United States Patent	12384842
Kind Code	B2
Date of Patent	August 12, 2025
Inventor(s)	Loew; Andreas et al.

Antibody molecules that bind to NKP30 and uses thereof

Abstract

Antibody molecules that specifically bind to NKp30 are disclosed. The anti-NKp30 antibody molecules can be used to treat, prevent and/or diagnose cancerous, autoimmune or infectious conditions and disorders.

Inventors: **Loew; Andreas (Boston, MA), Malhotra; Nidhi (Boston, MA), Katragadda; Madan (Acton, MA), Vash; Brian Edward (Cambridge, MA), Maiocco; Stephanie J. (Arlington, MA)**

Applicant: **Marengo Therapeutics, Inc.** (Cambridge, MA)

Family ID: **1000008750276**

Assignee: **Marengo Therapeutics, Inc. (Cambridge, MA)**

Appl. No.: **17/402320**

Filed: **August 13, 2021**

Prior Publication Data

Document Identifier	Publication Date
US 20210371523 A1	Dec. 02, 2021

Related U.S. Application Data

continuation parent-doc WO PCT/US2020/019329 20200221 PENDING child-doc US 17402320
us-provisional-application US 62808582 20190221

Publication Classification

Int. Cl.: **C07K16/28** (20060101); **A61K39/395** (20060101); A61K45/06 (20060101)

U.S. Cl.:

CPC **C07K16/2803** (20130101); **A61K39/3955** (20130101); C07K2317/24 (20130101); C07K2317/31 (20130101); C07K2317/52 (20130101); C07K2317/565 (20130101)

Field of Classification Search

CPC: C07K (16/2803); C07K (2317/24); C07K (2317/31); C07K (2317/52); C07K (2317/565); C07K (2317/74); A61K (39/3955); A61K (45/06); A61P (31/00); A61P (35/00); A61P (37/00)

References Cited

U.S. PATENT DOCUMENTS

Patent No.	Issued Date	Patentee Name	U.S. Cl.	CPC
861745	12/1906	Maxwell	N/A	N/A
4433059	12/1983	Chang et al.	N/A	N/A
4439196	12/1983	Higuchi	N/A	N/A
4444878	12/1983	Paulus	N/A	N/A
4447224	12/1983	DeCant, Jr. et al.	N/A	N/A
4447233	12/1983	Mayfield	N/A	N/A
4475196	12/1983	La Zor	N/A	N/A
4486194	12/1983	Ferrara	N/A	N/A
4487603	12/1983	Harris	N/A	N/A
4522811	12/1984	Eppstein et al.	N/A	N/A
4596556	12/1985	Morrow et al.	N/A	N/A
4676980	12/1986	Segal et al.	N/A	N/A
4737456	12/1987	Weng et al.	N/A	N/A
4790824	12/1987	Morrow et al.	N/A	N/A
4816567	12/1988	Cabilly et al.	N/A	N/A
4941880	12/1989	Burns	N/A	N/A
5057423	12/1990	Hiserodt et al.	N/A	N/A
5064413	12/1990	McKinnon et al.	N/A	N/A
5116615	12/1991	Gokcen et al.	N/A	N/A
5208020	12/1992	Chari et al.	N/A	N/A
5223409	12/1992	Ladner et al.	N/A	N/A
5225539	12/1992	Winter	N/A	N/A
5273743	12/1992	Ahlem et al.	N/A	N/A
5312335	12/1993	McKinnon et al.	N/A	N/A
5374548	12/1993	Caras	N/A	N/A
5383851	12/1994	McKinnon, Jr. et al.	N/A	N/A
5391377	12/1994	Barnwell	N/A	N/A
5399163	12/1994	Peterson et al.	N/A	N/A
5399331	12/1994	Loughrey et al.	N/A	N/A
5416016	12/1994	Low et al.	N/A	N/A
5416064	12/1994	Chari et al.	N/A	N/A
5500362	12/1995	Robinson et al.	N/A	N/A
5534254	12/1995	Huston et al.	N/A	N/A
5571894	12/1995	Wels et al.	N/A	N/A
5582996	12/1995	Curtis	N/A	N/A
5585089	12/1995	Queen et al.	N/A	N/A
5587458	12/1995	King et al.	N/A	N/A
5591828	12/1996	Bosslet et al.	N/A	N/A
5624821	12/1996	Winter et al.	N/A	N/A
5626561	12/1996	Butler et al.	N/A	N/A
5635483	12/1996	Pettit et al.	N/A	N/A
5635602	12/1996	Cantor et al.	N/A	N/A
5637481	12/1996	Ledbetter et al.	N/A	N/A
5641870	12/1996	Rinderknecht et al.	N/A	N/A
5648237	12/1996	Carter	N/A	N/A
5648260	12/1996	Winter et al.	N/A	N/A
5693761	12/1996	Queen et al.	N/A	N/A
5693762	12/1996	Queen et al.	N/A	N/A

5712374	12/1997	Kuntsmann et al.	N/A	N/A
5714586	12/1997	Kunstmann et al.	N/A	N/A
5731116	12/1997	Matsuo et al.	N/A	N/A
5731168	12/1997	Carter et al.	N/A	N/A
5739116	12/1997	Hamann et al.	N/A	N/A
5747036	12/1997	Brenner et al.	N/A	N/A
5750373	12/1997	Garrard et al.	N/A	N/A
5766947	12/1997	Rittershaus et al.	N/A	N/A
5767285	12/1997	Hamann et al.	N/A	N/A
5770429	12/1997	Lonberg et al.	N/A	N/A
5770701	12/1997	McGahren et al.	N/A	N/A
5770710	12/1997	McGahren et al.	N/A	N/A
5773001	12/1997	Hamann et al.	N/A	N/A
5780588	12/1997	Pettit et al.	N/A	N/A
5787900	12/1997	Butler et al.	N/A	N/A
5789199	12/1997	Joly et al.	N/A	N/A
5811097	12/1997	Allison et al.	N/A	N/A
5821337	12/1997	Carter et al.	N/A	N/A
5831012	12/1997	Nilsson et al.	N/A	N/A
5837242	12/1997	Holliger et al.	N/A	N/A
5837821	12/1997	Wu	N/A	N/A
5840523	12/1997	Simmons et al.	N/A	N/A
5843069	12/1997	Butler et al.	N/A	N/A
5844094	12/1997	Hudson et al.	N/A	N/A
5849500	12/1997	Breitling et al.	N/A	N/A
5849589	12/1997	Tedder et al.	N/A	N/A
5861155	12/1998	Lin	N/A	N/A
5864019	12/1998	King et al.	N/A	N/A
5869046	12/1998	Presta et al.	N/A	N/A
5869620	12/1998	Whitlow et al.	N/A	N/A
5877296	12/1998	Hamann et al.	N/A	N/A
5902745	12/1998	Butler et al.	N/A	N/A
5910573	12/1998	Plueckthun et al.	N/A	N/A
5913998	12/1998	Butler et al.	N/A	N/A
5932448	12/1998	Tso et al.	N/A	N/A
5959083	12/1998	Bosslet et al.	N/A	N/A
5959177	12/1998	Hein et al.	N/A	N/A
5968753	12/1998	Tseng-Law et al.	N/A	N/A
5980889	12/1998	Butler et al.	N/A	N/A
5989830	12/1998	Davis et al.	N/A	N/A
6005079	12/1998	Casterman et al.	N/A	N/A
6040498	12/1999	Stomp et al.	N/A	N/A
6075181	12/1999	Kucherlapati et al.	N/A	N/A
6120766	12/1999	Hale et al.	N/A	N/A
6150584	12/1999	Kucherlapati et al.	N/A	N/A
6171586	12/2000	Lam et al.	N/A	N/A
6171799	12/2000	Skibbens et al.	N/A	N/A
6172197	12/2000	McCafferty et al.	N/A	N/A
6194551	12/2000	Idusogie et al.	N/A	N/A
6239259	12/2000	Davis et al.	N/A	N/A
6248516	12/2000	Winter et al.	N/A	N/A
6267958	12/2000	Andya et al.	N/A	N/A
6291158	12/2000	Winter et al.	N/A	N/A
6294353	12/2000	Pack et al.	N/A	N/A
6333396	12/2000	Filpula et al.	N/A	N/A
6352694	12/2001	June et al.	N/A	N/A

6417429	12/2001	Hein et al.	N/A	N/A
6420548	12/2001	Vezina et al.	N/A	N/A
6476198	12/2001	Kang	N/A	N/A
6511663	12/2002	King et al.	N/A	N/A
6534055	12/2002	June et al.	N/A	N/A
6582915	12/2002	Griffiths et al.	N/A	N/A
6593081	12/2002	Griffiths et al.	N/A	N/A
6602684	12/2002	Umana et al.	N/A	N/A
6630579	12/2002	Chari et al.	N/A	N/A
6632427	12/2002	Finiels et al.	N/A	N/A
6670453	12/2002	Frenken et al.	N/A	N/A
6696245	12/2003	Winter et al.	N/A	N/A
6703199	12/2003	Koide	N/A	N/A
6737056	12/2003	Presta	N/A	N/A
6743896	12/2003	Filpula et al.	N/A	N/A
6756523	12/2003	Kahn et al.	N/A	N/A
6765087	12/2003	Casterman et al.	N/A	N/A
6809185	12/2003	Schoonjans et al.	N/A	N/A
6818418	12/2003	Lipovsek et al.	N/A	N/A
6833441	12/2003	Wang et al.	N/A	N/A
6838254	12/2004	Hamers et al.	N/A	N/A
6905680	12/2004	June et al.	N/A	N/A
6979546	12/2004	Moretta et al.	N/A	N/A
6982321	12/2005	Winter	N/A	N/A
7041870	12/2005	Tomizuka et al.	N/A	N/A
7083785	12/2005	Browning et al.	N/A	N/A
7087409	12/2005	Barbas, III et al.	N/A	N/A
7105149	12/2005	Dalla-Favera	N/A	N/A
7125978	12/2005	Vezina et al.	N/A	N/A
7129330	12/2005	Little et al.	N/A	N/A
7183076	12/2006	Arathoon et al.	N/A	N/A
7186804	12/2006	Gillies et al.	N/A	N/A
7189826	12/2006	Rodman	N/A	N/A
7250297	12/2006	Beste et al.	N/A	N/A
7276241	12/2006	Schneider et al.	N/A	N/A
7332581	12/2007	Presta	N/A	N/A
7361360	12/2007	Kitabwalla et al.	N/A	N/A
7371826	12/2007	Presta	N/A	N/A
7402314	12/2007	Sherman	N/A	N/A
7431380	12/2007	Buresh	N/A	N/A
7476724	12/2008	Dennis et al.	N/A	N/A
7498298	12/2008	Doronina et al.	N/A	N/A
7501121	12/2008	Tchistiakova et al.	N/A	N/A
7517966	12/2008	Moretta et al.	N/A	N/A
7521056	12/2008	Chang et al.	N/A	N/A
7521541	12/2008	Eigenbrot et al.	N/A	N/A
7527787	12/2008	Chang et al.	N/A	N/A
7527791	12/2008	Adams et al.	N/A	N/A
7534866	12/2008	Chang et al.	N/A	N/A
7563441	12/2008	Graus et al.	N/A	N/A
7601803	12/2008	Fiedler et al.	N/A	N/A
7612181	12/2008	Wu et al.	N/A	N/A
7642228	12/2009	Carter et al.	N/A	N/A
7700739	12/2009	Lacy et al.	N/A	N/A
7741446	12/2009	Pardridge et al.	N/A	N/A
7750128	12/2009	Gegg et al.	N/A	N/A

7767429	12/2009	Bookbinder et al.	N/A	N/A
7799902	12/2009	Browning et al.	N/A	N/A
7803376	12/2009	Velardi et al.	N/A	N/A
7807160	12/2009	Presta et al.	N/A	N/A
7829289	12/2009	Lantz et al.	N/A	N/A
7855275	12/2009	Eigenbrot et al.	N/A	N/A
7858759	12/2009	Brandt et al.	N/A	N/A
7906118	12/2010	Chang et al.	N/A	N/A
7919257	12/2010	Hoogenboom et al.	N/A	N/A
7943743	12/2010	Korman et al.	N/A	N/A
7999077	12/2010	Pastan et al.	N/A	N/A
8003774	12/2010	Stavenhagen et al.	N/A	N/A
8008449	12/2010	Korman et al.	N/A	N/A
8012465	12/2010	Elias et al.	N/A	N/A
8034326	12/2010	Hjorth et al.	N/A	N/A
8202517	12/2011	Bookbinder et al.	N/A	N/A
8216805	12/2011	Carter et al.	N/A	N/A
8227577	12/2011	Klein et al.	N/A	N/A
8299220	12/2011	Dalla-Favera	N/A	N/A
8354509	12/2012	Carven et al.	N/A	N/A
8362213	12/2012	Elkins et al.	N/A	N/A
8450470	12/2012	Bookbinder et al.	N/A	N/A
8466260	12/2012	Elkins et al.	N/A	N/A
8552156	12/2012	Takayanagi et al.	N/A	N/A
8580252	12/2012	Bookbinder et al.	N/A	N/A
8586713	12/2012	Davis et al.	N/A	N/A
8592562	12/2012	Kannan et al.	N/A	N/A
8609089	12/2012	Langermann et al.	N/A	N/A
8617545	12/2012	Hsu et al.	N/A	N/A
8617559	12/2012	Elkins et al.	N/A	N/A
8658135	12/2013	O'Connor-McCourt et al.	N/A	N/A
8703132	12/2013	Imhof-Jung et al.	N/A	N/A
8772246	12/2013	Bookbinder et al.	N/A	N/A
8790895	12/2013	Fiedler et al.	N/A	N/A
8821883	12/2013	Ambrose et al.	N/A	N/A
8846042	12/2013	Zhou	N/A	N/A
8871912	12/2013	Davis et al.	N/A	N/A
8920776	12/2013	Gaiger et al.	N/A	N/A
8945571	12/2014	Mössner et al.	N/A	N/A
8993524	12/2014	Bedi et al.	N/A	N/A
9000130	12/2014	Bhakta et al.	N/A	N/A
9034324	12/2014	Kalled et al.	N/A	N/A
9056905	12/2014	Olson et al.	N/A	N/A
9145588	12/2014	Throsby et al.	N/A	N/A
9200060	12/2014	Kannan et al.	N/A	N/A
9243058	12/2015	Armitage et al.	N/A	N/A
9309311	12/2015	Gurney et al.	N/A	N/A
9340621	12/2015	Kufer et al.	N/A	N/A
9358286	12/2015	De et al.	N/A	N/A
9359437	12/2015	Davis et al.	N/A	N/A
9382323	12/2015	Brinkmann et al.	N/A	N/A
9387237	12/2015	Kalled et al.	N/A	N/A
9416187	12/2015	Tedder et al.	N/A	N/A
9447159	12/2015	Ast et al.	N/A	N/A
9447185	12/2015	Romagne et al.	N/A	N/A
9545086	12/2016	Mackay et al.	N/A	N/A

9593376	12/2016	Zitvogel et al.	N/A	N/A
9663577	12/2016	Pierres et al.	N/A	N/A
9676863	12/2016	Lo	N/A	N/A
9833476	12/2016	Zhang et al.	N/A	N/A
10150816	12/2017	Abbot et al.	N/A	N/A
10294300	12/2018	Raum et al.	N/A	N/A
10308721	12/2018	Williams et al.	N/A	N/A
10478509	12/2018	Torgov et al.	N/A	N/A
10610571	12/2019	Ptacin et al.	N/A	N/A
10676516	12/2019	Viney et al.	N/A	N/A
10730942	12/2019	Pule et al.	N/A	N/A
10815311	12/2019	Wesche et al.	N/A	N/A
11033634	12/2020	Stull et al.	N/A	N/A
11291721	12/2021	Loew et al.	N/A	N/A
11292838	12/2021	Schendel et al.	N/A	N/A
11673953	12/2022	Zhang et al.	N/A	N/A
11692031	12/2022	Dahlhoff et al.	N/A	N/A
11845797	12/2022	Tan et al.	N/A	N/A
11965025	12/2023	Tan et al.	N/A	N/A
12152073	12/2023	Loew et al.	N/A	N/A
2002/0004587	12/2001	Miller et al.	N/A	N/A
2002/0041865	12/2001	Austin et al.	N/A	N/A
2002/0062010	12/2001	Arathoon et al.	N/A	N/A
2002/0076406	12/2001	Leung	N/A	N/A
2002/0103345	12/2001	Zhu	N/A	N/A
2002/0164328	12/2001	Shinkawa et al.	N/A	N/A
2003/0099647	12/2002	Deshpande	530/388.25	C07K 16/249
2003/0115614	12/2002	Kanda et al.	N/A	N/A
2003/0130496	12/2002	Winter et al.	N/A	N/A
2003/0157108	12/2002	Presta	N/A	N/A
2003/0175884	12/2002	Umana et al.	N/A	N/A
2003/0207346	12/2002	Arathoon et al.	N/A	N/A
2003/0211078	12/2002	Heavner	N/A	N/A
2004/0009530	12/2003	Wilson et al.	N/A	N/A
2004/0093621	12/2003	Shitara et al.	N/A	N/A
2004/0109865	12/2003	Niwa et al.	N/A	N/A
2004/0110282	12/2003	Kanda et al.	N/A	N/A
2004/0110704	12/2003	Yamane et al.	N/A	N/A
2004/0132140	12/2003	Satoh et al.	N/A	N/A
2004/0175756	12/2003	Kolkman et al.	N/A	N/A
2004/0219643	12/2003	Winter et al.	N/A	N/A
2004/0220388	12/2003	Mertens et al.	N/A	N/A
2004/0241817	12/2003	Umana et al.	N/A	N/A
2004/0242847	12/2003	Fukushima et al.	N/A	N/A
2005/0003403	12/2004	Rossi et al.	N/A	N/A
2005/0004352	12/2004	Kontermann et al.	N/A	N/A
2005/0014934	12/2004	Hinton et al.	N/A	N/A
2005/0048512	12/2004	Kolkman et al.	N/A	N/A
2005/0053973	12/2004	Kolkman et al.	N/A	N/A
2005/0069552	12/2004	Bleck et al.	N/A	N/A
2005/0079170	12/2004	Le Gall et al.	N/A	N/A
2005/0079574	12/2004	Bond	N/A	N/A
2005/0090648	12/2004	Tsurushita et al.	N/A	N/A
2005/0100543	12/2004	Hansen et al.	N/A	N/A
2005/0119455	12/2004	Fuh et al.	N/A	N/A
2005/0123546	12/2004	Umana et al.	N/A	N/A

2005/0136049	12/2004	Ledbetter et al.	N/A	N/A
2005/0136051	12/2004	Scallon	N/A	N/A
2005/0163782	12/2004	Glaser et al.	N/A	N/A
2005/0260186	12/2004	Bookbinder et al.	N/A	N/A
2005/0266000	12/2004	Bond et al.	N/A	N/A
2005/0266425	12/2004	Zauderer et al.	N/A	N/A
2006/0008844	12/2005	Stemmer et al.	N/A	N/A
2006/0025576	12/2005	Miller et al.	N/A	N/A
2006/0083747	12/2005	Winter et al.	N/A	N/A
2006/0104968	12/2005	Bookbinder et al.	N/A	N/A
2006/0120960	12/2005	Deyev et al.	N/A	N/A
2006/0141581	12/2005	Gillies et al.	N/A	N/A
2006/0204493	12/2005	Huang et al.	N/A	N/A
2006/0263367	12/2005	Fey et al.	N/A	N/A
2007/0004909	12/2006	Johnson et al.	N/A	N/A
2007/0036783	12/2006	Humeau et al.	N/A	N/A
2007/0061900	12/2006	Murphy et al.	N/A	N/A
2007/0087381	12/2006	Kojima	N/A	N/A
2007/0105105	12/2006	Clelland et al.	N/A	N/A
2007/0117126	12/2006	Sidhu et al.	N/A	N/A
2007/0128150	12/2006	Norman	N/A	N/A
2007/0141049	12/2006	Bredehorst et al.	N/A	N/A
2007/0154901	12/2006	Thogersen et al.	N/A	N/A
2007/0160598	12/2006	Dennis et al.	N/A	N/A
2007/0178106	12/2006	Romagne	N/A	N/A
2007/0184052	12/2006	Lin et al.	N/A	N/A
2007/0231322	12/2006	Romagne et al.	N/A	N/A
2007/0237764	12/2006	Birtalan et al.	N/A	N/A
2007/0274985	12/2006	Dubel et al.	N/A	N/A
2007/0292936	12/2006	Barthelemy et al.	N/A	N/A
2008/0050370	12/2007	Glaser et al.	N/A	N/A
2008/0063717	12/2007	Romagne et al.	N/A	N/A
2008/0069820	12/2007	Fuh et al.	N/A	N/A
2008/0152645	12/2007	Pardridge et al.	N/A	N/A
2008/0171855	12/2007	Rossi et al.	N/A	N/A
2008/0241884	12/2007	Shitara et al.	N/A	N/A
2008/0247944	12/2007	Graziano et al.	N/A	N/A
2008/0254512	12/2007	Capon	N/A	N/A
2008/0260738	12/2007	Moore et al.	N/A	N/A
2008/0299137	12/2007	Svendsen et al.	N/A	N/A
2009/0002360	12/2008	Chen et al.	N/A	N/A
2009/0010843	12/2008	Spee et al.	N/A	N/A
2009/0130106	12/2008	Christopherson et al.	N/A	N/A
2009/0148905	12/2008	Ashman et al.	N/A	N/A
2009/0155275	12/2008	Wu et al.	N/A	N/A
2009/0162359	12/2008	Klein et al.	N/A	N/A
2009/0162360	12/2008	Klein et al.	N/A	N/A
2009/0175851	12/2008	Klein et al.	N/A	N/A
2009/0175867	12/2008	Thompson et al.	N/A	N/A
2009/0214533	12/2008	Clynes	N/A	N/A
2009/0232811	12/2008	Klein et al.	N/A	N/A
2009/0234105	12/2008	Gervay-Hague et al.	N/A	N/A
2009/0263392	12/2008	Igawa et al.	N/A	N/A
2009/0274649	12/2008	Qu et al.	N/A	N/A
2009/0280116	12/2008	Smith et al.	N/A	N/A
2009/0324538	12/2008	Wong et al.	N/A	N/A

2010/0015133	12/2009	Igawa et al.	N/A	N/A
2010/0015153	12/2009	Moretta et al.	N/A	N/A
2010/0028330	12/2009	Collins et al.	N/A	N/A
2010/0047169	12/2009	Mandelboim et al.	N/A	N/A
2010/0168393	12/2009	Clube et al.	N/A	N/A
2010/0260704	12/2009	Berenguer et al.	N/A	N/A
2010/0316645	12/2009	Imhof-Jung et al.	N/A	N/A
2011/0014659	12/2010	Balazs et al.	N/A	N/A
2011/0054151	12/2010	Lazar et al.	N/A	N/A
2011/0091372	12/2010	Ghayur et al.	N/A	N/A
2011/0150892	12/2010	Thudium et al.	N/A	N/A
2011/0177073	12/2010	Van Berkel et al.	N/A	N/A
2011/0177093	12/2010	Kalled et al.	N/A	N/A
2011/0250170	12/2010	Pedretti et al.	N/A	N/A
2011/0287056	12/2010	Gu et al.	N/A	N/A
2011/0293613	12/2010	Brinkmann et al.	N/A	N/A
2012/0034221	12/2011	Bonvini et al.	N/A	N/A
2012/0039906	12/2011	Olive	N/A	N/A
2012/0114649	12/2011	Langermann et al.	N/A	N/A
2012/0149876	12/2011	Von Kreudenstein et al.	N/A	N/A
2012/0184716	12/2011	Fischer et al.	N/A	N/A
2012/0201746	12/2011	Liu et al.	N/A	N/A
2012/0213768	12/2011	Oh et al.	N/A	N/A
2012/0294857	12/2011	Sentman et al.	N/A	N/A
2013/0017200	12/2012	Scheer et al.	N/A	N/A
2013/0022601	12/2012	Brinkmann et al.	N/A	N/A
2013/0078249	12/2012	Ast et al.	N/A	N/A
2013/0129723	12/2012	Blankenship et al.	N/A	N/A
2013/0164293	12/2012	Florio et al.	N/A	N/A
2013/0165638	12/2012	Hsu et al.	N/A	N/A
2013/0178605	12/2012	Blein et al.	N/A	N/A
2013/0195849	12/2012	Spreter Von Kreudenstein et al.	N/A	N/A
2013/0243775	12/2012	Papadopoulos et al.	N/A	N/A
2013/0266568	12/2012	Brinkmann et al.	N/A	N/A
2013/0267686	12/2012	Brinkmann et al.	N/A	N/A
2013/0273055	12/2012	Borges et al.	N/A	N/A
2013/0273089	12/2012	Getts et al.	N/A	N/A
2013/0280208	12/2012	Stepkowski et al.	N/A	N/A
2013/0303396	12/2012	Igawa et al.	N/A	N/A
2013/0317200	12/2012	Elson et al.	N/A	N/A
2014/0037621	12/2013	Tsurushita et al.	N/A	N/A
2014/0044728	12/2013	Takayanagi et al.	N/A	N/A
2014/0051833	12/2013	Fischer et al.	N/A	N/A
2014/0051835	12/2013	Dixit et al.	N/A	N/A
2014/0072528	12/2013	Gerdes et al.	N/A	N/A
2014/0072581	12/2013	Dixit et al.	N/A	N/A
2014/0079689	12/2013	Elliott et al.	N/A	N/A
2014/0079691	12/2013	McConnell et al.	N/A	N/A
2014/0099254	12/2013	Chang et al.	N/A	N/A
2014/0154254	12/2013	Kannan et al.	N/A	N/A
2014/0199294	12/2013	Mimoto et al.	N/A	N/A
2014/0200331	12/2013	Corper et al.	N/A	N/A
2014/0227265	12/2013	Wu et al.	N/A	N/A
2014/0242075	12/2013	Parren et al.	N/A	N/A
2014/0242077	12/2013	Choi et al.	N/A	N/A

2014/0256916	12/2013	Kruip et al.	N/A	N/A
2014/0308285	12/2013	Yan et al.	N/A	N/A
2014/0322212	12/2013	Brogdon et al.	N/A	N/A
2014/0322221	12/2013	Miller et al.	N/A	N/A
2014/0348839	12/2013	Chowdhury et al.	N/A	N/A
2014/0363426	12/2013	Moore et al.	N/A	N/A
2014/0377269	12/2013	Mabry et al.	N/A	N/A
2015/0017187	12/2014	Thanos et al.	N/A	N/A
2015/0018529	12/2014	Humphreys et al.	N/A	N/A
2015/0056199	12/2014	Kumar et al.	N/A	N/A
2015/0098900	12/2014	Ebens et al.	N/A	N/A
2015/0133638	12/2014	Wranik et al.	N/A	N/A
2015/0166661	12/2014	Chen et al.	N/A	N/A
2015/0166670	12/2014	Castoldi et al.	N/A	N/A
2015/0175707	12/2014	De Jong et al.	N/A	N/A
2015/0203591	12/2014	Yancopoulos et al.	N/A	N/A
2015/0211001	12/2014	Ohrn et al.	N/A	N/A
2015/0218260	12/2014	Klein et al.	N/A	N/A
2015/0232560	12/2014	Heindl et al.	N/A	N/A
2015/0315296	12/2014	Schaefer et al.	N/A	N/A
2015/0337049	12/2014	Labrijn et al.	N/A	N/A
2015/0344570	12/2014	Igawa et al.	N/A	N/A
2015/0353636	12/2014	Parren et al.	N/A	N/A
2015/0368351	12/2014	Vu et al.	N/A	N/A
2015/0368352	12/2014	Liu	N/A	N/A
2015/0376287	12/2014	Vu et al.	N/A	N/A
2016/0015749	12/2015	Gottschalk et al.	N/A	N/A
2016/0039947	12/2015	Demarest et al.	N/A	N/A
2016/0075785	12/2015	Ast et al.	N/A	N/A
2016/0102135	12/2015	Escobar-Cabrera	N/A	N/A
2016/0114057	12/2015	Dixit et al.	N/A	N/A
2016/0130347	12/2015	Bruenker et al.	N/A	N/A
2016/0131654	12/2015	Berenson et al.	N/A	N/A
2016/0145340	12/2015	Borges et al.	N/A	N/A
2016/0145354	12/2015	Bacac et al.	N/A	N/A
2016/0176973	12/2015	Kufer et al.	N/A	N/A
2016/0194389	12/2015	Regula et al.	N/A	N/A
2016/0229915	12/2015	Igawa et al.	N/A	N/A
2016/0244523	12/2015	Blank et al.	N/A	N/A
2016/0257763	12/2015	Von Kreudenstein et al.	N/A	N/A
2016/0264685	12/2015	Fouque et al.	N/A	N/A
2016/0297885	12/2015	Kuo et al.	N/A	N/A
2016/0311915	12/2015	Pulé et al.	N/A	N/A
2016/0368985	12/2015	Hotzel et al.	N/A	N/A
2016/0368988	12/2015	Bakker et al.	N/A	N/A
2017/0022284	12/2016	Timmer et al.	N/A	N/A
2017/0035905	12/2016	Abrams et al.	N/A	N/A
2017/0037128	12/2016	Little et al.	N/A	N/A
2017/0051068	12/2016	Pillarisetti et al.	N/A	N/A
2017/0066827	12/2016	Pulé et al.	N/A	N/A
2017/0151281	12/2016	Wagner et al.	N/A	N/A
2017/0204176	12/2016	Bonvini et al.	N/A	N/A
2017/0269092	12/2016	Kralovics	N/A	N/A
2017/0275362	12/2016	Brentjens et al.	N/A	N/A
2017/0298445	12/2016	Ogg	N/A	N/A
2017/0334998	12/2016	Pulé et al.	N/A	N/A

2017/0368169	12/2016	Loew et al.	N/A	N/A
2018/0153938	12/2017	Keating et al.	N/A	N/A
2018/0235887	12/2017	Garidel et al.	N/A	N/A
2018/0256716	12/2017	Schendel et al.	N/A	N/A
2019/0062448	12/2018	Soros et al.	N/A	N/A
2019/0209612	12/2018	Pulé et al.	N/A	N/A
2019/0315883	12/2018	Ast et al.	N/A	N/A
2019/0322763	12/2018	Ast et al.	N/A	N/A
2020/0071417	12/2019	Loew et al.	N/A	N/A
2020/0109195	12/2019	Watkins et al.	N/A	N/A
2020/0129638	12/2019	Van Berkel et al.	N/A	N/A
2020/0140549	12/2019	Cordoba et al.	N/A	N/A
2020/0172591	12/2019	Hosse et al.	N/A	N/A
2020/0172868	12/2019	Wickham et al.	N/A	N/A
2020/0200756	12/2019	Pulé et al.	N/A	N/A
2020/0230208	12/2019	Wang et al.	N/A	N/A
2020/0277384	12/2019	Chang et al.	N/A	N/A
2020/0291089	12/2019	Loew et al.	N/A	N/A
2020/0299349	12/2019	Garcia et al.	N/A	N/A
2020/0306301	12/2019	Andresen et al.	N/A	N/A
2020/0308242	12/2019	Lowe et al.	N/A	N/A
2020/0317787	12/2019	Li et al.	N/A	N/A
2020/0332003	12/2019	Britanova et al.	N/A	N/A
2020/0377571	12/2019	Loew et al.	N/A	N/A
2020/0385472	12/2019	Loew et al.	N/A	N/A
2021/0009711	12/2020	Loew et al.	N/A	N/A
2021/0024631	12/2020	Kley et al.	N/A	N/A
2021/0079114	12/2020	Hudson	N/A	N/A
2021/0137982	12/2020	Loew et al.	N/A	N/A
2021/0198369	12/2020	Chang et al.	N/A	N/A
2021/0221863	12/2020	Kang et al.	N/A	N/A
2021/0230311	12/2020	Nezu et al.	N/A	N/A
2021/0238280	12/2020	Loew et al.	N/A	N/A
2021/0246227	12/2020	Loew et al.	N/A	N/A
2021/0277119	12/2020	Tan et al.	N/A	N/A
2021/0363250	12/2020	Kamikawaji et al.	N/A	N/A
2021/0380670	12/2020	Loew et al.	N/A	N/A
2021/0380682	12/2020	Loew et al.	N/A	N/A
2021/0380691	12/2020	Loew et al.	N/A	N/A
2021/0380692	12/2020	Loew et al.	N/A	N/A
2021/0380715	12/2020	Yoshida et al.	N/A	N/A
2022/0064255	12/2021	Loew et al.	N/A	N/A
2022/0064297	12/2021	Tan et al.	N/A	N/A
2022/0112286	12/2021	Britanova et al.	N/A	N/A
2022/0288200	12/2021	Loew et al.	N/A	N/A
2023/0025484	12/2022	Tan et al.	N/A	N/A
2023/0031734	12/2022	Tan et al.	N/A	N/A
2023/0034161	12/2022	Tan et al.	N/A	N/A
2023/0048244	12/2022	Loew	N/A	N/A
2023/0102344	12/2022	Katragadda et al.	N/A	N/A
2023/0127740	12/2022	Tan et al.	N/A	N/A
2023/0142522	12/2022	Tan et al.	N/A	N/A
2023/0174650	12/2022	Tan et al.	N/A	N/A
2023/0192848	12/2022	Loew	N/A	N/A
2023/0227552	12/2022	Tan et al.	N/A	N/A
2023/0333112	12/2022	Loew et al.	N/A	N/A

2023/0348593	12/2022	Loew et al.	N/A	N/A
2023/0357395	12/2022	Loew et al.	N/A	N/A
2023/0374133	12/2022	Tan et al.	N/A	N/A
2024/0002543	12/2023	Loew et al.	N/A	N/A
2024/0076377	12/2023	Tan et al.	N/A	N/A
2024/0301060	12/2023	Tan et al.	N/A	N/A

FOREIGN PATENT DOCUMENTS

Patent No.	**Application Date**	**Country**	**CPC**
2001278662	12/2005	AU	N/A
3016563	12/2016	CA	N/A
3214757	12/2021	CA	N/A
101802010	12/2009	CN	N/A
101985476	12/2010	CN	N/A
104203981	12/2013	CN	N/A
104769103	12/2014	CN	N/A
105916876	12/2015	CN	N/A
106103475	12/2015	CN	N/A
106163547	12/2015	CN	N/A
107206024	12/2016	CN	N/A
107903325	12/2017	CN	N/A
108026171	12/2017	CN	N/A
108949698	12/2017	CN	N/A
109153728	12/2018	CN	N/A
114026122	12/2021	CN	N/A
10261223	12/2003	DE	N/A
0125023	12/1983	EP	N/A
0171496	12/1985	EP	N/A
0173494	12/1985	EP	N/A
0184187	12/1985	EP	N/A
0346087	12/1988	EP	N/A
0368684	12/1989	EP	N/A
0388151	12/1989	EP	N/A
0404097	12/1989	EP	N/A
0519596	12/1991	EP	N/A
0171496	12/1992	EP	N/A
0616640	12/1993	EP	N/A
0425235	12/1995	EP	N/A
0403156	12/1996	EP	N/A
1176195	12/2001	EP	N/A
0125023	12/2001	EP	N/A
0368684	12/2003	EP	N/A
0616640	12/2003	EP	N/A
1301605	12/2004	EP	N/A
1870459	12/2006	EP	N/A
2581113	12/2012	EP	N/A
1846020	12/2012	EP	N/A
2699259	12/2013	EP	N/A
2467165	12/2014	EP	N/A
2847231	12/2014	EP	N/A
2982694	12/2015	EP	N/A
3023437	12/2015	EP	N/A
1870459	12/2015	EP	N/A
2982694	12/2015	EP	N/A
3029068	12/2015	EP	N/A
2699259	12/2015	EP	N/A

3055329	12/2015	EP	N/A
3137500	12/2016	EP	N/A
3059246	12/2017	EP	N/A
2723380	12/2018	EP	N/A
3294768	12/2018	EP	N/A
3149031	12/2018	EP	N/A
3590967	12/2019	EP	N/A
3626739	12/2019	EP	N/A
3642228	12/2019	EP	N/A
3189132	12/2019	EP	N/A
3303392	12/2019	EP	N/A
4087871	12/2021	EP	N/A
2188638	12/1986	GB	N/A
2599228	12/2021	GB	N/A
2616354	12/2022	GB	N/A
H0787994	12/1994	JP	N/A
H08502246	12/1995	JP	N/A
H09509307	12/1996	JP	N/A
2011524743	12/2010	JP	N/A
2013515509	12/2012	JP	N/A
2014527802	12/2013	JP	N/A
2016512557	12/2015	JP	N/A
6153947	12/2016	JP	N/A
2017143838	12/2016	JP	N/A
2018517712	12/2017	JP	N/A
2018531939	12/2017	JP	N/A
WO-8500817	12/1984	WO	N/A
WO-8601533	12/1985	WO	N/A
WO-8702671	12/1986	WO	N/A
WO-9002809	12/1989	WO	N/A
WO-9100906	12/1990	WO	N/A
WO-9103493	12/1990	WO	N/A
WO-9110741	12/1990	WO	N/A
WO-9117271	12/1990	WO	N/A
WO-9201047	12/1991	WO	N/A
WO-9203917	12/1991	WO	N/A
WO-9203918	12/1991	WO	N/A
WO-9209690	12/1991	WO	N/A
WO-9215679	12/1991	WO	N/A
WO-9218619	12/1991	WO	N/A
WO-9220791	12/1991	WO	N/A
WO-9209690	12/1991	WO	N/A
WO-9301161	12/1992	WO	N/A
WO-9301288	12/1992	WO	N/A
WO-9308829	12/1992	WO	N/A
WO-9311161	12/1992	WO	N/A
WO-9311236	12/1992	WO	N/A
WO-9323537	12/1992	WO	N/A
WO-9404678	12/1993	WO	N/A
WO-9405801	12/1993	WO	N/A
WO-9409131	12/1993	WO	N/A
WO-9411026	12/1993	WO	N/A
WO-9412625	12/1993	WO	N/A
WO-9425591	12/1993	WO	N/A
WO-9429351	12/1993	WO	N/A
WO-9509917	12/1994	WO	N/A

WO-9516038	12/1994	WO	N/A
WO-9637621	12/1995	WO	N/A
WO-9730087	12/1996	WO	N/A
WO-9814206	12/1997	WO	N/A
WO-9856915	12/1997	WO	N/A
WO-9858964	12/1997	WO	N/A
WO-9904820	12/1998	WO	N/A
WO-9916873	12/1998	WO	N/A
WO-9922764	12/1998	WO	N/A
WO-9945110	12/1998	WO	N/A
WO-9951642	12/1998	WO	N/A
WO-9964460	12/1998	WO	N/A
WO-0006605	12/1999	WO	N/A
WO-0034784	12/1999	WO	N/A
WO-0060070	12/1999	WO	N/A
WO-0061739	12/1999	WO	N/A
WO-0104144	12/2000	WO	N/A
WO-0129246	12/2000	WO	N/A
WO-0136630	12/2000	WO	N/A
WO-0164942	12/2000	WO	N/A
WO-0198357	12/2000	WO	N/A
WO-0231140	12/2001	WO	N/A
WO-02070647	12/2001	WO	N/A
WO-02072635	12/2001	WO	N/A
WO-03002609	12/2002	WO	N/A
WO-03011878	12/2002	WO	N/A
WO-03014161	12/2002	WO	N/A
WO-03056914	12/2002	WO	N/A
WO-03084570	12/2002	WO	N/A
WO-03085107	12/2002	WO	N/A
WO-03085119	12/2002	WO	N/A
WO-03093318	12/2002	WO	N/A
WO-2004003019	12/2003	WO	N/A
WO-2004024927	12/2003	WO	N/A
WO-2004033685	12/2003	WO	N/A
WO-2004056312	12/2003	WO	N/A
WO-2004056392	12/2003	WO	N/A
WO-2004056873	12/2003	WO	N/A
WO-2004057002	12/2003	WO	N/A
WO-2004058821	12/2003	WO	N/A
WO-2004065540	12/2003	WO	N/A
WO-2004081026	12/2003	WO	N/A
WO-2004081051	12/2003	WO	N/A
WO-2004101790	12/2003	WO	N/A
WO-2004106368	12/2003	WO	N/A
WO-2005035572	12/2004	WO	N/A
WO-2005035586	12/2004	WO	N/A
WO-2005035778	12/2004	WO	N/A
WO-2005053742	12/2004	WO	N/A
WO-2005100402	12/2004	WO	N/A
WO-2006000830	12/2005	WO	N/A
WO-2006020258	12/2005	WO	N/A
WO-2006029879	12/2005	WO	N/A
WO-2006044908	12/2005	WO	N/A
WO-2006079372	12/2005	WO	N/A
WO-2006106905	12/2005	WO	N/A

WO-2006121168	12/2005	WO	N/A
WO-2006135886	12/2005	WO	N/A
WO-2007005874	12/2006	WO	N/A
WO-2007044887	12/2006	WO	N/A
WO-2007059782	12/2006	WO	N/A
WO-2007005874	12/2006	WO	N/A
WO-2007095338	12/2006	WO	N/A
WO-2007110205	12/2006	WO	N/A
WO-2007137760	12/2006	WO	N/A
WO-2008017859	12/2007	WO	N/A
WO-2008077546	12/2007	WO	N/A
WO-2008087219	12/2007	WO	N/A
WO-2008119353	12/2007	WO	N/A
WO-2009021754	12/2008	WO	N/A
WO-2009068630	12/2008	WO	N/A
WO-2009077993	12/2008	WO	N/A
WO-2009089004	12/2008	WO	N/A
WO-2009101611	12/2008	WO	N/A
WO-2009103538	12/2008	WO	N/A
WO-2009114335	12/2008	WO	N/A
WO-2009147137	12/2008	WO	N/A
WO-2010019570	12/2009	WO	N/A
WO-2010027797	12/2009	WO	N/A
WO-2010027827	12/2009	WO	N/A
WO-2010029513	12/2009	WO	N/A
WO-2010077634	12/2009	WO	N/A
WO-2010129304	12/2009	WO	N/A
WO-2011066342	12/2010	WO	N/A
WO-2011090762	12/2010	WO	N/A
WO-2011131746	12/2010	WO	N/A
WO-2011155607	12/2010	WO	N/A
WO-2012079000	12/2011	WO	N/A
WO-2012088309	12/2011	WO	N/A
WO-2012107417	12/2011	WO	N/A
WO-2012131555	12/2011	WO	N/A
WO-2012138475	12/2011	WO	N/A
WO-2012143498	12/2011	WO	N/A
WO-2012170438	12/2011	WO	A61P 3/00
WO-2013019615	12/2012	WO	N/A
WO-2013033626	12/2012	WO	N/A
WO-2013037484	12/2012	WO	N/A
WO-2013060867	12/2012	WO	N/A
WO-2013079174	12/2012	WO	N/A
WO-2013103912	12/2012	WO	N/A
WO-2013170168	12/2012	WO	N/A
WO-2014008218	12/2013	WO	N/A
WO-2014100823	12/2013	WO	N/A
WO-2014159940	12/2013	WO	N/A
WO-2015052230	12/2014	WO	N/A
WO-2015066379	12/2014	WO	N/A
WO-2015095811	12/2014	WO	N/A
WO-2015107015	12/2014	WO	N/A
WO-2015107025	12/2014	WO	N/A
WO-2015107026	12/2014	WO	N/A
WO-2015121383	12/2014	WO	N/A
WO-2015127158	12/2014	WO	N/A

WO-2015132598	12/2014	WO	N/A
WO-2015164815	12/2014	WO	N/A
WO-2015166073	12/2014	WO	N/A
WO-2015181805	12/2014	WO	N/A
WO-2015197582	12/2014	WO	N/A
WO-2015197593	12/2014	WO	N/A
WO-2015197598	12/2014	WO	N/A
WO-2016016299	12/2015	WO	N/A
WO-2016019969	12/2015	WO	N/A
WO-2016026943	12/2015	WO	N/A
WO-2016033555	12/2015	WO	N/A
WO-2016071376	12/2015	WO	N/A
WO-2016071377	12/2015	WO	N/A
WO-2016079081	12/2015	WO	N/A
WO-2016087416	12/2015	WO	N/A
WO-2016087514	12/2015	WO	N/A
WO-2016087650	12/2015	WO	N/A
WO-2016090327	12/2015	WO	N/A
WO-2016110468	12/2015	WO	N/A
WO-2016110584	12/2015	WO	N/A
WO-2016115274	12/2015	WO	N/A
WO-2016118641	12/2015	WO	N/A
WO-2016168149	12/2015	WO	N/A
WO-2016180969	12/2015	WO	N/A
WO-2016193301	12/2015	WO	N/A
WO-2017021349	12/2016	WO	N/A
WO-2017021450	12/2016	WO	N/A
WO-2017037634	12/2016	WO	N/A
WO-2017040930	12/2016	WO	N/A
WO-2017055391	12/2016	WO	N/A
WO-2017059551	12/2016	WO	N/A
WO-2017062604	12/2016	WO	N/A
WO-2017077382	12/2016	WO	N/A
WO-2017134140	12/2016	WO	N/A
WO-2017165464	12/2016	WO	N/A
WO-2017167919	12/2016	WO	N/A
WO-2017180913	12/2016	WO	N/A
WO-2018057955	12/2017	WO	N/A
WO-2018067992	12/2017	WO	N/A
WO-2018098365	12/2017	WO	N/A
WO-2018144777	12/2017	WO	N/A
WO-2018201047	12/2017	WO	N/A
WO-2018224844	12/2017	WO	N/A
WO-2018237192	12/2017	WO	N/A
WO-2019005641	12/2018	WO	N/A
WO-2019035938	12/2018	WO	N/A
WO-2019040700	12/2018	WO	N/A
WO-2019040780	12/2018	WO	N/A
WO-2019055677	12/2018	WO	N/A
WO-2019067805	12/2018	WO	N/A
WO-2019086865	12/2018	WO	N/A
WO-2019101695	12/2018	WO	N/A
WO-2019132738	12/2018	WO	N/A
WO-2019139987	12/2018	WO	N/A
WO-2019158764	12/2018	WO	N/A
WO-2019178362	12/2018	WO	N/A

WO-2019178364	12/2018	WO	N/A
WO-2019178364	12/2018	WO	N/A
WO-2019191519	12/2018	WO	N/A
WO-2019226617	12/2018	WO	N/A
WO-2019231920	12/2018	WO	N/A
WO-2020005819	12/2019	WO	N/A
WO-2020010250	12/2019	WO	N/A
WO-2020018708	12/2019	WO	N/A
WO-2020010250	12/2019	WO	N/A
WO-2020025928	12/2019	WO	N/A
WO-2020057646	12/2019	WO	N/A
WO-2020082048	12/2019	WO	N/A
WO-2020084290	12/2019	WO	N/A
WO-2020086758	12/2019	WO	N/A
WO-2020088459	12/2019	WO	N/A
WO-2020089644	12/2019	WO	N/A
WO-2020091635	12/2019	WO	N/A
WO-2020106708	12/2019	WO	N/A
WO-2020139171	12/2019	WO	N/A
WO-2020139175	12/2019	WO	N/A
WO-2020142672	12/2019	WO	N/A
WO-2020142672	12/2019	WO	N/A
WO-2020172571	12/2019	WO	N/A
WO-2020172596	12/2019	WO	N/A
WO-2020172598	12/2019	WO	N/A
WO-2020172601	12/2019	WO	N/A
WO-2020172605	12/2019	WO	N/A
WO-2020183245	12/2019	WO	N/A
WO-2020249757	12/2019	WO	N/A
WO-2021089704	12/2020	WO	N/A
WO-2021097325	12/2020	WO	N/A
WO-2021138407	12/2020	WO	N/A
WO-2021138474	12/2020	WO	N/A
WO-2021140190	12/2020	WO	N/A
WO-2021138474	12/2020	WO	N/A
WO-2021188454	12/2020	WO	N/A
WO-2021217085	12/2020	WO	N/A
WO-2022046920	12/2021	WO	N/A
WO-2022046922	12/2021	WO	N/A
WO-2022047046	12/2021	WO	N/A
WO-2022046920	12/2021	WO	N/A
WO-2022046922	12/2021	WO	N/A
WO-2022175413	12/2021	WO	N/A
WO-2022179580	12/2021	WO	C07K 16/28
WO-2022216993	12/2021	WO	N/A
WO-2022216993	12/2021	WO	N/A
WO-2022240688	12/2021	WO	N/A
WO-2023081412	12/2022	WO	N/A
WO-2023122206	12/2022	WO	N/A
WO-2023141297	12/2022	WO	N/A
WO-2023081412	12/2022	WO	N/A
WO-2023122206	12/2022	WO	N/A
WO-2023141297	12/2022	WO	N/A
WO-2024081329	12/2023	WO	N/A
WO-2024081381	12/2023	WO	N/A
WO-2024197082	12/2023	WO	N/A

WO-2024226532	12/2023	WO	N/A
WO-2024227109	12/2023	WO	N/A
WO-2024197082	12/2023	WO	N/A
WO-2024254611	12/2023	WO	N/A
WO-2024226532	12/2024	WO	N/A

OTHER PUBLICATIONS

Almagro et al., Front. Immunol. 2018; 8:1751 (Year: 2018). cited by examiner

Chiu ML et al. Antibodies 2019 8, 55, 1-80 (Year: 2019). cited by examiner

Adachi, Osamu, et al., Targeted Disruption of the MyD88 Gene Results in Loss of IL-1-and IL-8-Mediated Function. Immunity 9(1):143-150 (1998). cited by applicant

Agostinis, Patrizia, et al., Photodynamic Therapy of Cancer: An Update. Ca: A Cancer Journal for Clinicians 61(4):250-281 (2011). cited by applicant

Aigner et al.: An effective tumor vaccine optimized for costimulation via bispecific and trispecific fusion proteins. Int J Oncol. 32(4):777-789 (2008). cited by applicant

Akiyama et al.: TNFalpha induces rapid activation and nuclear translocation of telomerase in human lymphocytes. Biochem Biophys Res Commun. 316(2):528-532 (2004). cited by applicant

Ala-Aho, Risto, et al., Collagenases in Cancer. Biochimie 87(3-4):273-286 (2005). cited by applicant

Al-Aghbar, M.A. et al., "High-affinity ligands can trigger T cell receptor signaling without CD45 segregation," Frontiers in Immunology, 2018;9(713):1-18. cited by applicant

Ali et al.: Modulation of human natural killer cytotoxicity by influenza virus and its subunit protein. Immunology 52(4):687-695 (1984). cited by applicant

Al-Lazikani, B. et al., "Standard Conformations for Canonical Structures of Immunoglobulins", J. Mol. Biol., 1997, vol. 273 ,pp. 927-948. cited by applicant

Altschul et al.: Basic Local Alignment Search Tool. Journal of Molecular Biology 215(3):403-410 (1990). cited by applicant

Altschul, et al. Gapped BLAST and PSI-BLAST: A New Generation Of Protein Database Search Programs. Nucleic Acids Research. 25(17):3389-3402 (1997). cited by applicant

Amarante-Mendes GP, Griffith TS. Therapeutic applications of TRAIL receptor agonists in cancer and beyond. Pharmacol Ther. Nov. 2015;155:117-31. Epub Sep. 5, 2015. cited by applicant

Arai, R. et al., "Design of the linkers which effectively separate domains of a bifunctional fusion protein", Protein Engineering, 2001, vol. 14, No. 8, pp. 529-532. cited by applicant

Arenas-Ramirez et al.: Interleukin-2: Biology, Design and Application. Trends in Immunology 36(12):763-777 (2015) cited by applicant

Arnon, T.I. et al., "Recognition of viral hemagglutinins by NKp44 but not by NKp30", Eur J. Immunol., 2001, vol. 31, No. 9, pp. 2680-2689. cited by applicant

Aslan, J.E et al., "S6K1 and mTOR regulate Rac1-driven platelet activation and aggregation", Blood, 2011, vol. 118, No. 11, pp. 3129-3136. cited by applicant

Aversa, Ilenia, et al., Molecular T-Cell Repertoire Analysis as Source of Prognostic and Predictive Biomarkers for Checkpoint blockade Immunotherapy. International Journal of Molecular Sciences 21(7):2378, 1-19 (2020). cited by applicant

Banerjee, Hridesh, et al., 33rd Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (SITC). Journal for Immunotherapy of Cancer 6(1):1-192 (2018). cited by applicant

Barbas, Carlos, et al., Assembly of Combinatorial Antibody Libraries on Phage Surfaces: The Gene III Site. Proceedings of the National Academy of Sciences of the United States of America 88(18):7978-7982 (1991). cited by applicant

Beidler, C B, et al., Cloning and High Level Expression of a Chimeric Antibody With Specificity for Human Carcinoembryonic Antigen. Journal of Immunology 141(11):4053-4060 (1988). cited by applicant

Berge, Ten, et al., Selective Expansion of a Peripheral Blood Cd8+ Memory T Cell Subset Expressing Both Granzyme B and L-selectin During Primary Viral Infection in Renal Allograft Recipients. Transplantation Proceedings 30(8):3975-3977 (1998). cited by applicant

Better, M. et al., "*Escherichia coli* Secretion of an Active Chimeric Antibody Fragment", Science, 1988, vol. 240, No. 4855, pp. 1041-1043. cited by applicant

Beun, G. et al., "T cell Retargeting Using Bispecific Monoclonal Antibodies in a Rat Colon Carcinoma Model", The Journal of Immunology, 1993, vol. 150, No. 6, pp. 2305-2315. cited by applicant

Bierer, B E, et al., Cyclosporin a and Fk506: Molecular Mechanisms of Immunosuppression and Probes for

Transplantation Biology. Current Opinion in Immunology 5(5):763-773 (1993). cited by applicant
Bird et al., Single-Chain Antigen-binding Proteins. Science 242(4877):423-426 (1988). cited by applicant
Bluemel, C. et al., "Epitope distance to the target cell membrane and antigen size determine the potency of T cell-mediated lysis by BiTE antibodies specific for a large melanoma surface antigen", Cancer Immunology, Immunotherapy, 2010, vol. 59, No. 8, pp. 1197-1209. cited by applicant
Bolt, S. et al., "The generation of a humanized, non-mitogenic CD3 monoclonal antibody which retains in vitro immunosuppressive properties," Eur. J. Immunol., 1993;23:403-411. cited by applicant
Breman, E. et al., "Overcoming target driven fratricide for T Cell Therapy," Frontiers in Immunology, 2018;9(2940):1-11. cited by applicant
Bruggemann, M. et al., Designer Mice: The Production of Human Antibody Repertories in Transgenic Animals, Terhorst C. Malavasi F, Albertini A (eds): Generation of Antibodies by Cell and Gene Immortalization, Year Immunol, 1993, vol. 7, pp. 33-40. cited by applicant
Bruggemann, M. et al., "Human antibody production in transgenic mice: expression from 100kb of the human IgH locus", Eur J. Immunol, 1991, vol. 21, pp. 1323-1326. cited by applicant
Buchwald et al. Long-term, continuous intravenous heparin administration by an implantable infusion pump in ambulatory patients with recurrent venous thrombosis. Surgery 88:507-516 (1980). cited by applicant
Cadwell, R. C. et al., "Randomization of Genes by PCR Mutagenesis", PCR Methods Appl., 1992, vol. 2, No. 1, pp. 28-33. cited by applicant
Cain, Chris, et al., Crossing over to Bispecificity. SciBX 4(28):1-3 (2011). cited by applicant
Chang et al.: A therapeutic T cell receptor mimic antibody targets tumor-associated PRAME peptide/HLA-I antigens. J Clin Invest. 127(7):2705-2718 (2017). cited by applicant
Chao, G. et al., "Isolating and engineering human antibodies using yeast surface display", Nature Protocols, 2006, vol. 1, No. 2, pp. 755-768. cited by applicant
Chaudry, et al. EpCAM an immunotherapeutic target for gastrointestinal malignancy: current experience and future challenges. Br J Cancer. Apr. 10, 2007;96(7):1013-9. Epub Feb. 27, 2007. cited by applicant
Chen et al.: Chromosome X-encoded cancer/testis antigens show distinctive expression patterns in developing gonads and in testicular seminoma. Hum Reprod. 26(12):3232-3243 doi:10.1093/humrep/der330 (2011). cited by applicant
Chen et al.: The nuclear localization sequences of the BRCA1 protein interact with the importin-alpha subunit of the nuclear transport signal receptor. J Biol Chem. 271(51):32863-32868 (1996). cited by applicant
Chiang, E. et al., "Abstract 3527: Potent anti-tumor activity of AbGn-100, an anti-CD326 x anti-TCR bispecific antibody to CD326-expressing solid tumors," Cancer Res., 2012;72(8_supplement):3527. cited by applicant
Chichili, V.P.R. et al., "Linkers in the structural biology of protein-protein interactions," Protein Science, 2013;22:153-167. cited by applicant
Chinese Patent Application No. 201780028089.4 2nd Office Action dated Apr. 18, 2022. cited by applicant
Cho, B.K. et al., "Single-Chain Fv/Folate Conjugates Mediate Efficient Lysis of Folate-Receptor-Positive Tumor Cells," Bioconjugate Chem., 1997;8:338-346. cited by applicant
Chothia, C. et al., "Canonical Structures for the Hypervariable Regions of Immunoglobulins", J. Mol. Biol, 1987, vol. 196, pp. 901-917. cited by applicant
Chothia et al., Structural repertoire of the human VH segments. J Mol Biol 227:799-817 (1992). cited by applicant
Ciccone, E. et al., "A monoclonal antibody specific for a common determinant of the human T cell receptor gamma/delta directly activates CD3+WT31-lymphocytes to express their functional program(s)," J Exp Med., 1988; 168(1):1-11. cited by applicant
Clackson, T. et al., Making antibody fragments using phage display libraries, Nature, 1991, vol. 352, pp. 624-628. cited by applicant
Colcher, David, et al., Single-Chain Antibodies in Pancreatic Cancer. Annals of the New York Academy of Sciences 880:263-280 (1999). cited by applicant
Coloma, J. et al., "Design and production of novel tetravalent bispecific antibodies", Nature Biotech, 1997, vol. 15, pp. 159-163. cited by applicant
Costa-Mattioli, Mauro, et al., RAPping Production of type I Interferon in pDCs through mTOR. Nature Immunology 9(10):1097-1099 (2008). cited by applicant
Cui, et al., "T cell receptor B-chain repertoire analysis of tumor-infiltrating lymphocytes in pancreatic cancer" Cancer Science (2018) 60-71. cited by applicant
Dao, Tao, et al., Targeting the Intracellular Wt1 Oncogene Product With a Therapeutic Human Antibody. Science Translational Medicine 5(176):176ra33, 1-22 (2013). cited by applicant
Davis, J. et al., "SEEDbodies: fusion proteins based on strand-exchange engineered domain (SEED) CH3 heterodimers in an Fc analogue platform for asymmetric binders or immunofusions and bispecific antibodies", Protein

Engineering, Design & Selection, 2010, vol. 23, No. 4, pp. 195-202. cited by applicant
Dela Cruz et al.: Anti-HER2/neu lgG3-(IL-2) and anti-HER2/neu lgG3-(GM-CSF) promote HER2/neu processing and presentation by dendritic cells: Implications in immunotherapy and vaccination strategies. Molecular Immunology 43(6):667-676 (2006). cited by applicant
Dickopf, S. et a., "Formal and geometries matter: Structure-based design defines the functionality of bispecific antibodies", Computational and Structural Biotechnology Journal, 2020, vol. 18, pp. 1221-1227. cited by applicant
Dimasi et al. Development of a trispecific antibody designed to simultaneously and efficiently target three different antigens on tumor cells. Mol Pharm 12(9):3490-3501 (2015). cited by applicant
Doyle, Sean, et al., IRF3 Mediates a TLR3/TLR4-Specific Antiviral Gene Program. Immunity 17(3):251-263 (2002). cited by applicant
Duhen et al., Co-expression of CD.SUB.39 .and CD.SUB.103 .identifies tumor-reactive CD8 T cells in human solid tumors. Nat Commun. 9(1):2724, pp. 1-13 (2018). cited by applicant
During, M J, et al., Controlled Release of Dopamine From a Polymeric Brain Implant: in Vivo Characterization. American Neurological Association 25(4):351-356 (1989). cited by applicant
El Achi, H. et al., "CD123 as a Biomarker in Hematolymphoid Malignancies: Principles of Detection and Targeted Therapies," Cancers, 2020;12(11):3087. cited by applicant
European Patent Application No. 17 718 441.3 Office Action dated Jan. 24, 2022. cited by applicant
European Search Report issued in EP20736073, dated Aug. 2, 2022. cited by applicant
Falini et al.: Cytoplasmic nucleophosmin in acute myelogenous leukemia with a normal karyotype. N Engl J Med. 352(3):254-266 doi:10.1056/NEJMoa041974 (2005). cited by applicant
Farrar et al.: The Molecular Cell Biology Of Interferon-gamma And Its Receptor. Annu Rev Immunol 11:571-611 (1993). cited by applicant
Fernandez-Malave, Edgar, et al., An Natural Anti-T-Cell Receptor Monoclonal Antibody Protects Against Experimental Autoimmune Encephalomyelitis. Journal of Neuroimmunology 234(1-2):63-70 (2011). cited by applicant
Foley, K.. et al., Combination immunotherapies implementing adoptive T-cell transfer for advanced-stage melanoma, Melanoma Research, vol. 28, 3 (2018):171-184. cited by applicant
Frost, Gregory, et al., A Microtiter-Based Assay for Hyaluronidase Activity Not Requiring Specialized Reagents. Analytical Biochemistry 251(2):263-269 (1997). cited by applicant
Fuchs, P. et al., "Targeting Recombinant Antibodies to the surface of *Escherichia coli*: Fusion to the Peptidoglycan associated Lipoprotein", Nature Publishing Group, 1991, vol. 9, No. 12, pp. 1369-1372. cited by applicant
Funayama et al.: Embryonic axis induction by the armadillo repeat domain of beta-catenin: evidence for intracellular signaling. J Cell Biol. 128(5):959-968 (1995). cited by applicant
Gao et al.: Alg14 recruits Alg13 to the cytoplasmic face of the endoplasmic reticulum to form a novel bipartite UDP-N-acetylglucosamine transferase required for the second step of N-linked glycosylation. J Biol Chem. 280(43):36254-36262 doi:10.1074/jbc.M507569200 (2005). cited by applicant
Garland, R.J., et al., "The use of Teflon cell culture bags to expand functionally active CD8+ cytotoxic T lymphocytes", Journal of Immunological Methods, 1999, vol. 227, pp. 53-63. cited by applicant
Garrard, L. et al., "FAB Assembly and Enrichment in a Monovalent Phage Display System", Nature Publishing Group, 1991, vol. 9, pp. 1373-1377. cited by applicant
Garrity, David, et al., The Activating NKG2D Receptor Assembles in the Membrane With Two Signaling Dimers Into a Hexameric Structure. Proceedings of the National Academy of Sciences of the United States of America 102(21):7641-7646 (2005). cited by applicant
GB Exam Report for GB2109794.4 dated Jun. 21, 2020. cited by applicant
Geissinger, E. et al., "Identification of the Tumor Cells in Peripheral T-Cell Lymphomas by Combined Polymerase Chain Reaction-Based T-Cell Receptor [3 Spectrotyping and Immunohistological Detection with T-Cell Receptor [3 Chain Variable Region Segment-Specific Antibodies," J. of Mol Diag., 2005;7(4):455-464. cited by applicant
Gillies, S.D. et al., "Bi-functional cytokine fusion proteins for gene therapy and antibody-targeted treatment of cancer," Cancer Immunol Immunotherapy, 2002;51:449-460. cited by applicant
Gjerstorff et al.: GAGE cancer-germline antigens are recruited to the nuclear envelope by germ cell-less (GCL). PLoS One 7(9):e45819:1-12 doi:10.1371/journal.pone.0045819 (2012). cited by applicant
Goel, M. et a., "Plasticity within the Antigen-Combining site may manifest as molecular mimicry in the humoral immune response," J Immunology, 2004;173(12):7358-7367. cited by applicant
Gohal, G, et al., "T-cell receptor phenotype pattern in atopic children using commercial fluorescently labeled antibodies against 21 human class-specific v segments for the tcrβ chain (vβ) of peripheral blood: a cross sectional study," Allergy Asthma Clin Immunol., 2016;12:10. cited by applicant

Gokden et al.: Diagnostic utility of renal cell carcinoma marker in cytopathology. Appl Immunohistochem Mol Morphol. Abstract Only. 11(2):116-119 doi:10.1097/00129039-200306000-00004 (2003). cited by applicant
Gordon, E.D. et al., "Alternative splicing of interleukin-33 and type 2 inflammation in asthma," PNAS, 2016;113(31):8765-8770. cited by applicant
Gram, H. et al., In vitro selection and affinity maturation of antibodies from a naïve combinatorial immunoglobulin library, PNAS, 1992, vol. 89, pp. 3576-3580. cited by applicant
Green, Edward, et al., TCR Validation Toward Gene Therapy for Cancer. Methods in Enzymology 629(21):419-441 (2019). cited by applicant
Green, L.L. et al., "Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light chain YACS", Nature Genet, 1994, vol. 7, pp. 13-21. cited by applicant
Griffiths, A.D. et al., "Human anti-self antibodies with high specificity from phage display libraries", The EMBO Journal, 1993, vol. 12, No. 2, pp. 725-734. cited by applicant
Gulley, J.L. et al., "New drugs on the horizon," Eur J Cancer, 2022;174(S1):S5. cited by applicant
Gupta, S. et al., "T cell activation via the T cell receptor: a comparison between WT31 (defining alpha/beta TcR)-induced and anti-CD3-induced activation of human T lymphocytes," Cell Immunol., 1991;132(1):26-44. cited by applicant
Haanen, J. et al., "Selective Expansion of Cross-reactive CD8+ Memory T Cells by Viral Variants", J. Exp. Med., 1999, vol. 190, No. 9, pp. 1319-1328. cited by applicant
Halin, C. et al., "Synergistic Therapeutic Effects of a Tumor Targeting Antibody Fragment, Fused to Interleukin 12 and to Tumor Necrosis Factor a1," Cancer Research, 2003;63:3202-3210. cited by applicant
Hall, MacLean, et al., Expansion of Tumor-Infiltrating Lymphocytes (TIL) from Human Pancreatic Tumors. Journal for Immuno Therapy of Cancer 4:61, 1-12 (2016). cited by applicant
Hamid, O. et al., "Safety and Tumor Responses with Lambrolizumab (Anti-PD-1) in Melanoma", The New England Journal of Medicine, 2013, vol. 369, No. 2, pp. 134-144. cited by applicant
Hamming et al. Crystal Structure of Interleukin-21 Receptor (IL-21R) Bound to IL-21 Reveals That Sugar Chain Interacting with WSXWS Motif Is Integral Part of IL-21R. The Journal of Biological Chemistry 287(12):9454-9460 (2012). cited by applicant
Hawkins, R. et al., "Selection of phage antibodies by binding affinity. Mimicking affinity maturation", J. Mol. Biol., 1992, vol. 226, No. 3, pp. 889-896. cited by applicant
Hay, B. et al., "Bacteriophage cloning and *Escherichia coli* expression of a human IgM Fab" Hum Antibodies Hybridomas, 1992, vol. 3, No. 2, pp. 81-85. cited by applicant
Henderson, D J, et al., Comparison of the Effects of FK-506, Cyclosporin A and Rapamycin on IL-2 Production. Immunology 73(3):316-321 (1991). cited by applicant
Herskovitz, O. et al., "NKp44 receptor mediates interaction of the envelope glycoproteins from the West-Nile and dengue viruses with Natural Killer cells," The Journal of Immunology, 2009;183(4):2610-2621. cited by applicant
Hirai et al.: Nucleolar scaffold protein, WDR46, determines the granular compartmental localization of nucleolin and DDX21. Genes Cells 18(9):780-797 (2013). cited by applicant
Hiyama, K, et al., Action of Chondroitinases. I. The Mode of Action of Two Chondroitinase-AC Preparations of Different Origin. Journal of Biochemistry 80(6):1201-1207 (1976). cited by applicant
Hiyama, K, et al., Crystallization and Some Properties of Chondroitinase from Arthrobacter Aurescens. The Journal of Biological Chemistry 250(5):1824-1828 (1975). cited by applicant
Hollinger, Philipp, et al., Engineered Antibody Fragments and the Rise of Single Domains. Nature Biotechnology 23(9):1126-1136 (2005). cited by applicant
Hombach, A.A. et al., "Antibody-IL2 Fusion Proteins for Tumor Targeting," Antibody Engineering, 2012:611-626. cited by applicant
"Hongyan, et al., "Fc Engineering for Developing Therapeutic Bispecific Antibodies and Novel Scaffolds" Frontiers In Immunology, (2017) vol. 8". cited by applicant
Hoogenboom, H.R. et al., "Multi-subunit proteins on the surface of filamentous phage: methodologies for displaying antibody (Fab) heavy and light chains", Nuc Acid Res, 1991, vol. 19, No. 15, pp. 4133-4137. cited by applicant
Howard, M A, et al., Intracerebral Drug Delivery in Rats with Lesion-induced Memory Deficits. Journal of Neurosurgery 71(1):105-112 (1989). cited by applicant
Hudson, K.R. et al., "Two Adjacent Residues in Staphylococcal EnterotoxIns A and E Determine T Cell Receptor Vbeta Specificity," J.Exp. Med., 1993;177:175-184. cited by applicant
Hudspeth et al.: Natural cytotoxicity receptors: broader expression patterns and functions in innate and adaptive immune cells. Frontiers in Immunology 4(69):1-15 (2013). cited by applicant
Hunig, T. et al., "A monoclonal antibody to a constant determinant of the rat t cell antigen receptor that induces t cell

activation", J. Exp. Med., 1989, vol. 169, pp. 73-86. cited by applicant
Huse, W. et al., "Generation of a large combinatorial library of the immunoglobulin repertoire in phage lambda" Science, 1989, vol. 246, No. 4935, pp. 1275-1281. cited by applicant
Huston, James, et al., Protein Engineering Of Antibody Binding Sites: Recovery Of Specific Activity In An Anti-digoxin Single-chain Fv Analogue Produced In *Escherichia coli*. Proceedings of the National Academy of Sciences of the United States of America 85(16):5879-5883 (1988). cited by applicant
International Preliminary Report on Patentability issued in PCT/US2017/023483, dated Sep. 25, 2018. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2019/040592, dated Jan. 5, 2021. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2020/012162, dated Jun. 16, 2021. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2020/019291, dated Aug. 10, 2021. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2020/019319, dated Aug. 10, 2021. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2020/019321, dated Aug. 10, 2021. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2020/060557 dated May 17, 2022. cited by applicant
International Preliminary Report on Patentability issued in PCT/US/2020/067543, dated Jul. 5, 2022. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2021/022408, dated Sep. 20, 2022. cited by applicant
International Preliminary Report on Patentability issued in PCT/US2021/028970, dated Oct. 25, 2022. cited by applicant
"International Search Report and Written Opinion for corresponding PCT Application No. PCT/US2019/012900 dated Jul. 5, 2019". cited by applicant
International Search Report and Written Opinion for corresponding PCT Application No. PCT/US2019/022282 issued Jul. 1, 2019. cited by applicant
International Search Report and Written Opinion issued in PCT/US2017/023483, mailed Aug. 29, 2017. cited by applicant
International Search Report and Written Opinion issued in PCT/US2019/040592, mailed Jan. 9, 2020. cited by applicant
International Search Report and Written Opinion issued in PCT/US2020/012162 mailed Jun. 26, 2020. cited by applicant
International Search Report and Written Opinion issued in PCT/US2020/019291, mailed Jun. 15, 2020. cited by applicant
International Search Report and Written Opinion issued in PCT/US2020/019319, mailed Jun. 26, 2020. cited by applicant
International Search Report and Written Opinion issued in PCT/US2020/019321, mailed Aug. 10, 2020. cited by applicant
International Search Report and Written Opinion issued in PCT/US2020/060557, mailed Mar. 30, 2021. cited by applicant
International Search Report and Written Opinion issued in PCT/US2020/067543, mailed Jul. 7, 2021. cited by applicant
International Search Report and Written Opinion issued in PCT/US2021/022408, mailed Aug. 31, 2021. cited by applicant
International Search Report and Written Opinion issued in PCT/US2021/028970 mailed Oct. 4, 2021. cited by applicant
International Search Report and Written Opinion issued in PCT/US2021/047571, dated Feb. 14, 2022. cited by applicant
International Search Report and Written Opinion issued in PCT/US2022/023922, mailed Oct. 17, 2022. cited by applicant
Islam, D, et al., Changes in the Peripheral Blood T-Cell Receptor V Beta Repertoire in Vivo and in Vitro During Shigellosis. Infection and Immunity 64(4):1391-1399 (1996). cited by applicant

Jameson, Stephen C., “T cell receptor antagonism in vivo, at last”, Proc. Natl. Acad. Sci., 1998, vol. 95, pp. 14001-14002. cited by applicant
Jiang, B. et al., “A novel peptide isolated from a phage display peptide library with trastuzumab can mimic antigen epitope of HER-2*,” The Journal of Biological Chemistry, 2005;280(6):4656-4662. cited by applicant
Jiang et al.: Nuclear expression of CDK4 correlates with disease progression and poor prognosis in human nasopharyngeal carcinoma. Histopathology 64(5):722-730 doi:10.1111/his.12319 (2013). cited by applicant
Jones et al., Replacing The Complementarity-determining Regions In A Human Antibody With Those From A Mouse. Nature 321(6069):522-525 (1986). cited by applicant
Ju et al.: Structure-function analysis of human interleukin-2. Identification of amino acid residues required for biological activity. The Journal of Biological Chemistry 262(12):5723-5731 (1987). cited by applicant
Kanagawa, et al., “In Vivo T Cell Tumor Therapy With Monoclonal Antibody Directed to the VB chain of T Cell Antigen Receptor” J. Exp. Med., vol. 170, (1989) p. 1513-1519. cited by applicant
Kanagawa, O, et al., The T Cell Receptor VB6 Domain Imparts Reactivity to the Mls-1a Antigen. Cellular Immunology 119(2):412-426 (1989). cited by applicant
Kato et al.: The structure and binding mode of interleukin-18. Nature Structural Biology 10(11):366-971 (2003). cited by applicant
Kato, Y. et al., “Molecular analysis of the pathophysiological binding of the platelet aggregation-inducing factor podoplanin to the C-type lectin-like receptor CLEC-2”, Cancer Sci, Jan. 2008, vol. 99, No. 1, pp. 54-61. cited by applicant
Kawaguchi, M, et al., Differential Activation Through the TCR-CD3 Complex Affects the Requirement for Costimulation of Human T Cells. Human immunology 43(2):136-148 (1995). cited by applicant
Kellner et al.: Enhancing natural killer cell-mediated lysis of lymphoma cells by combining therapeutic antibodies with CD20-specific immunoligands engaging NKG2D or NKp30. Oncoimmunology 5(1)e1058459 [1-12] (2016). cited by applicant
Kerkela, E, et al., Expression of Human Macrophage Metalloelastase (MMP-12) by Tumor Cells in Skin Cancer. Journal of Investigative Dermatology 114(6):1113-1119 (2000). cited by applicant
Kiefer, J.D. et al., “Immunocytokines and bispecific antibodies: two complementary strategies for the selective activation of immune cells at the tumor site,” Immunol Rev., 2016;270(1):178-192. cited by applicant
Kim, E.J. et al., “Interleukin-2 fusion protein with anti-CD3 single-chain Fv (sFv) selectively protects T cells from dexamethasone-induced apoptosis,” Vaccine, 2002;20:608-615. cited by applicant
Kirkin, et al. Melanoma-associated antigens recognized by cytotoxic T lymphocytes. APMIS. Jul. 1998;106(7):665-79. cited by applicant
Kitaura, K. et al., “A new high-throughput sequencing method for determining diversity and similarity of T cell receptor (TCR) α and β repertoires and identifying potential new invariant TCR α chains,” BMC Immunology, 2016, vol. 17, No. 38, pp. 1-16. cited by applicant
Klampfl, T. et al., “Somatic Mutations of Calreticulin in Myeloproliferative Neoplasms”, N Engl J Med., 2013, vol. 369, No. 25, pp. 2379-2390. cited by applicant
Klein, Christian, et al., Progress in Overcoming the Chain Association Issue in Bispecific Heterodimeric IgG Antibodies. mAbs 4(6):653-663 (2012). cited by applicant
Koch et al.: Activating natural cytotoxicity receptors of natural killer cells in cancer and infection. Trends Immunol. 34(4):182-191 doi:10.1016/j.it.2013.01.003 (2013). cited by applicant
Kunkel, Thomas A., “Rapid and efficient site-specific mutagenesis without phenotypic selection”, Proc Natl Acad Sci, 1985, vol. 82, No. 2, pp. 488-492. cited by applicant
Kushner et al.: Aberrant expression of cyclin A and cyclin B1 proteins in oral carcinoma. J Oral Pathol Med. 28(2):77-81 (1999). cited by applicant
Labrijn, Aran, et al., Controlled Fab-arm Exchange for the Generation of Stable Bispecific IgG1. Nature Protocols 9(10):2450-2463 (2014). cited by applicant
Labrijn, Aran, et al., Efficient Generation of Stable Bispecific IgG1 by Controlled Fab-arm Exchange. Proceedings of the National Academy of Sciences of the United States of America 110(13):5145-5150 (2013). cited by applicant
Lain et al.: Accumulating active p53 in the nucleus by inhibition of nuclear export: a novel strategy to promote the p53 tumor suppressor function. Exp Cell Res. 253(2):315-324 (1999). cited by applicant
Langer, Robert, et al., Chemical and Physical Structure of Polymers as Carriers for Controlled Release of Bioactive Agents: A Review. Journal of Macromolecular Science—Reviews in Macromolecular Chemistry and Physics 23(1):61-126 (1983). cited by applicant
Langer, Robert, et al., Medical Applications of Controlled Release. 2:115-138 (1984). cited by applicant
Langer, Robert, New Methods of Drug Delivery. Science 249(4976):1527-1533 (1990). cited by applicant

Lanier, L.L. et al., “Distinct epitopes on the t cell antigen receptor of HPB-ALL tumor cells identified by monoclonal antibodies,” 1986;137(7):2286-2292. cited by applicant
Leclercq, G. et al., “Dissecting the mechanism of cytokine release induced by T-cell engagers highlights the contribution of neutrophils,” Oncoimmunology, 2022;11(1):e2039432. cited by applicant
Lee, C. M. et al., “Selection of human antibody fragments by phage display”, Nat Protoc., 2007, vol. 2, No. 11, pp. 3001-3008. cited by applicant
Lee, K.D. et al., “Construction and characterization of a novel fusion protein consisting of anti-CD3 antibody fused to recombinant interleukin-2,” Oncology Reports, 2006;15:1211-1216. cited by applicant
Leonard, E.K. et al., “Engineered cytokine/antibody fusion proteins improve delivery of IL-2 to pro-inflammatory cells and promote antitumor activity,” bioRxiv, 2023:1-36. cited by applicant
Leong et al.: Optimized expression and specific activity of IL-12 by directed molecular evolution. Proc. Natl. Acad. Sci. USA; 100(3): 1163-1168 (2003). cited by applicant
Leutkens et al.: Functional autoantibodies against SSX-2 and NY-ESO-1 in multiple myeloma patients after allogeneic stem cell transplantation. Cancer Immunol Immunother. 63(11):1151-1162 (2014). cited by applicant
Levy, R J, et al., Inhibition of Calcification of Bioprosthetic Heart Valves by Local Controlled-Release Diphosphonate. Science 228(4696):190-192 (1985). cited by applicant
Li, B. et al., “Landscape of tumor-infiltrating T cell repertoire of human cancers,” Nature Genetics, 2016, vol. 48, No. 7, pp. 725-735. cited by applicant
Li, F. et al., “T cell receptor B-chain-targeting chimeric antigen receptor T cells against T cell malignancies,” Nature Communications, 2022;13:4334. cited by applicant
Li, Hanchen, et al., Tumor Microenvironment: The Role of the Tumor Stroma in Cancer. Journal of Cellular Biochemistry 101(4):805-815 (2007). cited by applicant
Li, Peng, et al., Design and Synthesis of Paclitaxel Conjugated with an ErbB2-recognizing Peptide, EC-1. Biopolymers 87(4):225-230 (2007). cited by applicant
Liddy et al.: Monoclonal TCR-redirected tumor cell killing. Nat Med. 18(6):980-987 doi:10.1038/nm.2764 (2012). cited by applicant
Liu, Alvin, et al., Chimeric Mouse-human IgG1 Antibody that can Mediate Lysis of Cancer Cells. Proceedings of the National Academy of Sciences of the United States of America 84(10):3439-3443 (1987). cited by applicant
Liu, Alvin, et al., Production of a Mouse-human Chimeric Monoclonal Antibody to CD20 With Potent Fc-dependent Biologic Activity. Journal of Immunology 139(10):3521-3526 (1987). cited by applicant
Liu, Der-Zen, et al., Synthesis of 2′-paclitaxel Methyl 2-glucopyranosyl Succinate for Specific Targeted Delivery to Cancer Cells. Bioorganic & Medicinal Chemistry Letters 17(3):617-620 (2007). cited by applicant
Liu, D.V. et al., “Engineered Interleukin-2 Antagonists for the Inhibition of Regulatory T Cells,” J. Immunother., 2009;32(9):887-894. cited by applicant
Liu, J, et al., Calcineurin is a Common Target of Cyclophilin-Cyclosporin A and FKBP-FK506 Complexes. Cell 66(4):807-815 (1991). cited by applicant
Liu, K. et al., “CD123 and its potential clinical application in leukemias,” Life Sciences, 2015;122:59-64. cited by applicant
Lloyd et al., Modelling the Human Immune Response: Performance of a 10″ Human Antibody Repertoire Against a Broad Panel of Therapeutically Relevant Antigens. Protein Engineering Design & Selection. 22(3):159-168 (2009). cited by applicant
Lobuglio, Albert, et al., Phase I Clinical Trial of CO17-1A Monoclonal Antibody. Hybridomia 5(1):S117-S123 (1986). cited by applicant
Lonberg, Nils, et al., Antigen-Specific Human Antibodies From Mice Comprising Four Distinct Genetic Modifications. Nature 368(6474):856-859 (1994). cited by applicant
Luo, S. et al., “Worldwide genetic variation of the IGHV and TRBV immune receptor gene families in humans” (2019) Life Sciences Alliance, vol. 2, No. 2, p. 1-9. cited by applicant
Lustgarten, J. et al., “Redirecting Effector T Cells through their IL-2 receptors,” J Immunology, 1999;162:359-365. cited by applicant
Maciocia, P. M. et al., “Targeting the T cell receptor B-chain constant region for immunotherapy of T cell malignancies”, Nature Medicine, 2017, vol. 23, No. 12, pp. 1416-1423. cited by applicant
Mackay, C.R. et al., “Gamma/delta T cells express a unique surface molecule appearing late during thymic development,” Eur J Immunol., 1989;19(8):1477-1483. cited by applicant
Macor, P. et al., “Bispecific antibodies targeting tumor-associated antigens and neutralizing complement regulators increase the efficacy of antibody-based immunotherapy in mice”, Leukemia, 2015, vol. 29, pp. 406-414. cited by applicant

Mandelboim, O. et al., “Recognition of hemagglutinins on virus-infected cells by NKp46 activates lysis by human NK cells”, Nature, 2001, vol. 409, No. 6823, pp. 1055-1060. cited by applicant
Mao et al.: Inhibition of human natural killer cell activity by influenza virions and hemagglutinin. Journal of Virology 84(9):4148-4157 (2010). cited by applicant
Martens, Tobias, et al., A Novel One-Armed Anti-c-Met Antibody Inhibits Glioblastoma Growth In Vivo. Clinical Cancer Research 12(20 Pt 1):6144-6152 (2006). cited by applicant
Martin, A. et al., “Chapter 3: Protein Sequence and Structure Analysis of Antibody Variable Domains”, In: Antibody Engineering Lab Manual (Ed: Duebel, S. and Kontermann, R., Springer- Verlag, Heidelberg), 2010, vol. 2, pp. 33-51. cited by applicant
Martin, F. et al., “The affinity-selection of a minibody polypeptide inhibitor of human interleukin-6”, EMBO J., 1994, vol. 13, No. 22, pp. 5303-5309. cited by applicant
McConnell, Stephen, et al., Tendamistat as a Scaffold for Conformationally Constrained Phage Peptide Libraries. Journal of Molecular Biology 250(4):460-470 (1995). cited by applicant
McElroy et al.: Structural and Biophysical Studies of the Human IL-7/IL-7R alpha Complex. Structure 17(1):54-65 (2009). cited by applicant
Merchant, A.M. et al., “An efficient route to human bispecific IgG,” Nature Biotechnology, 1998;16(7):677-681. cited by applicant
Meschendoerfer, W. et al., “SPR-based assays enable the full functional analysis of bispecific molecules,” Journal of Pharmaceutical and Biomedical Analysis, 2017, vol. 5, No. 132, pp. 141-147. cited by applicant
Meyers, E. et al., “Optimal alignments in linear space”, CABIOS,1988, vol. 4, No. 1, pp. 11-17. cited by applicant
Michelacci, Y M, et al., A Comparative Study Between a Chondroitinase B and a Chondroitinase AC From Flavobacterium Heparinum: Isolation of a Chondroitinase AC-Susceptible Dodecasaccharide From Chondroitin Sulphate B. The Biochemical Journal 151(1):121-129 (1975). cited by applicant
Michelacci, Yara, et al., Isolation and Partial Characterization of an Induced Chondroitinase B from Flavobacterium Heparinum. Biochemical and Biophysical Research Communications 56(4):973-980 (1974). cited by applicant
Miller et al.: Trispecific Killer Engagers (TrikEs) that contain IL-15 to make NK cells antigen specific and to sustain their persistence and expansion. Blood 126(23):232-232 (2015). cited by applicant
Milone, Michael, et al., Chimeric Receptors Containing CD137 Signal Transduction Domains Mediate Enhanced Survival of T Cells and Increased Antileukemic Efficacy in Vivo. Molecular Therapy 17(8):1453-1464 (2009). cited by applicant
Mitra, S. et al., “Interleukin-2 Activity can be Fine-Tuned with Engineering Receptor Signaling Clamps,” Immunity, 2015;42(5):826-838. cited by applicant
Miyahara, Y et al., Anti-TCRβ mAb induces long-term allograft survival by reducing antigen-reactive T cells and sparing regulatory T cells, American journal of transplantation: official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons, vol. 12, 6 (2012): 1409-18. cited by applicant
Modak et al.: Disialoganglioside GD2 and a novel tumor antigen: potential targets for immunotherapy of desmoplastic small round cell tumor. Med Pediatr Oncol. 39(6):547-551 (2002). cited by applicant
Moore, Gregory, et al., A Novel Bispecific Antibody Format Enables Simultaneous Bivalent and Monovalent Co-engagement of Distinct Target Antigens. mAbs 3(6):546-557 (2011). cited by applicant
Morel et al.: Processing of some antigens by the standard proteasome but not by the immunoproteasome results in poor presentation by dendritic cells. Immunity. 12(1):107-117 doi:10.1016/s1074-7613(00)80163-6 (2000). cited by applicant
Morrison, Sherie, et al., Chimeric Human Antibody Molecules: Mouse Antigen-binding Domains With Human Constant Region Domains. Proceedings of the National Academy of Sciences of the United States of America 81(21):6851-6855 (1984). cited by applicant
Morrison, Sherie, Transfectomas Provide Novel Chimeric Antibodies. Science 229(4719):1202-1207 (1985). cited by applicant
Muller, K.P. et al., “T cell receptor targeting to thymic cortical epithelial cells in vivo induces survival, activation and differentiation of immature thymocytes,” Eur. J. Immunol., 1993;23(7):1661-1670. cited by applicant
Murer, P. et al., “Antibody-cytokine fusion proteins: A novel class of biopharmaceuticals for the therapy of cancer and of chronic inflammation”, New Biotechnology, 2019, vol. 52, pp. 42-53. cited by applicant
Murzin, A G, et al., SCOP: A Structural Classification of Proteins Database for the Investigation of Sequences and Structures. Journal of Molecular Biology 247(4):536-540 (1995). cited by applicant
Nagarajan et al.: Ligand binding and phagocytosis by CD16 (Fc gamma receptor III) isoforms. Phagocytic signaling by associated zeta and gamma subunits in Chinese hamster ovary cells. Journal of Biological Chemistry J Biol Chem. 270(43):25762-25770 (1995). cited by applicant

Naing, et al., “Strategies for improving the management of immune-related adverse events” Journal for ImmunoTherapy of Cancer, (2020) p. 1-9. cited by applicant
Nandi et al.: CD28-mediated costimulation is necessary for optimal proliferation of murine NK cells. J Immunol. 152(7):3361-3369 (1994). cited by applicant
Nangalia, J. et al., “Somatic CALR Mutations in Myeloproliferative Neoplasms with Nonmutated JAK2”, N Engl J Med., 2013, vol. 369, No. 25, pp. 2391-2405. cited by applicant
Needleman, Saul, et al., A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins. Journal of Molecular Biology 48(3):444-453 (1970). cited by applicant
Newman et al.: Combining Early Heat Shock Protein Vaccination with Directed IL-2 Leads to Effective Anti-Tumor Immunity in Autologous Hematopoietic Cell Transplantation Recipients. 118(21):998-998 (2011). cited by applicant
Niederberger, N. et al., “Thymocyte stimulation by anti-TCR-b, but not by anti-TCR-a, leads to induction of developmental transcription program,” Journal of Leukoeyte Biology, 2005;77(5):830-841. cited by applicant
Nishimura, Yushi, et al., Recombinant Human-Mouse Chimeric Monoclonal Antibody Specific for Common Acute Lymphocytic Leukemia Antigen. Cancer Research 47(4):999-1005 (1987). cited by applicant
No Author “PE anti-human TCR VB23 Antibody” (2012). cited by applicant
No Author “PE anti-mouse TCR VB6 Antibody” (2012). cited by applicant
Nolo, R. et al., “Targeting P-selection blocks neuroblastoma growth”, Oncotarget, 2017, vol. 8, No. 49, pp. 86657-86670. cited by applicant
Novellino et al.: A listing of human tumor antigens recognized by T cells: Mar. 2004 update. Cancer Immunol Immunother. 54(3):187-207 doi:10.1007/s00262-004-0560-6 (2005). cited by applicant
Oh, Julyun, et al., Single Variable Domains From the T Cell Receptor B Chain Function as Mono- and Bifunctional CARs and TCRs. Scientific Reports 9(1):17291, 1-12 (2019). cited by applicant
Oi, Vernon, et al., Chimeric Antibodies. BioTechniques 4(3):214-221 (1986). cited by applicant
Ortiz-Sanchez, Elizabeth, et al., Antibody-Cytokine Fusion Proteins: Applications in Cancer Therapy. Expert Opinion on Biological Therapy 8(5):609-632 (2008). cited by applicant
Page, David, et al., Deep Sequencing of T-cell Receptor DNA as a Biomarker of Clonally Expanded TILs in Breast Cancer after Immunotherapy. Cancer Immunology Research 4(10):835-844 (2016). cited by applicant
Pardoll, D.M., “The blockade of immune checkpoints in cancer immunotherapy”, Nat Rev Cancer, 2012, Vo. 12, pp. 252-264. cited by applicant
Park, Y.P. et al., “Complex Regulation of human NKG2D-DAP10 cell surface expression: opposing roles of the yc cytokines and TGF-β1”, Blood, 2011, vol. 118, No. 11, pp. 3019-3027. cited by applicant
Pasche, N. et al., “Immunocytokines: a novel class of potent armed antibodies, ” Drug Discovery Today, 2012;17(11):583-590. cited by applicant
Paul, S. et al., “TCR beta chain-directed bispecific antibodies for the treatment of T-cell cancers,” Science Translational Medicine, 2021, pp. 1-21. cited by applicant
Payne, J. et al., “Two Monoclonal Rat Antibodies with Specificity for the β-Chain Variable Region Vβ6 of the Murine T-Cell Receptor”, Proc. Natl. Acad. Sci., 1988, vol. 85, pp. 7695-7698. cited by applicant
PCT/US2017/023483 International Search Report and Written Opinion dated Aug. 29, 2017. cited by applicant
PCT/US2018/029951 International Preliminary Report on Patentability dated Oct. 29, 2019. cited by applicant
PCT/US2018/029951 International Search Report and Written Opinion dated Mar. 7, 2018. cited by applicant
PCT/US2019/022284 International Preliminary Report on Patentability dated Sep. 15, 2020. cited by applicant
PCT/US2019/022284 International Search Report and Written Opinion dated Sep. 10, 2019. cited by applicant
PCT/US2020/019324 International Preliminary Report on Patentability dated Aug. 10, 2021. cited by applicant
PCT/US2020/019324 International Search Report and Written Opinion dated Jun. 10, 2020. cited by applicant
Pettit et al.: Structure-function studies of interleukin 15 using site-specific mutagenesis, polyethylene glycol conjugation, and homology modeling. J Biol Chem. 272(4):2312-2318 (1997). cited by applicant
Pilch, H, et al., Improved Assessment of T-Cell Receptor (TCR) VB Repertoire in Clinical Specimens: Combination o TCR-CDR3 Spectratyping with Flow Cytometry-Based TCR VB Frequency Analysis. Clinical and Diagnostic Laboratory Immunology 9(2):257-266 (2002). cited by applicant
Posnett, D.N. et al., “Inherited polymorphism of the human T-cell antigen receptor detected by a monoclonal antibody,” PNAS, 1986;83:7888-7892. cited by applicant
Presta, Leonard, Antibody Engineering. Current Opinion in Structural Biology 2(4):593-596 (1992). cited by applicant
Provenzano et al.: Enzymatic targeting of the stroma ablates physical barriers to treatment of pancreatic ductal adenocarcinoma. Cancer Cell. 21(3):418-429 doi:10.1016/j.ccr.2012.01.007 (2012). cited by applicant
Qi, et al., “Potent and selective antitumor activity of a T cell-engaging bispecific antibody targeting a membrane-proximal epitope of ROR1,” PNAS, 2018;115(24):E5467-E5476. cited by applicant

Rabia, L. et al., “Understanding and overcoming trade-offs between antibody affinity, specificity, stability and solubility,” Biochemical Engineering Journal, 2018;137:365-374. cited by applicant
Rakoff-Nahoum, Seth, et al., Toll-like Receptors and Cancer. Nature Reviews Cancer 9(1):57-63 (2009). cited by applicant
Rath, et al., “Engineering Strategies to Enhance TCR-Based Adoptive T Cell Therapy” (2020) Cells, 9, 1485, p. 1-34. cited by applicant
Reiter, Yoram, et al., Antibody Engineering of Recombinant Fv Immunotoxins for Improved Targeting of Cancer: Disulfide-stabilized Fv Immunotoxins. Clin Cancer Res 2(2):245-252 (1996). cited by applicant
Ridgway, John, et al., Knobs-Into-Holes Engineering of Antibody CH3 Domains for Heavy Chain Heterodimerization Protein Engineering 9(7):617-621 (1996). cited by applicant
Riechmann, L, et al., Reshaping Human Antibodies for Therapy. Nature 332(6162):323-327 (1988). cited by applicant
Riemer, A.B. et al., “Matching of trastuzumab (Herceptin) epitope mimics onto the surface of Her-2/neu—a new method of epitope definition,” Molecular Immunology, 2005;42:1121-1124. cited by applicant
Ring et al.: Mechanistic and structural insight into the functional dichotomy between interleukin-2 and interleukin-15. Nat Immunol. 13(12):1187-1195 (2012). cited by applicant
Roda-Navarro, P. et al., “Understanding the Spatial Topology of Artificial Immunology Synapses Assembled in T Cell-Redirecting Strategies: A Major Issue in Cancer Immunotherapy”, Frontiers in Cell and Developmental Biology, 2020, vol. 7, No. 370. cited by applicant
Rohena-Rivera et al.: IL-15 regulates migration, invasion, angiogenesis and genes associated with lipid metabolism and inflammation in prostate cancer. PloS one 12(4):e0172786:1-27 (2017). cited by applicant
Rosenberg, Steven, et al., Use of Tumor-Infiltrating Lymphocytes and Interleukin-2 in the Immunotherapy of Patients with Metastatic Melanoma. The New England Journal of Medicine 319(25):1676-1680 (1988). cited by applicant
Rudikoff et al.: Single Amino Acid Substitution Altering Antigen-binding Specificity. Pnas USA 79(6):1979-1983 (1982). cited by applicant
Ruggiero, Eliana, et al., High-resolution Analysis of the Human T-Cell Receptor Repertoire. Nature Communication 6:8081, 1-7 (2014). cited by applicant
Salameire, et al., “Accurate detection of the tumor clone in peripheral T-cell lymphoma biopsies by flow cytometric analysis of TCR-V B repertoire” Modern Pathology (2012) 25, p. 1246-1257. cited by applicant
Saleh, Mansoor, et al., A Phase II Trial of Murine Monoclonal Antibody 17-1A and Interferon-gamma: Clinical and Immunological Data. Cancer Immunology, Immunotherapy 32(3):185-190 (1990). cited by applicant
Sano, Y. et al., “Properties of Blocking and Non-blocking Monoclonal Antibodies Specific for Human Macrophage Galactose-type C-type Lectin (MGL/ClecSF10A/CD301),” J. Biochem., 2007;127-136. cited by applicant
Sastry, Konduru, et al., Targeting Hepatitis B virus-infected cells with a T-Cell Receptor-like Antibody. Journal of Virology 85(5):1935-1942 (2011). cited by applicant
Saudek et al. A preliminary trial of the programmable implantable medication system for insulin delivery. N. Engl. J. Med. 321(9):574-579 (1989). cited by applicant
Saunders, Kevin, Conceptual Approaches to Modulating Antibody Effector Functions and Circulation Half-Life. Frontiers in Immunology 10:1296, 1-20 (2019). cited by applicant
Schleinitz, N. et al., “Natural killer cells in human autoimmune diseases,” Immunology, 2010;131(4):451-458. cited by applicant
Schliemann et al.: Targeting interleukin-2 to the bone marrow stroma for therapy of acute myeloid leukemia relapsing after allogeneic hematopoietic stem cell transplantation. Cancer immunology research 3(5):547-556 (2015). cited by applicant
Schmittnaegel, Martina, et al., Activation of Cytomegalovirus-Specific CD8+ T-cell response by Antibody-Mediated peptide-major Histocompatibility class I Complexes. Oncolmmunology 5(1):e1052930, 1-3 (2015). cited by applicant
Scodeller, Pablo, Hyaluronidase and Other Extracellular Matrix Degrading Enzymes for Cancer Therapy: New Uses and Nano-Formulations, Journal of Carcinogenesis & Mutagenesis 5(4):1-5 (2014). cited by applicant
Sefton, Michael, Implantable Pumps. Critical Reviews in Biomedical Engineering 14(3):201-240 (1987). cited by applicant
Seidel, U. et al., “Natural killer cell mediated antibody-dependent cellular cytotoxicity in tumor immunotherapy with therapeutic antibodies”, frontiers in Immunology, 2013, vol. 4, No. 76, pp. 1-8. cited by applicant
Sekine, T. et al., “A feasible method for expansion of peripheral blood lymphocytes by culture with immobilized anti-CD3 monoclonal antibody and interleukin-2 for use in adoptive immunotherapy of cancer patients,” Biomed & Pharmacother, 1993;47:73-78. cited by applicant
Sen, S. et al., “Expression of epithelial cell adhesion molecule (EpCAM) in oral squamous cell carcinoma,” Histopathology, 2015:6:897-904. Abstract only. cited by applicant

Sergeeva, Anna, et al., An Anti-PR1/HLA-A2 T-cell Receptor-like Antibody Mediates Complement-Dependent Cytotoxicity Against Acute Myeloid Leukemia Progenitor Cells. Blood 117(16):4262-4272 (2011). cited by applicant
Shaw, Denise, et al., Mouse/Human Chimeric Antibodies to a Tumor-Associated Antigen: Biologic Activity of the Four Human IgG Subclasses. Journal of the National Cancer Institute 80(19):1553-1559 (1988). cited by applicant
Shi, M. et al., "A recombinant anti-erbB2, scFv-Fc-IL-2 fusion protein retains antigen specificity and cytokine function," Biotechnology letters, 2003;25:815-819. cited by applicant
Shimabukuro-Vornhagen, Alexander, et al., Cytokine Release Syndrome. Journal for Immuno Therapy of Cancer 6(56):1-14 (2018). cited by applicant
Shitaoka, Kiyomi, et al., Identification of Tumoricidal TCRs from Tumor-Infiltrating Lymphocytes by Single-Cell Analysis. Cancer Immunology Research 6(4):378-388 (2018). cited by applicant
Shpilberg, O, et al., Subcutaneous Administration of Rituximab (MabThera) and Trastuzumab (Herceptin) using Hyaluronidase. British Journal of Cancer 109(6):1556-1561 (2013). cited by applicant
Skegro, D. et al., "Immunoglobulin domain interface exchange as a platform technology for the generation of Fc heterodimers and bispecific antibodies," J Biol Chem, 2017, vol. 292, No. 23, pp. 9745-9759. cited by applicant
Spiess, C. et al., "Alternative molecular formats and therapeutic applications for bispecific antibodies", Molecular Immunology, 2015, vol. 67, pp. 95-106. cited by applicant
Stauber, D.J. et al., "Crystal structure of the IL-2 signaling complex: Paradigm for a heterotrimeric cytokine receptor," PNAS, 2006;103(8):2788-2793. cited by applicant
Stauber et al.: Nuclear and cytoplasmic survivin: molecular mechanism, prognostic, and therapeutic potential. Cancer Res. 67(13):5999-6002 (2007). cited by applicant
Stivala, Alex, et al., Automatic Generation of Protein Structure Cartoons With Pro-origami. Bioinformatics 27(23):3315-3316 (2011). cited by applicant
Sun, Lee, et al., Chimeric Antibody With Human Constant Regions and Mouse Variable Regions Directed Against Carcinoma-Associated Antigen 17-1A. Proceedings of the National Academy of Sciences of the United States of America 84(1):214-218 (1987). cited by applicant
Suzuki, Sakaru, et al., Formation of Three Types of Disulfated Disaccharides from Chondroitin Sulfates by Chondroitinase Digestion. The Journal of Biological Chemistry 243(7):1543-1550 (1968). cited by applicant
Swencki-Underwood, B. et al., "Engineering human IL-18 with increased bioactivity and bioavailability," Cytokine, 2006, vol. 34, pp. 114-124. cited by applicant
Tang, et al., "Anti-TCR Antibody Treatment Activates a Novel Population of Nonintestinal CD8aa+TCRaB+ Regulatory T Cells and Prevents Experimental Autoimmune Encephalomyelitis" The Journal of Immunology (2007) p. 1-9. cited by applicant
Tassev, D V, et al., Retargeting NK92 Cells using an HLA-A2-Restricted, EBNA3C-Specific Chimeric Antigen Receptor. Cancer Gene Ther 19(2):84-100 (2012). cited by applicant
"Stein, et al., "A new monoclonal antibody (CAL2) detects CALRETICULIN mutations in formalin-fixed and paraffin-embedded bone marrow biopsies," Leukemia, Jul. 23, 2015, vol. 30, No. 1, pp. 131-135". cited by applicant
"Ten Hacken, et al., "Calreticulin as a novel B-cell receptor antigen in chronic lymphocytic leukemia," Haematologica, Oct. 31, 2017, vol. 102, No. 10, pp. E394-e396". cited by applicant
Thorpe, Philip, Vascular Targeting Agents as Cancer Therapeutics. Clinical Cancer Research 10(2):415-427 (2004). cited by applicant
Tomlinson, Ian, et al., The Repertoire of Human Germline VH Sequences Reveals About Fifty Groups of VH Segments With Different Hypervariable Loops. Journal of Molecular Biology 227(3):776-798 (1992). cited by applicant
Tomonari, K. et al., "Epitope-specific binding of CD8 regulates activation of T cells and induction of cytotoxicity," International Immunology, 1990;2(12):1189-1194. cited by applicant
Tramontano et al.: The making of the minibody: an engineered beta-protein for the display of conformationally constrained peptides. J. Mol. Recognition. 7:9-24 (1994). cited by applicant
Trenevska et al.: Therapeutic Antibodies against Intracellular Tumor Antigens. Front Immunol. 8:1001 doi:10.3389/fimmu.2017.01001 [1-12] (2017). cited by applicant
Tsytsikov, V.N. et al., "Identification and Characterization of Two Alternative Splice Variants of Human Interleukin-2*" The Journal of Biological Chemistry, 1996;71(38):23055-23060. cited by applicant
Tuaillon, Nadine, et al., Human Immunoglobulin Heavy-Chain Minilocus Recombination in Transgenic Mice: Gene-Segment Use in Mu and Gamma Transcripts. Proceedings of the National Academy of Sciences of the United States o America 90(8):3720-3724 (1993). cited by applicant
U.S. Appl. No. 17/529,017 Non-Final Office Action dated Apr. 27, 2022. cited by applicant
Vallera et al.: Heterodimeric bispecific single-chain variable-fragment antibodies against EpCAM and CD16 induce

effective antibody-dependent cellular cytotoxicity against human carcinoma cells. Cancer Biother Radiopharm. 28(4):274-282 doi:10.1089/cbr.2012.1329 (2013). cited by applicant
Vannucchi, et al., "Calreticulin mutation-specific immunostaining in myeloproliferative neoplasms: pathogenetic insight and diagnostic value" Leukemia (2014) 28, p. 1811-1818. cited by applicant
Verhoeyen, M. et al., "Reshaping Human Antibodies: Grafting an Antilysozyme Activity", Science, 1988, vol. 239, pp 1534-1536. cited by applicant
Verma, Bhavna, et al., TCR Mimic Monoclonal Antibody Targets a Specific Peptide/HLA Class I Complex and Significantly Impedes Tumor Growth In Vivo Using Breast Cancer Models. J Immunol 184(4):2156-2165 (2010). cited by applicant
Verwilghen, J. et al., "Differences in the stimulating capacity of immobilized anti-CD3 monoclonal antibodies: variable dependence on interleukin-1 as a helper signal for T-cell activation," 1991;72:269-276. cited by applicant
Vonderheid, Eric, et al., Evidence for Restricted VB Usage in the Leukemic Phase of Cutaneous T Cell Lymphoma. The Journal of Investigative Dermatology 124(3):650-661 (2005). cited by applicant
Vyas, M. et al., "Natural ligands and antibody-based fusion proteins: harnessing the immune system against cancer", Trends in Molecular Medicine, 2014, vol. 20, No. 2, pp. 72-82. cited by applicant
Wadia, P. et al., "Impaired lymphocyte responses and their restoration in oral cancer patients expressing distinct TCR variable region," Cancer Investigation, 2008;26:471-480. cited by applicant
Wagner, E.K. et al., "Engineering therapeutics antibodies to combat infectious disease," Current Opinion in Chemical Engineering, 2018:19;131-141. cited by applicant
Wan, Y.Y. et al., "'Yin-Yang' functions of TGF-b and tregs in immune regulation," Immunol Rev., 2007;220:199-213. cited by applicant
Wang, Chun-Yan, et al., αβ T-Cell Receptor Bias in Disease and Therapy (Review). International Journal of Oncology 48(6):2247-2256 (2016). cited by applicant
Wang et al.: Cloning genes encoding MHC class II-restricted antigens: mutated CDC27 as a tumor antigen. Science 284(5418):1351-1354 doi:10.1126/science.284.5418.1351 (1999). cited by applicant
Wang et al.: RNA interference targeting CML66, a novel tumor antigen, inhibits proliferation, invasion and metastasis of HeLa cells. Cancer Lett. 269(1):127-138 (2008). cited by applicant
Wang, H. et al., "Preparation and functional identification of a monoclonal antibody against the recombinant soluble human NKp30 receptor," Internal Immunopharmacology, 2011;11(11):1732-1739. cited by applicant
Warren, H.S. et al., "Evidence that the cellular ligand for the Human NK Cell Activation Receptor NKp30 is not a Heparan Sulfate Glycosaminoglycan," The Journal of Immunology, 2005;175(1):207-212. cited by applicant
Wei, Shan, et al., Identification of a Novel Human T-cell Receptor Vβ Subfamily by Genomic Cloning. Human Immunology 41(3):201-206 (1994). cited by applicant
Weidle, U. et al., "The Intriguing Options of Multispecific Antibody Formats for Treatment of Cancer", Cancer Genomics & Proteomics, 2013, vol. 1, pp. 1-18. cited by applicant
Weidle, U.H. et al., "Tumor-Antigen-Binding Bispecific Antibodies for Cancer Treatment", Seminars in Oncology, 2014, vol. 41, No. 5, pp. 653-660. cited by applicant
Williemsen, R A, et al., A Phage Display Selected Fab Fragment with MHC Class I-Restricted Specificity for MAGE-A1 allows for Retargeting of Primary Human T Lymphocytes. Gene Therapy 8(21):1601-1608 (2001). cited by applicant
Wood, Clive, et al., The Synthesis and in Vivo Assembly of Functional Antibodies in Yeast. Nature 314(6010):446-449 (1985). cited by applicant
Wu, M.R. et al., "B7H6-Specific Bispecific T Cell Engagers Lead to Tumor Elimination and Host Antitumor Immunity", The Journal of Immunology, 2015, vol. 194, No. 11, pp. 5305-5311. cited by applicant
Wurzer et al.: Nuclear Ras: unexpected subcellular distribution of oncogenic forms.J Cell Biochem Suppl. Suppl 36:1-11 doi:10.1002/jcb.1070 (2001). cited by applicant
Xiao, Y.F. et al., "Peptide-based treatment: A promising cancer therapy", Journal of Immunology Research, 2015, pp. 1-14. cited by applicant
Xiaoying, C. et al., "Fusion protein linkers: Property, design and functionality", Advanced Drug Delivery Reviews, 2012, vol. 65, No. 10, pp. 1357-1369. cited by applicant
Xu, Xiao-Jun, et al., Cytokine Release Syndrome in Cancer Immunotherapy with Chimeric Antigen Receptor Engineered T Cells. Cancer Letters 343(2):172-178 (2014). cited by applicant
Yamagata, Tatsuya, et al., Purification and Properties of Bacterial Chondroitinases and Chondrosulfatases. The Journal of Biological Chemistry 243(7):1523-1535 (1968). cited by applicant
Yassai, Maryam, et al., A Clonotype Nomenclature for T Cell Receptors. Immunogenetics 61(7):493-502 (2009). cited by applicant

Yoon et al.: Charged residues dominate a unique interlocking topography in the heterodimeric cytokine interleukin-12. The EMBO J. 19(14):3530-3541 (2000). cited by applicant
Yoon, S.T. et al., "Both high and low avidity antibodies to the T cell receptor can have agonist or antagonist activity," Immunity, 1994;1(7):563-569. cited by applicant
Zhang, T. et al., "Cancer Immunotherapy Using a Bispecific NK Receptor Fusion Protein that Engages both T Cells and Tumor Cells", Cancer Research, 2011, vol. 71, No. 6, pp. 2066-2076. cited by applicant
Agata, Yasutoshi et al. Expression of the PD-1 Antigen on the Surface of Stimulated Mouse T and B Lymphocytes. International Immunology 8(5):765-772 (1996). cited by applicant
Aggen, DH et al. Single-chain VaVB T-cell Receptors Function Without Mispairing With Endogenous TCR Chains. Gene Therapy 19(4):365-374 (2012). cited by applicant
Akers, Michael J. et al. Formulation Development of Protein Dosage Forms. Pharmaceutical Biotechnology 14:47-127 (2002). cited by applicant
Akers, Michael J., et al. Peptides and proteins as parenteral solutions. Pharmaceutical formulation development of peptides and proteins. London: Taylor & Francis. pp. 145-77.(2000). cited by applicant
Allison, A C. The Mode of Action of Immunological Adjuvants. Developments in Biological Standardization 92:3-11 (1998). cited by applicant
Almagro, Juan C, and Johan Fransson. Humanization of Antibodies. Frontiers in Bioscience 13:1619-1633 (2008). cited by applicant
Anderson, et al. Anti-CD3 + IL-2-stimulated murine killer cells. In vitro generation and in vivo antitumor activity. J Immunol 142 (4): 1383-1394 (1989). cited by applicant
Baca, Manuel et al. Antibody Humanization Using Monovalent Phage Display. The Journal of Biological Chemistry 272(16):10678-10684 (1997). cited by applicant
Batzer, Mark A. et al. Enhanced Evolutionary PCR Using Oligonucleotides With Inosine At The 3′-Terminus. Nucleic Acids Research 19(18):5081 (1991). cited by applicant
Baxter, et al. Acquired mutation of the tyrosine kinase JAK2 in human myeloproliferative disorders. The Lancet. 2005. 365(9464):1054-1061. cited by applicant
Benati, Daniela et al. Public T Cell Receptors Confer High-avidity CD4 Responses to HIV Controllers. Journal of Clinical Investigation 126(6):2093-2108 (2016). cited by applicant
Bendig. Humanization of rodent monoclonal antibodies by CDR grafting. Methods: A Companion to Methods in Enzymology 8:83-93 (1995). cited by applicant
Berge, Stephen M. et al. Pharmaceutical Salts. Journal of Pharmaceutical Sciences 66(1):1-19 (1977). cited by applicant
Biomunex Pharmaceuticals, "Disruptive biological approaches in immunotherapy, based on next generation BiXAb® bi-and multi-specific antibody platform for cancer treatment," Mar. 2023 [PowerPoint Slides]. cited by applicant
Blank, Christian et al. Interaction of PD-L1 on Tumor Cells with PD-1 on Tumor-Specific T cells as a Mechanism of Immune Evasion: Implications for Tumor Immunotherapy. Cancer Immunology, Immunotherapy 54(4):307-314 (2005). Published Online on Dec. 15, 2004. cited by applicant
Bloeman, PGM. et al. Adhesion Molecules: A New Target for Immunoliposome-mediated Drug Delivery. FEBS Letters 357:140-144 (1995). cited by applicant
Boerner, Paula et al. Production Of Antigen-Specific Human Monoclonal Antibodies From In Vitro-primed Human Splenocytes. Journal of Immunology 147(1):86-95 (1991). cited by applicant
Bonsignori et al. Maturation Pathway from Germline to Broad HIV-1 Neutralizer of a CD4-Mimic Antibody. Cell 165(2):449-463 (2016). cited by applicant
Borrebaeck, Carl A K. Antibody Engineering, Second Edition. Oxford University Press: 1-11 (1995). cited by applicant
Bovay, Amandine et al. T Cell Receptor Alpha Variable 12-2 Bias in the Immunodominant Response to Yellow Fever Virus. European Journal of Immunology 48(2):258-272 (2018). cited by applicant
Brennan, Maureen et al. Preparation of Bispecific Antibodies by Chemical Recombination of Monoclonal Immunoglobulin G1 Fragments. Science 229(4708):81-83 (1985). cited by applicant
Brennan, Rebekah M. et al. Predictable Alphabeta T-cell Receptor Selection Toward an HLA-B*3501-restricted Human Cytomegalovirus Epitope. Journal of Virology 81(13):7269-7273 (2007). cited by applicant
Brey, et al. A gB/CD3 bispecific BiTE antibody construct for targeting Human Cytomegalovirus-infected cells. Sci Rep 28;8(1):17453 (2018). 12 pages. cited by applicant
Briscoe, Page et al. Delivery of Superoxide Dismutase to Pulmonary Epithelium via pH-sensitive Liposomes. American Journal of Physiology 268(3 Pt 1):L374-L380 (1995). cited by applicant
Brodeur, Bernard R. et al. Monoclonal Antibody Production Techniques and Applications. New York: Marcel

Dekker:51-63 (1987). cited by applicant
Buckland, et al. Fusion glycoprotein of measles virus: nucleotide sequence of the gene and comparison with other paramyxoviruses. Journal of General Virology 68(6):1695-1703 (1987). cited by applicant
Bulek, Anna M. et al. Structural Basis of Human B-cell Killing by CD8+ T cells in Type 1 Diabetes. Nature Immunology 13(3):283-289 (2012). cited by applicant
Cadwell, Craig R, and Gerald F. Joyce. Randomization of Genes by PCR Mutagenesis. PCR Methods and Applications 2(1):28-33 (1992). cited by applicant
Caldas, Cristina et al. Humanization of the anti-CD18 antibody 6.7: an unexpected effect of a framework residue in binding to antigen. Molecular immunology 39(15):941-952 (2003). cited by applicant
Campbell, Peter J. The long-term outlook for essential thrombocythemia. Mayo Clin Proc 81(2):157-8 (2006). cited by applicant
Campbell, Peter J. The myeloproliferative disorders. N Engl J Med 355(23):2452-66 (2006). cited by applicant
Campisi, Laura et al. Clonally Expanded CD8 T Cells Characterize Amyotrophic Lateral Sclerosis-4. Nature 606(7916):945-952 (2022). cited by applicant
Carnero Contentti, Edgar, et al. Mucosal-Associated Invariant T Cell Features and TCR Repertoire Characteristics During the Course of Multiple Sclerosis. Frontiers in Immunology 10:1-17 (2019). cited by applicant
Carter, Laura L et al. PD-1: PD-L Inhibitory Pathway Affects both CD4(+) and CD8(+) T Cells and is Overcome by IL-2. European Journal of Immunology 32(3):634-643 (2002). cited by applicant
Carter, Paul et al. Humanization of an Anti-p185HER2 Antibody for Human Cancer Therapy. PNAS USA 89(10):4285-4289 (1992). cited by applicant
Cazzola, Mario, and Robert Kralovics. From Janus Kinase 2 to Calreticulin: The Clinically Relevant Genomic Landscape of Myeloproliferative Neoplasms. Blood 123(24):3714-3719 (2014). cited by applicant
Chancellor, A. et al., “CD1b-restricted Gem T cell responses are modulated by *Mycobacterium tuberculosis* mycolic acid meromycolate chains,” PNAS, 2017;114(51):E10956-E10964. cited by applicant
Chang, et al. Opportunities and challenges for TCR mimic antibodies in cancer therapy. Expert Opinion on Biological Therapy 16(8):979-987 (2016). cited by applicant
Chari, Ravi V.J. et al. Immunoconjugates Containing Novel Maytansinoids: Promising Anticancer Drugs. Cancer Research 52(1):127-131 (1992). cited by applicant
Charlton, Keith A. Expression and Isolation of Recombinant Antibody Fragments in *E. coli*. Chapter 14. Methods in Molecular Biology 248:245-254 (2003). cited by applicant
Chen, Lan et al. The T Cell Repertoires from Nickel Sensitized Joint Implant Failure Patients. International Journal of Molecular Sciences 22(5):2428, 1-13 (2021). cited by applicant
Chen, Yvonne et al. Selection and Analysis of an Optimized Anti-VEGF Antibody: Crystal Structure of an Affinity-matured Fab in Complex With Antigen. Journal of Molecular Biology 293(4):865-881 (1999). cited by applicant
Choi, Yangwon et al. A method for production of antibodies to human T-cell receptor beta-chain variable regions. Proc Natl Acad Sci USA 88(19):8357-8361 (1991). cited by applicant
Chowdhury, Partha S. Engineering Hot Spots for Affinity Enhancement of Antibodies. Methods in Molecular Biology 207:179-196 (2003). cited by applicant
ClinicalTrials.gov Identifier: NCT00001846. Collection and Distribution of Blood Components From Healthy Donors for In Vitro Research Use, Record created Nov. 3, 1999. pp. 1-10. [retrieved on Aug. 22, 2024] Available at URL: https://clinicaltrials.gov/study/NCT00001846. cited by applicant
ClinicalTrials.gov Identifier: NCT01004822. A Safety, Tolerability, And Pharmacokinetic Trial With CVX-241 In Patients With Advanced Solid Tumors, Record created Oct. 28, 2009. pp. 1-17. [retrieved on Jul. 12, 2024] Available at URL: https://clinicaltrials.gov/study/NCT01004822?cond=NCT01004822&rank=1. cited by applicant
ClinicalTrials.gov Identifier: NCT03427411. M7824 in Subjects With HPV Associated Malignancies, Record created Feb. 8, 2018. pp. 1-19. [retrieved on Aug. 22, 2024] Available at URL: https://clinicaltrials.gov/study/NCT03427411?term=NCT03427411&rank=1. cited by applicant
Clynes, Raphael et al. Fc Receptors Are Required in Passive and Active Immunity to Melanoma. Proceedings of the National Academy of Sciences of the United States of America 95(2):652-656 (1998). cited by applicant
Cole, David K. et al. Germ Line-governed Recognition of a Cancer Epitope by an Immunodominant Human T-cell Receptor. Journal of Biological Chemistry 284(40):27281-27289 (2009). cited by applicant
Connolly, James L. et al. Tumor Structure and Tumor Stroma Generation. 6th Edition. Holland-Frei Cancer Medicine :1-5 (2003). cited by applicant
Consonni, M. et al., “Human T cells engineered with a leukemia lipid-specific TCR enables donor-unrestricted recognition of CD1c-expressing leukemia,” Nat Commun., 2021; 12(1):4844. cited by applicant
Co-pending U.S. Appl. No. 18/286,062, inventors Andreas; Loew et al., filed Oct. 6, 2023. cited by applicant

Co-pending U.S. Appl. No. 18/431,634, inventors Seng-Lai; Tan et al., filed Feb. 2, 2024. cited by applicant
Co-pending U.S. Appl. No. 18/654,860, inventors Hayday; Adrian et al., filed May 3, 2024. cited by applicant
Co-pending U.S. Appl. No. 18/659,544, inventors Andreas; Loew et al., filed May 9, 2024. cited by applicant
Co-pending U.S. Appl. No. 18/749,969, inventors Hsu; Jonathan et al., filed Jun. 21, 2024. cited by applicant
Co-pending U.S. Appl. No. 18/779,692, inventor Andreas; Loew, filed Jul. 22, 2024. cited by applicant
Cragg, Mark S, and Martin J Glennie et al. Antibody Specificity Controls in Vivo Effector Mechanisms of anti-CD20 Reagents. Blood 103(7):2738-2743 (2004). cited by applicant
Cragg, Mark S. et al. Complement-mediated Lysis by Anti-CD20 mAb Correlates with Segregation into Lipid Rafts. Blood 101(3):1045-1052 (2003). cited by applicant
Crowther, Michael D. et al. Genome-wide CRISPR-Cas9 Screening Reveals Ubiquitous T Cell Cancer Targeting via the Monomorphic MHC Class I-related Protein MR1. Nature Immunology 21(2):178-185 (2020). cited by applicant
Cunningham, Brian C, and James A. Wells. High-resolution Epitope Mapping of hGH-receptor Interactions by Alanine-scanning Mutagenesis. Science 244(4908):1081-1085 (1989). cited by applicant
Dahal-Koirala, S. et al. TCR Sequencing of Single Cells Reactive to DQ2.5-glia-α2 and DQ2.5-glia-ω2 Reveals Clonal Expansion and Epitope-specific V-gene Usage. 9(3):587-596 (2016). cited by applicant
Dall'Acqua, William F. et al. Antibody Humanization by Framework Shuffling. Methods 36(1):43-60 (2005). cited by applicant
Deak, Laura Codarri, et al., PD-1-cis IL-2R Agonism Yields Better Effectors from Stem-like CD8+ T Cells. Nature 610(7930):161-172 (2022). cited by applicant
Delhommeau, François et al. Mutation in TET2 in Myeloid Cancers. N Engl J Med 360(22):2289-2301 (2009). cited by applicant
Dimasi, Nazzareno et al. The Design and Characterization of Oligospecific Antibodies for Simultaneous Targeting of Multiple Disease Mediators. Journal of Molecular Biology 393(3):672-692 (2009). cited by applicant
Diskin, Ron et al. Increasing the Potency and Breadth of an HIV Antibody by Using Structure-based Rational Design. Science 334(6060):1289-1293 (2011). cited by applicant
Dong, Haidong, and Lieping Chen. B7-H1 Pathway and its Role in the Evasion of Tumor Immunity. Journal of Molecular Medicine 81(5):281-287 (2003). cited by applicant
Draghi, et al. P530 Novel bispecific antibody targeting NKp30 receptor enhances NK-mediated killing activity against multiple myeloma cells and overcomes CD16A deficiency. Abstract. In Meeting Abstracts: 33rd Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (STIC 2018). 8 pages. cited by applicant
Du, Jiamu et al. Molecular basis of recognition of human osteopontin by 23C3, a potential therapeutic antibody for treatment of rheumatoid arthritis. Journal of molecular biology 382(4):835-842 (2008). cited by applicant
Dubowchik, Gene M. et al. Doxorubicin Immunoconjugates Containing Bivalent, Lysosomally-cleavable Dipeptide Linkages. Bioorganic & Medicinal Chemistry Letters 12(11):1529-1532 (2002). cited by applicant
Duncan, Alexander R, and Greg Winter. The Binding Site for C1q on IgG. Nature 332(6166):738-740 (1988). cited by applicant
Dupuis, Marc et al. Dendritic Cells Internalize Vaccine Adjuvant After Intramuscular Injection. Cell Immunology 186(1):18-27 (1998). cited by applicant
Edwards, Bryan M. et al. The Remarkable Flexibility of the Human Antibody Repertoire; Isolation of Over One Thousand Different Antibodies to a Single Protein, BLyS. Journal of Molecular Biology 334(1):103-118 (2003). cited by applicant
Ernst, et al. Inactivating mutations of the histone methyltransferase gene EZH2 in myeloid disorders. Nat Genet 42(8):722-6 (2010). cited by applicant
Fellouse, Frederic A. et al. Synthetic Antibodies From a Four-amino-acid Code: a Dominant Role for Tyrosine in Antigen Recognition. Proceedings of the National Academy of Sciences 24:101(34):12467-12472 (2004). cited by applicant
Fernandez-Sesma, Ana et al. A bispecific antibody recognizing influenza A virus M2 protein redirects effector cells to inhibit virus replication in vitro. Journal of virology 70(7):4800-4804 (1996). cited by applicant
Ferrari De Andrade, et al. Natural killer cells are essential for the ability of BRAF inhibitors to control BRAFV600E-mutant metastatic melanoma. Cancer research 74(24):7298-7308 (2014). cited by applicant
Fix, J A et al. Oral Controlled Release Technology for Peptides: Status and Future Prospects. Pharmaceutical research 13(12):1760-1764 (1996). cited by applicant
Flatman, Stephen et al. Process Analytics for Purification of Monoclonal Antibodies. Journal of Chromatography 848:79-87 (2007). Published Online on Dec. 11, 2006. cited by applicant
Fontana, Angelo et al. Probing the Partly Folded States of Proteins by Limited Proteolysis. Folding & Design 2(2):R17-R26 (1997). cited by applicant

Freeman, Gordon et al. Engagement of the PD-1 Immunoinhibitory Receptor by a Novel B7 Family Member Leads To Negative Regulation Of Lymphocyte Activation. Journal Of Experimental Medicine 192(7):1027-1034 (2000). cited by applicant
Frick, Rahel et al. A TRAV26-1-encoded Recognition Motif Focuses the Biased T Cell Response in Celiac Disease. European Journal of Immunology 50(1):142-145 (2020). cited by applicant
Gabrilovich, D I. et al. IL-12 And Mutant P53 Peptide-Pulsed Dendritic Cells For The Specific Immunotherapy Of Cancer. Journal of Immunotherapy with Emphasis on Tumor Immunology 19(6):414-418 (1996). cited by applicant
Gacerez, Albert T. et al. How Chimeric Antigen Receptor Design Affects Adoptive T Cell Therapy. Journal of cellular physiology 231(12):2590-2598 (2016). cited by applicant
Galvin, Teresa A. Effect of different promoters on immune responses elicited by HIV-1 gag/env multigenic DNA vaccine in Macaca mulatta and Macaca nemestrina. Vaccine 18(23):2566-2583 (2000). cited by applicant
Gamvrellis, Anita et al. Vaccines That Facilitate Antigen Entry Into Dendritic Cells. Immunology & Cell Biology 82(5):506-516 (2004). cited by applicant
Gazzano-Santoro, Helene et al. A Non-radioactive Complement-dependent Cytotoxicity Assay For Anti-cd20 Monoclonal Antibody. Journal Of Immunological Methods 202(2):163-171 (1996). cited by applicant
Gedda, Mallikarjuna R. et al. Longitudinal transcriptional analysis of peripheral blood leukocytes in COVID-19 convalescent donors. J Transl Med 20(1):587, 1-16 (2022). cited by applicant
GenBank Accession No. 2ERJ_D. Version 2ERJ_D. Chain D, Interleukin-2. Record created Mar. 21, 2006. 2 pages. Retrieved Jul. 15, 2024 at URL: https://www.ncbi.nlm.nih.gov/protein/90109213. cited by applicant
GenBank Accession No. AAA62478.2. Version No. AAA62478.2. induced by lymphocyte activation; similar to Human receptor protein encoded by GenBank Accession No. U03397 [*Homo sapiens*]. Record created Jun. 12, 1993. 2 Pages. Retrieved Aug. 1, 2024 at URL: https://www.ncbi.nlm.nih.gov/protein/AAA62478. cited by applicant
GenBank Accession No. AAH66254. Version No. AAH66254.1. Interleukin 2 [*Homo sapiens*]. Record created Feb. 12, 2004. 2 Pages. Retrieved Jul. 12, 2024 at URL: https://www.ncbi.nlm.nih.gov/protein/AAH66254. cited by applicant
GenBank Accession No. BAG36664. Version No. BAG36664.1. unnamed protein product [*Homo sapiens*]. Record created May 23, 2008. 2 Pages. Retrieved Aug. 1, 2024 at URL: https://www.ncbi.nlm.nih.gov/protein/BAG36664. cited by applicant
GenBank Accession No. NM_005191. Version No. NM_005191.4. *Homo sapiens* CD80 Molecule (CD80), mRNA. Record created May 24, 1999. Retrieved Aug. 2, 2024. Retrieved from: https://www.ncbi.nlm.nih.gov/nuccore/NM_005191. cited by applicant
GenBank Accession No. NP002174. Version No. NP_002174.1. interleukin-3 receptor subunit alpha isoform 1 precursor [*Homo sapiens*]. Record created Mar. 14, 2021. 3 Pages. Retrieved Aug. 1, 2024 at URL: https://www.ncbi.nlm.nih.gov/protein/NP_002174. cited by applicant
Gerngross, Tillman U. Advances In The Production Of Human Therapeutic Proteins In Yeasts and Filamentous Fungi. Nature Biotechnology 22(11):1409-1414 (2004). cited by applicant
Giaccone, Giuseppe. et al. A phase I study of the natural killer T-cell ligand alpha-galactosylceramide (KRN7000) in patients with solid tumors. Clinical cancer research 8(12):3702-3709 (2002). cited by applicant
Godfrey, Dale I. et al. The Burgeoning Family of Unconventional T Cells. Nature Immunology 16(11):1114-1123 (2015). cited by applicant
Graham, Frank L. et al. Characteristics of a Human Cell line Transformed by DNA from Human Adenovirus type 5. Journal of General Virology 36(1):59-72 (1977). cited by applicant
Gruber, Meegan et al. Efficient Tumor Cell Lysis Mediated By A Bispecific Single Chain Antibody Expressed In *Escherichia coli*. Journal Of Immunology 152(11):5368-5374 (1994). cited by applicant
Gussow et al., Chapter 5: Humanization of Monoclonal Antibodies. Methods in Enzymology. 203:99-121 (1991). cited by applicant
Hamers-Casterman, C. et al. Naturally Occurring Antibodies Devoid of Light Chains. Nature 363(6428):446-448 (1993). cited by applicant
Harutyunyan, et al. p53 lesions in leukemic transformation. N Engl J Med 364(5):488-90 (2011). cited by applicant
Harutyunyan, et al. Rare germline variants in regions of loss of heterozygosity may influence clinical course of hematological malignancies. Leukemia 25(11):1782-4 (2011). cited by applicant
Hashimoto, M, et al., PD-1 Combination Therapy with IL-2 Modifies CD8+ T Cell Exhaustion Program. Nature 610(7930):173-181 (2022). cited by applicant
He, X.Y. et al. TRAV gene expression in PBMCs and TILs in patients with breast cancer analyzed by a DNA melting curve (FQ-PCR) technique for TCR a chain CDR3 spectratyping. Neoplasma 59(6):693-699 (2012). cited by applicant
Helliwell, P S, and W J Taylor. Classification and Diagnostic Criteria for Psoriatic Arthritis. Annals of the Rheumatic

Diseases 64(Suppl 2):ii3-ii8 (2005). cited by applicant
Hinks, Timothy S. C. and Xia-Wei Zhang. MAIT Cell Activation and Functions. Frontiers in Immunology 11:1014, 1-10 (2020). cited by applicant
Hinman, Lois M. et al. Preparation And Characterization Of Monoclonal Antibody Conjugates Of The Calicheamicins: A Novel And Potent Family Of Antitumor Antibiotics. Cancer Research 53(14):3336-3342 (1993). cited by applicant
Holliger, Philipp et al. "Diabodies": Small Bivalent and Bispecific Antibody Fragments. Proceedings of the National Academy of Sciences of the United States of America 90(14):6444-6448 (1993). cited by applicant
Holmström, M O. et al. The calreticulin (CALR) exon 9 mutations are promising targets for cancer immune therapy. Leukemia 32(2):429-437 (2018). cited by applicant
Holmström, Morten Orebo, and Hans Carl Hasselbalch. Cancer immune therapy for myeloid malignancies: present and future. Seminars in Immunopathology 41(1):97-109 (2019). cited by applicant
Holmstrom, M O. et al. The CALR Exon 9 Mutations Are Shared Neoantigens in Patients With Calr Mutant Chronic Myeloproliferative Neoplasms. Leukemia 30(12):2413-2416 (2016). cited by applicant
Hong, Sung Noh et al. Reduced diversity of intestinal T-cell receptor repertoire in patients with Crohn's disease. Frontiers in Cellular and Infection Microbiology 12:1-12 (2022). cited by applicant
Hoogenboom, Hennie R, and Greg Winter. By-Passing Immunisation: Human Antibodies From Synthetic Repertoires Of Germline VH Gene Segments Rearranged In Vitro. Journal of Molecular Biology 227(2):381-388 (1992). cited by applicant
Hoogenboom, Hennie R. Overview Of Antibody Phage-display Technology And Its Applications. Methods In Molecular Biology 178:1-37 (2002). cited by applicant
Horna, Pedro et al. Utility of TRBC1 expression in the diagnosis of peripheral blood involvement by cutaneous T-cell lymphoma. Journal of Investigative Dermatology 141(4):821-829.e2 (2021). cited by applicant
Howson, Lauren J. et al. MAIT cell clonal expansion and TCR repertoire shaping in human volunteers challenged with Salmonella Paratyphi A. Nat Commun 9(1):253, 1-11 (2018). cited by applicant
Hsu, Jonathan et al. AT cell receptor β chain-directed antibody fusion molecule activates and expands subsets of T cells to promote antitumor activity. Science translational medicine 15(724):eadi0258, 1-18 (2023). cited by applicant
Hsu, Jonathan et al. Supplementary Materials for: A T Cell Receptor β Chain-directed Antibody Fusion Molecule Activates and Expands Subsets of T Cells to Promote Antitumor Activity. Science Translational Medicine 15(724):eadi0258, 1-39 (2023). cited by applicant
Huang, Huang et al. Select sequencing of clonally expanded CD8+ T cells reveals limits to clonal expansion. Proc Natl Acad Sci U S A 116(18):8995-9001 (2019). cited by applicant
Huda, Taha I. et al. Specific HLA Alleles, Paired With TCR V- and J-gene Segment Usage, Link to Distinct Multiple Myeloma Survival Rates. Leukemia & Lymphoma 62(7):1711-1720 (2021). cited by applicant
Hudson, Peter J, and Christelle Souriau. Engineered Antibodies. Nature Medicine 9(1):129-134 (2003). cited by applicant
Human NKp30/NCR3 Antibody. Catalog No. MAB1849. Clone 210845 was used by HLDA to establish CD designation. [Website] R&D Systems. Retrieved Jul. 27, 2024 at URL: https://www.rndsystems.com/products/human-nkp30-ncr3-antibody-210845_mab1849. 7 pages. cited by applicant
Human NKp30/NCR3 Antibody. Catalog No. MAB18491. Source: Monoclonal Mouse IgG2A Clone No. 210847. [Website] R&D Systems. Retrieved Nov. 23, 2023 at URL: https://www.rndsystems.com/products/human-nkp30-ncr3-antibody-210847_mab18491#productdetails. 6 pages. cited by applicant
Hussain, Khiyam et al. 1392 An Atypical Central Memory like Phenotype Can be Induced in Human T Cells by Innate TCRa Engagement. J. Immuno Ther. Cancer 10(suppl 2):A1447 (2022). cited by applicant
Idusogie, Eshoe E. et al. Mapping of the C1q Binding Site on Rituxan, A Chimeric Antibody with a Human IgG1 Fc. The Journal of Immunology 164(8):4178-4184 (2000). cited by applicant
Imai-Nishiya, Harue et al. Double Knockdown of Alpha1,6-fucosyltransferase (FUT8) And GDP-mannose 4,6-dehydratase (GMD) In Antibody-producing Cells: A New Strategy For Generating Fully Non-fucosylated Therapeutic Antibodies With Enhanced ADCC. BMC Biotechnology 7:84, 1-13 (2007). cited by applicant
Ipilimumab. CAS 477202-00-9. chemicalbook.com [Website] Retrieved Oct. 8, 2024 at: https://www.chemicalbook.com/CASEN_477202-00-9.htm. 3 pages. cited by applicant
James, et al. A JAK2 mutation in myeloproliferative disorders: pathogenesis and therapeutic and scientific prospects. Trends Mol Med 11(12):546-54 (2005). cited by applicant
James, et al. A unique clonal JAK2 mutation leading to constitutive signalling causes polycythaemia vera. Nature. 2005;434:1144-1148. cited by applicant
Jeffrey, Scott C. et al. Dipeptide-based Highly Potent Doxorubicin Antibody Conjugates. Bioorganic Medicinal

Chemistry Letters 16(2):358-362 (2006). cited by applicant
Johnsson, Bo. et al. Comparison Of Methods for Immobilization To Carboxymethyl Dextran Sensor Surfaces By Analysis Of The Specific Activity Of Monoclonal Antibodies. Journal of Molecular Recognition 8(1-2):125-131 (1995). cited by applicant
Johnsson, Bo. et al. Immobilization of Proteins To A Carboxymethyldextran-modified Gold Surface For Biospecific Interaction Analysis In Surface Plasmon Resonance Sensors. Analytical Biochemistry 198(2):268-277 (1991). cited by applicant
Jonsson, U. et al. Introducing a Biosensor Based Technology for Real-time Biospecific Interaction Analysis. Annals of Clinical Biology 51(1):19-26 (1993). cited by applicant
Jonsson, U. et al. Real-time Biospecific Interaction Analysis Using Surface Plasmon Resonance and a Sensor Chip Technology. BioTechniques 11(5):620-627 (1991). cited by applicant
Jung, S. et al. Prevention and therapy of experimental autoimmune neuritis by an antibody against T cell receptors-alpha/beta. Journal of immunology 148(12):3768-3775 (1992). cited by applicant
Kabat, Elvin A. et al. Sequences of Proteins of Immunological Interest. Fifth Edition, NIH Pub. No. 91-3242. Public Health Service, U.S. Department of Health and Human Services, National Institutes of Health: 647-669 (1991). cited by applicant
Kam, Nadine Wong Shi et al. Carbon Nanotubes as Multifunctional Biological Transporters and Near-infrared Agents for Selective Cancer Cell Destruction. Proceedings of the National Academy of Sciences of the United States of America 102(33):11600-11605 (2005). cited by applicant
Kanda, Yutaka et al. Comparison of Cell Lines for Stable Production of Fucose-negative Antibodies With Enhanced ADCC. Biotechnology and Bioengineering 94(4):680-688 (2006). cited by applicant
Karlin, S, and S F Altschul. Applications and Statistics for Multiple High-scoring Segments in Molecular Sequences. Proceedings of the National Academy of Sciences of the United States of America 90(12):5873-5877 (1993). cited by applicant
Kashmiri, Syed V S. et al. SDR Grafting—a New Approach to Antibody Humanization. Methods 36(1):25-34 (2005). cited by applicant
Kasmar, A.G. et al., "CD1b tetramers bind aβ T cell receptors to identify a mycobacterial glycolipid-reactive T cell repertoire in humans," J Exp Med., 2011;208(9):1741-1747. cited by applicant
Keinanen, A, and M L Laukkanen. Biosynthetic Lipid-tagging of Antibodies. FEBS letters 346(1):123-126 (1994). cited by applicant
Killion, J J, and I J Fidler. Systemic Targeting of Liposome-encapsulated Immunomodulators to Macrophages for Treatment of Cancer Metastasis. ImmunoMethods 4(3):273-279 (1994). cited by applicant
King, H Dalton et al. Monoclonal Antibody Conjugates of Doxorubicin Prepared With Branched Peptide Linkers: Inhibition of Aggregation by Methoxytriethyleneglycol Chains. Journal of Medicinal Chemistry 45(19):4336-4343 (2002). cited by applicant
Klampfl, Thorsten et al. Genome Integrity of Myeloproliferative Neoplasms in Chronic Phase and During Disease Progression. Blood 118(1): 167-176 (2011). cited by applicant
Klimka, A et al. Human Anti-CD30 Recombinant Antibodies by Guided Phage Antibody Selection Using Cell Panning. British Journal of Cancer 83(2):252-260 (2000). cited by applicant
Knappik, et al. Fully synthetic human combinatorial antibody libraries (HuCAL) based on modular consensus frameworks and CDRs randomized with trinucleotides. J Mol Biol. Feb. 11, 2000;296(1):57-86. cited by applicant
Konishi, Jun et al. B7-H1 Expression on Non-small Cell Lung Cancer Cells and Its Relationship With Tumor-infiltrating Lymphocytes and Their PD-1 Expression. Clinical Cancer Research 10(15):5094-5100 (2004). cited by applicant
Kostelny, S A. et al. Formation of a Bispecific Antibody by the Use of Leucine Zippers. Journal of Immunology 148(5):1547-1553 (1992). cited by applicant
Kozbor, D. et al. A Human Hybrid Myeloma for Production of Human Monoclonal Antibodies. Journal of Immunology 133(6):3001-3005 (1984). cited by applicant
Kralovics, et al. Altered gene expression in myeloproliferative disorders correlates with activation of signaling by the V617F mutation of Jak2. Blood 106(10):3374-6 (2005). cited by applicant
Kralovics, et al. Molecular pathogenesis of Philadelphia chromosome negative myeloproliferative disorders. Blood Rev 19(1):1-13 (2005). cited by applicant
Kralovics, Robert et al. A Gain-of-function Mutation of JAK2 in Myeloproliferative Disorders. The New England Journal of Medicine 352(17):1779-1790 (2005). cited by applicant
Kralovics, Robert. Genetic Complexity of Myeloproliferative Neoplasms. Leukemia 22(10):1841-1848 (2008). cited by applicant

Kratz, F. et al. Prodrugs of Anthracyclines in Cancer Chemotherapy. Current Medicinal Chemistry 13(5):477-523 (2006). cited by applicant
Kronenberg, M. et al., "A 'Gem' of a cell," Nat Immunol., 2013;14(7):694-695. cited by applicant
Kunik, Vered et al. Structural consensus among antibodies defines the antigen binding site. PLoS computational biology 8(2):e1002388, 1-12 (2012). cited by applicant
Latchman, Yvette et al. PD-L2 is a Second Ligand for PD-1 and Inhibits T Cell Activation. Nature Immunology 2(3):261-268 (2001). cited by applicant
Lee, Chingwei V. et al. Bivalent Antibody Phage Display Mimics Natural Immunoglobulin. Journal of Immunological Methods 284(1-2):119-132 (2004). cited by applicant
Lee, Chingwei V. et al. High-affinity Human Antibodies From Phage-displayed Synthetic Fab Libraries With a Single Framework Scaffold. Journal of Molecular Biology 340(5):1073-1093 (2004). cited by applicant
Lepore, Marco et al. Functionally Diverse Human T cells Recognize non-microbial Antigens Presented by MR1.Elife 6:e24476, 1-22 (2017). cited by applicant
Levine, et al. The JAK2V617F activating mutation occurs in chronic myelomonocytic leukemia and acute myeloid leukemia, but not in acute lymphoblastic leukemia or chronic lymphocytic leukemia. Blood 106(10):3377-9 (2005). cited by applicant
Levine, Ross L. et al. Activating Mutation in the Tyrosine Kinase JAK2 in Polycythemia Vera, Essential Thrombocythemia, and Myeloid Metaplasia With Myelofibrosis. Cancer Cell 7(4):387-397 (2005). cited by applicant
Li, Huijuan et al. Optimization of Humanized IgGs in Glycoengineered Pichia Pastoris. Nature Biotechnology 24(2):210-215 (2006). cited by applicant
Li, Jian. et al. Human Antibodies for Immunotherapy Development Generated via a Human B Cell Hybridoma Technology. Proceedings of the National Academy of Sciences of the United States of America 103(10):3557-3562 (2006). cited by applicant
Li, Yangqiu et al. Restricted TRBV repertoire in CD4+ and CD8+ T-cell subsets from CML patients. Hematology 16(1):43-49 (2011). cited by applicant
Lifely, M R. et al. Glycosylation and biological activity of CAMPATH-1H Expressed in different Cell lines and Grown under different Culture Conditions. Glycobiology 5(8):813-822 (1995). cited by applicant
Lode, Holger N. et al. Targeted Therapy With a Novel Enediyene Antibiotic Calicheamicin Theta(I)1 Effectively Suppresses Growth and Dissemination of Liver Metastases in a Syngeneic Model of Murine Neuroblastoma. Cancer Research 58(14):2925-2928 (1998). cited by applicant
Lonberg, Nils. Fully Human Antibodies From Transgenic Mouse and Phage Display Platforms. Current Opinion in Immunology 20(4):450-459 (2008). cited by applicant
Lonberg, Nils. Human Antibodies From Transgenic Animals. Nature Biotechnology 23(9):1117-1125 (2005). cited by applicant
Lopez, K. et al., "CD1b Tetramers Broadly Detect T Cells That Correlate With Mycobacterial Exposure but Not Tuberculosis Disease State," Front Immunol., 2020; 11:199. cited by applicant
Lossius, Andreas. et al. High-throughput Sequencing of TCR Repertoires in Multiple Sclerosis Reveals Intrathecal Enrichment of EBV-reactive CD8+ T Cells. European Of Journal Immunnology 44(11):3439-3452 (2014). cited by applicant
Lu, Chenyang et al. Clinical Significance of T Cell Receptor Repertoire in Primary Sjogren's Syndrome. EBioMedicine 84:104252, 1-12 (2022). cited by applicant
Maciocia, Paul M. et al. Supplemental Figures: Targeting the T cell receptor β-chain constant region for immunotherapy of T cell malignancies. Nature Medicine 23(12):1416-1423 (2017). Retrieved Oct. 8, 2024 at URL: https://static-content.springer.com/esm/art%3A10.1038%2Fnm.4444/MediaObjects/41591_2017_BFnm4444_MOESM1_ESM.pdf 6 pages. cited by applicant
Maeda, T. et al. Amelioration of acute graft-versus-host disease and re-establishment of tolerance by short-term treatment with an anti-TCR antibody. Journal of immunology 153(9):4311-4320 (1994). cited by applicant
Marks, James D, and Andrew Bradbury. Selection of Human Antibodies From Phage Display Libraries. Methods in Molecular Biology 48:161-176 (2004). cited by applicant
Marks, James D. et al. By-passing Immunization Human Antibodies from V-gene Libraries Displayed on Phage. Journal of Molecular Biology 222(3):581-597 (1991). cited by applicant
Martin, Andrew C. et al., Chapter 3: Protein Sequence and Structure Analysis of Antibody Variable Domains. In: Antibody Engineering Lab Manual (Ed: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg) 2:33-51 (2010) cited by applicant
Martin, Andrew CR. Protein Sequence and Structure Analysis of Antibody Variable Domains. Antibody

Engineering:422-439 (2001). cited by applicant
Matsumoto, Y. et al. Successful prevention and treatment of autoimmune encephalomyelitis by short-term administration of anti-T-cell receptor alpha beta antibody. Immunology 81(1):1-7 (1994). cited by applicant
Mayer, Gene et al. Chapter 10: Major Histocompatibility Complex (MHC) And T-Cell Receptors—Role In Immune Responses. In: Microbiology and Immunology on-line, University of South Carolina School of Medicine: 1-6 (2010). cited by applicant
McCafferty, J. et al. Phage Antibodies: Filamentous Phage Displaying Antibody Variable Domains. Nature 348(6301):552-554 (1990). cited by applicant
McGoff, Paul, and David S. Scher. Solution Formulation of Proteins/Peptides:In McNally EJ., ed, Protein Formulation and Delivery:139-158 (2000). cited by applicant
McLellan, Jason S. et al. Structure of HIV-1 gp120 V1/V2 Domain with Broadly Neutralizing Antibody PG9. Nature 480(7377):336-343 (2011). cited by applicant
Meermeier, Erin W. et al. Human TRAV1-2-negative MR1-restricted T cells detect S. pyogenes and alternatives to MAIT riboflavin-based antigens. Nat Commun 7:12506, 1-12 (2016). cited by applicant
Meeting Abstracts. 33rd Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (SITC 2018). Journal for Immunotherapy of Cancer 6(Suppl 1):207-398 (2018). cited by applicant
Meilleur, Courtney et al. Bacterial Superantigens Expand and Activate, Rather than Delete or Incapacitate, Preexisting Antigen-Specific Memory CD8+ T Cells. J Infect Dis 219(8):1307-1317 (2019). Published online Nov. 12, 2018. cited by applicant
Milosevic, Jelena D, and Robert Kralovics. Genetic and Epigenetic Alterations of Myeloproliferative Disorders. International Journal of Hematology 97(2):183-197 (2013). Published Online Dec. 12, 2012. cited by applicant
Milstein, C, and A C Cuello. Hybrid Hybridomas and Their Use in Immunohistochemistry. Nature 305(5934):537-540 (1983). cited by applicant
Moore, et al. Abstract C180: A novel bispecific platform for potent redirected killing of B-cell lymphoma. Mol Cancer Ther 8 (12_Supplement): C180 (2009). cited by applicant
Mosca, Paul J. et al. Dendritic cell vaccines. Frontiers in Bioscience 12:4050-4060 (2007). cited by applicant
Motozono, Chihiro et al. Molecular Basis of a Dominant T Cell Response to an HIV Reverse Transcriptase 8-mer Epitope Presented by the Protective Allele HLA-B*51:01. Journal of Immunology 192(7):3428-3434 (2014). cited by applicant
Myers, et al. Optimal alignments in linear space. CABIOS 4(1):11-17 (1988). cited by applicant
Nagy, Attila et al. Stability of Cytotoxic Luteinizing Hormone-releasing Hormone Conjugate (AN-152) Containing Doxorubicin 14-O-Hemiglutarate in Mouse and Human Serum in vitro: Implications for the Design of Preclinical Studies. Proc Natl Acad Sci U S A 97(2):829-834 (2000). cited by applicant
Nair et al., Epitope Recognition by Diverse Antibodies Suggests Conformational Convergence in an Antibody Response. The Journal of Immunology, 168:2371-2382 (2002). cited by applicant
Natsume, Akito et al. Engineered Antibodies of IgG1/IgG3 Mixed Isotype with Enhanced Cytotoxic Activities. Cancer Research 68(10):3863-3872 (2008). cited by applicant
Ni, Jian. Research Progress and Prospects of Antibodymoics and Antibody-Based Drugs, Modern Immunology 26(4):265-268 (2006). Abstract Only. One page. cited by applicant
No Author, “33rd Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (SITC 2018)”, Journal for Immuno Therapy of Cancer, 2018, vol. 6(1), No. 115, pp. 1-192. cited by applicant
Nomoto, K. et al. Tolerance induction in a fully allogeneic combination using anti-T cell receptor-alpha beta monoclonal antibody, low dose irradiation, and donor bone marrow transfusion. Transplantation 59(3):395-401 (1995). cited by applicant
Ohtsuka, Eiko et al. An Alternative Approach to Deoxyoligonucleotides as Hybridization Probes by Insertion of Deoxyinosine at Ambiguous Codon Positions. Journal of Biological Chemistry 260(5):2605-2608 (1985). cited by applicant
Okazaki, Akira et al. Fucose Depletion From Human IgG1 Oligosaccharide Enhances Binding Enthalpy and Association Rate Between IgG1 and FcgammaRIIIa. Journal of Molecular Biology 336(5):1239-1249 (2004). cited by applicant
Osbourn, Jane et al. From Rodent Reagents to Human Therapeutics Using Antibody Guided Selection. Methods 36(1):61-68 (2005). cited by applicant
Owais, Mohammad et al. Chloroquine Encapsulated in Malaria-infected Erythrocyte-specific Antibody-bearing Liposomes Effectively Controls Chloroquine-resistant Plasmodium Berghei Infections in Mice. Antimicrobial Agents and Chemotherapy 39(1):180-184 (1995). cited by applicant
Padlan, Eduardo A. A Possible Procedure for Reducing the Immunogenicity of Antibody Variable Domains While

Preserving Their Ligand-binding Properties. Molecular Immunology 28(4-5):489-498 (1991). cited by applicant
Panka et al. Variable region framework differences result in decreased or increased affinity of variant anti-digoxin antibodies. PNAS USA 85:3080-3084 (1988). cited by applicant
Pardanani, Animesh D. et al. MPL515 Mutations in Myeloproliferative and Other Myeloid Disorders: a Study of 1182 Patients. Blood 108(10):3472-3476 (2006). cited by applicant
Pardanani, et al. Discordant distribution of JAK2V617F mutation in siblings with familial myeloproliferative disorders. Blood 107(11):4572-3 (2006). cited by applicant
Paul: Fundamental Immunology. 3rd Edition. 292-295 (1993). cited by applicant
PCT/US2020/019329 International Search Report and Written Opinion dated Jun. 26, 2020. cited by applicant
PCT/US2020/060557 International Search Report and Written Opinion dated Mar. 30, 2021. cited by applicant
PCT/US2021/047574 International Search Report and Written Opinion dated Feb. 17, 2022. cited by applicant
PCT/US2021/047773 International Search Report and Written Opinion dated Dec. 23, 2021. cited by applicant
PCT/US2022/023922 International Search Report and Written Opinion dated Oct. 6, 2022. cited by applicant
PCT/US2022/049039 International Search Report and Written Opinion dated May 10, 2023. cited by applicant
PCT/US2022/053705 International Search Report and Written Opinion dated Jul. 7, 2023. cited by applicant
PCT/US2023/011280 International Search Report and Written Opinion dated Jun. 28, 2023. cited by applicant
PCT/US2023/034966 International Search Report and Written Opinion dated Mar. 29, 2024. cited by applicant
PCT/US2023/035056 International Search Report and Written Opinion dated Mar. 5, 2024. cited by applicant
PCT/US2024/026686 International Search Report and Written Opinion dated Sep. 23, 2024. cited by applicant
Pearson, William R, and David J Lipman. Improved Tools For Biological Sequence Comparison. PNAS USA 85(8):2444-2448 (1988). cited by applicant
Pejchal, Robert et al. A Potent and Broad Neutralizing Antibody Recognizes and Penetrates the HIV Glycan Shield. Science 334(6059):1097-1103 (2011). cited by applicant
Petersen, Jan. et al. Diverse T Cell Receptor Gene Usage in HLA-DQ8-associated Celiac Disease Converges Into a Consensus Binding Solution. Structure 24(10):1643-1657 (2016). cited by applicant
Petkova, Stefka B. et al. Enhanced Half-life of Genetically Engineered Human IgG1 Antibodies in a Humanized FcRn Mouse Model: Potential Application in Humorally Mediated Autoimmune Disease. International Immunology 18(12):1759-1769 (2006). cited by applicant
Pikman, et al. MPLW515L Is a Novel Somatic Activating Mutation in Myelofibrosis with Myeloid Metaplasia. PLoS Med. 2006;3(7):e270. cited by applicant
Pluckthun, A. Chapter 11: Antibodies From *Escherichia coli*. The Pharmacology of Monoclonal Antibodies 113:269-315 (1994). cited by applicant
Porritt, Rebecca A. et al. HLA Class I-associated Expansion of TRBV11-2 T Cells in Multisystem Inflammatory Syndrome in Children. The Journal of Clinical Investigation 131(10):e146614, 1-13 (2021). cited by applicant
Presta, Leonard G. et al. Humanization of an Antibody Directed Against IgE. Journal of Immunology 151(5): 2623-2632 (1993). cited by applicant
Presta, Leonard G. et al. Humanization of an Anti-vascular Endothelial Growth Factor Monoclonal Antibody for the Therapy of Solid Tumors and Other Disorders. Cancer Research 57(20):4593-4599 (1997). cited by applicant
Queen, Cary et al. A Humanized Antibody That Binds to the Interleukin 2 Receptor. Proceedings of the National Academy of Sciences 86(24):10029-10033 (1989). cited by applicant
Ranade, Vasant V. Drug Delivery Systems. 1. Site-specific Drug Delivery Using Liposomes as Carriers. Journal of Clinical Pharmacology 29(8):685-694 (1989). cited by applicant
Reinink, P. et al., “A Tcr β-Chain Motif Biases toward Recognition of Human CD1 Proteins,” J Immunol., 2019;203(12):3395-3406. cited by applicant
Ripka, James et al. Two Chinese Hamster Ovary Glycosylation Mutants Affected in the Conversion of GDP-mannose to GDP-fucose. Archives of Biochemistry and Biophysics 249(2):533-545 (1986). cited by applicant
Rosok, Mae Joanne et al. A Combinatorial Library Strategy for the Rapid Humanization of Anticarcinoma BR96 Fab. The Journal of Biological Chemistry 271(37):22611-22618 (1996). cited by applicant
Rossolini, Gian Maria et al. Use of Deoxyinosine-containing Primers vs Degenerate Primers for Polymerase Chain Reaction Based on Ambiguous Sequence Information. Molecular and Cellular Probes 8(2):91-98 (1994). cited by applicant
Rowntree, Louise C. et al. A Shared TCR Bias Toward an Immunogenic EBV Epitope Dominates in HLA-B*07:02-Expressing Individuals. Journal of Immunology 205(6):1524-1534 (2020). cited by applicant
Samanen, James. et al. Chemical Approaches to Improve the Oral Bioavailability of Peptidergic Molecules. Journal of Pharmacy and Pharmacology 48(2):119-135 (1996). cited by applicant
Sanchez-Ruiz, Jose M. et al. Differential Scanning Calorimetry of the Irreversible Thermal Denaturation of

Thermolysin. Biochemistry 27(5):1648-1652 (1988). cited by applicant
Schachter, Harry. et al. Biosynthetic Controls that Determine the Branching and Microheterogeneity of Protein-bound Oligosaccharides. Biochemistry and Cell Biology 64(3):163-181 (1986). cited by applicant
Scheid, Johannes F. et al. Sequence and Structural Convergence of Broad and Potent HIV Antibodies that Mimic CD4 Binding. Science 333(6049):1633-1637 (2011). cited by applicant
Scheuermann, R.H. and Racila, E. CD19 Antigen in Leukemia and Lymphoma Diagnosis and Immunotherapy. Leukemia & Lymphoma 18(5-6):385-397 (1995). cited by applicant
Schreier, Hans et al. Targeting of Liposomes to Cells Expressing CD4 Using Glycosylphosphatidylinositol-anchored gp120. Influence of Liposome Composition on Intracellular Trafficking. The Journal of Biological Chemistry 269(12):9090-9098 (1994). cited by applicant
Scott, et al. JAK2 exon 12 mutations in polycythemia vera and idiopathic erythrocytosis. N Engl J Med 356(5):459-68 (2007). cited by applicant
Shields, Robert L. et al. High Resolution Mapping of the Binding Site on Human IgG1 for Fc Gamma RI, Fc Gamma RII, Fc Gamma RIII, and FcRn and design of IgG1 Variants with Improved Binding to the Fc Gamma R. Journal of Biological Chemistry 276(9):6591-6604 (2001). cited by applicant
Sidhu, Sachdev S. et al. Phage-displayed Antibody Libraries of Synthetic Heavy Chain Complementarity Determining Regions. Journal of Molecular Biology 338(2):299-310 (2004). cited by applicant
Sim, Gek Kee et al. Primary Structure Of Human T-Cell Receptor Alpha-chain. Nature 312(5996):771-775 (1984). cited by applicant
Sims, Martin J. et al. A Humanized CD18 Antibody Can Block Function Without Cell Destruction. Journal of Immunology 151(4):2296-2308 (1993). cited by applicant
Smith, et al. T cell inactivation and cytokine deviation promoted by anti-CD3 mAbs. Curr Opin Immunol 9(5):648-54 (1997). cited by applicant
Smith, Temple F, and Waterman Michael S. Comparison of Biosequences. Advances in applied mathematics 2(4):482-489 (1981). cited by applicant
Song, De-Gang et al. CD27 Costimulation Augments the Survival and Antitumor Activity of Redirected Human T cells in vivo. Blood 119(3):696-706 (2012). cited by applicant
Srivastava, Shivani, and Stanley R Riddell. Engineering CAR-T cells: Design concepts. Trends in immunology 36(8):494-502 (2015). cited by applicant
Staerz, Uwe D, and Michael J. Bevan. Activation of resting T lymphocytes by a monoclonal antibody directed against an allotypic determinant on the T cell receptor. Eur. J. Immunol 16:263-270 (1986). cited by applicant
Stegelmann, F. et al. DNMT3a Mutations in Myeloproliferative Neoplasms. Leukemia 25(7):1217-1219 (2011). cited by applicant
Stein, et al. Disruption of the ASXL1 gene is frequent in primary, post-essential thrombocytosis and post-polycythemia vera myelofibrosis, but not essential thrombocytosis or polycythemia vera: analysis of molecular genetics and clinical phenotypes. Haematologica 96(10):1462-9 (2011). cited by applicant
Stein, et al. Natural Killer (NK)- and T-Cell Engaging Antibody-Derived Therapeutics. Antibodies 1(1):88-123 (2012) cited by applicant
Stein, Sokrates et al. Protective Roles of SIRT1 in Atherosclerosis. Cell Cycle 10(4):640-647 (2011). cited by applicant
Streltsov, Victor A. et al. Structure of a Shark IgNAR Antibody Variable Domain and Modeling of an Early-developmental Isotype. Protein Science 14(11):2901-2909 (2005). cited by applicant
Surman, Sherri L. et al. Clonally Related CD8+ T Cells Responsible for Rapid Population of Both Diffuse Nasal-associated Lymphoid Tissue and Lung After Respiratory Virus Infection. Journal of Immunology 187(2):835-841 (2011). cited by applicant
Suzuki-Inoue, et al. Involvement of the Snake Toxin Receptor CLEC-2, in Podoplanin-mediated Platelet Activation, by Cancer Cells. The Journal of Biological Chemistry, 282(36):25993-26001 (2007). cited by applicant
Szeto, Christopher et al. Molecular Basis of a Dominant SARS-CoV-2 Spike-Derived Epitope Presented by HLA-A*02:01 Recognised by a Public TCR. Cells 10(10):2646, 1-15 (2021). cited by applicant
Tan, Huo et al. Clonal expanded TRA and TRB subfamily T cells in peripheral blood from patients with diffuse large B-cell lymphoma. Hematology 15(2):81-87 (2010). cited by applicant
Tang, Yong. et al. Regulation of Antibody-dependent Cellular Cytotoxicity by lgG Intrinsic and Apparent Affinity for Target Antigen. Journal of Immunology 179(5):2815-2823 (2007). cited by applicant
Tastan, Cihan et al. Tuning of human MAIT cell activation by commensal bacteria species and MR1-dependent T-cell presentation. Mucosal Immunol 11(6):1591-1605 (2018). cited by applicant
Torgov, Michael Y. et al. Generation of an Intensely Potent Anthracycline by a Monoclonal Antibody-beta-

galactosidase Conjugate. Bioconjugate Chemistry 16(3):717-721 (2005). cited by applicant
Traunecker, André et al. Bispecific Single Chain Molecules (Janusins) Target Cytotoxic Lymphocytes on HIV Infected Cells. The EMBO Journal 10(12):3655-3659 (1991). cited by applicant
Tutt, Alison et al. Trispecific F(ab')3 Derivatives that Use Cooperative Signaling via the TCR/CD3 Complex and CD2 to Activate and Redirect Resting Cytotoxic T cells. Journal of Immunology 147(1):60-69 (1991). cited by applicant
Umezawa, F, and Y Eto. Liposome Targeting to Mouse Brain: Mannose as a Recognition Marker. Biochemical and Biophysical Research Communications 153(3):1038-1044 (1988). cited by applicant
UniProt reference No. P04626. Receptor Tyrosine-Protein Kinase erbB-2. Record created Nov. 1, 1988. pp. 1-19. Retrieved Sep. 27, 2024 at URL: https://www.uniprot.org/uniprotkb/P04626/entry. cited by applicant
UniProt reference No. Q9HBE4. Interleukin-21. Record created Mar. 1, 2001. pp. 1-9. Retrieved Sep. 27, 2024 at URL: https://www.uniprot.org/uniprotkb/Q9HBE4/entry. cited by applicant
UniProtKB Accession No. A0A075B6N4. T cell receptor beta variable 25-1. Record created Oct. 1, 2014. pp. 1-9. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/A0A075B6N4/entry. cited by applicant
UniProtKB Accession No. A0A0B4J240. T cell receptor alpha variable 10. Record created Mar. 11, 2015. pp. 1-9. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/A0A0B4J240/entry. cited by applicant
UniProtKB Accession No. A0A1G7UTW6_9SPHI. Uncharacterized protein Pedobacter terrae (Nov. 22, 2017). Retrieved Jul. 16, 2024 at URL: https://rest.uniprot.org/unisave/A0A1G7UTW6?format=txt&versions=1. One page. cited by applicant
UniProtKB Accession No. A0A2V7GPM2_9BACT. Uncharacterized protein Gemmatimonadetes bacterium (Sep. 12, 2018). Retrieved Jul. 16, 2024 at URL: https://rest.uniprot.org/unisave/A0A2V7GPM2?format=txt&versions=1. One page. cited by applicant
UniProtKB Accession No. 000220. Tumor necrosis factor receptor superfamily member 10A. Record created Jul. 1, 1997. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/O00220/entry pp. 1-9. cited by applicant
UniProtKB Accession No. 014763. Tumor necrosis factor receptor superfamily member 10B. Record created Jan. 1, 1998. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/014763/entry pp. 1-10. cited by applicant
UniProtKB Accession No. 095760. Interleukin-33. Record created May 1, 1999. pp. 1-10. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/O95760/entry. cited by applicant
UniProtKB Accession No. 095866. Megakaryocyte and platelet inhibitory receptor G6b. Record created May 1, 1999. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/O95866/entry pp. 1-11. cited by applicant
UniProtKB Accession No. P01137. Transforming growth factor beta-1 proprotein. Record created Nov. 1, 1988. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P01137/entry pp. 1-17. cited by applicant
UniProtKB Accession No. P01562. Interferon alpha-1/13. Record created Nov. 1, 1988. pp. 1-10. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01562/entry. cited by applicant
UniProtKB Accession No. P01563. Interferon alpha-2. Record created Nov. 1, 1988. pp. 1-12. Retrieved Oct. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01563/entry. cited by applicant
UniProtKB Accession No. P01566. Interferon alpha-10. Record created Nov. 1, 1988. pp. 1-10. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01566/entry. cited by applicant
UniProtKB Accession No. P01567. Interferon alpha-7. Record created Nov. 1, 1988. pp. 1-7. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01567/entry. cited by applicant
UniProtKB Accession No. P01568. IFN21_HUMAN. Record created Nov. 1, 1988. pp. 1-7. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01568/entry. cited by applicant
UniProtKB Accession No. P01569. Interferon alpha-5. Record created Nov. 1, 1988. pp. 1-10. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01569/entry. cited by applicant
UniProtKB Accession No. P01570. IFN14_HUMAN. Record created Nov. 1, 1988. pp. 1-7. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01570/entry. cited by applicant
UniProtKB Accession No. P01574. Interferon beta. Record created Nov. 1, 1988. pp. 1-9. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P01574/entry. cited by applicant
UniProtKB Accession No. P05013. Interferon alpha-6. Record created Nov. 1, 1988. pp. 1-11. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P05013/entry. cited by applicant
UniProtKB Accession No. P05014. Interferon alpha-4. Record created Nov. 1, 1988. pp. 1-11. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P05014/entry. cited by applicant
UniProtKB Accession No. P05106. Integrin beta-3. Record created Nov. 1, 1988. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P05106/entry pp. 1-20. cited by applicant
UniProtKB Accession No. P05107. Integrin beta-2. Record created Nov. 1, 1988. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P05107/entry pp. 1-15. cited by applicant
UniProtKB Accession No. P07359. Platelet glycoprotein Ib alpha chain. Record created Nov. 1, 1988. Retrieved Aug.

16, 2024 at URL: https://www.uniprot.org/uniprotkb/P07359/entry pp. 1-15. cited by applicant
UniProtKB Accession No. P08514. Integrin alpha-IIb. Record created Nov. 1, 1988. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P08514/entry pp. 1-15. cited by applicant
UniProtKB Accession No. P0DOX5. Immunoglobulin gamma-1 heavy chain. Record created Mar. 15, 2017. Retrieved Nov. 6, 2024 at URL: https://www.uniprot.org/uniprotkb/P0DOX5/entry pp. 1-4. cited by applicant
UniProtKB Accession No. P10600. Transforming growth factor beta-3 proprotein. Record created Jul. 1, 1989. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P10600/entry pp. 1-11. cited by applicant
UniProtKB Accession No. P10721. Mast/stem cell growth factor receptor Kit. Record created Jul. 1, 1989. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P10721/entry pp. 1-20. cited by applicant
UniProtKB Accession No. P12318. Low affinity immunoglobulin gamma Fc region receptor II-a. Record created Oct. 1, 1989. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P12318/entry pp. 1-9. cited by applicant
UniProtKB Accession No. P16109. P-selectin. Record created Apr. 1, 1990. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P16109/entry pp. 1-12. cited by applicant
UniProtKB Accession No. P28906. Hematopoietic progenitor cell antigen CD34. Record created Dec. 1, 1992. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P28906/entry pp. 1-10. cited by applicant
UniProtKB Accession No. P29459. Interleukin-12 subunit alpha. Record created Apr. 1, 1993. pp. 1-13. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P29459/entry. cited by applicant
UniProtKB Accession No. P29460. Interleukin-12 subunit beta. Record created Apr. 1, 1993. pp. 1-10. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P29460/entry. cited by applicant
UniProtKB Accession No. P30408. Transmembrane 4 L6 family member 1. Record created Apr. 1, 1993. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P30408/entry pp. 1-7. cited by applicant
UniProtKB Accession No. P32881. Interferon alpha-8. Record created Oct. 1, 1993. pp. 1-7. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P32881/entry. cited by applicant
UniProtKB Accession No. P36888. Receptor-type tyrosine-protein kinase FLT3. Record created Jun. 1, 1994. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P36888/entry pp. 1-13. cited by applicant
UniProtKB Accession No. P36897. TGF-beta receptor type-1. Record created Jun. 1, 1994. Retrieved Aug. 16, 2024 a URL: https://www.uniprot.org/uniprotkb/P36897/entry pp. 1-16. cited by applicant
UniProtKB Accession No. P37173. TGF-beta receptor type-2. Record created Oct. 1, 1994. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P37173/entry pp. 1-18. cited by applicant
UniProtKB Accession No. P40238. Thrombopoietin receptor. Record created Feb. 1, 1995. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P40238/entry pp. 1-11. cited by applicant
UniProtKB Accession No. P40933. Interleukin-15. Record created Feb. 1, 1995. pp. 1-9. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/P40933/entry. cited by applicant
UniProtKB Accession No. P56856. Cld_Human. 14 pages. Retrieved Oct. 7, 2024 at URL: https://www.uniprot.org/uniprotkb/P56856/entry. cited by applicant
UniProtKB Accession No. P60568. Interleukin-2. Record created Mar. 15, 2004. pp. 1-12. Retrieved Jul. 12, 2024 at URL: https://www.uniprot.org/uniprotkb/P60568/entry. cited by applicant
UniProtKB Accession No. P61812. Transforming growth factor beta-2 proprotein. Record created Jun. 7, 2004. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/P61812/entry pp. 1-12. cited by applicant
UniProtKB Accession No. Q02487. Desmocollin-2. Record created Feb. 1, 1994. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/Q02487/entry pp. 1-15. cited by applicant
UniProtKB Accession No. Q03167. Transforming growth factor beta receptor type 3. Record created Feb. 1, 1994. Retrieved Aug. 16, 2024 at URL: https://www.uniprot.org/uniprotkb/Q03167/entry pp. 1-10. cited by applicant
UniProtKB Accession No. Q14116. Interleukin-18. Record created Nov. 1, 1996. pp. 1-10. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/Q14116/entry. cited by applicant
UniProtKB Accession No. Q9H293. Interleukin-25. Record created Mar. 1, 2001. pp. 1-11. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/Q9H293/entry. cited by applicant
UniProtKB Accession No. Q9NPF7. Interleukin-23 subunit alpha. Record created Oct. 1, 2000. pp. 1-13. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/Q9NPF7/entry. cited by applicant
UniProtKB Accession No. Q9NYJ7. Delta-like protein 3. Record created Oct. 1, 2000. pp. 1-9. Retrieved Oct. 10, 2024 at URL: https://www.uniprot.org/uniprotkb/Q9NYJ7/entry. cited by applicant
Urakami, Akane et al. An Envelope-Modified Tetravalent Dengue Virus-Like-Particle Vaccine Has Implications for Flavivirus Vaccine Design. Journal of virology 91(23):e00090-17, 1-16 (2017). cited by applicant
U.S. Appl. No. 15/465,564 Notice of Allowance dated Nov. 10, 2021. cited by applicant
U.S. Appl. No. 15/465,564 Notice of Allowance dated Oct. 29, 2021. cited by applicant
U.S. Appl. No. 15/465,564 Office Action dated Apr. 29, 2020. cited by applicant

U.S. Appl. No. 15/465,564 Office Action dated May 26, 2021. cited by applicant
U.S. Appl. No. 15/465,564 Office Action dated Oct. 13, 2020. cited by applicant
U.S. Appl. No. 15/465,564 Office Action dated Sep. 9, 2019. cited by applicant
U.S. Appl. No. 16/960,704 Office Action dated Dec. 22, 2023. cited by applicant
U.S. Appl. No. 16/960,704 Office Action dated Jul. 5, 2024. cited by applicant
U.S. Appl. No. 16/980,730 Notice of Allowance dated Jun. 13, 2024. cited by applicant
U.S. Appl. No. 16/980,730 Office Action dated Feb. 12, 2024. cited by applicant
U.S. Appl. No. 16/980,771 Office Action dated Jan. 10, 2024. cited by applicant
U.S. Appl. No. 17/256,917 Notice of Allowance dated Sep. 7, 2023. cited by applicant
U.S. Appl. No. 17/366,638 Office Action dated Apr. 25, 2024. cited by applicant
U.S. Appl. No. 17/366,638 Office Action dated Aug. 27, 2024. cited by applicant
U.S. Appl. No. 17/402,325 Office Action dated Sep. 24, 2024. cited by applicant
U.S. Appl. No. 17/402,329 Office Action dated Nov. 5, 2024. cited by applicant
U.S. Appl. No. 17/529,017 Office Action dated Nov. 18, 2022. cited by applicant
U.S. Appl. No. 17/820,634 Office Action dated Apr. 19, 2023. cited by applicant
U.S. Appl. No. 17/820,634 Office Action dated Aug. 11, 2023. cited by applicant
U.S. Appl. No. 17/820,634 Office Action dated Aug. 15, 2023. cited by applicant
U.S. Appl. No. 17/820,794 Notice of Allowance dated Feb. 1, 2024. cited by applicant
U.S. Appl. No. 17/820,794 Office Action dated Dec. 29, 2023. cited by applicant
U.S. Appl. No. 17/820,794 Office Action dated Mar. 31, 2023. cited by applicant
U.S. Appl. No. 17/820,794 Office Action dated Sep. 15, 2023. cited by applicant
U.S. Appl. No. 17/820,800 Office Action dated Feb. 21, 2023. cited by applicant
U.S. Appl. No. 17/820,800 Office Action dated Jun. 1, 2023. cited by applicant
U.S. Appl. No. 17/820,805 Office Action dated Apr. 26, 2024. cited by applicant
U.S. Appl. No. 17/820,805 Office Action dated Aug. 14, 2023. cited by applicant
U.S. Appl. No. 17/820,805 Office Action dated Oct. 31, 2024. cited by applicant
U.S. Appl. No. 17/820,806 Office Action dated Apr. 12, 2023. cited by applicant
U.S. Appl. No. 17/820,806 Office Action dated Aug. 15, 2023. cited by applicant
U.S. Appl. No. 17/820,811 Office Action dated May 25, 2023. cited by applicant
U.S. Appl. No. 17/820,818 Office Action dated Jun. 1, 2023. cited by applicant
U.S. Appl. No. 17/820,818 Office Action dated Mar. 12, 2024. cited by applicant
U.S. Appl. No. 18/341,688 Office Action dated Jan. 25, 2024. cited by applicant
U.S. Appl. No. 18/341,688 Office Action dated May 10, 2024. cited by applicant
U.S. Appl. No. 18/472,920 Office Action dated Nov. 4, 2024. cited by applicant
Valkenburg, Sophie A. et al. Molecular Basis for Universal HLA-A*0201-restricted CD8+ T-cell Immunity Against Influenza Viruses. Proceedings of the National Academy of Sciences of the United States of America 113(16):4440-4445 (2016). cited by applicant
Van Dijk, Marc A. et al. Human Antibodies as Next Generation Therapeutics. Current Opinion in Chemical Biology 5(4):368-374 (2001). cited by applicant
Van Mierlo, Carlo PM, and Elles Steensma. Protein Folding and Stability Investigated by Fluorescence, Circular Dichroism (CD), and Nuclear Magnetic Resonance (NMR) Spectroscopy: the Flavodoxin Story. Journal of Biotechnology 79(3):281-298 (2000). cited by applicant
Van Rhijn, I. et al., “A conserved human T cell population targets mycobacterial antigens presented by CD1b,” Nat Immunol., 2013;14(7):706-713. cited by applicant
Van Rhijn, I. et al., “TCR bias and affinity define two compartments of the CD1b-glycolipid-specific T Cell repertoire,” J Immunol., 2014;192(9):4054-4060. cited by applicant
Vantourout, Pierre et al. Innate TCRβ-chain engagement drives human T cells toward distinct memory-like effector phenotypes with immunotherapeutic potentials. Science Advances 9(49):eadj6174, 1-19 (2023). cited by applicant
Viney, Joanne L. et al. Generation of Monoclonal Antibodies Against a Human T Cell Receptor Beta Chain Expressed in Transgenic Mice. Hybridoma 11(6):701-713 (1992). cited by applicant
Vitetta, Ellen S. et al. Redesigning Nature's Poisons to Create Anti-tumor Reagents. Science 238(4830):1098-1104 (1987). cited by applicant
Vollmers, H P. et al. Death by Stress: Natural IgM-induced Apoptosis. Methods and Findings in Experimental and Clinical Pharmacology 27(3):185-191 (2005). cited by applicant
Vollmers, H P. et al. The “Early Birds”: Natural IgM Antibodies and Immune Surveillance. Histology and Histopathology 20(3):927-937 (2005). cited by applicant

Walker, Laura M. et al. Broad and Potent Neutralizing Antibodies from an African Donor Reveal a New HIV-1 Vaccine Target. Science 326(5950):285-289 (2009). cited by applicant
Walker, Laura M. et al. Broad Neutralization Coverage of Hiv by Multiple Highly Potent Antibodies. Nature 477(7365):466-470 (2011). cited by applicant
Wang, Zhenguang et al. Current status and perspectives of chimeric antigen receptor modified T cells for cancer treatment. Protein and Cell 8(12):896-925 (2017). cited by applicant
Watanabe, M. et al. Interleukin-21 Can Efficiently Restore Impaired Antibody-dependent Cell- mediated Cytotoxicity in Patients With Oesophageal Squamous Cell Carcinoma. British Journal of Cancer 102(3):520-529 (2010). cited by applicant
Willemsen, R A. et al. Grafting Primary Human T Lymphocytes With Cancer-specific Chimeric Single Chain and Two Chain TCR. Gene Therapy 7(16):1369-1377 (2000). cited by applicant
Winkler et al., Changing the Antigen Binding Specificity by Single Point Mutations of an Anti-p24 (HIV-1) Antibody. Journal of Immunology 165(8):4505-4514 (2000). cited by applicant
Winter, Greg. et al. Making Antibodies by Phage Display Technology. Annual Review of Immunology 12(1):433-455 (1994). cited by applicant
Wright, Ann, and Sherie L. Morrison et al. Effect of Glycosylation on Antibody Function: Implications for Genetic Engineering. Trends in Biotechnology 15(1):26-32 (1997). cited by applicant
Xiang, Jianhua H. et al. Modification in Framework Region I Results in a Decreased Affinity of Chimeric Anti-TAG72 antibody. Molecular Immunology 28(1-2):141-148 (1991). cited by applicant
Xu, Jian et al. MIR548P and TRAV39 Are Potential Indicators of Tumor Microenvironment and Novel Prognostic Biomarkers of Esophageal Squamous Cell Carcinoma. Journal of Clinical Oncology 2022:3152114, 1-20 (2022). cited by applicant
Yamane-Ohnuki, Naoko. et al. Establishment of FUT8 Knockout Chinese Hamster Ovary Cells: an Ideal Host Cell Line for Producing Completely Defucosylated Antibodies With Enhanced Antibody-dependent Cellular Cytotoxicity. Biotechnology and Bioengineering 87(5):614-622 (2004). cited by applicant
Yang, Xinbo et al. Structural basis for clonal diversity of the human T-cell response to a dominant influenza virus epitope. J Biol Chem 292(45):18618-18627 (2017). cited by applicant
Yazaki, Paul J, and Anna M Wu. Expression of Recombinant Antibodies in Mammalian Cell Lines. Methods in Molecular Biology 248:255-268 (2004). cited by applicant
Yohannes, Dawit A. et al. Deep Sequencing of Blood and Gut T-cell Receptor B-chains Reveals Gluten-induced Immune Signatures in Celiac Disease. Scientific Reports 7(1):17977, 1-12 (2017). cited by applicant
Zhang, Tong. et al. An NKp30-Based Chimeric Antigen Receptor Promotes T cell Effector Functions and Antitumor Efficacy In Vivo. Journal of Immunology 189(5):2290-2299 (2012). cited by applicant
Zhang, Tong. et al. Transgenic TCR Expression: Comparison of Single Chain With Full-length Receptor Constructs for T-cell Function. Cancer Gene Therapy 11(7):487-496 (2004). cited by applicant
Zhou, Hongyu. et al. A Novel Risk Score System of Immune Genes Associated With Prognosis in Endometrial Cancer. Cancer Cell International 20:240, 1-12 (2020). cited by applicant
Zitti, et al. Natural killer cells in inflammation and autoimmunity. Cytokine & Growth Factor Reviews 42:37-46 (2018). cited by applicant
Barthelemy, Pierre A. et al. Comprehensive analysis of the factors contributing to the stability and solubility of autonomous human VH domains. The Journal of biological chemistry 283(6):3639-3654 (2008). cited by applicant
Beiboer, Sigrid HW. et al. Guided selection of a pan carcinoma specific antibody reveals similar binding characteristics yet structural divergence between the original murine antibody and its human equivalent. Journal of Molecular Biology 296(3):833-849 (2000). cited by applicant
Blythe, Martin J, and Darren R Flower. Benchmarking B cell epitope prediction: underperformance of existing methods. Protein science 14(1):246-248 (2005). Published online Dec. 2, 2004. cited by applicant
British Medical Association. Definition of Polypeptide. p. 457. The British Medical Association Illustrated Medical Dictionary, First UK Edition, 2002, Dorling Kindersley, London, England. cited by applicant
Choi, Yoonjoo, and Charlotte M Deane. Predicting antibody complementarity determining region structures without classification. Molecular bioSystems 7(12):3327-3334 (2011). cited by applicant
Couzi, Lionel et al. Antibody-dependent anti-cytomegalovirus activity of human Gamma delta T cells expressing CD16 (FcgammaRIIIa). Blood 119(6):1418-1427 (2012). cited by applicant
De Genst, Erwin et al. Antibody Repertoire Development in Camelids. Developmental and Comparative Immunology 30(1-2):187-198 (2006). cited by applicant
Desmyter, Aline. et al. Camelid Nanobodies: Killing Two Birds with One Stone. Current Opinion in Structural Biology 32:1-8 (2015). cited by applicant

Dondelinger, Mathieu et al. Understanding the Significance and Implications of Antibody Numbering and Antigen-Binding Surface/Residue Definition. Frontiers in Immunology 9:2278, 1-15 (2018). cited by applicant
Gershoni, Jonathan M. et al. Epitope mapping: the first step in developing epitope-based vaccines. BioDrugs 21(3):145-156 (2007). cited by applicant
Gherardin, Nicholas A. et al. Human blood MAIT cell subsets defined using MR1 tetramers. Immunology and cell biology 96(5):507-525 (2018). cited by applicant
Grabstein, et al. Cloning of a T cell growth factor that interacts with the ß chain of the interleukin-2 receptor. Science 264(5161): 965-968 (1994). cited by applicant
International Search Report and Written Opinion issued in PCT/US2019/040592, mailed Jan. 3, 2020. cited by applicant
Janeway Jr, Charles A. et al. The rearrangement of antigen-receptor gene segments controls lymphocyte development. Immunobiology: The Immune System in Health and Disease. 5th Edition. New York: Garland Science. 1-17 (2001). cited by applicant
Ladner, Robert C. Mapping the epitopes of antibodies. Biotechnology and genetic engineering reviews 24(1):1-30 (2007). cited by applicant
Lin, Yuan et al. Improved Affinity of a Chicken Single-chain Antibody to Avian Infectious Bronchitis Virus by Site-directed Mutagenesis of Complementarity-determining Region H3. African Journal of Biotechnology 10(79):18294-18302 (2011). cited by applicant
Lydard, Peter. et al. In Antibodies: Generation of diversity. Immunology :76-85 (2011). cited by applicant
Makins, Marian, ed. Definition of Polypeptide. p. 1207. Collins English Dictionary, Third Edition, Updated 1995, HarperCollins Publishers, Glasgow, Scotland. cited by applicant
McLaughlin-Taylor, Elizabeth et al. Identification of the major late human cytomegalovirus matrix protein pp65 as a target antigen for CD8+ virus-specific cytotoxic T lymphocytes. Journal of medical virology 43(1):103-110 (1994). cited by applicant
PCT/US2018/029951 International Search Report and Written Opinion dated Jul. 3, 2018. cited by applicant
PCT/US2024/025875 International Search Report and Written Opinion dated Dec. 17, 2024. cited by applicant
PCT/US2024/033300 International Search Report and Written Opinion dated Jan. 29, 2025. cited by applicant
PCT/US2024/044469 International Search Report and Written Opinion dated Feb. 14, 2025. cited by applicant
Riechmann, Lutz et al. Reshaping Human Antibodies For Therapy. Nature 332(6162):323-327 (1988). cited by applicant
Rosenberg, Steven A. et al. Use of Tumor-infiltrating Lymphocytes and Interleukin-2 in the Immunotherapy of Patients with Metastatic Melanoma. The New England Journal of Medicine 319(25):1676-1680 (1988). cited by applicant
Schreiber, Andreas et al. 3D-Epitope-Explorer (3DEX): localization of conformational epitopes within three-dimensional structures of proteins. Journal of computational chemistry 26(9):879-887 (2005). cited by applicant
Sze, Daniel M. et al. Clonal cytotoxic T cells are expanded in myeloma and reside in the CD8(+)CD57(+)CD28(−) compartment. Blood 98(9):2817-2827 (2001). cited by applicant
Tutt, Alison L. et al. Activation and preferential expansion of rat cytotoxic (CD8) T cells in vitro and in vivo with a bispecific (anti-TCR alpha/beta x anti-CD2) F(ab')2 antibody. Journal of immunology 155(6):2960-2971 (1995). cited by applicant
UniProtKB Accession No. O14931. Natural cytotoxicity triggering receptor 3. Record created Jan. 1, 1998. Retrieved Nov. 14, 2024 at URL: https://www.uniprot.org/uniprotkb/014931/entry pp. 1-10. cited by applicant
UniProtKB Accession No. P01854. Immunoglobulin heavy constant epsilon. Record created Nov. 1, 1988. Retrieved Nov. 15, 2024 at URL: https://www.uniprot.org/uniprotkb/P01854/entry pp. 1-10. cited by applicant
UniProtKB Accession No. P01859. Immunoglobulin heavy constant gamma 2. Record created Nov. 1, 1988. pp. 1-9. Retrieved Oct. 11, 2024 at URL: https://www.uniprot.org/uniprotkb/P01859/entry. cited by applicant
UniProtKB Accession No. P01860. Immunoglobulin heavy constant gamma 3. Record created Nov. 1, 1988. pp. 1-14. Retrieved Oct. 11, 2024 at URL: https://www.uniprot.org/uniprotkb/P01860/entry. cited by applicant
UniProtKB Accession No. P01861. Immunoglobulin heavy constant gamma 4. Record created Nov. 1, 1988. pp. 1-13. Retrieved Oct. 11, 2024 at URL: https://www.uniprot.org/uniprotkb/P01861/entry. cited by applicant
UniProtKB Accession No. P01871. Immunoglobulin heavy constant mu. Record created Nov. 1, 1988. Retrieved Nov. 15, 2024 at URL: https://www.uniprot.org/uniprotkb/P01871/entry pp. 1-12. cited by applicant
UniProtKB Accession No. P01876. Immunoglobulin heavy constant alpha 1. Record created Nov. 1, 1988. Retrieved Nov. 15, 2024 at URL: https://www.uniprot.org/uniprotkb/P01876/entry pp. 1-9. cited by applicant
UniProtKB Accession No. P01877. Immunoglobulin heavy constant alpha 2. Record created Nov. 1, 1988. Retrieved Nov. 15, 2024 at URL: https://www.uniprot.org/uniprotkb/P01877/entry pp. 1-9. cited by applicant

UniProtKB Accession No. Q9H293. Interleukin-25. Record created Mar. 1, 2001. pp. 1-7. Retrieved Sep. 9, 2024 at URL: https://www.uniprot.org/uniprotkb/Q9H293/entry. cited by applicant
U.S. Appl. No. 16/960,704 Corrected Notice of Allowability dated Dec. 20, 2024. cited by applicant
U.S. Appl. No. 16/960,704 Notice of Allowance dated Dec. 19, 2024. cited by applicant
U.S. Appl. No. 17/402,322 Office Action dated Nov. 19, 2024. cited by applicant
U.S. Appl. No. 17/584,892 Office Action dated Feb. 3, 2025. cited by applicant
U.S. Appl. No. 17/820,805 Notice of Allowance dated Jan. 24, 2025. cited by applicant
U.S. Appl. No. 18/341,688 Office Action dated Mar. 5, 2025. cited by applicant
Ward, E Sally et al. Binding Activities of a Repertoire of Single Immunoglobulin Variable Domains Secreted from *Escherichia coli*. Nature 341(6242):544-546 (1989). cited by applicant
Weisser, Nina E, and J Christopher Hall. Applications of single-chain variable fragment antibodies in therapeutics and diagnostics. Biotechnology advances 27(4):502-520 (2009). cited by applicant
Wu, Zhihua. et al. T cell receptor beta-chain CDR3 spectratyping and cytomegalovirus activation in allogeneic hematopoietic stem cell transplant recipients. Journal of Zhejiang University Medical Sciences 45(5):515-521 (2016). With English abstract. cited by applicant

---

Primary Examiner: Epps-Smith; Janet L

Assistant Examiner: Cunningchen; Kathleen

Attorney, Agent or Firm: Wilson Sonsini Goodrich & Rosati

Background/Summary

RELATED APPLICATIONS (1) This application is a continuation of International Application No. PCT/US2020/019329, filed on Feb. 21, 2020, which claims the benefit of U.S. Provisional Application 62/808,582 filed Feb. 21, 2019, the entire contents of each of which are hereby incorporated by reference.

SEQUENCE LISTING
(1) The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Feb. 20, 2020, is named 53676-735.301_SL.txt and is 517,567 bytes in size.
BACKGROUND
(2) Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKp30, NKp44 and NKp46.
(3) Given the importance of immune checkpoint pathways in regulating an immune response, the need exists for developing novel agents that modulate the activity of immunoinhibitory proteins, such as PD-1, thus leading to activation of the immune system. Such agents can be used, e.g., for cancer immunotherapy and treatment of other conditions, such as chronic infection.
SUMMARY OF THE INVENTION
(4) Disclosed herein are antibody molecules (e.g., humanized antibody molecules) that bind to NKp30 with high affinity and specificity. Nucleic acid molecules encoding the antibody molecules, expression vectors, host cells and methods for making the antibody molecules are also provided. Multi- or bispecific or multifunctional antibody molecules and pharmaceutical compositions comprising the antibody molecules are also provided. The anti-NKp30antibody molecules disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent and/or diagnose disorders, such as cancerous disorders (e.g., solid and soft-tissue tumors), as well as autoimmune and infectious diseases. Thus, compositions and methods for detecting NKp30, as well as methods for treating various disorders including cancer, autoimmune and/or infectious diseases, using the anti-NKp30 antibody molecules are disclosed herein.
(5) Accordingly, in one aspect, the invention features an antibody molecule (e.g., an isolated or recombinant antibody molecule), comprising one or more sequences according to the following enumerated embodiments. Additional features of any of the disclosed antibody molecules, multifunctional molecules, nucleic acids, vectors, host cells, or methods include one or more of the following enumerated embodiments.

(6) Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following enumerated embodiments.

ENUMERATED EMBODIMENTS

(7) 1. An isolated antibody molecule that binds to NKp30, comprising: (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 7315 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 7327 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7329 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

(8) 2. The antibody molecule of embodiment 1, wherein the antigen binding domain comprises: (i) a VH comprising the amino acid sequence of any of SEQ ID NOs: 7298 or 7300-7304 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to any of SEQ ID NOs: 7298 or 7300-7304), and/or (ii) a VL comprising the amino acid sequence of any of SEQ ID NOs: 7299 or 7305-7309 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to any of SEQ ID NOs: 7299 or 7305-7309).

(9) 3. The antibody molecule of embodiment 2, wherein the antigen binding domain comprises: (i) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7305 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7305); or (ii) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7309 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7309).

(10) 4. The antibody molecule of any of embodiments 1-3, wherein the antigen binding domain comprises: (i) an amino acid sequence of SEQ ID NO: 7310 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7310); or (ii) an amino acid sequence of SEQ ID NO: 7311 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7311).

(11) 5. An isolated antibody molecule that binds to NKp30, comprising: (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

(12) 6. The antibody molecule of embodiment 5, wherein the antigen binding domain comprises: (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

(13) 7. The antibody molecule of embodiment 5 or 6, wherein the antigen binding domain comprises: (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with

no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6006 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or (2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6069 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(14) 8. The antibody molecule of embodiment 7, wherein the antigen binding domain comprises: (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and (3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

(15) 9. The antibody molecule of any one of embodiments 5-8, wherein the antigen binding domain comprises: (i) a VH comprising the amino acid sequence of SEQ ID NO: 6121 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6121), and/or (ii) a VL comprising the amino acid sequence of SEQ ID NO: 7294 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 7294).

(16) 10. The antibody molecule of any one of embodiments 5-9, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6148 or 6149 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6148 or 6149).

(17) 11. The antibody molecule of either of embodiments 5-10, wherein the antigen binding domain comprises a light chain comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6150).

(18) 12. The antibody molecule of either of embodiments 5-11, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6148 or 6149 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6148 or 6149), and a light chain comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6150).

(19) 13. The antibody molecule of any of embodiments 5-12, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6015 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6016 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6017 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(20) 14. The antibody molecule of embodiment 13, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014, a VHFWR2 amino acid sequence of SEQ ID NO: 6015, a VHFWR3 amino acid sequence of SEQ ID NO: 6016, or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

(21) 15. The antibody molecule of embodiment 14, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6123 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6123).

(22) 16. The antibody molecule of any of embodiments 5-15, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6019 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6020 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g.,

substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6021 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(23) 17. The antibody molecule of embodiment 16, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018, a VHFWR2 amino acid sequence of SEQ ID NO: 6019, a VHFWR3 amino acid sequence of SEQ ID NO: 6020, or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.
(24) 18. The antibody molecule of embodiment 17, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6124 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6124).
(25) 19. The antibody molecule of any of embodiments 5-18, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6022 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6023 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6024 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6025 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(26) 20. The antibody molecule of embodiment 19, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6022, a VHFWR2 amino acid sequence of SEQ ID NO: 6023, a VHFWR3 amino acid sequence of SEQ ID NO: 6024, or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.
(27) 21. The antibody molecule of embodiment 20, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6125 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6125).
(28) 22. The antibody molecule of any of embodiments 5-21, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6027 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6028 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6029 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(29) 23. The antibody molecule of embodiment 22, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026, a VHFWR2 amino acid sequence of SEQ ID NO: 6027, a VHFWR3 amino acid sequence of SEQ ID NO: 6028, or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.
(30) 24. The antibody molecule of embodiment 23, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6126 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6126).
(31) 25. The antibody molecule of any of embodiments 5-24, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6032 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6033 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6034 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(32) 26. The antibody molecule of embodiment 25, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030, a VHFWR2 amino acid sequence of SEQ ID NO: 6032, a VHFWR3 amino acid sequence of SEQ ID NO: 6033, or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.
(33) 27. The antibody molecule of embodiment 26, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6127 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6127).
(34) 28. The antibody molecule of any of embodiments 5-27, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid

sequence of SEQ ID NO: 6035 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6036 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6037 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6038 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(35) 29. The antibody molecule of embodiment 28, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6035, a VHFWR2 amino acid sequence of SEQ ID NO: 6036, a VHFWR3 amino acid sequence of SEQ ID NO: 6037, or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.
(36) 30. The antibody molecule of embodiment 29, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6128 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6128).
(37) 31. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6078 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6079 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6080 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(38) 32. The antibody molecule of embodiment 31, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077, a VLFWR2 amino acid sequence of SEQ ID NO: 6078, a VLFWR3 amino acid sequence of SEQ ID NO: 6079, or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.
(39) 33. The antibody molecule of embodiment 32, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6137 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6137).
(40) 34. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6082 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6083 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6084 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(41) 35. The antibody molecule of embodiment 34, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081, a VLFWR2 amino acid sequence of SEQ ID NO: 6082, a VLFWR3 amino acid sequence of SEQ ID NO: 6083, or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.
(42) 36. The antibody molecule of embodiment 35, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6138 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6138).
(43) 37. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6085 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6086 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6087 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6088 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(44) 38. The antibody molecule of embodiment 37, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID

NO: 6085, a VLFWR2 amino acid sequence of SEQ ID NO: 6086, a VLFWR3 amino acid sequence of SEQ ID NO: 6087, or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.
(45) 39. The antibody molecule of embodiment 38, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6139 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6139).
(46) 40. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6090 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6091 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6092 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(47) 41. The antibody molecule of embodiment 40, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089, a VLFWR2 amino acid sequence of SEQ ID NO: 6090, a VLFWR3 amino acid sequence of SEQ ID NO: 6091, or a VLFWR4 amino acid sequence of SEQ ID NO: 6092.
(48) 42. The antibody molecule of embodiment 41, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6140 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6140).
(49) 43. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6094 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6095 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6096 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(50) 44. The antibody molecule of embodiment 43, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093, a VLFWR2 amino acid sequence of SEQ ID NO: 6094, a VLFWR3 amino acid sequence of SEQ ID NO: 6095, or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.
(51) 45. The antibody molecule of embodiment 44, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6141 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6141).
(52) 46. An isolated antibody molecule that binds to NKp30, comprising: (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).
(53) 47. The antibody molecule of embodiment 46, wherein the antigen binding domain comprises: (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072.
(54) 48. The antibody molecule of embodiments 46 or 47, wherein the antigen binding domain comprises: (1) a

heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6013 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or (2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6076 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(55) 49. The antibody molecule of embodiment 48, wherein the antigen binding domain comprises: (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and (3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

(56) 50. The antibody molecule of any one of embodiments 46-49, wherein the antigen binding domain comprises: (i) a VH comprising the amino acid sequence of SEQ ID NO: 6122 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6122), and/or (ii) a VL comprising the amino acid sequence of SEQ ID NO: 6136 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6136).

(57) 51. The antibody molecule of any of embodiments 46-50, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6151 or 6152 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6151 or 6152).

(58) 52. The antibody molecule of any of embodiments 46-51, wherein the antigen binding domain comprises a light chain comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6153).

(59) 53. The antibody molecule of any of embodiments 46-51, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6151 or 6152 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6151 or 6152), and a light chain comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6153).

(60) 54. The antibody molecule of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6040 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6041 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6042 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(61) 55. The antibody molecule of embodiment 54, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039, a VHFWR2 amino acid sequence of SEQ ID NO: 6040, a VHFWR3 amino acid sequence of SEQ ID NO: 6041, or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

(62) 56. The antibody molecule of embodiment 55, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6129 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6129).

(63) 57. The antibody molecule of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions,

additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6044 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6045 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6046 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(64) 58. The antibody molecule of embodiment 57, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043, a VHFWR2 amino acid sequence of SEQ ID NO: 6044, a VHFWR3 amino acid sequence of SEQ ID NO: 6045, or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.

(65) 59. The antibody molecule of embodiment 58, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6130 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6130).

(66) 60. The antibody molecule of any of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6048 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6049 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6050 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(67) 61. The antibody molecule of embodiment 60, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047, a VHFWR2 amino acid sequence of SEQ ID NO: 6048, a VHFWR3 amino acid sequence of SEQ ID NO: 6049, or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

(68) 62. The antibody molecule of embodiment 61, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6131 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6131).

(69) 63. The antibody molecule of any of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6052 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6053 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6054 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(70) 64. The antibody molecule of embodiment 63, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051, a VHFWR2 amino acid sequence of SEQ ID NO: 6052, a VHFWR3 amino acid sequence of SEQ ID NO: 6053, or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

(71) 65. The antibody molecule of embodiment 64, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6132 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6132).

(72) 66. The antibody molecule of any of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6058 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(73) 67. The antibody molecule of embodiment 66, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055, a VHFWR2 amino acid sequence of SEQ ID NO: 6056, a VHFWR3 amino acid sequence

of SEQ ID NO: 6057, or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.
(74) 68. The antibody molecule of embodiment 67, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6133 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6133).
(75) 69. The antibody molecule of any of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6062 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(76) 70. The antibody molecule of embodiment 69, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.
(77) 71. The antibody molecule of embodiment 70, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6134 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6134).
(78) 72. The antibody molecule of any of embodiments 46, 47, or 54-71, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6098 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6099 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6100 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(79) 73. The antibody molecule of embodiment 72, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097, a VLFWR2 amino acid sequence of SEQ ID NO: 6098, a VLFWR3 amino acid sequence of SEQ ID NO: 6099, or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.
(80) 74. The antibody molecule of embodiment 73, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6142 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6142).
(81) 75. The antibody molecule of any of embodiments 46, 47, or 54-74, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6102 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6103 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6104 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
(82) 76. The antibody molecule of embodiment 75, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101, a VLFWR2 amino acid sequence of SEQ ID NO: 6102, a VLFWR3 amino acid sequence of SEQ ID NO: 6103, or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.
(83) 77. The antibody molecule of embodiment 76, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6143 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6143).
(84) 78. The antibody molecule of any of embodiments 46, 47, or 54-77, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6106 (or a

sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6107 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6108 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(85) 79. The antibody molecule of embodiment 78, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105, a VLFWR2 amino acid sequence of SEQ ID NO: 6106, a VLFWR3 amino acid sequence of SEQ ID NO: 6107, or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

(86) 80. The antibody molecule of embodiment 79, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6144 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6144).

(87) 81. The antibody molecule of any of embodiments 46, 47, or 54-80, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6110 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6111 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6112 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(88) 82. The antibody molecule of embodiment 81, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109, a VLFWR2 amino acid sequence of SEQ ID NO: 6110, a VLFWR3 amino acid sequence of SEQ ID NO: 6111, or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

(89) 83. The antibody molecule of embodiment 78, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6145 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6145).

(90) 84. The antibody molecule of any of embodiments 46, 47, or 54-83, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6116 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(91) 85. The antibody molecule of embodiment 84, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

(92) 86. The antibody molecule of embodiment 85, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6146 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6146).

(93) 87. The antibody molecule of any of embodiments 46, 47, or 54-86, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6120 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

(94) 88. The antibody molecule of embodiment 87, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID

NO: 6119, or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.
(95) 89. The antibody molecule of embodiment 88, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6147 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6147).
(96) 90. The antibody molecule of any one of the preceding embodiments, wherein the antigen binding domain comprises:
(97) (i) a VH comprising the amino acid sequence of SEQ ID NO: 6122 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6122), and/or
(98) (ii) a VL comprising the amino acid sequence of SEQ ID NO: 6136 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6136).
(99) 91. A multispecific molecule comprising the antibody molecule of any of embodiments 1-90.
(100) 92. The multispecific molecule of embodiment 91, further comprising one, two, three, four or more of: a. a tumor targeting moiety, e.g., as described herein; b. a cytokine molecule, e.g., as described herein; c. a T cell engager, e.g., as described herein; or d. a stromal modifying moiety, e.g., as described herein.
(101) 93. The multispecific molecule of embodiment 91, further comprising a binding specificity that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.
(102) 94. The multispecific molecule of embodiment 91, further comprising a binding specificity that binds to an infected cell, e.g., a viral or bacterial infected cell.
(103) 95. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which is a monospecific antibody molecule, a bispecific antibody molecule, or a trispecific antibody molecule.
(104) 96. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which is a monovalent antibody molecule, a bivalent antibody molecule, or a trivalent antibody molecule.
(105) 97. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which is a full antibody (e.g., an antibody that includes at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains), or an antigen-binding fragment (e.g., a Fab, F(ab′).sub.2, Fv, a single chain Fv, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).
(106) 98. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which comprises a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, or a fragment thereof.
(107) 99. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof.
(108) 100. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, wherein the immunoglobulin chain constant region (e.g., Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.
(109) 101. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, wherein an interface of a first and second immunoglobulin chain constant regions (e.g., Fc region) is altered, e.g., mutated, to increase or decrease dimerization, e.g., relative to a non-engineered interface.
(110) 102. The antibody molecule or the multispecific molecule of embodiment 101, wherein the dimerization of the immunoglobulin chain constant region (e.g., Fc region) is enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired cavity-protuberance (“knob-in-a hole”), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer:homomultimer forms, e.g., relative to a non-engineered interface.
(111) 103. The antibody molecule or the multispecific molecule of embodiment 101 or 102, wherein the immunoglobulin chain constant region (e.g., Fc region) comprises an amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1.
(112) 104. The antibody molecule or the multispecific molecule of embodiment 103, wherein the immunoglobulin chain constant region (e.g., Fc region) comprises an amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), or T366W (e.g., corresponding to a protuberance or knob), or a combination thereof.
(113) 105. The antibody molecule or the multispecific molecule of any of embodiments 1-104, further comprising a linker, e.g., a linker between one or more of: the targeting moiety and the cytokine molecule or the stromal modifying moiety, the targeting moiety and the immune cell engager, the cytokine molecule or the

stromal modifying moiety, and the immune cell engager, the cytokine molecule or the stromal modifying moiety and the immunoglobulin chain constant region (e.g., the Fc region), the targeting moiety and the immunoglobulin chain constant region, or the immune cell engager and the immunoglobulin chain constant region.

(114) 106. The antibody molecule or the multispecific molecule of embodiment 105, wherein the linker is selected from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker.

(115) 107. The antibody molecule or the multispecific molecule of embodiment 106, wherein the linker is a peptide linker.

(116) 108. The antibody molecule or the multispecific molecule of embodiment 107, wherein the peptide linker comprises Gly and Ser.

(117) 109. An isolated nucleic acid molecule, which comprises the nucleotide sequence encoding any of the antibody molecules or multispecific or multifunctional molecules described herein, or a nucleotide sequence substantially homologous thereto (e.g., at least 95% to 99.9% identical thereto).

(118) 110. An isolated nucleic acid encoding the antibody molecule or the multispecific molecule of any of embodiments 1-108.

(119) 111. A vector, e.g., an expression vector, comprising one or more of the nucleic acid molecules of any of embodiments 109 or 110.

(120) 112. A host cell comprising the nucleic acid molecule or the vector of embodiment 111.

(121) 113. A method of making, e.g., producing, the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of embodiments 1-108, comprising culturing the host cell of embodiment 112, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

(122) 114. A pharmaceutical composition comprising the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of embodiments 1-108 and a pharmaceutically acceptable carrier, excipient, or stabilizer.

(123) 115. A method of treating a cancer, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the cancer.

(124) 116. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating cancer.

(125) 117. The method of embodiment 115 or the use of embodiment 116, wherein the cancer is a solid tumor cancer, or a metastatic lesion.

(126) 118. The method of embodiment 117 or the use of embodiment 117, wherein the solid tumor cancer is one or more of pancreatic (e.g., pancreatic adenocarcinoma), breast, colorectal, lung (e.g., small or non-small cell lung cancer), skin, ovarian, or liver cancer.

(127) 119. The method of embodiment 115 or the use of embodiment 116, wherein the cancer is a hematological cancer.

(128) 120. The method of any of embodiments 115 or 116-119 or the use of any of embodiments 116-119, further comprising administering a second therapeutic treatment.

(129) 121. The method of embodiment 120 or the use of embodiment 120, wherein the second therapeutic treatment comprises a therapeutic agent (e.g., a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery.

(130) 122. The method of embodiment 121 or the use of embodiment 121, wherein the therapeutic agent is selected from: a chemotherapeutic agent, or a biologic agent.

(131) 123. A method of treating an autoimmune or an inflammatory disorder, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the autoimmune or the inflammatory disorder.

(132) 124. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating an autoimmune or an inflammatory disorder.

(133) 125. A method of treating an infectious disorder, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the infectious disorder.

(134) 126. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating an infectious disorder.

Description

BRIEF DESCRIPTION OF THE DRAWINGS

(1) FIG. **1** is a graph showing binding of NKp30 antibodies to NK92 cells. Data was calculated as the percent-AF747 positive population.

(2) FIG. **2** is a graph showing activation of NK92 cells by NKp30 antibodies. Data were generated using hamster anti-NKp30 mAbs.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

(3) Certain terms are defined below.

(4) As used herein, the articles “a” and “an” refer to one or more than one, e.g., to at least one, of the grammatical object of the article. The use of the words “a” or “an” when used in conjunction with the term “comprising” herein may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.”

(5) As used herein, “about” and “approximately” generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given range of values.

(6) As used herein, the term “molecule” as used in, e.g., antibody molecule, cytokine molecule, receptor molecule, includes full-length, naturally-occurring molecules, as well as variants, e.g., functional variants (e.g., truncations, fragments, mutated (e.g., substantially similar sequences) or derivatized form thereof), so long as at least one function and/or activity of the unmodified (e.g., naturally-occurring) molecule remains.

(7) “Antibody molecule” as used herein refers to a protein, e.g., an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. An antibody molecule encompasses antibodies (e.g., full-length antibodies) and antibody fragments. In an embodiment, an antibody molecule comprises an antigen binding or functional fragment of a full-length antibody, or a full-length immunoglobulin chain. For example, a full-length antibody is an immunoglobulin (Ig) molecule (e.g., an IgG antibody) that is naturally occurring or formed by normal immunoglobulin gene fragment recombinatorial processes). In embodiments, an antibody molecule refers to an immunologically active, antigen-binding portion of an immunoglobulin molecule, such as an antibody fragment. An antibody fragment, e.g., functional fragment, is a portion of an antibody, e.g., Fab, Fab′, F(ab′).sub.2, F(ab).sub.2, variable fragment (Fv), domain antibody (dAb), or single chain variable fragment (scFv). A functional antibody fragment binds to the same antigen as that recognized by the intact (e.g., full-length) antibody. The terms “antibody fragment” or “functional fragment” also include isolated fragments consisting of the variable regions, such as the “Fv” fragments consisting of the variable regions of the heavy and light chains or recombinant single chain polypeptide molecules in which light and heavy variable regions are connected by a peptide linker (“scFv proteins”). In some embodiments, an antibody fragment does not include portions of antibodies without antigen binding activity, such as Fc fragments or single amino acid residues. Exemplary antibody molecules include full length antibodies and antibody fragments, e.g., dAb (domain antibody), single chain, Fab, Fab′, and F(ab′).sub.2 fragments, and single chain variable fragments (scFvs).

(8) As used herein, an “immunoglobulin variable domain sequence” refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids, or may include other alterations that are compatible with formation of the protein structure.

(9) In embodiments, an antibody molecule is monospecific, e.g., it comprises binding specificity for a single epitope. In some embodiments, an antibody molecule is multispecific, e.g., it comprises a plurality of immunoglobulin variable domain sequences, where a first immunoglobulin variable domain sequence has binding specificity for a first epitope and a second immunoglobulin variable domain sequence has binding specificity for a second epitope. In some embodiments, an antibody molecule is a bispecific antibody molecule. “Bispecific antibody molecule” as used herein refers to an antibody molecule that has specificity for more than one (e.g., two, three, four, or more) epitope and/or antigen.

(10) “Antigen” (Ag) as used herein refers to a molecule that can provoke an immune response, e.g., involving activation of certain immune cells and/or antibody generation. Any macromolecule, including almost all proteins or peptides, can be an antigen. Antigens can also be derived from genomic recombinant or DNA. For example, any DNA comprising a nucleotide sequence or a partial nucleotide sequence that encodes a protein

capable of eliciting an immune response encodes an “antigen.” In embodiments, an antigen does not need to be encoded solely by a full-length nucleotide sequence of a gene, nor does an antigen need to be encoded by a gene at all. In embodiments, an antigen can be synthesized or can be derived from a biological sample, e.g., a tissue sample, a tumor sample, a cell, or a fluid with other biological components. As used, herein a “tumor antigen” or interchangeably, a “cancer antigen” includes any molecule present on, or associated with, a cancer, e.g., a cancer cell or a tumor microenvironment that can provoke an immune response. As used, herein an “immune cell antigen” includes any molecule present on, or associated with, an immune cell that can provoke an immune response.

(11) The “antigen-binding site,” or “binding portion” of an antibody molecule refers to the part of an antibody molecule, e.g., an immunoglobulin (Ig) molecule, that participates in antigen binding. In embodiments, the antigen binding site is formed by amino acid residues of the variable (V) regions of the heavy (H) and light (L) chains. Three highly divergent stretches within the variable regions of the heavy and light chains, referred to as hypervariable regions, are disposed between more conserved flanking stretches called “framework regions,” (FRs). FRs are amino acid sequences that are naturally found between, and adjacent to, hypervariable regions in immunoglobulins. In embodiments, in an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface, which is complementary to the three-dimensional surface of a bound antigen. The three hypervariable regions of each of the heavy and light chains are referred to as “complementarity-determining regions,” or “CDRs.” The framework region and CDRs have been defined and described, e.g., in Kabat, E. A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242, and Chothia, C. et al. (1987) J. Mol. Biol. 196:901-917. Each variable chain (e.g., variable heavy chain and variable light chain) is typically made up of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the amino acid order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

(12) “Cancer” as used herein can encompass all types of oncogenic processes and/or cancerous growths. In embodiments, cancer includes primary tumors as well as metastatic tissues or malignantly transformed cells, tissues, or organs. In embodiments, cancer encompasses all histopathologies and stages, e.g., stages of invasiveness/severity, of a cancer. In embodiments, cancer includes relapsed and/or resistant cancer. The terms “cancer” and “tumor” can be used interchangeably. For example, both terms encompass solid and liquid tumors. As used herein, the term “cancer” or “tumor” includes premalignant, as well as malignant cancers and tumors.

(13) As used herein, an “immune cell” refers to any of various cells that function in the immune system, e.g., to protect against agents of infection and foreign matter. In embodiments, this term includes leukocytes, e.g., neutrophils, eosinophils, basophils, lymphocytes, and monocytes. Innate leukocytes include phagocytes (e.g., macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. Innate leukocytes identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms, and are mediators in the activation of an adaptive immune response. The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are important types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response. The term “immune cell” includes immune effector cells.

(14) “Immune effector cell,” as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include, but are not limited to, T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NK T) cells, and mast cells.

(15) The term “effector function” or “effector response” refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

(16) The compositions and methods of the present invention encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, e.g., sequences at least 80%, 85%, 90%, 95% identical or higher to the sequence specified. In the context of an amino acid sequence, the term “substantially identical” is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 80%, 85%, 90%. 91%, 92%, 93%, 94%, 95%, 96%, 97%,

98% or 99% identity to a reference sequence, e.g., a sequence provided herein.
(17) In the context of nucleotide sequence, the term “substantially identical” is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For example, nucleotide sequences having at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, e.g., a sequence provided herein.
(18) The term “variant” refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence. In some embodiments, the variant is a functional variant.
(19) The term “functional variant” refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence, and is capable of having one or more activities of the reference amino acid sequence.
(20) Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.
(21) To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid “identity” is equivalent to amino acid or nucleic acid “homology”).
(22) The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.
(23) The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.
(24) The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) *CABIOS,* 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.
(25) The nucleic acid and protein sequences described herein can be used as a “query sequence” to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and) XBLAST programs (version 2.0) of Altschul, et al. (1990) *J Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to a nucleic acid molecule of the invention. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See ncbi.nlm.nih.gov.
(26) It is understood that the molecules of the present invention may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.
(27) The term “amino acid” is intended to embrace all molecules, whether natural or synthetic, which include

both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term “amino acid” includes both the D- or L-optical isomers and peptidomimetics.

(28) A “conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

(29) The terms “polypeptide”, “peptide” and “protein” (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

(30) The terms “nucleic acid,” “nucleic acid sequence,” “nucleotide sequence,” or “polynucleotide sequence,” and “polynucleotide” are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

(31) The term “isolated,” as used herein, refers to material that is removed from its original or native environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of the environment in which it is found in nature.

(32) Various aspects of the invention are described in further detail below. Additional definitions are set out throughout the specification.

(33) Natural Killer Cell Engagers

(34) Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKp30, NKp44 and NKp46. The NCRs initiate tumor targeting by recognition of heparan sulfate on cancer cells. NKG2D is a receptor that provides both stimulatory and costimulatory innate immune responses on activated killer (NK) cells, leading to cytotoxic activity. DNAM1 is a receptor involved in intercellular adhesion, lymphocyte signaling, cytotoxicity and lymphokine secretion mediated by cytotoxic T-lymphocyte (CTL) and NK cell. DAP10 (also known as HCST) is a transmembrane adapter protein which associates with KLRK1 to form an activation receptor KLRK1-HCST in lymphoid and myeloid cells; this receptor plays a major role in triggering cytotoxicity against target cells expressing cell surface ligands such as MHC class I chain-related MICA and MICB, and U (optionally L1)6-binding proteins (ULBPs); it KLRK1-HCST receptor plays a role in immune surveillance against tumors and is required for cytolysis of tumors cells; indeed, melanoma cells that do not express KLRK1 ligands escape from immune surveillance mediated by NK cells. CD16 is a receptor for the Fc region of IgG, which binds complexed or aggregated IgG and also monomeric IgG and thereby mediates antibody-dependent cellular cytotoxicity (ADCC) and other antibody-dependent responses, such as phagocytosis.

(35) The present disclosure provides, inter alia, antibody molecules, e.g., multispecific (e.g., bi-, tri-, quad-specific) or multifunctional molecules, that are engineered to contain one or more NK cell engagers that

mediate binding to and/or activation of an NK cell. Accordingly, in some embodiments, the NK cell engager is selected from an antigen binding domain or ligand that binds to (e.g., activates): NKp30, NKp40, NKp44, NKp46, NKG2D, DNAM1, DAP10, CD16 (e.g., CD16a, CD16b, or both), CRTAM, CD27, PSGL1, CD96, CD100 (SEMA4D), NKp80, CD244 (also known as SLAMF4 or 2B4), SLAMF6, SLAMF7, KIR2DS2, KIR2DS4, KIR3DS1, KIR2DS3, KIR2DS5, KIR2DS1, CD94, NKG2C, NKG2E, or CD160.

(36) In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Tables 7-10. In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in U.S. Pat. Nos. 6,979,546, 9,447,185, PCT Application No. WO2015121383A1, PCT Application No. WO2016110468A1, PCT Application No. WO2004056392A1, or U.S. Application Publication No. US20070231322A1, the sequences of which are hereby incorporated by reference. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp30, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKp30, the NK cell, or both.

(37) In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more CDRs (e.g., VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and/or VLCDR3) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more framework regions (e.g., VHFWR1, VHFWR2, VHFWR3, VHFWR4, VLFWR1, VLFWR2, VLFWR3, and/or VLFWR4) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH and/or a VL disclosed in Table 9, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, any of the VH domains disclosed in Table 9 may be paired with any of the VL domains disclosed in Table 9 to form the antigen binding domain that binds to NKp30. In some embodiments, the antigen binding domain that binds to NKp30 comprises an amino acid sequence disclosed in Table 10, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto.

(38) In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1), a VHCDR2, and a VHCDR3, and a VL comprising a light chain complementarity determining region 1 (VLCDR1), a VLCDR2, and a VLCDR3.

(39) In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 6002, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6008, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

(40) In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7326, 7327, and 7329, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

(41) In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 7315, 7326, 7327, and 7329, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs:

7313, 6001, 6002, 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6008, 6009, 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, 7315, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, 6009, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

(42) In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7298 or 7300-7304 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7299 or 7305-7309 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7302 and 7305, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7302 and 7309, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

(43) In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6121 or 6123-6128 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7294 or 6137-6141 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6122 or 6129-6134 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6136 or 6142-6147 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7295 and 7296, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7297 and 7296, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 6122 and 6136, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

(44) In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 7310 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 7311 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 6187, 6188, 6189 or 6190 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

(45) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002.

(46) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

(47) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a

sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

(48) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009.

(49) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

(50) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

(51) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.

(52) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

(53) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.
(54) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.
(55) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.
(56) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.
(57) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.
(58) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.
(59) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.
(60) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.
(61) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid

sequence of SEQ ID NO: 6075 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

(62) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

(63) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014, a VHFWR2 amino acid sequence of SEQ ID NO: 6015, a VHFWR3 amino acid sequence of SEQ ID NO: 6016, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

(64) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6014 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6015 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6016 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

(65) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077, a VLFWR2 amino acid sequence of SEQ ID NO: 6078, a VLFWR3 amino acid sequence of SEQ ID NO: 6079, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

(66) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6077 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6078 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6079 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

(67) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018, a VHFWR2 amino acid sequence of SEQ ID NO: 6019, a VHFWR3 amino acid sequence of SEQ ID NO: 6020, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

(68) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6018 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6019 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6020 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

(69) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081, a VLFWR2 amino acid sequence of SEQ ID NO: 6082, a VLFWR3 amino acid sequence of SEQ ID NO: 6083, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.

(70) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6081 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6082 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6083 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.

(71) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6022, a VHFWR2 amino acid sequence of SEQ ID NO: 6023, a VHFWR3 amino acid sequence of SEQ ID NO: 6024, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.
(72) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6022 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6023 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6024 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.
(73) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6085, a VLFWR2 amino acid sequence of SEQ ID NO: 6086, a VLFWR3 amino acid sequence of SEQ ID NO: 6087, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.
(74) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6085 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6086 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6087 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.
(75) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026, a VHFWR2 amino acid sequence of SEQ ID NO: 6027, a VHFWR3 amino acid sequence of SEQ ID NO: 6028, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.
(76) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6026 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6027 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6028 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.
(77) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089, a VLFWR2 amino acid sequence of SEQ ID NO: 6090, a VLFWR3 amino acid sequence of SEQ ID NO: 6091, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6092.
(78) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6089 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6090 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6091 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6092.
(79) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030, a VHFWR2 amino acid sequence of SEQ ID NO: 6032, a VHFWR3 amino acid sequence of SEQ ID NO: 6033, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.
(80) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6030 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6032 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6033 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.
(81) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093, a VLFWR2 amino acid sequence of SEQ ID NO: 6094, a VLFWR3 amino acid sequence of SEQ ID NO: 6095, and/or a VLFWR4

amino acid sequence of SEQ ID NO: 6096.
(82) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6093 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6094 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6095 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.
(83) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6035, a VHFWR2 amino acid sequence of SEQ ID NO: 6036, a VHFWR3 amino acid sequence of SEQ ID NO: 6037, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.
(84) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6035 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6036 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6037 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.
(85) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039, a VHFWR2 amino acid sequence of SEQ ID NO: 6040, a VHFWR3 amino acid sequence of SEQ ID NO: 6041, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.
(86) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6039 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6040 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6041 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.
(87) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097, a VLFWR2 amino acid sequence of SEQ ID NO: 6098, a VLFWR3 amino acid sequence of SEQ ID NO: 6099, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.
(88) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6097 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6098 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6099 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.
(89) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043, a VHFWR2 amino acid sequence of SEQ ID NO: 6044, a VHFWR3 amino acid sequence of SEQ ID NO: 6045, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.
(90) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6043 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6044 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6045 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.
(91) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101, a VLFWR2 amino acid sequence of SEQ ID NO: 6102, a VLFWR3 amino acid sequence of SEQ ID NO: 6103, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.
(92) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6101 (or a sequence with no more than 1, 2, or 3 mutations,

e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6102 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6103 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.

(93) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047, a VHFWR2 amino acid sequence of SEQ ID NO: 6048, a VHFWR3 amino acid sequence of SEQ ID NO: 6049, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

(94) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6047 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6048 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6049 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

(95) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105, a VLFWR2 amino acid sequence of SEQ ID NO: 6106, a VLFWR3 amino acid sequence of SEQ ID NO: 6107, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

(96) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6105 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6106 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6107 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

(97) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051, a VHFWR2 amino acid sequence of SEQ ID NO: 6052, a VHFWR3 amino acid sequence of SEQ ID NO: 6053, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

(98) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6051 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6052 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6053 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

(99) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109, a VLFWR2 amino acid sequence of SEQ ID NO: 6110, a VLFWR3 amino acid sequence of SEQ ID NO: 6111, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

(100) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6109 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6110 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6111 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

(101) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055, a VHFWR2 amino acid sequence of SEQ ID NO: 6056, a VHFWR3 amino acid sequence of SEQ ID NO: 6057, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.

(102) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6055 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino

acid sequence of SEQ ID NO: 6058.
(103) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.
(104) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.
(105) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.
(106) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.
(107) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID NO: 6119, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.
(108) In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.
(109) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6148). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6149). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6150). In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150.
(110) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148, and a VL comprising the amino acid sequence of SEQ ID NO: 6150. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149, and a VL comprising the amino acid sequence of SEQ ID NO: 6150.
(111) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6151). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6152). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 93%, 95%, or 99%

sequence identity to SEQ ID NO: 6153). In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153.

(112) In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151, and a VL comprising the amino acid sequence of SEQ ID NO: 6153. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152, and a VL comprising the amino acid sequence of SEQ ID NO: 6153.

(113) In some embodiments, the antigen binding domain that targets NKp30 comprises an scFv. In some embodiments, the scFv comprises an amino acid sequence selected from SEQ ID NOs: 6187-6190, or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto.

(114) TABLE-US-00001 TABLE 7 Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains Ab ID VHFWR1 VHCDR1 VHFWR2 VHCDR2 VHFWR3 VHCDR3 VHFWR4 9G1-HC QIQLQESG TGGYHW WIRQFP YIYSSGS RISITRDT GNWHYF WGQGTM PGLVKPSQ N (SEQ GKKLEW TSYNPSL SKNQFFLQ DF VTVSS SLSLTCSV ID NO: MG KS (SEQ LNSVTTED (SEQ (SEQ TGFSIN 6000) (SEQ ID NO: TATYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6006) NO: 6003) 6004) NO: 6005) 15H6-HC QIQLQESG TGGYHW WIRQFP YIYSSGT RISITRDT GNWHYF WGQGTL PGLVKPSQ N (SEQ GKKLEW TRYNPSL SKNQFFLQ DY VAVSS SLSLTCSV ID NO: MG KS (SEQ LNSVTPED (SEQ (SEQ TGFSIN 6007) (SEQ ID NO: TATYYCTR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6013) NO: 6010) 6011) NO: 6012) 9G1-HC_1 QIQLQESG TGGYHW WIRQPA YIYSSGS RVTMSRDT GNWHYF WGQGTM PGLVKPSE N (SEQ GKGLEW TSYNPSL SKNQFSLK DF VTVSS TLSLTCTV ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ SGFSIN 6000) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6017) NO: 6014) 6015) NO: 6016) 9G1-HC_2 QIQLQESG TGGYHW WIRQHP YIYSSGS LVTISRDT GNWHYF WGQGTM PGLVKPSQ N (SEQ GKGLEW TSYNPSL SKNQFSLK DF VTVSS TLSLTCTV ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ SGFSIN 6000) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6021) NO: 6018) 6019) NO: 6020) 9G1-HC_3 EIQLLESG TGGYHW WVRQAP YIYSSGS RFTISRDT GNWHYF WGQGTM GGLVQPGG N (SEQ GKGLEW TSYNPSL SKNTFYLQ DF VTVSS SLRLSCAV ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ SGFSIN 6000) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6025) NO: 6022) 6023) NO: 6024) 9G1-HC_4 QIQLVQSG TGGYHW WVRQAP YIYSSGS RVTITRDT GNWHYF WGQGTM AEVKKPGS N (SEQ GQGLEW TSYNPSL STNTFYME DF VTVSS SVKVSCKV ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ SGFSIN 6000) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6029) NO: 6026) 6027) NO: 6028) 9G1-HC_5 EIQLVESG TGGYHW WVRQAP YIYSSGS RFTISRDT GNWHYF WGQGTM GGLVQPGG N (SEQ GKGLEW TSYNPSL AKNSFYLQ DF VTVSS SLRLSCAV ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ SGFSIN 6000) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6034) NO: 6030) 6032) NO: 6033) 9G1-HC_6 QIQLVQSG TGGYHW WVRQAP YIYSSGS RVTMTRDT GNWHYF WGQGTM AEVKKPGA N (SEQ GQGLEW TSYNPSL STNTFYME DF VTVSS SVKVSCKV ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ SGFSIN 6000) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6001) (SEQ ID 6002) 6038) NO: 6035) 6036) NO: 6037) 15H6-HC_1 QIQLQESG TGGYHW WIRQHP YIYSSGT LVTISRDT GNWHYF WGQGTL PGLVKPSQ N (SEQ GKGLEW TRYNPSL SKNQFSLK DY VTVSS TLSLTCTV ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ SGFSIN 6007) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6042) NO: 6039) 6040) NO: 6041) 15H6-HC_2 QIQLQESG TGGYHW WIRQPA YIYSSGT RVTMSRDT GNWHYF WGQGTL PGLVKPSE N (SEQ GKGLEW TRYNPSL SKNQFSLK DY VTVSS TLSLTCTV ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ SGFSIN 6007) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6046) NO: 6043) 6044) NO: 6045) 15H6-HC_3 EIQLLESG TGGYHW WVRQAP YIYSSGT RFTISRDT GNWHYF WGQGTL GGLVQPGG N (SEQ GKGLEW TRYNPSL SKNTFYLQ DY VTVSS SLRLSCAV ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ SGFSIN 6007) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6050) NO: 6047) 6048) NO: 6049) 15H6-HC_4 QIQLVESG TGGYHW WIRQAP YIYSSGT RFTISRDT GNWHYF WGQGTL GGLVKPGG N (SEQ GKGLEW TRYNPSL AKNSFYLQ DY VTVSS SLRLSCAV ID NO: VG

KS (SEQ MNSLRAED (SEQ (SEQ SGFSIN 6007) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6054) NO: 6051) 6052) NO: 6053) 15H6-HC_5 QIQLVQSG TGGYHW WVRQAP YIYSSGT RVTMTRDT GNWHYF WGQGTL AEVKKPGA N (SEQ GQGLEW TRYNPSL STNTFYME DY VTVSS SVKVSCKV ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ SGFSIN 6007) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6058) NO: 6055) 6056) NO: 6057) 15H6-HC_6 EIQLVQSG TGGYHW WVQQAP YIYSSGT RVTITRDT GNWHYF WGQGTL AEVKKPGA N (SEQ GKGLEW TRYNPSL STNTFYME DY VTVSS TVKISCKV ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ SGFSIN 6007) (SEQ ID NO: TAVYYCAR ID NO: ID NO: (SEQ ID ID NO: 6008) (SEQ ID 6009) 6062) NO: 6059) 6060) NO: 6061)

(115) TABLE-US-00002 TABLE 18 Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains (according to the Kabat numbering scheme) Ab ID VHFWR1 VHCDR1 VHFWR2 VHCDR2 VHFWR3 VHCDR3 VHFWR4 9G1-HC QIQLQES GYHWN WIRQFP YIYSSGS RISITRDT GNWHY WGQGTM GPGLVKP (SEQ GKKLEW TSYNPSL SKNQFFLQ FDF VTVSS SQSLSLT ID NO: MG KS (SEQ LNSVTTED (SEQ (SEQ CSVTGFS 7313) (SEQ ID NO: TATYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6006) (SEQ 6004) ID NO: ID NO: 6005) 7317) 15H6-HC QIQLQES GYHWN WIRQFP YIYSSGT RISITRDT GNWHY WGQGTL GPGLVKP (SEQ GKKLEW TRYNPSL SKNQFFLQ FDY VAVSS SQSLSLT ID NO: MG KS (SEQ LNSVTPED (SEQ (SEQ CSVTGFS 7313) (SEQ ID NO: TATYYCTR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6013) (SEQ 6011) ID NO: ID NO: 6012) 7317) 9G1-HC_1 QIQLQES GYHWN WIRQPA YIYSSGS RVTMSRDT GNWHY WGQGTM GPGLVKP (SEQ GKGLEW TSYNPSL SKNQFSLK FDF VTVSS SETLSLT ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ CTVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6017) (SEQ 6015) ID NO: ID NO: 6016) 7371) 9G1-HC_2 QIQLQES GYHWN WIRQHP YIYSSGS LVTISRDT GNWHY WGQGTM GPGLVKP (SEQ GKGLEW TSYNPSL SKNQFSLK FDF VTVSS SQTLSLT ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ CTVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6021) (SEQ 6019) ID NO: ID NO: 6020) 7372) 9G1-HC_3 EIQLLES GYHWN WVRQAP YIYSSGS RFTISRDT GNWHY WGQGTM GGGLVQP (SEQ GKGLEW TSYNPSL SKNTFYLQ FDF VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6025) (SEQ 6023) ID NO: ID NO: 6024) 7373) 9G1-HC_4 QIQLVQS GYHWN WVRQAP YIYSSGS RVTITRDT GNWHY WGQGTM GAEVKKP (SEQ GQGLEW TSYNPSL STNTFYME FDF VTVSS GSSVKVS ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ CKVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6029) (SEQ 6027) ID NO: ID NO: 6028) 7374) 9G1-HC_5 EIQLVES GYHWN WVRQAP YIYSSGS RFTISRDT GNWHY WGQGTM GGGLVQP (SEQ GKGLEW TSYNPSL AKNSFYLQ FDF VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6034) (SEQ 6032) ID NO: ID NO: 6033) 7375) 9G1-HC_6 QIQLVQS GYHWN WVRQAP YIYSSGS RVTMTRDT GNWHY WGQGTM GAEVKKP (SEQ GQGLEW TSYNPSL STNTFYME FDF VTVSS GASVKVS ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ CKVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6001) (SEQ 6002) 6038) (SEQ 6036) ID NO: ID NO: 6037) 7376) 15H6-HC_1 QIQLQES GYHWN WIRQHP YIYSSGT LVTISRDT GNWHY WGQGTL GPGLVKP (SEQ GKGLEW TRYNPSL SKNQFSLK FDY VTVSS SQTLSLT ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ CTVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6042) (SEQ 6040) ID NO: ID NO: 6041) 7372) 15H6-HC_2 QIQLQES GYHWN WIRQPA YIYSSGT RVTMSRDT GNWHY WGQGTL GPGLVKP (SEQ GKGLEW TRYNPSL SKNQFSLK FDY VTVSS SETLSLT ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ CTVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6046) (SEQ 6044) ID NO: ID NO: 6045) 7371) 15H6-HC_3 EIQLLES GYHWN WVRQAP YIYSSGT RFTISRDT GNWHY WGQGTL GGGLVQP (SEQ GKGLEW TRYNPSL SKNTFYLQ FDY VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6050) (SEQ 6048) ID NO: ID NO: 6049) 7373) 15H6-HC_4 QIQLVES GYHWN WIRQAP YIYSSGT RFTISRDT GNWHY WGQGTL GGGLVKP (SEQ GKGLEW TRYNPSL AKNSFYLQ FDY VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6054) (SEQ 6052) ID NO: ID NO: 6053) 7377) 15H6-HC_5 QIQLVQS GYHWN WVRQAP YIYSSGT RVTMTRDT GNWHY WGQGTL GAEVKKP (SEQ GQGLEW TRYNPS STNTFYME FDY VTVSS GASVKVS ID NO: MG LKS LSSLRSED (SEQ (SEQ CKVSGFS 7313) (SEQ (SEQ ID

TAVYYCAR ID NO: ID NO: INTG ID NO: NO: (SEQ 6009) 6058) (SEQ 6056) 6008) ID NO: ID NO: 6057) 7376) 15H6-HC_6 EIQLVQS GYHWN WVQQAP YIYSSGT RVTITRDT GNWHY WGQGTL GAEVKKP (SEQ GKGLEW TRYNPSL STNTFYME FDY VTVSS GATVKIS ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ CKVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6062) (SEQ 6060) ID NO: ID NO: 6061) 7378) 9D9-HC QIQLQES GYHWN WIRQFP YIYSSGT RISITRDT GDWHY WGQGTM GPGLVKP (SEQ GKKVEW TKYNPSL SKNQFFLQ FDY VAVSS SQSLSLS ID NO: MG KS (SEQ LNSVTTED (SEQ (SEQ CSVTGFS 7313) (SEQ ID NO: TATYYCAR ID NO: ID NO: INTG ID NO: 7385) (SEQ 7315) 7316) (SEQ 7314) ID NO: ID NO: 6005) 7312) 3A12-HC QIQLQES GYHWN WIRQFP YIYSSGS RFSITRDT GNWHY WGQGTL GPGLVKP (SEQ GKKLEW TRYNPSL SKNQFFLQ FDY VAVSS SQSLSLT ID NO: MG KS (SEQ LNSVTTED (SEQ (SEQ CSVTGFS 7313) (SEQ ID NO: TATYYCTR ID NO: ID NO: INTG ID NO: 7318) (SEQ 6009) 6013) (SEQ 6004) ID NO: ID NO: 7319) 7317) 12D10-HC QIQLQES GYHWN WIRQFP YIYSSGT RISITRDT GNWHY WGQGTL GPGLVKP (SEQ GKKLEW TRYNPSL SKNQFFLQ FDY VAVSS SQSLSLT ID NO: MG KS (SEQ LNSVTPED (SEQ (SEQ CSVTGFS 7313) (SEQ ID NO: TATYYCTR ID NO: ID NO: INTG ID NO: 6008) (SEQ 6009) 6013) (SEQ 6004) ID NO: ID NO: 6012) 7317) 15E1-HC QIQLQES GYHWN WIRQFP YIYSSGS RFSITRDT GDWHY WGPGTM GPGLVKP (SEQ GKKLEW TSYNPSL SKNQFFLQ FDY VTVSS SQSLSLS ID NO: MG KS (SEQ LNSVTTED (SEQ (SEQ CSVTGFS 7313) (SEQ ID NO: TATYYCAR ID NO: ID NO: ITTT ID NO: 6001) (SEQ 7315) 7324) (SEQ 6004) ID NO: ID NO: 7323) 7322) 15E1_Humanized QIQLQES GYHWN WIRQHP YIYSSGS LVTISRDT GDWHY WGQGTM variant_VH1 GPGLVKP (SEQ GKGLEW TSYNPSL SKNQFSLK FDY VTVSS SQTLSLT ID NO: IG KS (SEQ LSSVTAAD (SEQ (SEQ CTVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: ITTT ID NO: 6001) (SEQ 7315) 6006) (SEQ 6019) ID NO: ID NO: 6020) 7330) 15E1_Humanized QIQLVES GYHWN WIRQAP YIYSSGS RFTISRDT GDWHY WGQGTM variant_VH2 GGGLVKP (SEQ GKGLEW TSYNPSL AKNSFYLQ FDY VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: ITTT ID NO: 6001) (SEQ 7315) 6006) (SEQ 6052) ID NO: ID NO: 6033) 7331) 15E1_Humanized EIQLLES GYHWN WVRQAP YIYSSGS RFTISRDT GDWHY WGQGTM variant_VH3 GGGLVQP (SEQ GKGLEW TSYNPSL SKNTFYLQ FDY VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: ITTT ID NO: 6001) (SEQ 7315) 6006) (SEQ 6023) ID NO: ID NO: 6024) 7332) 15E1_Humanized EIQLVES GYHWN WVRQAP YIYSSGS RFTISRDT GDWHY WGQGTM variant_VH4 GGGLVQP (SEQ GKGLEW TSYNPSL AKNSFYLQ FDY VTVSS GGSLRLS ID NO: VG KS (SEQ MNSLRAED (SEQ (SEQ CAVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: ITTT ID NO: 6001) (SEQ 7315) 6006) (SEQ 6023) ID NO: ID NO: 6033) 7333) 15E1_Humanized QIQLVQS GYHWN WVRQAP YIYSSGS RVTMTRDT GDWHY WGQGTM variant_VH5 GAEVKKP (SEQ GQGLEW TSYNPSL STNTFYME FDY VTVSS GASVKVS ID NO: MG KS (SEQ LSSLRSED (SEQ (SEQ CKVSGFS 7313) (SEQ ID NO: TAVYYCAR ID NO: ID NO: ITTT ID NO: 6001) (SEQ 7315) 6006) (SEQ 6027) ID NO: ID NO: 6037) 7334)

(116) TABLE-US-00003 TABLE 8 Exemplary light chain CDRs and FWRs of NKp30-targeting antigen binding domains Ab ID VLFWR1 VLCDR1 VLFWR2 VLCDR2 VLFWR3 VLCDR3 VLFWR4 9G1-LC SYTLTQ SGERLS WYQQKP ENDKRP GIPDQFSG QSWDST FGSGTQ PPLLSV DKYVH GRAPVM S (SEQ SNSGNIAT NSAV LTVL ALGHKA (SEQ VIY ID NO: LTISKAQA (SEQ (SEQ TITC ID NO: (SEQ 6064) GYEADYYC ID NO: ID NO: (SEQ 6063) ID NO: (SEQ ID 7293) 6069) ID NO: 6067) NO: 7292) 6066) 15H6-LC SYTLTQ SGENLS WYQQKP ENEKRP GIPDQFSG HYWESI FGSGTH PPSLSV DKYVH GRAPVM S (SEQ SNSGNIAT NSVV LTVL APGQKA (SEQ VIY ID NO: LTISKAQP (SEQ (SEQ TIIC ID NO: (SEQ 6071) GSEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6076) ID NO: 6074) NO: 6075) 6073) 9G1-LC_1 QSVTTQ SGERLS WYQQLP ENDKRP GVPDRFSG QSWDST FGGGTQ PPSVSG DKYVH GTAPKM S (SEQ SNSGNSAS NSAV LTVL APGQRV (SEQ LIY ID NO: LAITGLQA (SEQ (SEQ TISC ID NO: (SEQ 6064) EDEADYYC ID NO: ID NO: (SEQ 6063) ID NO: (SEQ ID 7293) 6080) ID NO: 6078) NO: 6079) 6077) 9G1-LC_2 QSVTTQ SGERLS WYQQLP ENDKRP GVPDRFSG QSWDST FGGGTQ PPSASG DKYVH GTAPKM S (SEQ SNSGNSAS NSAV LTVL TPGQRV (SEQ LIY ID NO: LAISGLQS (SEQ (SEQ TISC ID NO: (SEQ 6064) EDEADYYC ID NO: ID NO: (SEQ 6063) ID NO: (SEQ ID 7293) 6084) ID NO: 6082) NO: 6083) 6081) 9G1-LC_3 QSVTTQ SGERLS WYQQLP ENDKRP GVPDRFSG QSWDST FGGGTQ PPSASG DKYVH GTAPKM S (SEQ SNSGNSAS NSAV LTVL TPGQRV (SEQ LIY ID NO: LAISGLRS (SEQ (SEQ TISC ID NO: (SEQ 6064) EDEADYYC ID NO: ID NO: (SEQ 6063) ID NO: (SEQ ID 7293)

6088) ID NO: 6086) NO: 6087) 6085) 9G1-LC_4 SSETTQ SGERLS WYQQKP ENDKRP GIPERFSG QSWDST FGGGTQ PHSVSV DKYVH GQDPVM S (SEQ SNPGNTAT NSAV LTVL ATAQMA (SEQ VIY ID NO: LTISRIEA (SEQ (SEQ RITC ID NO: (SEQ 6064) GDEADYYC ID NO: ID NO: (SEQ 6063) ID NO: (SEQ ID 7293) 6092) ID NO: 6090) NO: 6091) 6089) 9G1-LC_5 DIQMTQ SGERLS WYQQKP ENDKRP GVPSRFSG QSWDST FGQGTK SPSTLS DKYVH GKAPKM S (SEQ SNSGNEAT NSAV VEIK ASVGDR (SEQ LIY ID NO: LTISSLQP (SEQ (SEQ VTITC ID NO: (SEQ 6064) DDFATYYC ID NO: ID NO: (SEQ 6063) ID NO: (SEQ ID 7293) 6096) ID NO: 6094) NO: 6095) 6093) 15H6-LC_1 QYVLTQ SGENLS WYQQLP ENEKRP GVPDRFSG HYWESI FGEGTE PPSASG DKYVH GTAPKM S (SEQ SNSGNSAS NSVV LTVL TPGQRV (SEQ LIY ID NO: LAISGLQS (SEQ (SEQ TISC ID NO: (SEQ 6071) EDEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6100) ID NO: 6098) NO: 6099) 6097) 15H6-LC_2 QYVLTQ SGENLS WYQQLP ENEKRP GVPDRFSG HYWESI FGEGTE PPSASG DKYVH GTAPKM S (SEQ SNSGNSAS NSVV LTVL TPGQRV (SEQ LIY ID NO: LAISGLRS (SEQ (SEQ TISC ID NO: (SEQ 6071) EDEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6104) ID NO: 6102) NO: 6103) 6101) 15H6-LC_3 SYELTQ SGENLS WYQQKP ENEKRP GIPERFSG HYWESI FGEGTE PPSVSV DKYVH GQSPVM S (SEQ SNSGNTAT NSVV LTVL SPGQTA (SEQ VIY ID NO: LTISGTQA (SEQ (SEQ SITC ID NO: (SEQ 6071) MDEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6108) ID NO: 6106) NO: 6107) 6105) 15H6-LC_4 DYVLTQ SGENLS WYLQKP ENEKRP GVPDRFSG HYWESI FGQGTK SPLSLP DKYVH GQSPQM S (SEQ SNSGNDAT NSVV VEIK VTPGEP (SEQ LIY ID NO: LKISRVEA (SEQ (SEQ ASISC ID NO: (SEQ 6071) EDVGVYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6112) ID NO: 6110) NO: 6111) 6109) 15H6-LC_5 AYQLTQ SGENLS WYQQKP ENEKRP GVPSRFSG HYWESI FGQGTK SPSSLS DKYVH GKAPKM S (SEQ SNSGNDAT NSVV VEIK ASVGDR (SEQ LIY ID NO: LTISSLQP (SEQ (SEQ VTITC ID NO: (SEQ 6071) EDFATYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6116) ID NO: 6114) NO: 6115) 6113) 15H6-LC_6 EYVLTQ SGENLS WYQQKP ENEKRP GIPARFSG HYWESI FGQGTK SPATLS DKYVH GQAPRM S (SEQ SNSGNEAT NSVV VEIK VSPGER (SEQ LIY ID NO: LTISSLQS (SEQ (SEQ ATLSC ID NO: (SEQ 6071) EDFAVYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6120) ID NO: 6118) NO: 6119) 6117) 9D9-LC SYTLTQ SGENLS WYQQKP ENDKRP GIPDQFSG HCWDST FGSGTH PPLVSV DKYVH GRAPVM S (SEQ SNSGNIAT NSAV LTVL ALGQKA (SEQ VIY ID NO: LTISKAQA (SEQ (SEQ TIIC ID NO: (SEQ 6064) GYEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 7321) 6076) ID NO: 6067) NO: 7292) 7320) 3A12-LC SYTLTQ SGENLS WYQQKP ENDKRP GIPDQFSG HCWDST FGSGTH PPLVSV DKYVH GRAPVM S (SEQ SNSGNIAT NSAV LTVL ALGQKA (SEQ VIY ID NO: LTISKAQA (SEQ (SEQ TIIC ID NO: (SEQ 6064) GYEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 7321) 6076) ID NO: 6067) NO: 7292) 7320) 12D10-LC SYTLTQ SGENLS WYQQKP ENEKRP GIPDQFSG HYWESI FGSGTH PPSLSV DKYVH GRAPVM S (SEQ SNSGNIAT NSVV LTVL APGQKA (SEQ VIY ID NO: LTISKAQP (SEQ (SEQ TIIC ID NO: (SEQ 6071) GSEADYYC ID NO: ID NO: (SEQ 6070) ID NO: (SEQ ID 6072) 6076) ID NO: 6074) NO: 6075) 6073) 15E1-LC SFTLTQ SGEKLS WYQQKP ENDRRP GIPDQFSG QFWDST FGGGTQ PPLVSV DKYVH GRAPVM S (SEQ SNSGNIAS NSAV LTVL AVGQVA (SEQ VIY ID NO: LTISKAQA (SEQ (SEQ TITC ID NO: (SEQ 7327) GDEADYFC ID NO: ID NO: (SEQ 7326) ID NO: (SEQ ID 7329) 6080) ID NO: 6067) NO: 7328) 7325) 15E1_Humanized SSETTQ SGEKLS WYQQKP ENDRRP GIPERFSG QFWDST FGGGTQ variant_VL1 PPSVSV DKYVH GQSPVM S (SEQ SNSGNTAT NSAV LTVL SPGQTA (SEQ VIY ID NO: LTISGTQA (SEQ (SEQ SITC ID NO: (SEQ 7327) MDEADYFC ID NO: ID NO: (SEQ 7326) ID NO: (SEQ ID 7329) 6080) ID NO: 6106) NO: 7336) 7335) 15E1_Humanized SSETTQ SGEKLS WYQQKP ENDRRP GIPERFSG QFWDST FGGGTQ variant_VL2 PHSVSV DKYVH GQDPVM S (SEQ SNPGNTAT NSAV LTVL ATAQMA (SEQ VIY ID NO: LTISRIEA (SEQ (SEQ RITC ID NO: (SEQ 7327) GDEADYFC ID NO: ID NO: (SEQ 7326) ID NO: (SEQ ID 7329) 6080) ID NO: 6090) NO: 7337) 6089) 15E1_Humanized QSVTTQ SGEKLS WYQQLP ENDRRP GVPDRFSG QFWDST FGGGTQ variant_VL3 PPSASG DKYVH GTAPKM S (SEQ SNSGNSAS NSAV LTVL TPGQRV (SEQ LIY ID NO: LAISGLRS (SEQ (SEQ TISC ID NO: (SEQ 7327) EDEADYFC ID NO: ID NO: (SEQ 7326) ID NO: (SEQ ID 7329) 6080) ID NO: 6078) NO: 7338) 6081) 15E1_Humanized QSVTTQ SGEKLS WYQQLP ENDRRP GVPDRFSG QFWDST FGGGTQ variant_VL4 PPSVSG DKYVH GTAPKM S (SEQ SNSGNSAS NSAV LTVL APGQRV (SEQ LIY ID NO: LAITGLQA (SEQ (SEQ TISC ID NO: (SEQ 7327) EDEADYFC ID NO: ID NO: (SEQ 7326) ID NO: (SEQ ID 7329) 6080) ID NO: 6078) NO: 7339) 6077) 15E1_Humanized DSVTTQ SGEKLS WYQQRP ENDRRP GVPDRFSG QFWDST FGGGTK variant_VL5 SPLSLP DKYVH GQSPRM S (SEQ SNSGNDAT NSAV VEIK VTLGQP (SEQ LIY ID NO:

LKISRVEA (SEQ (SEQ ASISC ID NO: (SEQ 7327) EDVGVYFC ID NO: ID NO: (SEQ 7326) ID NO: (SEQ ID 7329) 233) ID NO: 7341) NO: 7342) 7340)

(117) TABLE-US-00004 TABLE 9 Exemplary variable regions of NKp30-targeting antigen binding domains SEQ ID NO Ab ID Description Sequence SEQ 9G1-HC 9G1 heavy QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWN ID NO: chain variable WIRQFPGKKLEWMGYIYSSGSTSYNPSLKSRISITRD 6121 region TSKNQFFLQLNSVTTEDTATYYCARGNWHYFDFWGQG TMVTVSS SEQ 15H6-HC 15H6 heavy QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWN ID NO: chain variable WIRQFPGKKLEWMGYIYSSGTTRYNPSLKSRISITRD 6122 region TSKNQFFLQLNSVTPEDTATYYCTRGNWHYFDYWGQG TLVAVSS SEQ 9G1-HC_1 9G1 heavy QIQLQESGPGLVKPSETLSLTCTVSGFSINTGGYHWN ID NO: chain variable WIRQPAGKGLEWIGYIYSSGSTSYNPSLKSRVTMSRD 6123 region TSKNQFSLKLSSVTAADTAVYYCARGNWHYFDFWGQG humanized TMVTVSS variant 1 SEQ 9G1-HC_2 9G1 heavy QIQLQESGPGLVKPSQTLSLTCTVSGFSINTGGYHWN ID NO: chain variable WIRQHPGKGLEWIGYIYSSGSTSYNPSLKSLVTISRD 6124 region TSKNQFSLKLSSVTAADTAVYYCARGNWHYFDFWGQG humanized TMVTVSS variant 2 SEQ 9G1-HC_3 9G1 heavy EIQLLESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN ID NO: chain variable WVRQAPGKGLEWVGYIYSSGSTSYNPSLKSRFTISRD 6125 region TSKNTFYLQMNSLRAEDTAVYYCARGNWHYFDFWGQG humanized TMVTVSS variant 3 SEQ 9G1-HC_4 9G1 heavy QIQLVQSGAEVKKPGSSVKVSCKVSGFSINTGGYHWN ID NO: chain variable WVRQAPGQGLEWMGYIYSSGSTSYNPSLKSRVTITRD 6126 region TSTNTFYMELSSLRSEDTAVYYCARGNWHYFDFWGQG humanized TMVTVSS variant 4 SEQ 9G1-HC_5 9G1 heavy EIQLVESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN ID NO: chain variable WVRQAPGKGLEWVGYIYSSGSTSYNPSLKSRFTISRD 6127 region TAKNSFYLQMNSLRAEDTAVYYCARGNWHYFDFWGQG humanized TMVTVSS variant 5 SEQ 9G1-HC_6 9G1 heavy QIQLVQSGAEVKKPGASVKVSCKVSGFSINTGGYHWN ID NO: chain variable WVRQAPGQGLEWMGYIYSSGSTSYNPSLKSRVTMTRD 6128 region TSTNTFYMELSSLRSEDTAVYYCARGNWHYFDFWGQG humanized TMVTVSS variant 6 SEQ 15H6-HC_1 15H6 heavy QIQLQESGPGLVKPSQTLSLTCTVSGFSINTGGYHWN ID NO: chain variable WIRQHPGKGLEWIGYIYSSGTTRYNPSLKSLVTISRD 6129 region TSKNQFSLKLSSVTAADTAVYYCARGNWHYFDYW humanized GQGTLVTVSS variant 1 SEQ 15H6-HC_2 15H6 heavy QIQLQESGPGLVKPSETLSLTCTVSGFSINTGGYHWN ID NO: chain variable WIRQPAGKGLEWIGYIYSSGTTRYNPSLKSRVTMSRD 6130 region TSKNQFSLKLSSVTAADTAVYYCARGNWHYFDYWGQG humanized TLVTVSS variant 2 SEQ 15H6-HC_3 15H6 heavy EIQLLESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN ID NO: chain variable WVRQAPGKGLEWVGYIYSSGTTRYNPSLKSRFTISRD 6131 region TSKNTFYLQMNSLRAEDTAVYYCARGNWHYFDYWGQG humanized TLVTVSS variant 3 SEQ 15H6-HC_4 15H6 heavy QIQLVESGGGLVKPGGSLRLSCAVSGFSINTGGYHWN ID NO: chain variable WIRQAPGKGLEWVGYIYSSGTTRYNPSLKSRFTISRD 6132 region TAKNSFYLQMNSLRAEDTAVYYCARGNWHYFDYWGQG humanized TLVTVSS variant 4 SEQ 15H6-HC_5 15H6 heavy QIQLVQSGAEVKKPGASVKVSCKVSGFSINTGGYHWN ID NO: chain variable WVRQAPGQGLEWMGYIYSSGTTRYNPSLKSRVTMTRD 6133 region TSTNTFYMELSSLRSEDTAVYYCARGNWHYFDYWGQG humanized TLVTVSS variant 5 SEQ 15H6-HC_6 15H6 heavy EIQLVQSGAEVKKPGATVKISCKVSGFSINTGGYHWN ID NO: chain variable WVQQAPGKGLEWMGYIYSSGTTRYNPSLKSRVTITRD 6134 region TSTNTFYMELSSLRSEDTAVYYCARGNWHYFDYWGQG humanized TLVTVSS variant 6 SEQ 9G1-LC 9G1 light SYTLTQPPLLSVALGHKATITCSGERLSDKYVHWYQQ ID NO: chain variable KPGRAPVMVIYENDKRPSGIPDQFSGSNSGNIATLTI 7294 region SKAQAGYEADYYCQSWDSTNSAVFGSGTQLTVL SEQ 15H6-LC 15H6 light SYTLTQPPSLSVAPGQKATIICSGENLSDKYVHWYQQ ID NO: chain variable KPGRAPVMVIYENEKRPSGIPDQFSGSNSGNIATLTI 6136 region SKAQPGSEADYYCHYWESINSVVFGSGTHLTVL SEQ 9G1-LC_1 9G1 light QSVTTQPPSVSGAPGQRVTISCSGERLSDKYVHWYQQ ID NO: chain variable LPGTAPKMLIYENDKRPSGVPDRFSGSNSGNSASLAI 6137 region TGLQAEDEADYYCQSWDSTNSAVFGGGTQLTVL humanized variant 1 SEQ 9G1-LC_2 9G1 light QSVTTQPPSASGTPGQRVTISCSGERLSDKYVHWYQQ ID NO: chain variable

LPGTAPKMLIYENDKRPSGVPDRFSGSNSGNSASLAI 6138 region
SGLQSEDEADYYCQSWDSTNSAVFGGGTQLTVL humanized variant 2 SEQ 9G1-LC_3 9G1 light
QSVTTQPPSASGTPGQRVTISCSGERLSDKYVHWYQQ ID NO: chain variable
LPGTAPKMLIYENDKRPSGVPDRFSGSNSGNSASLAI 6139 region
SGLRSEDEADYYCQSWDSTNSAVFGGGTQLTVL humanized variant 3 SEQ 9G1-LC_4 9G1 light
SSETTQPHSVSVATAQMARITCSGERLSDKYVHWYQQ ID NO: chain variable
KPGQDPVMVIYENDKRPSGIPERFSGSNPGNTATLTI 6140 region
SRIEAGDEADYYCQSWDSTNSAVFGGGTQLTVL humanized variant 4 SEQ 9G1-LC_5 9G1 light
DIQMTQSPSTLSASVGDRVTITCSGERLSDKYVHWYQ ID NO: chain variable
QKPGKAPKMLIYENDKRPSGVPSRFSGSNSGNEATLT 6141 region
ISSLQPDDFATYYCQSWDSTNSAVFGQGTKVEIK humanized variant 5 SEQ 15H6-LC_1 15H6 light
QYVLTQPPSASGTPGQRVTISCSGENLSDKYVHWYQQ ID NO: chain variable
LPGTAPKMLIYENEKRPSGVPDRFSGSNSGNSASLAI 6142 region
SGLQSEDEADYYCHYWESINSVVFGEGTELTVL humanized variant 1 SEQ 15H6-LC_2 15H6 light
QYVLTQPPSASGTPGQRVTISCSGENLSDKYVHWYQQ ID NO: chain variable
LPGTAPKMLIYENEKRPSGVPDRFSGSNSGNSASLAI 6143 region
SGLRSEDEADYYCHYWESINSVVFGEGTELTVL humanized variant 2 SEQ 15H6-LC_3 15H6 light
SYELTQPPSVSVSPGQTASITCSGENLSDKYVHWYQQ ID NO: chain variable
KPGQSPVMVIYENEKRPSGIPERFSGSNSGNTATLTI 6144 region
SGTQAMDEADYYCHYWESINSVVFGEGTELTVL humanized variant 3 SEQ 15H6-LC_4 15H6 light
DYVLTQSPLSLPVTPGEPASISCSGENLSDKYVHWYL ID NO: chain variable
QKPGQSPQMLIYENEKRPSGVPDRFSGSNSGNDATLK 6145 region
ISRVEAEDVGVYYCHYWESINSVVFGQGTKVEIK humanized variant 4 SEQ 15H6-LC_5 15H6 light
AYQLTQSPSSLSASVGDRVTITCSGENLSDKYVHWYQ ID NO: chain variable
QKPGKAPKMLIYENEKRPSGVPSRFSGSNSGNDATLT 6146 region
ISSLQPEDFATYYCHYWESINSVVFGQGTKVEIK humanized variant 5 SEQ 15H6-LC_6 15H6 light
EYVLTQSPATLSVSPGERATLSCSGENLSDKYVHWYQ ID NO: chain variable
QKPGQAPRMLIYENEKRPSGIPARFSGSNSGNEATLT 6147 region
ISSLQSEDFAVYYCHYWESINSVVFGQGTKVEIK humanized variant 6 SEQ 9D9-HC 9D9 heavy
QIQLQESGPGLVKPSQSLSLSCSVTGFSINTGGYHWN ID NO: chain variable
WIRQFPGKKVEWMGYIYSSGTTKYNPSLKSRISITRD 7295 region
TSKNQFFLQLNSVTTEDTATYYCARGDWHYFDYWGQG TMVAVSS SEQ 9D9-LC 9D9 light
SYTLTQPPLVSVALGQKATIICSGENLSDKYVHWYQQ ID NO: chain variable
KPGRAPVMVIYENDKRPSGIPDQFSGSNSGNIATLTI 7296 region
SKAQAGYEADYYCHCWDSTNSAVFGSGTHLTVL SEQ 3A12-HC 3Al2 heavy
QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWN ID NO: chain variable
WIRQFPGKKLEWMGYIYSSGSTRYNPSLKSRFSITRD 7297 region
TSKNQFFLQLNSVTTEDTATYYCTRGNWHYFDYWGQG TLVAVSS SEQ 3A12-LC 3Al2 light
SYTLTQPPLVSVALGQKATIICSGENLSDKYVHWYQQ ID NO: chain variable
KPGRAPVMVIYENDKRPSGIPDQFSGSNSGNIATLTI 7296 region
SKAQAGYEADYYCHCWDSTNSAVFGSGTHLTVL SEQ 12D10-HC 12D10 heavy
QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWN ID NO: chain variable
WIRQFPGKKLEWMGYIYSSGTTRYNPSLKSRISITRD 6122 region
TSKNQFFLQLNSVTPEDTATYYCTRGNWHYFDYWGQG TLVAVSS SEQ 12D10-LC 12D 10 light
SYTLTQPPSLSVAPGQKATIICSGENLSDKYVHWYQQ ID NO: chain variable
KPGRAPVMVIYENEKRPSGIPDQFSGSNSGNIATLTI 6136 region
SKAQPGSEADYYCHYWESINSVVFGSGTHLTVL SEQ 15E1-HC 15E1 heavy
QIQLQESGPGLVKPSQSLSLSCSVTGFSITTTGYHWN ID NO: chain variable
WIRQFPGKKLEWMGYIYSSGSTSYNPSLKSRFSITRD 7298 region
TSKNQFFLQLNSVTTEDTATYYCARGDWHYFDYWG PGTMVTVSS SEQ 15E1-LC 15E1 light
SFTLTQPPLVSVAVGQVATITCSGEKLSDKYVHWYQQ ID NO: chain variable
KPGRAPVMVIYENDRRPSGIPDQFSGSNSGNIASLTI 7299 region
SKAQAGDEADYFCQFWDSTNSAVFGGGTQLTVL SEQ 15E1_Humanized 15E1 heavy
QIQLQESGPGLVKPSQTLSLTCTVSGFSITTTGYHWN ID NO: variant_VH1 chain variable
WIRQHPGKGLEWIGYIYSSGSTSYNPSLKSLVTISRD 7300 region
TSKNQFSLKLSSVTAADTAVYYCARGDWHYFDYWGQG humanized TMVTVSS variant 1 SEQ

15E1_Humanized 15E1 heavy QIQLVESGGGLVKPGGSLRLSCAVSGFSITTTGYHWN ID NO:
variant_VH2 chain variable WIRQAPGKGLEWVGYIYSSGSTSYNPSLKSRFTISRD 7301 region
TAKNSFYLQMNSLRAEDTAVYYCARGDWHYFDYWGQG humanized TMVTVSS variant 2 SEQ
15E1_Humanized 15E1 heavy EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN ID NO:
variant_VH3 chain variable WVRQAPGKGLEWVGYIYSSGSTSYNPSLKSRFTISRD 7302 (BJM0407
region TSKNTFYLQMNSLRAEDTAVYYCARGDWHYFDYWGQG VH and humanized TMVTVSS
BJM0411VH) variant 3 SEQ 15E1_Humanized 15E1 heavy
EIQLVESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN ID NO: variant_VH4 chain variable
WVRQAPGKGLEWVGYIYSSGSTSYNPSLKSRFTISRD 7303 region
TAKNSFYLQMNSLRAEDTAVYYCARGDWHYFDYWGQG humanized TMVTVSS variant 4 SEQ
15E1_Humanized 15E1 heavy QIQLVQSGAEVKKPGASVKVSCKVSGFSITTTGYHWN ID NO:
variant_VH5 chain variable WVRQAPGQGLEWMGYIYSSGSTSYNPSLKSRVTMTRD 7304 region
TSTNTFYMELSSLRSEDTAVYYCARGDWHYFDYWGQG humanized TMVTVSS variant 5 SEQ
15E1_Humanized 15E1 light SSETTQPPSVSVSPGQTASITCSGEKLSDKYVHWYQQ ID NO:
variant_VL1 chain variable KPGQSPVMVIYENDRRPSGIPERFSGSNSGNTATLTI 7305 (BJM0407VL)
region SGTQAMDEADYFCQFWDSTNSAVFGGGTQLTVL humanized variant 1 SEQ 15E1_Humanized
15E1 light SSETTQPHSVSVATAQMARITCSGEKLSDKYVHWYQQ ID NO: variant_VL2 chain
variable KPGQDPVMVIYENDRRPSGIPERFSGSNPGNTATLTI 7306 region
SRIEAGDEADYFCQFWDSTNSAVFGGGTQLTVL humanized variant 2 SEQ 15E1_Humanized 15E1
light QSVTTQPPSASGTPGQRVTISCSGEKLSDKYVHWYQQ ID NO: variant_VL3 chain variable
LPGTAPKMLIYENDRRPSGVPDRFSGSNSGNSASLAI 7307 region
SGLRSEDEADYFCQFWDSTNSAVFGGGTQLTVL humanized variant 3 SEQ 15E1_Humanized 15E1
light QSVTTQPPSVSGAPGQRVTISCSGEKLSDKYVHWYQQ ID NO: variant_VL4 chain variable
LPGTAPKMLIYENDRRPSGVPDRFSGSNSGNSASLAI 7308 region
TGLQAEDEADYFCQFWDSTNSAVFGGGTQLTVL humanized variant 4 SEQ 15E1_Humanized 15E1
light DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVHWYQ ID NO: variant_VL5 chain variable
QRPGQSPRMLIYENDRRPSGVPDRFSGSNSGNDATLK 7309 (BJM0411VL) region
ISRVEAEDVGVYFCQFWDSTNSAVFGGGTKVEIK humanized variant 5
(118) TABLE-US-00005 TABLE 10 Exemplary NKp30-targeting antigen binding domains/antibody
molecules SEQ ID NO Ab ID Description Sequence SEQ Ch(anti- 9G1 heavy
QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWNWIRQ ID NO: NKp30 chain
FPGKKLEWMGYIYSSGSTSYNPSLKSRISITRDTSKNQFFL 6148 9G1)HC
QLNSVTTEDTATYYCARGNWHYFDFWGQGTMVTVSSASTKG N297A
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
KPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVCTLPPSREEMTKNQVSLSCA
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSK
LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ Ch(anti- 9G1 heavy
QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWNWIRQ ID NO: NKp30 chain
FPGKKLEWMGYIYSSGSTSYNPSLKSRISITRDTSKNQFFL 6149 9G1)HC
QLNSVTTEDTATYYCARGNWHYFDFWGQGTMVTVSSASTKG
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
KPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVCTLPPSREEMTKNQVSLSCA
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSK
LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ Ch(anti- 9G1 light
SYTLTQPPLLSVALGHKATITCSGERLSDKYVHWYQQKPGR ID NO: NKp30 chain
APVMVIYENDKRPSGIPDQFSGSNSGNIATLTISKAQAGYE 6150 9G1)LC
ADYYCQSWDSTNSAVFGSGTQLTVLGQPKANPTVTLFPPSS
EELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTK

PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEK TVAPTECS SEQ Ch(anti- 15H6 heavy
QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWNWIRQ ID NO: NKp30 chain
FPGKKLEWMGYIYSSGTTRYNPSLKSRISITRDTSKNQFFL 6151 15H6)HC
QLNSVTPEDTATYYCTRGNWHYFDYWGQGTLVAVSSASTKG N297A
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
KPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVCTLPPSREEMTKNQVSLSCA
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSK
LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ Ch(anti- 15H6 heavy
QIQLQESGPGLVKPSQSLSLTCSVTGFSINTGGYHWNWIRQ ID NO: NKp30 chain
FPGKKLEWMGYIYSSGTTRYNPSLKSRISITRDTSKNQFFL 6152 15H6)HC
QLNSVTPEDTATYYCTRGNWHYFDYWGQGTLVAVSSASTKG (hole)
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
KPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVCTLPPSREEMTKNQVSLSCA
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSK
LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ Ch(anti- 15H6 light
SYTLTQPPSLSVAPGQKATIICSGENLSDKYVHWYQQKPGR ID NO: NKp30 chain
APVMVIYENEKRPSGIPDQFSGSNSGNIATLTISKAQPGSE 6153 15H6)LC
ADYYCHYWESINSVVFGSGTHLTVLGQPKANPTVTLFPPSS
EELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTK
PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEK TVAPTECS SEQ BJM0859
EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWNWVRQ ID NO: lambda
APGKGLEWVGYIYSSGSTSYNPSLKSRFTISRDTSKNTFYL 7310 scFv
QMNSLRAEDTAVYYCARGDWHYFDYWGQGTMVTVSSGGGGS
GGGGSGGGGSGGGGSSSETTQPPSVSVSPGQTASITCSGEK
LSDKYVHWYQQKPGQSPVMVIYENDRRPSGIPERFSGSNSG
NTATLTISGTQAMDEADYFCQFWDSTNSAVFGGGTQLTVL SEQ BJM0860
EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWNWVRQ ID NO: kappa
APGKGLEWVGYIYSSGSTSYNPSLKSRFTISRDTSKNTFYL 7311 scFv
QMNSLRAEDTAVYYCARGDWHYFDYWGQGTMVTVSSGGGGS
GGGGSGGGGSGGGGSDSVTTQSPLSLPVTLGQPASISCSGE
KLSDKYVHWYQQRPGQSPRMLIYENDRRPSGVPDRFSGSNS
GNDATLKISRVEAEDVGVYFCQFWDSTNSAVFGGGTKVEIK

(119) In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp46 (e.g., NKp46 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp46, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp46 (e.g., NKp46 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKp46, the NK cell, or both.

(120) In some embodiments, the NK cell engager is an antigen binding domain that binds to NKG2D (e.g., NKG2D present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKG2D, to the NK cell activates the NK cell. An antigen binding domain that binds to NKG2D (e.g., NKG2D present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKG2D, the NK cell, or both.

(121) In some embodiments, the NK cell engager is an antigen binding domain that binds to CD16 (e.g., CD16 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid

sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to CD16, to the NK cell activates the NK cell. An antigen binding domain that binds to CD16 (e.g., CD16 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target CD16, the NK cell, or both.

(122) TABLE-US-00006 TABLE 15 Exemplary variable regions of NKp46, NKG2D, or CD16-targeting antigen binding domains SEQ ID NO Ab ID Description Sequence SEQ NKG2D_1scFv scFv that QVHLQESGPGLVKPSETLSLTCTVSDDSISSYYWSWIRQ ID NO: binds PPGKGLEWIGHISYSGSANYNPSLKSRVTISVDTSKNQF 6175 NKG2D SLKLSSVTAADTAVYYCANWDDAFNIWGQGTMVTVSSGG GGSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATL SCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTF GQGTKVEIK SEQ NKG2D_1VH VH that QVHLQESGPGLVKPSETLSLTCTVSDDSISSYYWSWIRQ ID NO: binds PPGKGLEWIGHISYSGSANYNPSLKSRVTISVDTSKNQF 6176 NKG2D SLKLSSVTAADTAVYYCANWDDAFNIWGQGTMVTVSS SEQ NKG2D_1VL VL that EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQ ID NO: binds KPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISR 6177 NKG2D LEPEDFAVYYCQQYGSSPWTFGQGTKVEIK SEQ NKG2D_2scFv scFv that EVQLVQSGAEVKEPGESLKISCKNSGYSFTNYWVGWVRQ ID NO: binds MPGKGLEWMGIIYPGDSDTRYSPSFQGQVTISADKSINT 6178 NKG2D AYLQWSSLKASDTAMYYCGRLTMFRGIIIGYFDYWGQGT LVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPATLSL SPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDAS NRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQR SNWPWTFGQGTKVEIK SEQ NKG2D_2VH VH that EVQLVQSGAEVKEPGESLKISCKNSGYSFTNYWVGWVRQ ID NO: binds MPGKGLEWMGIIYPGDSDTRYSPSFQGQVTISADKSINT 6179 NKG2D AYLQWSSLKASDTAMYYCGRLTMFRGIIIGYFDYWGQGT LVTVSS SEQ NKG2D_2VL VL that EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQK ID NO: binds PGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSL 6180 NKG2D EPEDFAVYYCQQRSNWPWTFGQGTKVEIK SEQ NKp46scFv scFv that QVQLQQSGPELVKPGASVKMSCKASGYTFTDYVINWGKQ ID NO: binds NKp46 RSGQGLEWIGEIYPGSGTNYYNEKFKAKATLTADKSSNI 6181 AYMQLSSLTSEDSAVYFCARRGRYGLYAMDYWGQGTSVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQTTSSLSASLG DRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLH SGVPSRFSGSGSGTDYSLTINNLEQEDIATYFCQQGNTR PWTFGGGTKLEIK SEQ NKp46VH VH that QVQLQQSGPELVKPGASVKMSCKASGYTFTDYVINWGKQ ID NO: binds NKp46 RSGQGLEWIGEIYPGSGTNYYNEKFKAKATLTADKSSNI 6182 AYMQLSSLTSEDSAVYFCARRGRYGLYAMDYWGQGTSVT VSS SEQ NKp46VL VL that DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQK ID NO: binds NKp46 PDGTVKLLIYYTSRLHSGVPSRFSGSGSGTDYSLTINNL 6183 EQEDIATYFCQQGNTRPWTFGGGTKLEIK SEQ CD16scFv scFv that EVQLVESGGGVVRPGGSLRLSCAASGFTFDDYGMSWVRQ ID NO: binds CD16 APGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKNS 6184 LYLQMNSLRAEDTAVYYCARGRSLLFDYWGQGTLVTVSR GGGGSGGGGSGGGGSSELTQDPAVSVALGQTVRITCQGD SLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGS SSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGT KLTVL SEQ CD16VH VH that EVQLVESGGGVVRPGGSLRLSCAASGFTFDDYGMSWVRQ ID NO: binds CD16 APGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKNS 6185 LYLQMNSLRAEDTAVYYCARGRSLLFDYWGQGTLVTVSR SEQ CD16VL VL that SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKP ID NO: binds CD16 GQAPVLVIYGKNNRPSGIPDRFSGSSSGNTASLTITGAQ 6186 AEDEADYYCNSRDSSGNHVVFGGGTKLTVL

(123) In one embodiment, the NK cell engager is a ligand of NKp30, e.g., is a B7-6, e.g., comprises the amino acid sequence of:

DLKVEMMAGGTQITPLNDNVTIFCNIFYSQPLNITSMGITWFWKSLTFDKEVKVFEFFGD
HQEAFRPGAIVSPWRLKSGDASLRLPGIQLEEAGEYRCEVVVTPLKAQGTVQLEVVASP
ASRLLLDQVGMKENEDKYMCESSGFYPEAINITWEKQTQKFPHPIEISEDVITGPTIKNM
DGTFNVTSCLKLNSSQEDPGTVYQCVVRHASLHTPLRSNFTLTAARHSLSETEKTDNFS (SEQ ID NO: 7233), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7233.

(124) In other embodiments, the NK cell engager is a ligand of NKp44 or NKp46, which is a viral HA. Viral hemagglutinins (HA) are glyco proteins which are on the surface of viruses. HA proteins allow viruses to bind to the membrane of cells via sialic acid sugar moieties which contributes to the fusion of viral membranes with the cell membranes (see e.g., Eur J Immunol. 2001 September; 31(9):2680-9 “Recognition of viral hemagglutinins by NKp44 but not by NKp30”; and Nature. 2001 Feb. 22; 409(6823):1055-60 “Recognition of haemaglutinins on virus-infected cells by NKp46 activates lysis by human NK cells” the contents of each of which are incorporated by reference herein).

(125) In other embodiments, the NK cell engager is a ligand of NKG2D chosen from MICA, MICB, or ULBP1, e.g., wherein: (i) MICA comprises the amino acid sequence:
EPHSLRYNLTVLSWDGSVQSGFLTEVHLDGQPFLRCDRQKCRAKPQGQWAEDVLGNK
TWDRETRDLTGNGKDLRMTLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQHFYYDGEL
FLSQNLETKEWTMPQSSRAQTLAMNVRNFLKEDAMKTKTHYHAMHADCLQELRRYLK
SGVVLRRTVPPMVNVTRSEASEGNITVTCRASGFYPWNITLSWRQDGVSLSHDTQQWG
DVLPDGNGTYQTWVATRICQGEEQRFTCYMEHSGNHSTHPVPSGKVLVLQSHW (SEQ ID NO: 7234), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7234; (ii) MICB comprises the amino acid sequence:
AEPHSLRYNLMVLSQDESVQSGFLAEGHLDGQPFLRYDRQKRRAKPQGQWAEDVLGA
KTWDTETEDLTENGQDLRRTLTHIKDQKGGLHSLQEIRVCEIHEDSSTRGSRHFYYDGEL
FLSQNLETQESTVPQSSRAQTLAMNVTNFWKEDAMKTKTHYRAMQADCLQKLQRYLK
SGVAIRRTVPPMVNVTCSEVSEGNITVTCRASSFYPRNITLTWRQDGVSLSHNTQQWGD
VLPDGNGTYQTWVATRIRQGEEQRFTCYMEHSGNHGTHPVPSGKVLVLQSQRTD (SEQ ID NO: 7235), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7235; or (iii) ULBP1 comprises the amino acid sequence:
GWVDTHCLCYDFIITPKSRPEPQWCEVQGLVDERPFLHYDCVNHKAKAFASLGKKVNV
TKTWEEQTETLRDVVDFLKGQLLDIQVENLIPIEPLTLQARMSCEHEAHGHGRGSWQFL
FNGQKFLLFDSNNRKWTALHPGAKKMTEKWEKNRDVTMFFQKISLGDCKMWLEEFL
MYWEQMLDPTKPPSLAPG (SEQ ID NO: 7236), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7236.

(126) In other embodiments, the NK cell engager is a ligand of DNAM1 chosen from NECTIN2 or NECL5, e.g., wherein: (i) NECTIN2 comprises the amino acid sequence:
QDVRVQVLPEVRGQLGGTVELPCHLLPPVPGLYISLVTWQRPDAPANHQNVAAFHPKM
GPSFPSPKPGSERLSFVSAKQSTGQDTEAELQDATLALHGLTVEDEGNYTCEFATFPKGS
VRGMTWLRVIAKPKNQAEAQKVTFSQDPTTVALCISKEGRPPARISWLSSLDWEAKETQ
VSGTLAGTVTVTSRFTLVPSGRADGVTVTCKVEHESFEEPALIPVTLSVRYPPEVSISGYD
DNWYLGRTDATLSCDVRSNPEPTGYDWSTTSGTFPTSAVAQGSQLVIHAVDSLFNTTFV
CTVTNAVGMGRAEQVIFVRETPNTAGAGATGG (SEQ ID NO: 7237), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7237; or (ii) NECL5 comprises the amino acid sequence:
WPPPGTGDVVVQAPTQVPGFLGDSVTLPCYLQVPNMEVTHVSQLTWARHGESGSMAV
FHQTQGPSYSESKRLEFVAARLGAELRNASLRMFGLRVEDEGNYTCLFVTFPQGSRSVD

IWLRVLAKPQNTAEVQKVQLTGEPVPMARCVSTGGRPPAQITWHSDLGGMPNTSQVPG
FLSGTVTVTSLWILVPSSQVDGKNVTCKVEHESFEKPQLLTVNLTVYYPPEVSISGYDNN
WYLGQNEATLTCDARSNPEPTGYNWSTTMGPLPPFAVAQGAQLLIRPVDKPINTTLICN
VTNALGARQAELTVQVKEGPPSEHSGISRN (SEQ ID NO: 7238), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7238.

(127) In yet other embodiments, the NK cell engager is a ligand of DAP10, which is an adapter for NKG2D (see e.g., Proc Natl Acad Sci USA. 2005 May 24; 102(21): 7641-7646; and Blood, 15 Sep. 2011 Volume 118, Number 11, the full contents of each of which is incorporated by reference herein).

(128) In other embodiments, the NK cell engager is a ligand of CD16, which is a CD16a/b ligand, e.g., a CD16a/b ligand further comprising an antibody Fc region (see e.g., Front Immunol. 2013; 4: 76 discusses how antibodies use the Fc to trigger NK cells through CD16, the full contents of which are incorporated herein).

(129) In other embodiments, the NK cell engager is a ligand of CRTAM, which is NECL2, e.g., wherein NECL2 comprises the amino acid sequence:
QNLFTKDVTVIEGEVATISCQVNKSDDSVIQLLNPNRQTIYFRDFRPLKDSRFQLLNFSSS
ELKVSLTNVSISDEGRYFCQLYTDPPQESYTTITVLVPPRNLMIDIQKDTAVEGEEIEVNC
TAMASKPATTIRWFKGNTELKGKSEVEEWSDMYTVTSQLMLKVHKEDDGVPVICQVE
HPAVTGNLQTQRYLEVQYKPQVHIQMTYPLQGLTREGDALELTCEAIGKPQPVMVTWV
RVDDEMPQHAVLSGPNLFINNLNKTDNGTYRCEASNIVGKAHSDYMLYVYDPPTTIPPP
TTTTTTTTTTTTTILTIITDSRAGEEGSIRAVDH (SEQ ID NO: 7239), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7239.

(130) In other embodiments, the NK cell engager is a ligand of CD27, which is CD70, e.g., wherein CD70 comprises the amino acid sequence:
QRFAQAQQQLPLESLGWDVAELQLNHTGPQQDPRLYWQGGPALGRSFLHGPELDKGQ
LRIHRDGIYMVHIQVTLAICSSTTASRHHPTTLAVGICSPASRSISLLRLSFHQGCTIASQR
LTPLARGDTLCTNLTGTLLPSRNTDETFFGVQWVRP (SEQ ID NO: 7240), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7240.

(131) In other embodiments, the NK cell engager is a ligand of PSGL1, which is L-selectin (CD62L), e.g., wherein L-selectin comprises the amino acid sequence:
WTYHYSEKPMNWQRARRFCRDNYTDLVAIQNKAEIEYLEKTLPFSRSYYWIGIRKIGGI
WTWVGTNKSLTEEAENWGDGEPNNKKNKEDCVEIYIKRNKDAGKWNDDACHKLKAA
LCYTASCQPWSCSGHGECVEIINNYTCNCDVGYYGPQCQFVIQCEPLEAPELGTMDCTH
PLGNFSFSSQCAFSCSEGTNLTGIEETTCGPFGNWSSPEPTCQVIQCEPLSAPDLGIMNCSH
PLASFSFTSACTFICSEGTELIGKKKTICESSGIWSNPSPICQKLDKSFSMIKEGDYN (SEQ ID NO: 7241), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7241.

(132) In other embodiments, the NK cell engager is a ligand of CD96, which is NECL5, e.g., wherein NECL5 comprises the amino acid sequence:
WPPPGTGDVVVQAPTQVPGFLGDSVTLPCYLQVPNMEVTHVSQLTWARHGESGSMAV
FHQTQGPSYSESKRLEFVAARLGAELRNASLRMFGLRVEDEGNYTCLFVTFPQGSRSVD
IWLRVLAKPQNTAEVQKVQLTGEPVPMARCVSTGGRPPAQITWHSDLGGMPNTSQVPG
FLSGTVTVTSLWILVPSSQVDGKNVTCKVEHESFEKPQLLTVNLTVYYPPEVSISGYDNN
WYLGQNEATLTCDARSNPEPTGYNWSTTMGPLPPFAVAQGAQLLIRPVDKPINTTLICN
VTNALGARQAELTVQVKEGPPSEHSGISRN (SEQ ID NO: 7238), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7238.

(133) In other embodiments, the NK cell engager is a ligand of CD100 (SEMA4D), which is CD72, e.g., wherein CD72 comprises the amino acid sequence:

RYLQVSQQLQQTNRVLEVTNSSLRQQLRLKITQLGQSAEDLQGSRRELAQSQEALQVEQ
RAHQAAEGQLQACQADRQKTKETLQSEEQQRRALEQKLSNMENRLKPFFTCGSADTCC
PSGWIMHQKSCFYISLTSKNWQESQKQCETLSSKLATFSEIYPQSHSYYFLNSLLPNGGS
GNSYWTGLSSNKDWKLTDDTQRTRTYAQSSKCNKVHKTWSWWTLESESCRSSLPYICE MTAFRFPD
(SEQ ID NO: 7242), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7242.

(134) In other embodiments, the NK cell engager is a ligand of NKp80, which is CLEC2B (AICL), e.g., wherein CLEC2B (AICL) comprises the amino acid sequence:
KLTRDSQSLCPYDWIGFQNKCYYFSKEEGDWNSSKYNCSTQHADLTIIDNIEEMNFLRR
YKCSSDHWIGLKMAKNRTGQWVDGATFTKSFGMRGSEGCAYLSDDGAATARCYTER KWICRKRIH
(SEQ ID NO: 7243), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7243.

(135) In other embodiments, the NK cell engager is a ligand of CD244, which is CD48, e.g., wherein CD48 comprises the amino acid sequence:
QGHLVHMTVVSGSNVTLNISESLPENYKQLTWFYTFDQKIVEWDSRKSKYFESKFKGR
VRLDPQSGALYISKVQKEDNSTYIMRVLKKTGNEQEWKIKLQVLDPVPKPVIKIEKIEDM
DDNCYLKLSCVIPGESVNYTWYGDKRPFPKELQNSVLETTLMPHNYSRCYTCQVSNSVS
SKNGTVCLSPPCTLARS (SEQ ID NO: 7244), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7244.

(136) In some embodiments, the NK cell engager is a viral hemagglutinin (HA), HA is a glycoprotein found on the surface of influenza viruses. It is responsible for binding the virus to cells with sialic acid on the membranes, such as cells in the upper respiratory tract or erythrocytes. HA has at least 18 different antigens. These subtypes are named H1 through H18. NCRs can recognize viral proteins. NKp46 has been shown to be able to interact with the HA of influenza and the HA-NA of Paramyxovirus, including Sendai virus and Newcastle disease virus. Besides NKp46, NKp44 can also functionally interact with HA of different influenza subtypes.

(137) Antibody Molecules

(138) In an embodiment, the anti-NKp30 antibody molecule is a monospecific antibody molecule and binds a single epitope on NKp30. E.g., a monospecific antibody molecule having a plurality of immunoglobulin variable domain sequences, each of which binds the same epitope.

(139) In another embodiment, the anti-NKp30 antibody molecule is a multispecific or multifunctional antibody molecule, e.g., it comprises a plurality of immunoglobulin variable domains sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, e.g., the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, e.g., the different proteins (or different subunits of a multimeric protein). In an embodiment a multispecific antibody molecule comprises a third, fourth or fifth immunoglobulin variable domain. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule, a trispecific antibody molecule, or a tetraspecific antibody molecule.

(140) In an embodiment a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, e.g., the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, e.g., the different proteins (or different subunits of a multimeric protein). In an embodiment a bispecific antibody molecule comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for

a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody having binding specificity for a first epitope and a half antibody having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a scFv or a Fab, or fragment thereof, have binding specificity for a first epitope and a scFv or a Fab, or fragment thereof, have binding specificity for a second epitope.

(141) In an embodiment, an antibody molecule comprises a diabody, and a single-chain molecule, as well as an antigen-binding fragment of an antibody (e.g., Fab, F(ab′).sub.2, and Fv). For example, an antibody molecule can include a heavy (H) chain variable domain sequence (abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein as VL). In an embodiment an antibody molecule comprises or consists of a heavy chain and a light chain (referred to herein as a half antibody. In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab′, F(ab′).sub.2, Fc, Fd, Fd′, Fv, single chain antibodies (scFv for example), single variable domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (e.g., humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (e.g., IgG1, IgG2, IgG3, and IgG4) of antibodies. The preparation of antibody molecules can be monoclonal or polyclonal. An antibody molecule can also be a human, humanized, CDR-grafted, or in vitro generated antibody. The antibody can have a heavy chain constant region chosen from, e.g., IgG1, IgG2, IgG3, or IgG4. The antibody can also have a light chain chosen from, e.g., kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

(142) Examples of antigen-binding fragments of an antibody molecule include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab′)2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb) fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), see e.g., Bird et al. (1988) *Science* 242:423-426; and Huston et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883); (viii) a single domain antibody. These antibody fragments are obtained using conventional techniques known to those with skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

(143) Antibody molecules include intact molecules as well as functional fragments thereof. Constant regions of the antibody molecules can be altered, e.g., mutated, to modify the properties of the antibody (e.g., to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

(144) Antibody molecules can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to another aspect of the invention, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are disclosed in WO 9404678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from antibodies raised in Camelidae species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides Camelidae may produce heavy chain antibodies naturally devoid of light chain; such VHHs are within the scope of the invention.

(145) The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW).

(146) The extent of the framework region and CDRs has been precisely defined by a number of methods (see,

Kabat, E. A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C. et al. (1987) *J. Mol. Biol.* 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software. See, generally, e.g., *Protein Sequence and Structure Analysis of Antibody Variable Domains*. In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg).

(147) The terms “complementarity determining region,” and “CDR,” as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. In general, there are three CDRs in each heavy chain variable region (HCDR1, HCDR2, HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, LCDR3).

(148) The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of known schemes, including those described by Kabat et al. (1991), “Sequences of Proteins of Immunological Interest,” 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (“Kabat” numbering scheme), Al-Lazikani et al., (1997) *JMB* 273, 927-948 (“Chothia” numbering scheme). As used herein, the CDRs defined according the “Chothia” number scheme are also sometimes referred to as “hypervariable loops.”

(149) For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3). Under Chothia, the CDR amino acids in the VH are numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3).

(150) Each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

(151) The antibody molecule can be a polyclonal or a monoclonal antibody.

(152) The terms “monoclonal antibody” or “monoclonal antibody composition” as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope. A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (e.g., recombinant methods).

(153) The antibody can be recombinantly produced, e.g., produced by phage display or by combinatorial methods.

(154) Phage display and combinatorial methods for generating antibodies are known in the art (as described in, e.g., Ladner et al. U.S. Pat. No. 5,223,409; Kang et al. International Publication No. WO 92/18619; Dower et al. International Publication No. WO 91/17271; Winter et al. International Publication WO 92/20791; Markland et al. International Publication No. WO 92/15679; Breitling et al. International Publication WO 93/01288; McCafferty et al. International Publication No. WO 92/01047; Garrard et al. International Publication No. WO 92/09690; Ladner et al. International Publication No. WO 90/02809; Fuchs et al. (1991) Bio/Technology 9:1370-1372; Hay et al. (1992) *Hum Antibody Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffths et al. (1993) *EMBO J* 12:725-734; Hawkins et al. (1992) *J Mol Biol* 226:889-896; Clackson et al. (1991) *Nature* 352:624-628; Gram et al. (1992) *PNAS* 89:3576-3580; Garrad et al. (1991) *Bio/Technology* 9:1373-1377; Hoogenboom et al. (1991) *Nuc Acid Res* 19:4133-4137; and Barbas et al. (1991) *PNAS* 88:7978-7982, the contents of all of which are incorporated by reference herein).

(155) In one embodiment, the antibody is a fully human antibody (e.g., an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, e.g., a rodent (mouse or rat), goat, primate (e.g., monkey), camel antibody. Preferably, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

(156) Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (see, e.g., Wood et al. International Application WO 91/00906, Kucherlapati et al. PCT publication WO 91/10741; Lonberg et al. International Application WO 92/03918; Kay et al. International Application 92/03917; Lonberg, N. et al. 1994 *Nature* 368:856-859; Green, L. L. et al. 1994 *Nature Genet.* 7:13-21; Morrison, S. L. et al. 1994 *Proc. Natl. Acad. Sci. USA* 81:6851-6855; Bruggeman et al. 1993 *Year Immunol* 7:33-40; Tuaillon et al. 1993 *PNAS* 90:3720-3724; Bruggeman et al. 1991 *Eur J Immunol* 21:1323-1326).

(157) An antibody molecule can be one in which the variable region, or a portion thereof, e.g., the CDRs, are generated in a non-human organism, e.g., a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies

are within the invention. Antibody molecules generated in a non-human organism, e.g., a rat or mouse, and then modified, e.g., in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

(158) An “effectively human” protein is a protein that does substantially not evoke a neutralizing antibody response, e.g., the human anti-murine antibody (HAMA) response. HAMA can be problematic in a number of circumstances, e.g., if the antibody molecule is administered repeatedly, e.g., in treatment of a chronic or recurrent disease condition. A HAMA response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (see, e.g., Saleh et al., *Cancer Immunol. Immunother.*, 32:180-190 (1990)) and also because of potential allergic reactions (see, e.g., LoBuglio et al., *Hybridoma*, 5:5117-5123 (1986)).

(159) Chimeric antibodies can be produced by recombinant DNA techniques known in the art (see Robinson et al., International Patent Publication PCT/US86/02269; Akira, et al., European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison et al., European Patent Application 173,494; Neuberger et al., International Application WO 86/01533; Cabilly et al. U.S. Pat. No. 4,816,567; Cabilly et al., European Patent Application 125,023; Better et al. (1988 *Science* 240:1041-1043); Liu et al. (1987) *PNAS* 84:3439-3443; Liu et al., 1987, *J Immunol.* 139:3521-3526; Sun et al. (1987) *PNAS* 84:214-218; Nishimura et al., 1987, *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al., 1988, *J. Natl Cancer Inst.* 80:1553-1559).

(160) A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and or light immuoglobulin chains) replaced with a donor CDR. The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding to the antigen. Preferably, the donor will be a rodent antibody, e.g., a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the immunoglobulin providing the CDRs is called the “donor” and the immunoglobulin providing the framework is called the “acceptor.” In one embodiment, the donor immunoglobulin is a non-human (e.g., rodent). The acceptor framework is a naturally-occurring (e.g., a human) framework or a consensus framework, or a sequence about 85% or higher, preferably 90%, 95%, 99% or higher identical thereto.

(161) As used herein, the term “consensus sequence” refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (See e.g., Winnaker, From Genes to Clones (Verlagsgesellschaft, Weinheim, Germany 1987). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A “consensus framework” refers to the framework region in the consensus immunoglobulin sequence.

(162) An antibody molecule can be humanized by methods known in the art (see e.g., Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi et al., 1986, *BioTechniques* 4:214, and by Queen et al. U.S. Pat. Nos. 5,585,089, 5,693,761 and 5,693,762, the contents of all of which are hereby incorporated by reference).

(163) Humanized or CDR-grafted antibody molecules can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced. See e.g., U.S. Pat. No. 5,225,539; Jones et al. 1986 *Nature* 321:552-525; Verhoeyan et al. 1988 *Science* 239:1534; Beidler et al. 1988 *J. Immunol.* 141:4053-4060; Winter U.S. Pat. No. 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare the humanized antibodies of the present invention (UK Patent Application GB 2188638A, filed on Mar. 26, 1987; Winter U.S. Pat. No. 5,225,539), the contents of which is expressly incorporated by reference.

(164) Also within the scope of the invention are humanized antibody molecules in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in U.S. Pat. No. 5,585,089, e.g., columns 12-16 of U.S. Pat. No. 5,585,089, e.g., columns 12-16 of U.S. Pat. No. 5,585,089, the contents of which are hereby incorporated by reference. Other techniques for humanizing antibodies are described in Padlan et al. EP 519596 A1, published on Dec. 23, 1992.

(165) The antibody molecule can be a single chain antibody. A single-chain antibody (scFv) may be engineered (see, for example, Colcher, D. et al. (1999) *Ann NY Acad Sci* 880:263-80; and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

(166) In yet other embodiments, the antibody molecule has a heavy chain constant region chosen from, e.g., the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, e.g., the (e.g., human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another

embodiment, the antibody molecule has a light chain constant region chosen from, e.g., the (e.g., human) light chain constant regions of kappa or lambda. The constant region can be altered, e.g., mutated, to modify the properties of the antibody (e.g., to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement function). In one embodiment the antibody has: effector function; and can fix complement. In other embodiments the antibody does not; recruit effector cells; or fix complement. In another embodiment, the antibody has reduced or no ability to bind an Fc receptor. For example, it is a isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, e.g., it has a mutagenized or deleted Fc receptor binding region.
(167) Methods for altering an antibody constant region are known in the art. Antibodies with altered function, e.g. altered affinity for an effector ligand, such as FcR on a cell, or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (see e.g., EP 388,151 A1, U.S. Pat. Nos. 5,624,821 and 5,648,260, the contents of all of which are hereby incorporated by reference). Similar type of alterations could be described which if applied to the murine, or other species immunoglobulin would reduce or eliminate these functions.
(168) An antibody molecule can be derivatized or linked to another functional molecule (e.g., another peptide or protein). As used herein, a “derivatized” antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin. Accordingly, the antibody molecules of the invention are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (e.g., a bispecific antibody or a diabody), a detectable agent, a cytotoxic agent, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).
(169) One type of derivatized antibody molecule is produced by crosslinking two or more antibodies (of the same type or of different types, e.g., to create bispecific antibodies). Suitable crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (e.g., m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (e.g., disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.
(170) Multispecific or Multifunctional Antibody Molecules
(171) Exemplary structures of multispecific and multifunctional molecules defined herein are described throughout. Exemplary structures are further described in: Weidle U et al. (2013) The Intriguing Options of Multispecific Antibody Formats for Treatment of Cancer. *Cancer Genomics* & *Proteomics* 10: 1-18 (2013); and Spiess C et al. (2015) Alternative molecular formats and therapeutic applications for bispecific antibodies. *Molecular Immunology* 67: 95-106; the full contents of each of which is incorporated by reference herein).
(172) In embodiments, multispecific antibody molecules can comprise more than one antigen-binding site, where different sites are specific for different antigens. In embodiments, multispecific antibody molecules can bind more than one (e.g., two or more) epitopes on the same antigen. In embodiments, multispecific antibody molecules comprise an antigen-binding site specific for a target cell (e.g., cancer cell) and a different antigen-binding site specific for an immune effector cell. In one embodiment, the multispecific antibody molecule is a bispecific antibody molecule. Bispecific antibody molecules can be classified into five different structural groups: (i) bispecific immunoglobulin G (BsIgG); (ii) IgG appended with an additional antigen-binding moiety; (iii) bispecific antibody fragments; (iv) bispecific fusion proteins; and (v) bispecific antibody conjugates.
(173) BsIgG is a format that is monovalent for each antigen. Exemplary BsIgG formats include but are not limited to crossMab, DAF (two-in-one), DAF (four-in-one), DutaMab, DT-IgG, knobs-in-holes common LC, knobs-in-holes assembly, charge pair, Fab-arm exchange, SEEDbody, triomab, LUZ-Y, Fcab, κλ-body, orthogonal Fab. See Spiess et al. Mol. Immunol. 67(2015):95-106. Exemplary BsIgGs include catumaxomab (Fresenius Biotech, Trion Pharma, Neopharm), which contains an anti-CD3 arm and an anti-EpCAM arm; and ertumaxomab (Neovii Biotech, Fresenius Biotech), which targets CD3 and HER2. In some embodiments, BsIgG comprises heavy chains that are engineered for heterodimerization. For example, heavy chains can be engineered for heterodimerization using a “knobs-into-holes” strategy, a SEED platform, a common heavy chain (e.g., in κλ-bodies), and use of heterodimeric Fc regions. See Spiess et al. Mol. Immunol. 67(2015):95-106. Strategies that have been used to avoid heavy chain pairing of homodimers in BsIgG include knobs-in-holes, duobody, azymetric, charge pair, HA-TF, SEEDbody, and differential protein A affinity. See Id. BsIgG can be produced by separate expression of the component antibodies in different host cells and subsequent purification/assembly into a BsIgG. BsIgG can also be produced by expression of the component antibodies in

a single host cell. BsIgG can be purified using affinity chromatography, e.g., using protein A and sequential pH elution.

(174) IgG appended with an additional antigen-binding moiety is another format of bispecific antibody molecules. For example, monospecific IgG can be engineered to have bispecificity by appending an additional antigen-binding unit onto the monospecific IgG, e.g., at the N- or C-terminus of either the heavy or light chain. Exemplary additional antigen-binding units include single domain antibodies (e.g., variable heavy chain or variable light chain), engineered protein scaffolds, and paired antibody variable domains (e.g., single chain variable fragments or variable fragments). See Id. Examples of appended IgG formats include dual variable domain IgG (DVD-Ig), IgG(H)-scFv, scFv-(H)IgG, IgG(L)-scFv, scFv-(L)IgG, IgG(L,H)-Fv, IgG(H)-V, V(H)-IgG, IgG(L)-V, V(L)-IgG, KIH IgG-scFab, 2scFv-IgG, IgG-2scFv, scFv4-Ig, zybody, and DVI-IgG (four-in-one). See Spiess et al. Mol. Immunol. 67(2015):95-106. An example of an IgG-scFv is MM-141 (Merrimack Pharmaceuticals), which binds IGF-1R and HER3. Examples of DVD-Ig include ABT-981 (AbbVie), which binds IL-1α and IL-1β; and ABT-122 (AbbVie), which binds TNF and IL-17A.

(175) Bispecific antibody fragments (BsAb) are a format of bispecific antibody molecules that lack some or all of the antibody constant domains. For example, some BsAb lack an Fc region. In embodiments, bispecific antibody fragments include heavy and light chain regions that are connected by a peptide linker that permits efficient expression of the BsAb in a single host cell. Exemplary bispecific antibody fragments include but are not limited to nanobody, nanobody-HAS, BiTE, Diabody, DART, TandAb, scDiabody, scDiabody-CH3, Diabody-CH3, triple body, miniantibody, minibody, TriBi minibody, scFv-CH3 KIH, Fab-scFv, scFv-CH-CL-scFv, F(ab′)2, F(ab′)2-scFv2, scFv-KIH, Fab-scFv-Fc, tetravalent HCAb, scDiabody-Fc, Diabody-Fc, tandem scFv-Fc, and intrabody. See Id. For example, the BiTE format comprises tandem scFvs, where the component scFvs bind to CD3 on T cells and a surface antigen on cancer cells

(176) Bispecific fusion proteins include antibody fragments linked to other proteins, e.g., to add additional specificity and/or functionality. An example of a bispecific fusion protein is an immTAC, which comprises an anti-CD3 scFv linked to an affinity-matured T-cell receptor that recognizes HLA-presented peptides. In embodiments, the dock-and-lock (DNL) method can be used to generate bispecific antibody molecules with higher valency. Also, fusions to albumin binding proteins or human serum albumin can be extend the serum half-life of antibody fragments. See Id.

(177) In embodiments, chemical conjugation, e.g., chemical conjugation of antibodies and/or antibody fragments, can be used to create BsAb molecules. See Id. An exemplary bispecific antibody conjugate includes the CovX-body format, in which a low molecular weight drug is conjugated site-specifically to a single reactive lysine in each Fab arm or an antibody or fragment thereof. In embodiments, the conjugation improves the serum half-life of the low molecular weight drug. An exemplary CovX-body is CVX-241 (NCT01004822), which comprises an antibody conjugated to two short peptides inhibiting either VEGF or Ang2. See Id.

(178) The antibody molecules can be produced by recombinant expression, e.g., of at least one or more component, in a host system. Exemplary host systems include eukaryotic cells (e.g., mammalian cells, e.g., CHO cells, or insect cells, e.g., SF9 or S2 cells) and prokaryotic cells (e.g., *E. coli*). Bispecific antibody molecules can be produced by separate expression of the components in different host cells and subsequent purification/assembly. Alternatively, the antibody molecules can be produced by expression of the components in a single host cell. Purification of bispecific antibody molecules can be performed by various methods such as affinity chromatography, e.g., using protein A and sequential pH elution. In other embodiments, affinity tags can be used for purification, e.g., histidine-containing tag, myc tag, or streptavidin tag.

(179) CDR-Grafted Scaffolds

(180) In embodiments, the antibody molecule is a CDR-grafted scaffold domain. In embodiments, the scaffold domain is based on a fibronectin domain, e.g., fibronectin type III domain. The overall fold of the fibronectin type III (Fn3) domain is closely related to that of the smallest functional antibody fragment, the variable domain of the antibody heavy chain. There are three loops at the end of Fn3; the positions of BC, DE and FG loops approximately correspond to those of CDR1, 2 and 3 of the VH domain of an antibody. Fn3 does not have disulfide bonds; and therefore Fn3 is stable under reducing conditions, unlike antibodies and their fragments (see, e.g., WO 98/56915; WO 01/64942; WO 00/34784). An Fn3 domain can be modified (e.g., using CDRs or hypervariable loops described herein) or varied, e.g., to select domains that bind to an antigen/marker/cell described herein.

(181) In embodiments, a scaffold domain, e.g., a folded domain, is based on an antibody, e.g., a “minibody” scaffold created by deleting three beta strands from a heavy chain variable domain of a monoclonal antibody (see, e.g., Tramontano et al., 1994, J Mol. Recognit. 7:9; and Martin et al., 1994, EMBO J. 13:5303-5309). The “minibody” can be used to present two hypervariable loops. In embodiments, the scaffold domain is a V-like

domain (see, e.g., Coia et al. WO 99/45110) or a domain derived from tendamistatin, which is a 74 residue, six-strand beta sheet sandwich held together by two disulfide bonds (see, e.g., McConnell and Hoess, 1995, J Mol. Biol. 250:460). For example, the loops of tendamistatin can be modified (e.g., using CDRs or hypervariable loops) or varied, e.g., to select domains that bind to a marker/antigen/cell described herein. Another exemplary scaffold domain is a beta-sandwich structure derived from the extracellular domain of CTLA-4 (see, e.g., WO 00/60070).

(182) Other exemplary scaffold domains include but are not limited to T-cell receptors; MHC proteins; extracellular domains (e.g., fibronectin Type III repeats, EGF repeats); protease inhibitors (e.g., Kunitz domains, ecotin, BPTI, and so forth); TPR repeats; trifoil structures; zinc finger domains; DNA-binding proteins; particularly monomeric DNA binding proteins; RNA binding proteins; enzymes, e.g., proteases (particularly inactivated proteases), RNase; chaperones, e.g., thioredoxin, and heat shock proteins; and intracellular signaling domains (such as SH2 and SH3 domains). See, e.g., US 20040009530 and U.S. Pat. No. 7,501,121, incorporated herein by reference.

(183) In embodiments, a scaffold domain is evaluated and chosen, e.g., by one or more of the following criteria: (1) amino acid sequence, (2) sequences of several homologous domains, (3) 3-dimensional structure, and/or (4) stability data over a range of pH, temperature, salinity, organic solvent, oxidant concentration. In embodiments, the scaffold domain is a small, stable protein domain, e.g., a protein of less than 100, 70, 50, 40 or 30 amino acids. The domain may include one or more disulfide bonds or may chelate a metal, e.g., zinc.

(184) Antibody-Based Fusions

(185) A variety of formats can be generated which contain additional binding entities attached to the N or C terminus of antibodies. These fusions with single chain or disulfide stabilized Fvs or Fabs result in the generation of tetravalent molecules with bivalent binding specificity for each antigen. Combinations of scFvs and scFabs with IgGs enable the production of molecules which can recognize three or more different antigens.

(186) Antibody-Fab Fusion

(187) Antibody-Fab fusions are bispecific antibodies comprising a traditional antibody to a first target and a Fab to a second target fused to the C terminus of the antibody heavy chain. Commonly the antibody and the Fab will have a common light chain. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. et al. (1997) *Nature Biotech* 15:159.

(188) Antibody-scFv Fusion

(189) Antibody-scFv Fusions are bispecific antibodies comprising a traditional antibody and a scFv of unique specificity fused to the C terminus of the antibody heavy chain. The scFv can be fused to the C terminus through the Heavy Chain of the scFv either directly or through a linker peptide. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. et al. (1997) *Nature Biotech* 15:159.

(190) Variable Domain Immunoglobulin DVD

(191) A related format is the dual variable domain immunoglobulin (DVD), which are composed of VH and VL domains of a second specificity place upon the N termini of the V domains by shorter linker sequences.

(192) Other exemplary multispecific antibody formats include, e.g., those described in the following US20160114057A1, US20130243775A1, US20140051833, US20130022601, US20150017187A1, US20120201746A1, US20150133638A1, US20130266568A1, US20160145340A1, WO2015127158A1, US20150203591A1, US20140322221A1, US20130303396A1, US20110293613, US20130017200A1, US20160102135A1, WO2015197598A2, WO2015197582A1, U.S. Pat. No. 9,359,437, US20150018529, WO2016115274A1, WO2016087416A1, US20080069820A1, U.S. Pat. Nos. 9,145,588B, 7,919,257, and US20150232560A1. Exemplary multispecific molecules utilizing a full antibody-Fab/scFab format include those described in the following, U.S. Pat. No. 9,382,323B2, US20140072581A1, US20140308285A1, US20130165638A1, US20130267686A1, US20140377269A1, U.S. Pat. No. 7,741,446B2, and WO1995009917A1. Exemplary multispecific molecules utilizing a domain exchange format include those described in the following, US20150315296A1, WO2016087650A1, US20160075785A1, WO2016016299A1, US20160130347A1, US20150166670, U.S. Pat. No. 8,703,132B2, US20100316645, U.S. Pat. No. 8,227,577B2, US20130078249.

(193) Fc-Containing Entities (Mini-Antibodies)

(194) Fc-containing entities, also known as mini-antibodies, can be generated by fusing scFv to the C-termini

of constant heavy region domain 3 (CH3-scFv) and/or to the hinge region (scFv-hinge-Fc) of an antibody with a different specificity. Trivalent entities can also be made which have disulfide stabilized variable domains (without peptide linker) fused to the C-terminus of CH3 domains of IgGs.

(195) Fc-Containing Multispecific Molecules

(196) In some embodiments, the multispecific molecules disclosed herein includes an immunoglobulin constant region (e.g., an Fc region). Exemplary Fc regions can be chosen from the heavy chain constant regions of IgG1, IgG2, IgG3 or IgG4; more particularly, the heavy chain constant region of human IgG1, IgG2, IgG3, or IgG4.

(197) In some embodiments, the immunoglobulin chain constant region (e.g., the Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.

(198) In other embodiments, an interface of a first and second immunoglobulin chain constant regions (e.g., a first and a second Fc region) is altered, e.g., mutated, to increase or decrease dimerization, e.g., relative to a non-engineered interface, e.g., a naturally-occurring interface. For example, dimerization of the immunoglobulin chain constant region (e.g., the Fc region) can be enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired protuberance-cavity ("knob-in-a hole"), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer to homomultimer forms, e.g., relative to a non-engineered interface.

(199) In some embodiments, the multispecific molecules include a paired amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1 For example, the immunoglobulin chain constant region (e.g., Fc region) can include a paired an amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), and T366W (e.g., corresponding to a protuberance or knob).

(200) In other embodiments, the multifunctional molecule includes a half-life extender, e.g., a human serum albumin or an antibody molecule to human serum albumin.

(201) Heterodimerized Antibody Molecules & Methods of Making

(202) Various methods of producing multispecific antibodies have been disclosed to address the problem of incorrect heavy chain pairing. Exemplary methods are described below. Exemplary multispecific antibody formats and methods of making said multispecific antibodies are also disclosed in e.g., Speiss et al. Molecular Immunology 67 (2015) 95-106; and Klein et al mAbs 4:6, 653-663; November/December 2012; the entire contents of each of which are incorporated by reference herein.

(203) Heterodimerized bispecific antibodies are based on the natural IgG structure, wherein the two binding arms recognize different antigens. IgG derived formats that enable defined monovalent (and simultaneous) antigen binding are generated by forced heavy chain heterodimerization, combined with technologies that minimize light chain mispairing (e.g., common light chain). Forced heavy chain heterodimerization can be obtained using, e.g., knob-in-hole OR strand exchange engineered domains (SEED).

(204) Knob-in-Hole

(205) Knob-in-Hole as described in U.S. Pat. Nos. 5,731,116, 7,476,724 and Ridgway, J. et al. (1996) *Prot. Engineering* 9(7): 617-621, broadly involves: (1) mutating the CH3 domain of one or both antibodies to promote heterodimerization; and (2) combining the mutated antibodies under conditions that promote heterodimerization. "Knobs" or "protuberances" are typically created by replacing a small amino acid in a parental antibody with a larger amino acid (e.g., T366Y or T366W); "Holes" or "cavities" are created by replacing a larger residue in a parental antibody with a smaller amino acid (e.g., Y407T, T366S, L368A and/or Y407V).

(206) For bispecific antibodies including an Fc domain, introduction of specific mutations into the constant region of the heavy chains to promote the correct heterodimerization of the Fc portion can be utilized. Several such techniques are reviewed in Klein et al. (mAbs (2012) 4:6, 1-11), the contents of which are incorporated herein by reference in their entirety. These techniques include the "knobs-into-holes" (KiH) approach which involves the introduction of a bulky residue into one of the CH3 domains of one of the antibody heavy chains. This bulky residue fits into a complementary "hole" in the other CH3 domain of the paired heavy chain so as to promote correct pairing of heavy chains (see e.g., U.S. Pat. No. 7,642,228).

(207) Exemplary KiH mutations include S354C, T366W in the "knob" heavy chain and Y349C, T366S, L368A, Y407V in the "hole" heavy chain. Other exemplary KiH mutations are provided in Table 1, with additional optional stabilizing Fc cysteine mutations.

(208) TABLE-US-00007 TABLE 1 Exemplary Fc KiH mutations and optional Cysteine mutations Position Knob Mutation Hole Mutation T366 T366W T366S L368 — L368A Y407 — Y407V Additional Cysteine Mutations to form a stabilizing disulfide bridge Position Knob CH3 Hole CH3 S354 S354C — Y349 — Y349C

(209) Other Fc mutations are provided by Igawa and Tsunoda who identified 3 negatively charged residues in the CH3 domain of one chain that pair with three positively charged residues in the CH3 domain of the other chain. These specific charged residue pairs are: E356-K439, E357-K370, D399-K409 and vice versa. By introducing at least two of the following three mutations in chain A: E356K, E357K and D399K, as well as K370E, K409D, K439E in chain B, alone or in combination with newly identified disulfide bridges, they were able to favor very efficient heterodimerization while suppressing homodimerization at the same time (Martens T et al. A novel one-armed antic-Met antibody inhibits glioblastoma growth in vivo. Clin Cancer Res 2006; 12:6144-52; PMID:17062691). Xencor defined 41 variant pairs based on combining structural calculations and sequence information that were subsequently screened for maximal heterodimerization, defining the combination of S364H, F405A (HA) on chain A and Y349T, T394F on chain B (TF) (Moore G L et al. A novel bispecific antibody format enables simultaneous bivalent and monovalent co-engagement of distinct target antigens. MAbs 2011; 3:546-57; PMID: 22123055).
(210) Other exemplary Fc mutations to promote heterodimerization of multispecific antibodies include those described in the following references, the contents of each of which is incorporated by reference herein, WO2016071377A1, US20140079689A1, US20160194389A1, US20160257763, WO2016071376A2, WO2015107026A1, WO2015107025A1, WO2015107015A1, US20150353636A1, US20140199294A1, U.S. Pat. No. 7,750,128B2, US20160229915A1, US20150344570A1, U.S. Pat. No. 8,003,774A1, US20150337049A1, US20150175707A1, US20140242075A1, US20130195849A1, US20120149876A1, US20140200331A1, U.S. Pat. No. 9,309,311B2, U.S. Pat. No. 8,586,713, US20140037621A1, US20130178605A1, US20140363426A1, US20140051835A1 and US20110054151A1.
(211) Stabilizing cysteine mutations have also been used in combination with KiH and other Fc heterodimerization promoting variants, see e.g., U.S. Pat. No. 7,183,076. Other exemplary cysteine modifications include, e.g., those disclosed in US20140348839A1, U.S. Pat. No. 7,855,275B2, and U.S. Pat. No. 9,000,130B2.
(212) Strand Exchange Engineered Domains (SEED)
(213) Heterodimeric Fc platform that support the design of bispecific and asymmetric fusion proteins by devising strand-exchange engineered domain (SEED) C(H)3 heterodimers are known. These derivatives of human IgG and IgA C(H)3 domains create complementary human SEED C(H)3 heterodimers that are composed of alternating segments of human IgA and IgG C(H)3 sequences. The resulting pair of SEED C(H)3 domains preferentially associates to form heterodimers when expressed in mammalian cells. SEEDbody (Sb) fusion proteins consist of [IgG1 hinge]-C(H)2-[SEED C(H)3], that may be genetically linked to one or more fusion partners (see e.g., Davis J H et al. SEEDbodies: fusion proteins based on strand exchange engineered domain (SEED) CH3 heterodimers in an Fc analogue platform for asymmetric binders or immunofusions and bispecific antibodies. Protein Eng Des Sel 2010; 23:195-202; PMID:20299542 and U.S. Pat. No. 8,871,912. The contents of each of which are incorporated by reference herein).
(214) Duobody
(215) “Duobody” technology to produce bispecific antibodies with correct heavy chain pairing are known. The DuoBody technology involves three basic steps to generate stable bispecific human IgG1 antibodies in a post-production exchange reaction. In a first step, two IgG1s, each containing single matched mutations in the third constant (CH3) domain, are produced separately using standard mammalian recombinant cell lines. Subsequently, these IgG1 antibodies are purified according to standard processes for recovery and purification. After production and purification (post-production), the two antibodies are recombined under tailored laboratory conditions resulting in a bispecific antibody product with a very high yield (typically >95%) (see e.g., Labrijn et al, PNAS 2013; 110(13):5145-5150 and Labrijn et al. Nature Protocols 2014; 9(10):2450-63, the contents of each of which are incorporated by reference herein).
(216) Electrostatic Interactions
(217) Methods of making multispecific antibodies using CH3 amino acid changes with charged amino acids such that homodimer formation is electrostatically unfavorable are disclosed. EP1870459 and WO 2009089004 describe other strategies for favoring heterodimer formation upon co-expression of different antibody domains in a host cell. In these methods, one or more residues that make up the heavy chain constant domain 3 (CH3), CH3-CH3 interfaces in both CH3 domains are replaced with a charged amino acid such that homodimer formation is electrostatically unfavorable and heterodimerization is electrostatically favorable. Additional methods of making multispecific molecules using electrostatic interactions are described in the following references, the contents of each of which is incorporated by reference herein, include US20100015133, U.S. Pat. No. 8,592,562B2, U.S. Pat. No. 9,200,060B2, US20140154254A1, and U.S. Pat. No. 9,358,286A1.
(218) Common Light Chain

(219) Light chain mispairing needs to be avoided to generate homogenous preparations of bispecific IgGs. One way to achieve this is through the use of the common light chain principle, i.e. combining two binders that share one light chain but still have separate specificities. An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable light chain to interact with each of the heteromeric variable heavy chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common light chain as disclosed in, e.g., U.S. Pat. No. 7,183,076B2, US20110177073A1, EP2847231A1, WO2016079081A1, and EP3055329A1, the contents of each of which is incorporated by reference herein.
(220) CrossMab
(221) Another option to reduce light chain mispairing is the CrossMab technology which avoids non-specific L chain mispairing by exchanging CH1 and CL domains in the Fab of one half of the bispecific antibody. Such crossover variants retain binding specificity and affinity, but make the two arms so different that L chain mispairing is prevented. The CrossMab technology (as reviewed in Klein et al. Supra) involves domain swapping between heavy and light chains so as to promote the formation of the correct pairings. Briefly, to construct a bispecific IgG-like CrossMab antibody that could bind to two antigens by using two distinct light chain-heavy chain pairs, a two-step modification process is applied. First, a dimerization interface is engineered into the C-terminus of each heavy chain using a heterodimerization approach, e.g., Knob-into-hole (KiH) technology, to ensure that only a heterodimer of two distinct heavy chains from one antibody (e.g., Antibody A) and a second antibody (e.g., Antibody B) is efficiently formed. Next, the constant heavy 1 (CH1) and constant light (CL) domains of one antibody are exchanged (Antibody A), keeping the variable heavy (VH) and variable light (VL) domains consistent. The exchange of the CH1 and CL domains ensured that the modified antibody (Antibody A) light chain would only efficiently dimerize with the modified antibody (antibody A) heavy chain, while the unmodified antibody (Antibody B) light chain would only efficiently dimerize with the unmodified antibody (Antibody B) heavy chain; and thus only the desired bispecific CrossMab would be efficiently formed (see e.g., Cain, C. SciBX 4(28); doi:10.1038/scibx.2011.783, the contents of which are incorporated by reference herein).
(222) Common Heavy Chain
(223) An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable heavy chain to interact with each of the heteromeric variable light chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common heavy chain are disclosed in, e.g., US20120184716, US20130317200, and US20160264685A1, the contents of each of which is incorporated by reference herein.
(224) Amino Acid Modifications
(225) Alternative compositions and methods of producing multispecific antibodies with correct light chain pairing include various amino acid modifications. For example, Zymeworks describes heterodimers with one or more amino acid modifications in the CH1 and/or CL domains, one or more amino acid modifications in the VH and/or VL domains, or a combination thereof, which are part of the interface between the light chain and heavy chain and create preferential pairing between each heavy chain and a desired light chain such that when the two heavy chains and two light chains of the heterodimer pair are co-expressed in a cell, the heavy chain of the first heterodimer preferentially pairs with one of the light chains rather than the other (see e.g., WO2015181805). Other exemplary methods are described in WO2016026943 (Argen-X), US20150211001, US20140072581A1, US20160039947A1, and US20150368352.
(226) Lambda/Kappa Formats
(227) Multispecific molecules (e.g., multispecific antibody molecules) that include the lambda light chain polypeptide and a kappa light chain polypeptides, can be used to allow for heterodimerization. Methods for generating bispecific antibody molecules comprising the lambda light chain polypeptide and a kappa light chain polypeptides are disclosed in PCT/US17/53053 filed on Sep. 22, 2017, incorporated herein by reference in its entirety.
(228) In embodiments, the multispecific molecules includes a multispecific antibody molecule, e.g., an antibody molecule comprising two binding specificities, e.g., a bispecific antibody molecule. The multispecific antibody molecule includes: a lambda light chain polypeptide 1 (LLCP1) specific for a first epitope; a heavy chain polypeptide 1 (HCP1) specific for the first epitope; a kappa light chain polypeptide 2 (KLCP2) specific for a second epitope; and a heavy chain polypeptide 2 (HCP2) specific for the second epitope.
(229) “Lambda light chain polypeptide 1 (LLCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises

all or a fragment of a CH1 region. In an embodiment, an LLCP1 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP1. LLCP1, together with its HCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope). As described elsewhere herein, LLCP1 has a higher affinity for HCP1 than for HCP2.

(230) "Kappa light chain polypeptide 2 (KLCP2)", as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP2. In an embodiments it comprises all or a fragment of a CH1 region. In an embodiment, a KLCP2 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP2. KLCP2, together with its HCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

(231) "Heavy chain polypeptide 1 (HCP1)", as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiments it comprises all or a fragment of a CH1 region. In an embodiment, it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an LLCP1, (ii) to complex preferentially, as described herein to LLCP1 as opposed to KLCP2; and (iii) to complex preferentially, as described herein, to an HCP2, as opposed to another molecule of HCP1. HCP1, together with its LLCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope).

(232) "Heavy chain polypeptide 2 (HCP2)", as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiments it comprises all or a fragment of a CH1 region. In an embodiments it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an KLCP2, (ii) to complex preferentially, as described herein to KLCP2 as opposed to LLCP1; and (iii) to complex preferentially, as described herein, to an HCP1, as opposed to another molecule of HCP2. HCP2, together with its KLCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

(233) In some embodiments of the multispecific antibody molecule disclosed herein: LLCP1 has a higher affinity for HCP1 than for HCP2; and/or KLCP2 has a higher affinity for HCP2 than for HCP1.

(234) In embodiments, the affinity of LLCP1 for HCP1 is sufficiently greater than its affinity for HCP2, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75, 80, 90, 95, 98, 99, 99.5, or 99.9% of the multispecific antibody molecule molecules have a LLCP1 complexed, or interfaced with, a HCP1.

(235) In some embodiments of the multispecific antibody molecule disclosed herein: the HCP1 has a greater affinity for HCP2, than for a second molecule of HCP1; and/or the HCP2 has a greater affinity for HCP1, than for a second molecule of HCP2.

(236) In embodiments, the affinity of HCP1 for HCP2 is sufficiently greater than its affinity for a second molecule of HCP1, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75%, 80, 90, 95, 98, 99 99.5 or 99.9% of the multispecific antibody molecule molecules have a HCP1 complexed, or interfaced with, a HCP2.

(237) In another aspect, disclosed herein is a method for making, or producing, a multispecific antibody molecule. The method includes: (i) providing a first heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both)); (ii) providing a second heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both)); (iii) providing a lambda chain polypeptide (e.g., a lambda light variable region (VLλ), a lambda light constant chain (VLλ), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH); and (iv) providing a kappa chain polypeptide (e.g., a lambda light variable region (VLκ), a lambda light constant chain (VLκ), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH), under conditions where (i)-(iv) associate.

(238) In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization.
(239) In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in a single cell, e.g., a single mammalian cell, e.g., a CHO cell. In embodiments, (i)-(iv) are expressed in the cell.
(240) In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in different cells, e.g., different mammalian cells, e.g., two or more CHO cell. In embodiments, (i)-(iv) are expressed in the cells.
(241) In one embodiment, the method further comprises purifying a cell-expressed antibody molecule, e.g., using a lambda-and/or-kappa-specific purification, e.g., affinity chromatography.
(242) In embodiments, the method further comprises evaluating the cell-expressed multispecific antibody molecule. For example, the purified cell-expressed multispecific antibody molecule can be analyzed by techniques known in the art, include mass spectrometry. In one embodiment, the purified cell-expressed antibody molecule is cleaved, e.g., digested with papain to yield the Fab moieties and evaluated using mass spectrometry.
(243) In embodiments, the method produces correctly paired kappa/lambda multispecific, e.g., bispecific, antibody molecules in a high yield, e.g., at least 75%, 80, 90, 95, 98, 99 99.5 or 99.9%.
(244) In other embodiments, the multispecific, e.g., a bispecific, antibody molecule that includes: (i) a first heavy chain polypeptide (HCP1) (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both)), e.g., wherein the HCP1 binds to a first epitope; (ii) a second heavy chain polypeptide (HCP2) (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both)), e.g., wherein the HCP2 binds to a second epitope; (iii) a lambda light chain polypeptide (LLCP1) (e.g., a lambda light variable region (VLl), a lambda light constant chain (VLl), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH), e.g., wherein the LLCP1 binds to a first epitope; and (iv) a kappa light chain polypeptide (KLCP2) (e.g., a lambda light variable region (VLk), a lambda light constant chain (VLk), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH), e.g., wherein the KLCP2 binds to a second epitope.
(245) In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization. In embodiments, the multispecific antibody molecule has a first binding specificity that includes a hybrid VLl-CLl heterodimerized to a first heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a knob modification) and a second binding specificity that includes a hybrid VLk-CLk heterodimerized to a second heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a hole modification).
(246) Linkers
(247) The multispecific or multifunctional molecule disclosed herein can further include a linker, e.g., a linker between one or more of: the antigen binding domain and the cytokine molecule, the antigen binding domain and the immune cell engager, the antigen binding domain and the stromal modifying moiety, the cytokine molecule and the immune cell engager, the cytokine molecule and the stromal modifying moiety, the immune cell engager and the stromal modifying moiety, the antigen binding domain and the immunoglobulin chain constant region, the cytokine molecule and the immunoglobulin chain constant region, the immune cell engager and the immunoglobulin chain constant region, or the stromal modifying moiety and the immunoglobulin chain constant region. In embodiments, the linker is chosen from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker, or a combination thereof.
(248) In one embodiment, the multispecific molecule can include one, two, three or four linkers, e.g., a peptide linker. In one embodiment, the peptide linker includes Gly and Ser. In some embodiments, the peptide linker is selected from GGGGS (SEQ ID NO: 42); GGGGSGGGGS (SEQ ID NO: 43); GGGGSGGGGSGGGGS (SEQ ID NO: 44); and DVPSGPGGGGGSGGGGS (SEQ ID NO: 45). In some embodiments, the peptide linker is a A(EAAAK)nA (SEQ ID NO: 6154) family of linkers (e.g., as described in Protein Eng. (2001) 14 (8): 529-532). These are stiff helical linkers with n ranging from 2-5. In some embodiments, the peptide linker is selected from AEAAAKEAAAKAAA (SEQ ID NO: 75); AEAAAKEAAAKEAAAKAAA (SEQ ID NO: 76); AEAAAKEAAAKEAAAKEAAAKAAA (SEQ ID NO: 77); and AEAAAKEAAAKEAAAKEAAAKEAAAKAAA(SEQ ID NO: 78).
(249) Targeting Moieties
(250) In one embodiment, the anti-NKp30 antibody molecule further comprises a second antigen binding moiety, e.g., tumor targeting moiety, that binds to a cancer antigen, e.g., a tumor antigen or a stromal antigen. In some embodiments, the cancer antigen is, e.g., a mammalian, e.g., a human, cancer antigen. In other

embodiments, the antibody molecule further comprises a second binding moiety that binds to an immune cell antigen, e.g., a mammalian, e.g., a human, immune cell antigen. In other embodiments, the antibody molecule further comprises a second binding moiety that binds to a viral antigen. For example, the antibody molecule binds specifically to an epitope, e.g., linear or conformational epitope, on the cancer antigen, the immune cell antigen.

(251) In some embodiments, the multispecific (e.g., bi-, tri-, tetra-specific) molecule, includes, e.g., is engineered to contain, one or more tumor specific targeting moieties that direct the molecule to a tumor cell. In certain embodiments, the multispecific molecules disclosed herein include a tumor-targeting moiety. The tumor targeting moiety can be chosen from an antibody molecule (e.g., an antigen binding domain as described herein), a receptor or a receptor fragment, or a ligand or a ligand fragment, or a combination thereof. In some embodiments, the tumor targeting moiety associates with, e.g., binds to, a tumor cell (e.g., a molecule, e.g., antigen, present on the surface of the tumor cell). In certain embodiments, the tumor targeting moiety targets, e.g., directs the multispecific molecules disclosed herein to a cancer (e.g., a cancer or tumor cells). In some embodiments, the cancer is chosen from a hematological cancer, a solid cancer, a metastatic cancer, or a combination thereof.

(252) In some embodiments, the multispecific molecule, e.g., the tumor-targeting moiety, binds to a solid tumor antigen or a stromal antigen. The solid tumor antigen or stromal antigen can be present on a solid tumor, or a metastatic lesion thereof. In some embodiments, the solid tumor is chosen from one or more of pancreatic (e.g., pancreatic adenocarcinoma), breast, colorectal, lung (e.g., small or non-small cell lung cancer), skin, ovarian, or liver cancer. In one embodiment, the solid tumor is a fibrotic or desmoplastic solid tumor. For example, the solid tumor antigen or stromal antigen can be present on a tumor, e.g., a tumor of a class typified by having one or more of: limited tumor perfusion, compressed blood vessels, or fibrotic tumor interstitium.

(253) In certain embodiments, the solid tumor antigen is chosen from one or more of: PDL1, CD47, mesothelin, ganglioside 2 (GD2), prostate stem cell antigen (PSCA), prostate specific membrane antigen (PMSA), prostate-specific antigen (PSA), carcinoembryonic antigen (CEA), Ron Kinase, c-Met, Immature laminin receptor, TAG-72, BING-4, Calcium-activated chloride channel 2, Cyclin-B1, 9D7, Ep-CAM, EphA3, Her2/neu, Telomerase, SAP-1, Survivin, NY-ESO-1/LAGE-1, PRAME, SSX-2, Melan-A/MART-1, Gp100/pmel17, Tyrosinase, TRP-1/-2, MC1R, β-catenin, BRCA1/2, CDK4, CML66, Fibronectin, p53, Ras, TGF-B receptor, AFP, ETA, MAGE, MUC-1, CA-125, BAGE, GAGE, NY-ESO-1, β-catenin, CDK4, CDC27, CD47, a actinin-4, TRP1/gp75, TRP2, gp100, Melan-A/MART1, gangliosides, WT1, EphA3, Epidermal growth factor receptor (EGFR), CD20, MART-2, MART-1, MUC1, MUC2, MUM1, MUM2, MUM3, NA88-1, NPM, OA1, OGT, RCC, RUI1, RUI2, SAGE, TRG, TRP1, TSTA, Folate receptor alpha, L1-CAM, CAIX, EGFRvIII, gpA33, GD3, GM2, VEGFR, Intergrins (Integrin alphaVbeta3, Integrin alpha5Beta1), Carbohydrates (Le), IGF1R, EPHA3, TRAILR1, TRAILR2, or RANKL. In some embodiments, the solid tumor antigen is chosen from: PDL1, Mesothelin, CD47, GD2, PMSA, PSCA, CEA, Ron Kinase, or c-Met. Exemplary amino acid and nucleotide sequences for tumor targeting moieties are disclosed in WO 2017/165464, see e.g., pages 102-108, 172-290, incorporated herein by reference.

(254) In some embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises a targeting moiety, e.g., a binding specificity, that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.

(255) In some embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises a targeting moiety, e.g., a binding specificity, that binds to an infected cell, e.g., a viral infected cell.

(256) T Cell Engagers

(257) In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more T cell engager that mediate binding to and/or activation of a T cell. Accordingly, in some embodiments, the T cell engager is selected from an antigen binding domain or ligand that binds to (e.g., and in some embodiments activates) one or more of CD3, TCRα, TCRβ, TCRγ, TCRζ, ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226. In other embodiments, the T cell engager is selected from an antigen binding domain or ligand that binds to and does not activate one or more of CD3, TCRα, TCRβ, TCRγ, TCRζ, ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226.

(258) Exemplary T cell engagers are disclosed in WO 2017/165464, incorporated herein by reference.

(259) Cytokine Molecules

(260) In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule)

further comprises one or more cytokine molecules, e.g., immunomodulatory (e.g., proinflammatory) cytokines and variants, e.g., functional variants, thereof. Accordingly, in some embodiments, the cytokine molecule is an interleukin or a variant, e.g., a functional variant thereof. In some embodiments the interleukin is a proinflammatory interleukin. In some embodiments the interleukin is chosen from interleukin-2 (IL-2), interleukin-12 (IL-12), interleukin-15 (IL-15), interleukin-18 (IL-18), interleukin-21 (IL-21), interleukin-7 (IL-7), or interferon gamma. In some embodiments, the cytokine molecule is a proinflammatory cytokine.

(261) In certain embodiments, the cytokine is a single chain cytokine. In certain embodiments, the cytokine is a multichain cytokine (e.g., the cytokine comprises 2 or more (e.g., 2) polypeptide chains. An exemplary multichain cytokine is IL-12.

(262) Examples of useful cytokines include, but are not limited to, GM-CSF, IL-1α, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-21, IFN-α, IFN-γ, MIP-1α, MIP-1β, TGF-β, TNF-α, and TNFβ. In one embodiment the cytokine of the multispecific or multifunctional polypeptide is a cytokine selected from the group of GM-CSF, IL-2, IL-7, IL-8, IL-10, IL-12, IL-15, IL-21, IFN-α, IFN-γ, MIP-1α, MIP-1β and TGF-β. In one embodiment the cytokine of the i the multispecific or multifunctional polypeptide is a cytokine selected from the group of IL-2, IL-7, IL-10, IL-12, IL-15, IFN-α, and IFN-γ. In certain embodiments the cytokine is mutated to remove N- and/or O-glycosylation sites. Elimination of glycosylation increases homogeneity of the product obtainable in recombinant production.

(263) In one embodiment, the cytokine of the multispecific or multifunctional polypeptide is IL-2. In a specific embodiment, the IL-2 cytokine can elicit one or more of the cellular responses selected from the group consisting of: proliferation in an activated T lymphocyte cell, differentiation in an activated T lymphocyte cell, cytotoxic T cell (CTL) activity, proliferation in an activated B cell, differentiation in an activated B cell, proliferation in a natural killer (NK) cell, differentiation in a NK cell, cytokine secretion by an activated T cell or an NK cell, and NK/lymphocyte activated killer (LAK) antitumor cytotoxicity. In another particular embodiment the IL-2 cytokine is a mutant IL-2 cytokine having reduced binding affinity to the .alpha.-subunit of the IL-2 receptor. Together with the beta- and gamma-subunits (also known as CD122 and CD132, respectively), the .alpha.-subunit (also known as CD25) forms the heterotrimeric high-affinity IL-2 receptor, while the dimeric receptor consisting only of the β- and γ-subunits is termed the intermediate-affinity IL-2 receptor. As described in PCT patent application number PCT/EP2012/051991, which is incorporated herein by reference in its entirety, a mutant IL-2 polypeptide with reduced binding to the .alpha.-subunit of the IL-2 receptor has a reduced ability to induce IL-2 signaling in regulatory T cells, induces less activation-induced cell death (AICD) in T cells, and has a reduced toxicity profile in vivo, compared to a wild-type IL-2 polypeptide. The use of such an cytokine with reduced toxicity is particularly advantageous in a multispecific or multifunctional polypeptide according to the invention, having a long serum half-life due to the presence of an Fc domain. In one embodiment, the mutant IL-2 cytokine of the multispecific or multifunctional polypeptide according to the invention comprises at least one amino acid mutation that reduces or abolishes the affinity of the mutant IL-2 cytokine to the .alpha.-subunit of the IL-2 receptor (CD25) but preserves the affinity of the mutant IL-2 cytokine to the intermediate-affinity IL-2 receptor (consisting of the β and γ subunits of the IL-2 receptor), compared to the non-mutated IL-2 cytokine. In one embodiment the one or more amino acid mutations are amino acid substitutions. In a specific embodiment, the mutant IL-2 cytokine comprises one, two or three amino acid substitutions at one, two or three position(s) selected from the positions corresponding to residue 42, 45, and 72 of human IL-2. In a more specific embodiment, the mutant IL-2 cytokine comprises three amino acid substitutions at the positions corresponding to residue 42, 45 and 72 of human IL-2. In an even more specific embodiment, the mutant IL-2 cytokine is human IL-2 comprising the amino acid substitutions F42A, Y45A and L72G. In one embodiment the mutant IL-2 cytokine additionally comprises an amino acid mutation at a position corresponding to position 3 of human IL-2, which eliminates the 0-glycosylation site of IL-2. Particularly, said additional amino acid mutation is an amino acid substitution replacing a threonine residue by an alanine residue. A particular mutant IL-2 cytokine useful in the invention comprises four amino acid substitutions at positions corresponding to residues 3, 42, 45 and 72 of human IL-2. Specific amino acid substitutions are T3A, F42A, Y45A and L72G. As demonstrated in PCT patent application number PCT/EP2012/051991 and in the appended Examples, said quadruple mutant IL-2 polypeptide (IL-2 qm) exhibits no detectable binding to CD25, reduced ability to induce apoptosis in T cells, reduced ability to induce IL-2 signaling in T.sub.reg cells, and a reduced toxicity profile in vivo. However, it retains ability to activate IL-2 signaling in effector cells, to induce proliferation of effector cells, and to generate IFN-γ as a secondary cytokine by NK cells.

(264) The IL-2 or mutant IL-2 cytokine according to any of the above embodiments may comprise additional mutations that provide further advantages such as increased expression or stability. For example, the cysteine at

position 125 may be replaced with a neutral amino acid such as alanine, to avoid the formation of disulfide-bridged IL-2 dimers. Thus, in certain embodiments the IL-2 or mutant IL-2 cytokine of the multispecific or multifunctional polypeptide according to the invention comprises an additional amino acid mutation at a position corresponding to residue 125 of human IL-2. In one embodiment said additional amino acid mutation is the amino acid substitution C125A.

(265) Exemplary cytokine molecules are disclosed in WO 2017/165464, see e.g., pages 108-118, 169-172, incorporated herein by reference.

(266) TGF-β Inhibitor

(267) In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more modulators of TGF-β (e.g., a TGF-β inhibitor). In some embodiments, the TGF-β inhibitor binds to and inhibits TGF-β, e.g., reduces the activity of TGF-β. In some embodiments, the TGF-β inhibitor inhibits (e.g., reduces the activity of) TGF-β1. In some embodiments, the TGF-β inhibitor inhibits (e.g., reduces the activity of) TGF-β2. In some embodiments, the TGF-β inhibitor inhibits (e.g., reduces the activity of) TGF-β3. In some embodiments, the TGF-β inhibitor inhibits (e.g., reduces the activity of) TGF-β1 and TGF-β3. In some embodiments, the TGF-β inhibitor inhibits (e.g., reduces the activity of) TGF-β1, TGF-β2, and TGF-β3.

(268) In some embodiments, the TGF-β inhibitor comprises a portion of a TGF-β receptor (e.g., an extracellular domain of a TGF-β receptor) that is capable of inhibiting (e.g., reducing the activity of) TGF-β, or functional fragment or variant thereof. In some embodiments, the TGF-β inhibitor comprises a TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof). In some embodiments, the TGF-β inhibitor comprises a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof). In some embodiments, the TGF-β inhibitor comprises a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof). In some embodiments, the TGF-β inhibitor comprises a TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof) and a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof). In some embodiments, the TGF-β inhibitor comprises a TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof) and a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof). In some embodiments, the TGF-β inhibitor comprises a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof) and a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof).

(269) Exemplary TGF-β receptor polypeptides that can be used as TGF-β inhibitors have been disclosed in U.S. Pat. Nos. 8,993,524, 9,676,863, 8,658,135, US20150056199, US20070184052, and WO2017037634, all of which are herein incorporated by reference in their entirety.

(270) In some embodiments, the TGF-β inhibitor comprises an extracellular domain of TGFBR1 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3095, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3096, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3097, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3104, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3105, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

(271) In some embodiments, the TGF-β inhibitor comprises an extracellular domain of TGFBR2 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3098, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3099, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3100, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3101, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical

thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3102, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3103, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

(272) In some embodiments, the TGF-β inhibitor comprises an extracellular domain of TGFBR3 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3106, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises an extracellular domain of SEQ ID NO: 3107, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-β inhibitor comprises the amino acid sequence of SEQ ID NO: 3108, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

(273) In some embodiments, the TGF-β inhibitor comprises no more than one TGF-β receptor extracellular domain. In some embodiments, the TGF-β inhibitor comprises two or more (e.g., two, three, four, five, or more) TGF-β receptor extracellular domains, linked together, e.g., via a linker.

(274) TABLE-US-00008 TABLE 4 Exemplary amino acid sequences of TGF-β polypeptides or TGF-β receptor polypeptides SEQ ID NO Description Amino acid sequence SEQ Immature MPPSGLRLLLLLLPLLWLLVLTPGRPAAGLSTCKTIDMELVKRKRIE ID NO: human TGF-β AIRGQILSKLRLASPPSQGEVPPGPLPEAVLALYNSTRDRVAGESAE 3092 1 (P01137-1) PEPEPEADYYAKEVTRVLMVETHNEIYDKFKQSTHSIYMFFNTSELR EAVPEPVLLSRAELRLLRLKLKVEQHVELYQKYSNNSWRYLSNRLLA PSDSPEWLSFDVTGVVRQWLSRGGEIEGFRLSAHCSCDSRDNTLQVD INGFTTGRRGDLATIHGMNRPFLLLMATPLERAQHLQSSRHRRALDT NYCFSSTEKNCCVRQLYIDFRKDLGWKWIHEPKGYHANFCLGPCPYI WSLDTQYSKVLALYNQHNPGASAAPCCVPQALEPLPIVYYVGRKPKV EQLSNMIVRSCKCS SEQ Human TGF-β LSTCKTIDMELVKRKRIEAIRGQILSKLRLASPPSQGEVPPGPLPEA ID NO: 1 (P01137-1) VLALYNSTRDRVAGESAEPEPEPEADYYAKEVTRVLMVETHNEIYDK 3117 FKQSTHSIYMFFNTSELREAVPEPVLLSRAELRLLRLKLKVEQHVEL YQKYSNNSWRYLSNRLLAPSDSPEWLSFDVTGVVRQWLSRGGEIEGF RLSAHCSCDSRDNTLQVDINGFTTGRRGDLATIHGMNRPFLLLMATP LERAQHLQSSRHRRALDTNYCFSSTEKNCCVRQLYIDFRKDLGWKWI HEPKGYHANFCLGPCPYIWSLDTQYSKVLALYNQHNPGASAAPCCVP QALEPLPIVYYVGRKPKVEQLSNMIVRSCKCS SEQ Immature MHYCVLSAFLILHLVTVALSLSTCSTLDMDQFMRKRIEAIRGQILSK ID NO: human TGF-β LKLTSPPEDYPEPEEVPPEVISIYNSTRDLLQEKASRRAAACERERS 3093 2 (P61812-1) DEEYYAKEVYKIDMPPFFPSENAIPPTFYRPYFRIVRFDVSAMEKNA SNLVKAEFRVFRLQNPKARVPEQRIELYQILKSKDLTSPTQRYIDSK VVKTRAEGEWLSFDVTDAVHEWLHHKDRNLGFKISLHCPCCTFVPSN NYIIPNKSEELEARFAGIDGTSTYTSGDQKTIKSTRKKNSGKTPHLL LMLLPSYRLESQQTNRRKKRALDAAYCFRNVQDNCCLRPLYIDFKRD LGWKWIHEPKGYNANFCAGACPYLWSSDTQHSRVLSLYNTINPEASA SPCCVSQDLEPLTILYYIGKTPKIEQLSNMIVKSCKCS SEQ Human TGF-β LSTCSTLDMDQFMRKRIEAIRGQILSKLKLTSPPEDYPEPEEVPPEV ID NO: 2 (P61812-1) ISIYNSTRDLLQEKASRRAAACERERSDEEYYAKEVYKIDMPPFFPS 3118 ENAIPPTFYRPYFRIVRFDVSAMEKNASNLVKAEFRVFRLQNPKARV PEQRIELYQILKSKDLTSPTQRYIDSKVVKTRAEGEWLSFDVTDAVH EWLHHKDRNLGFKISLHCPCCTFVPSNNYIIPNKSEELEARFAGIDG TSTYTSGDQKTIKSTRKKNSGKTPHLLLMLLPSYRLESQQTNRRKKR ALDAAYCFRNVQDNCCLRPLYIDFKRDLGWKWIHEPKGYNANFCAGA CPYLWSSDTQHSRVLSLYNTINPEASASPCCVSQDLEPLTILYYIGK TPKIEQLSNMIVKSCKCS SEQ Immature MKMHLQRALVVLALLNFATVSLSLSTCTTLDFGHIKKKRVEAIRGQI ID NO: human TGF-β LSKLRLTSPPEPTVMTHVPYQVLALYNSTRELLEEMHGEREEGCTQE 3094 3 (P10600-1) NTESEYYAKEIHKFDMIQGLAEHNELAVCPKGITSKVFRFNVSSVEK NRTNLFRAEFRVLRVPNPSSKRNEQRIELFQILRPDEHIAKQRYIGG

KNLPTRGTAEWLSFDVTDTVREWLLRRESNLGLEISIHCPCHTFQPN
GDILENIHEVMEIKFKGVDNEDDHGRGDLGRLKKQKDHHNPHLILMM
IPPHRLDNPGQGGQRKKRALDTNYCFRNLEENCCVRPLYIDFRQDLG
WKWVHEPKGYYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASASP
CCVPQDLEPLTILYYVGRTPKVEQLSNMVVKSCKCS SEQ Human TGF-β
LSTCTTLDFGHIKKKRVEAIRGQILSKLRLTSPPEPTVMTHVPYQVL ID NO: 3 (P10600-1)
ALYNSTRELLEEMHGEREEGCTQENTESEYYAKEIHKFDMIQGLAEH 3119
NELAVCPKGITSKVFRFNVSSVEKNRTNLFRAEFRVLRVPNPSSKRN
EQRIELFQILRPDEHIAKQRYIGGKNLPTRGTAEWLSFDVTDTVREW
LLRRESNLGLEISIHCPCHTFQPNGDILENIHEVMEIKFKGVDNEDD
HGRGDLGRLKKQKDFIHNPHLILMMIPPHRLDNPGQGGQRKKRALDT
NYCFRNLEENCCVRPLYIDFRQDLGWKWVHEPKGYYANFCSGPCPYL
RSADTTHSTVLGLYNTLNPEASASPCCVPQDLEPLTILYYVGRTPKV EQLSNMVVKSCKCS SEQ
Immature MEAAVAAPRPRLLLLVLAAAAAAAAALLPGATALQCFCHLCTKDNFT ID NO: human
CVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGS 3095 TGFBR1
VTTTYCCNQDHCNKIELPTTVKSSPGLGPVELAAVIAGPVCFVCISL isoform 1
MLMVYICHNRTVIFIHRVPNEEDPSLDRPFISEGTTLKDLIYDMTTS (P36897-1)
GSGSGLPLLVQRTIARTIVLQESIGKGRFGEVWRGKWRGEEVAVKIF
SSREERSWFREAEIYQTVMLRHENILGFIAADNKDNGTWTQLWLVSD
YHEHGSLFDYLNRYTVTVEGMIKLALSTASGLAHLHMEIVGTQGKPA
IAHRDLKSKNILVKKNGTCCIADLGLAVRHDSATDTIDIAPNHRVGT
KRYMAPEVLDDSINMKHFESFKRADIYAMGLVFWEIARRCSIGGIHE
DYQLPYYDLVPSDPSVEEMRKVVCEQKLRPNIPNRWQSCEALRVMAK
IMRECWYANGAARLTALRIKKTLSQLSQQEGIKM SEQ Human
LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR ID NO: TGFBR1
DRPFVCAPSSKTGSVTTTYCCNQDHCNKIELPTTVKSSPGLGPVELA 3120 isoform 1
AVIAGPVCFVCISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFISEG (P36897-1)
TTLKDLIYDMTTSGSGSGLPLLVQRTIARTIVLQESIGKGRFGEVWR
GKWRGEEVAVKIFSSREERSWFREAEIYQTVMLRHENILGFIAADNK
DNGTWTQLWLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTASGLAH
LHMEIVGTQGKPAIAHRDLKSKNILVKKNGTCCIADLGLAVRHDSAT
DTIDIAPNHRVGTKRYMAPEVLDDSINMKHFESFKRADIYAMGLVFW
EIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLRPNIPN
RWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQQEGIKM SEQ Immature
MEAAVAAPRPRLLLLVLAAAAAAAAALLPGATALQCFCHLCTKDNFT ID NO: human
CVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGS 3096 TGFBR1
VTTTYCCNQDHCNKIELPTTGPFSVKSSPGLGPVELAAVIAGPVCFV isoform 2
CISLMLMVYICHNRTVIFIHRVPNEEDPSLDRPFISEGTTLKDLIYD (P36897-2)
MTTSGSGSGLPLLVQRTIARTIVLQESIGKGRFGEVWRGKWRGEEVA
VKIFSSREERSWFREAEIYQTVMLRHENILGFIAADNKDNGTWTQLW
LVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTASGLAHLHMEIVGTQ
GKPAIAHRDLKSKNILVKKNGTCCIADLGLAVRHDSATDTIDIAPNH
RVGTKRYMAPEVLDDSINMKHFESFKRADIYAMGLVFWEIARRCSIG
GIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLRPNIPNRWQSCEALR
VMAKIMRECWYANGAARLTALRIKKTLSQLSQQEGIKM SEQ Human
LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR ID NO: TGFBR1
DRPFVCAPSSKTGSVTTTYCCNQDHCNKIELPTTGPFSVKSSPGLGP 3121 isoform 2
VELAAVIAGPVCFVCISLMLMVYICHNRTVIFIHRVPNEEDPSLDRP (P36897-2)
FISEGTTLKDLIYDMTTSGSGSGLPLLVQRTIARTIVLQESIGKGRF
GEVWRGKWRGEEVAVKIFSSREERSWFREAEIYQTVMLRHENILGFI
AADNKDNGTWTQLWLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTA
SGLAHLHMEIVGTQGKPAIAHRDLKSKNILVKKNGTCCIADLGLAVR
HDSATDTIDIAPNHRVGTKRYMAPEVLDDSINMKHFESFKRADIYAM
GLVFWEIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLR
PNIPNRWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQQ EGIKM SEQ Immature
MEAAVAAPRPRLLLLVLAAAAAAAAALLPGATALQCFCHLCTKDNFT ID NO: human

CVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGS 3097 TGFBR1
VTTTYCCNQDHCNKIELPTTGLPLLVQRTIARTIVLQESIGKGRFGE isoform 3
VWRGKWRGEEVAVKIFSSREERSWFREAEIYQTVMLRHENILGFIAA (P36897-3)
DNKDNGTWTQLWLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTASG
LAHLHMEIVGTQGKPAIAHRDLKSKNILVKKNGTCCIADLGLAVRHD
SATDTIDIAPNHRVGTKRYMAPEVLDDSINMKHFESFKRADIYAMGL
VFWEIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLRPN
IPNRWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQQEG IKM SEQ Human
LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR ID NO: TGFBR1
DRPFVCAPSSKTGSVTTTYCCNQDHCNKIELPTTGLPLLVQRTIART 3122 isoform 3
IVLQESIGKGRFGEVWRGKWRGEEVAVKIFSSREERSWFREAEIYQT (P36897-3)
VMLRHENILGFIAADNKDNGTWTQLWLVSDYHEHGSLFDYLNRYTVT
VEGMIKLALSTASGLAHLHMEIVGTQGKPAIAHRDLKSKNILVKKNG
TCCIADLGLAVRHDSATDTIDIAPNHRVGTKRYMAPEVLDDSINMKH
FESFKRADIYAMGLVFWEIARRCSIGGIHEDYQLPYYDLVPSDPSVE
EMRKVVCEQKLRPNIPNRWQSCEALRVMAKIMRECWYANGAARLTAL RIKKTLSQLSQQEGIKM
SEQ Human LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR ID NO: TGFBR1
DRPFVCAPSSKTGSVTTTYCCNQDHCNKIELPTTVKSSPGLGPVEL 3104 fragment 1 SEQ Human
ALQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIP ID NO: TGFBR1
RDRPFVCAPSSKTGSVTTTYCCNQDHCNKIEL 3105 fragment 2 SEQ Immature
MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKF ID NO: human
PQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDEN 3098 TGFBR2
ITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSD isoform B
ECNDNIIFSEEYNTSNPDLLLVIFQVTGISLLPPLGVAISVIIIFYC (short
YRVNRQQKLSSTWETGKTRKLMEFSEHCAIILEDDRSDISSTCANNI isoform)
NHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYE (P37173-1)
EYASWKTEKDIFSDINLKHENILQFLTAEERKTELGKQYWLITAFHA
KGNLQEYLTRHVISWEDLRKLGSSLARGIAHLHSDHTPCGRPKMPIV
HRDLKSSNILVKNDLTCCLCDFGLSLRLDPTLSVDDLANSGQVGTAR
YMAPEVLESRMNLENVESFKQTDVYSMALVLWEMTSRCNAVGEVKDY
EPPFGSKVREHPCVESMKDNVLRDRGRPEIPSFWLNHQGIQMVCETL
TECWDHDPEARLTAQCVAERFSELEHLDRLSGRSCSEEKIPEDGSLN TTK SEQ Human
TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS ID NO: TGFBR2
NCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDA 3123 isoform B
ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLV (short
IFQVTGISLLPPLGVAISVIIIFYCYRVNRQQKLSSTWETGKTRKLM isoform)
EFSEHCAIILEDDRSDISSTCANNINHNTELLPIELDTLVGKGRFAE (P37173-1)
VYKAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENI
LQFLTAEERKTELGKQYWLITAFHAKGNLQEYLTRHVISWEDLRKLG
SSLARGIAHLHSDHTPCGRPKMPIVHRDLKSSNILVKNDLTCCLCDF
GLSLRLDPTLSVDDLANSGQVGTARYMAPEVLESRMNLENVESFKQT
DVYSMALVLWEMTSRCNAVGEVKDYEPPFGSKVREHPCVESMKDNVL
RDRGRPEIPSFWLNHQGIQMVCETLTECWDHDPEARLTAQCVAERFS
ELEHLDRLSGRSCSEEKIPEDGSLNTTK SEQ Immature
MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSDVEMEAQKDEIICPSC ID NO: human
NRTAHPLRHINNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS 3099 TGFBR2
NCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDA isoform A
ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLV (long isoform)
IFQVTGISLLPPLGVAISVIIIFYCYRVNRQQKLSSTWETGKTRKLM (P37173-2)
EFSEHCAIILEDDRSDISSTCANNINHNTELLPIELDTLVGKGRFAE
VYKAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENI
LQFLTAEERKTELGKQYWLITAFHAKGNLQEYLTRHVISWEDLRKLG
SSLARGIAHLHSDHTPCGRPKMPIVHRDLKSSNILVKNDLTCCLCDF
GLSLRLDPTLSVDDLANSGQVGTARYMAPEVLESRMNLENVESFKQT
DVYSMALVLWEMTSRCNAVGEVKDYEPPFGSKVREHPCVESMKDNVL
RDRGRPEIPSFWLNHQGIQMVCETLTECWDHDPEARLTAQCVAERFS

ELEHLDRLSGRSCSEEKIPEDGSLNTTK SEQ Human
TIPPHVQKSDVEMEAQKDEIICPSCNRTAHPLRHINNDMIVTDNNGA ID NO: TGFBR2
VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKN 3124 isoform A
DENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSC (long isoform)
SSDECNDNIIFSEEYNTSNPDLLLVIFQVTGISLLPPLGVAISVIII (P37173-2)
FYCYRVNRQQKLSSTWETGKTRKLMEFSEHCAIILEDDRSDISSTCA
NNININHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIF
PYEEYASWKTEKDIFSDINLKHENILQFLTAEERKTELGKQYWLITA
FHAKGNLQEYLTRHVISWEDLRKLGSSLARGIAHLHSDHTPCGRPKM
PIVHRDLKSSNILVKNDLTCCLCDFGLSLRLDPTLSVDDLANSGQVG
TARYMAPEVLESRMNLENVESFKQTDVYSMALVLWEMTSRCNAVGEV
KDYEPPFGSKVREHPCVESMKDNVLRDRGRPEIPSFWLNHQGIQMVC
ETLTECWDHDPEARLTAQCVAERFSELEHLDRLSGRSCSEEKIPEDG SLNTTK SEQ Human
TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS ID NO: TGFBR2
NCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDA 3100 fragment 1
ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPD (ECD of human TGFBR2 isoform B)
SEQ Human IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSN ID NO: TGFBR2
CSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAA 3101 fragment 2
SPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPD SEQ Human
TIPPHVQKSDVEMEAQKDEIICPSCNRTAHPLRHINNDMIVTDNNGA ID NO: TGFBR2
VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKN 3102 fragment 3
DENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSC (ECD of
SSDECNDNIIFSEEYNTSNPD human TGFBR2 isoform A) SEQ Human
QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENI ID NO: TGFBR2
TLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDE 3103 fragment 4 CNDNIIF SEQ
Immature MTSHYVIAIFALMSSCLATAGPEPGALCELSPVSASHPVQALMESFT ID NO: human
VLSGCASRGTTGLPQEVHVLNLRTAGQGPGQLQREVTLHLNPISSV 3106 TGFBR3
HIHHKSVVFLLNSPHPLVWHLKTERLATGVSRLFLVSEGSVVQFSSA isoform 1
NFSLTAETEERNFPHGNEHLLNWARKEYGAVTSFTELKIARNIYIKV (Q03167-1)
GEDQVFPPKCNIGKNFLSLNYLAEYLQPKAAEGCVMSSQPQNEEVHI
IELITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLILILKCKKSVNW
VIKSFDVKGSLKIIAPNSIGFGKESERSMTMTKSIRDDIPSTQGNLV
KWALDNGYSPITSYTMAPVANRFHLRLENNAEEMGDEEVHTIPPELR
ILLDPGALPALQNPPIRGGEGQNGGLPFPFPDISRRVWNEEGEDGLP
RPKDPVIPSIQLFPGLREPEEVQGSVDIALSVKCDNEKMIVAVEKDS
FQASGYSGMDVTLLDPTCKAKMNGTHFVLESPLNGCGTRPRWSALDG
VVYYNSIVIQVPALGDSSGWPDGYEDLESGDNGFPGDMDEGDASLFT
RPEIVVFNCSLQQVRNPSSFQEQPHGNITFNMELYNTDLFLVPSQGV
FSVPENGHVYVEVSVTKAEQELGFAIQTCFISPYSNPDRMSHYTIIE
NICPKDESVKFYSPKRVHFPIPQADMDKKRFSFVFKPVFNTSLLFLQ
CELTLCTKMEKHPQKLPKCVPPDEACTSLDASIIWAMMQNKKTFTKP
LAVIHHEAESKEKGPSMKEPNPISPPIFHGLDTLTVMGIAFAAFVIG
ALLTGALWYIYSHTGETAGRQQVPTSPPASENSSAAHSIGSTQSTPC SSSSTA SEQ Human
GPEPGALCELSPVSASHPVQALMESFTVLSGCASRGTTGLPQEVHVL ID NO: TGFBR3
NLRTAGQGPGQLQREVTLHLNPISSVHIFIHKSVVFLLNSPHPLVWH 3125 isoform 1
LKTERLATGVSRLFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHL (Q03167-1)
LNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLN
YLAEYLQPKAAEGCVMSSQPQNEEVHIIELITPNSNPYSAFQVDITI
DIRPSQEDLEVVKNLILILKCKKSVNWVIKSFDVKGSLKIIAPNSIG
FGKESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYTMAPVA
NRFHLRLENNAEEMGDEEVHTIPPELRILLDPGALPALQNPPIRGGE
GQNGGLPFPFPDISRRVWNEEGEDGLPRPKDPVIPSIQLFPGLREPE
EVQGSVDIALSVKCDNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKA
KMNGTHFVLESPLNGCGTRPRWSALDGVVYYNSIVIQVPALGDSSGW
PDGYEDLESGDNGFPGDMDEGDASLFTRPEIVVFNCSLQQVRNPSSF
QEQPHGNITFNMELYNTDLFLVPSQGVFSVPENGHVYVEVSVTKAEQ

ELGFAIQTCFISPYSNPDRMSHYTIIENICPKDESVKFYSPKRVHFP
IPQADMDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHPQKLPKCV
PPDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMKEP
NPISPPIFHGLDTLTVMGIAFAAFVIGALLTGALWYIYSHTGETAGR
QQVPTSPPASENSSAAHSIGSTQSTPCSSSSTA SEQ Immature
MTSHYVIAIFALMSSCLATAGPEPGALCELSPVSASHPVQALMESFT ID NO: human
VLSGCASRGTTGLPQEVHVLNLRTAGQGPGQLQREVTLHLNPISSVH 3107 TGFBR3
IHHKSVVFLLNSPHPLVWHLKTERLATGVSRLFLVSEGSVVQFSSAN isoform 2
FSLTAETEERNFPHGNEHLLNWARKEYGAVTSFTELKIARNIYIKVG (Q03167-2)
EDQVFPPKCNIGKNFLSLNYLAEYLQPKAAEGCVMSSQPQNEEVHII
ELITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLILILKCKKSVNWV
IKSFDVKGSLKIIAPNSIGFGKESERSMTMTKSIRDDIPSTQGNLVK
WALDNGYSPITSYTMAPVANRFHLRLENNEEMGDEEVHTIPPELRIL
LDPGALPALQNPPIRGGEGQNGGLPFPFPDISRRVWNEEGEDGLPRP
KDPVIPSIQLFPGLREPEEVQGSVDIALSVKCDNEKMIVAVEKDSFQ
ASGYSGMDVTLLDPTCKAKMNGTHFVLESPLNGCGTRPRWSALDGVV
YYNSIVIQVPALGDSSGWPDGYEDLESGDNGFPGDMDEGDASLFTRP
EIVVFNCSLQQVRNPSSFQEQPHGNITFNMELYNTDLFLVPSQGVFS
VPENGHVYVEVSVTKAEQELGFAIQTCFISPYSNPDRMSHYTIIENI
CPKDESVKFYSPKRVHFPIPQADMDKKRFSFVFKPVFNTSLLFLQCE
LTLCTKMEKHPQKLPKCVPPDEACTSLDASIIWAMMQNKKTFTKPLA
VIHHEAESKEKGPSMKEPNPISPPIFHGLDTLTVMGIAFAAFVIGAL
LTGALWYIYSHTGETAGRQQVPTSPPASENSSAAHSIGSTQSTPCSS SSTA SEQ Human
GPEPGALCELSPVSASHPVQALMESFTVLSGCASRGTTGLPQEVHVL ID NO: TGFBR3
NLRTAGQGPGQLQREVTLHLNPISSVHIFIHKSVVFLLNSPHPLVWH 3126 isoform 2
LKTERLATGVSRLFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHL (Q03167-2)
LNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLN
YLAEYLQPKAAEGCVMSSQPQNEEVHIIELITPNSNPYSAFQVDITI
DIRPSQEDLEVVKNLILILKCKKSVNWVIKSFDVKGSLKIIAPNSIG
FGKESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYTMAPVA
NRFHLRLENNEEMGDEEVHTIPPELRILLDPGALPALQNPPIRGGEG
QNGGLPFPFPDISRRVWNEEGEDGLPRPKDPVIPSIQLFPGLREPEE
VQGSVDIALSVKCDNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKAK
MNGTHFVLESPLNGCGTRPRWSALDGVVYYNSIVIQVPALGDSSGWP
DGYEDLESGDNGFPGDMDEGDASLFTRPEIVVFNCSLQQVRNPSSFQ
EQPHGNITFNMELYNTDLFLVPSQGVFSVPENGHVYVEVSVTKAEQE
LGFAIQTCFISPYSNPDRMSHYTIIENICPKDESVKFYSPKRVHFPI
PQADMDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHPQKLPKCVP
PDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMKEPN
PISPPIFHGLDTLTVMGIAFAAFVIGALLTGALWYIYSHTGETAGRQ
QVPTSPPASENSSAAHSIGSTQSTPCSSSSTA SEQ Human
GPEPGALCELSPVSASHPVQALMESFTVLSGCASRGTTGLPQEVHVL ID NO: TGFBR3
NLRTAGQGPGQLQREVTLHLNPISSVHIFIHKSVVFLLNSPHPLVWH 3108 fragment 1
LKTERLATGVSRLFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHL
LNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLN
YLAEYLQPKAAEGCVMSSQPQNEEVHIIELITPNSNPYSAFQVDITI
DIRPSQEDLEVVKNLILILKCKKSVNWVIKSFDVKGSLKIIAPNSIG
FGKESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYTMAPVA
NRFHLRLENNAEEMGDEEVHTIPPELRILLDPGALPALQNPPIRGGE
GQNGGLPFPFPDISRRVWNEEGEDGLPRPKDPVIPSIQLFPGLREPE
EVQGSVDIALSVKCDNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKA
KMNGTHFVLESPLNGCGTRPRWSALDGVVYYNSIVIQVPALGDSSGW
PDGYEDLESGDNGFPGDMDEGDASLFTRPEIVVFNCSLQQVRNPSSF
QEQPHGNITFNMELYNTDLFLVPSQGVFSVPENGHVYVEVSVTKAEQ
ELGFAIQTCFISPYSNPDRMSHYTIIENICPKDESVKFYSPKRVHFP
IPQADMDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHPQKLPKCV

PPDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMKEP NPISPPIFHGLDTLTV SEQ
hCH1-hFc_Hole- ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT ID NO: 3x4GS-
TGFbR2 SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV 3192
DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLP
PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
XGGGGSGGGGSGGGGSIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFC
DVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVC
HDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNII FSEEYNTSNPD, where in
X is K or absent SEQ hCH1-hFc_Knob-
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT ID NO: 3x4GS-TGFbR2
SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV 3193
DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
XGGGGSGGGGSGGGGSIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFC
DVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVC
HDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNII FSEEYNTSNPD, where in
X is K or absent SEQ hFc_Hole-
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS ID NO: 3x4GS-TGFbR2
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL 3194
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPSREEMTKN
QVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVS
KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGXGGGGSGGG
GSGGGGSIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDN
QKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHD
FILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSN PD, where in X is K or
absent SEQ hFc_Knob- DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS ID NO:
3x4GS-TGFbR2 HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL 3195
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREEMTKN
QVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS
KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGXGGGGSGGG
GSGGGGSIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDN
QKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHD
FILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSN PD, where in X is K or
absent SEQ TGFbR2-3x4GS- IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSN
ID NO: hCH1-hFc_Hole CSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAA 3196
SPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGGS
GGGGSGGGGSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICN
VNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGX, where
in X is K or absent SEQ TGFbR2-3x4GS-
IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSN ID NO: hCH1-hFc_Knob
CSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAA 3197
SPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGGS
GGGGSGGGGSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICN
VNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK

DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGX, where in X is K or absent SEQ TGFbR2-3x4G5-
IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSN ID NO: hCLIg_v1
CSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAA 3198
SPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGGS
GGGGSGGGGSGQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGA
VTVAWKADGSPVKAGVETTKPSKQSNNKYAASSYLSLTPEQWKSHRS
YSCQVTHEGSTVEKTVAPTECS SEQ TGFβR2-3x4GS-
IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSN ID NO: hCLIg_vk
CSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAA 3199
SPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGGS
GGGGSGGGGSRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKFIK
VYACEVTHQGLSSPVTKSFNRGEC

Stromal Modifying Moieties

(275) In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more stromal modifying moieties. Stromal modifying moieties described herein include moieties (e.g., proteins, e.g., enzymes) capable of degrading a component of the stroma, e.g., an ECM component, e.g., a glycosaminoglycan, e.g., hyaluronan (also known as hyaluronic acid or HA), chondroitin sulfate, chondroitin, dermatan sulfate, heparin sulfate, heparin, entactin, tenascin, aggrecan and keratin sulfate; or an extracellular protein, e.g., collagen, laminin, elastin, fibrinogen, fibronectin, and vitronectin.

(276) In some embodiments, the stromal modifying moiety is an enzyme. For example, the stromal modifying moiety can include, but is not limited to a hyaluronidase, a collagenase, a chondroitinase, a matrix metalloproteinase (e.g., macrophage metalloelastase).

(277) Exemplary amino acid and nucleotide sequences for stromal modifying moieties are disclosed in WO 2017/165464, see e.g., pages 131-136, 188-193, incorporated herein by reference.

(278) Nucleic Acids

(279) Nucleic acids encoding the aforementioned antibody molecules, e.g., multispecific or multifunctional molecules. are also disclosed.

(280) In certain embodiments, the invention features nucleic acids comprising nucleotide sequences that encode heavy and light chain variable regions and CDRs or hypervariable loops of the antibody molecules, as described herein. For example, the invention features a first and second nucleic acid encoding heavy and light chain variable regions, respectively, of an antibody molecule chosen from one or more of the antibody molecules disclosed herein. The nucleic acid can comprise a nucleotide sequence as set forth in the tables herein, or a sequence substantially identical thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in the tables herein.

(281) In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a heavy chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, e.g., conserved substitutions). In other embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a light chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, e.g., conserved substitutions). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs or hypervariable loops from heavy and light chain variable regions having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, e.g., conserved substitutions).

(282) In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a heavy chain variable region having the nucleotide sequence as set forth in the tables herein, a sequence substantially homologous thereto (e.g., a sequence at least about 85%,

90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a light chain variable region having the nucleotide sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs or hypervariable loops from heavy and light chain variable regions having the nucleotide sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein).

(283) In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding a cytokine molecule, an immune cell engager, or a stromal modifying moiety disclosed herein.

(284) In another aspect, the application features host cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell, as described in more detail hereinbelow.

(285) Vectors

(286) Further provided herein are vectors comprising the nucleotide sequences encoding a multispecific or multifunctional molecule described herein. In one embodiment, the vectors comprise nucleotides encoding a multispecific or multifunctional molecule described herein. In one embodiment, the vectors comprise the nucleotide sequences described herein. The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

(287) Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

(288) Additionally, cells which have stably integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow for the selection of transfected host cells. The marker may provide, for example, prototropy to an auxotrophic host, biocide resistance (e.g., antibiotics), or resistance to heavy metals such as copper, or the like. The selectable marker gene can be either directly linked to the DNA sequences to be expressed, or introduced into the same cell by cotransformation. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcriptional promoters, enhancers, and termination signals.

(289) Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity

(290) Methods and conditions for culturing the resulting transfected cells and for recovering the antibody molecule produced are known to those skilled in the art, and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

(291) Cells

(292) In another aspect, the application features host cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell. The host cell can be a eukaryotic cell, e.g., a mammalian cell, an insect cell, a yeast cell, or a prokaryotic cell, e.g., *E. coli*. For example, the mammalian cell can be a cultured cell or a cell line. Exemplary mammalian cells include lymphocytic cell lines (e.g., NSO), Chinese hamster ovary cells (CHO), COS cells, oocyte cells, and cells from a transgenic animal, e.g., mammary epithelial cell.

(293) The invention also provides host cells comprising a nucleic acid encoding an antibody molecule as described herein.

(294) In one embodiment, the host cells are genetically engineered to comprise nucleic acids encoding the antibody molecule.

(295) In one embodiment, the host cells are genetically engineered by using an expression cassette. The phrase “expression cassette,” refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or

without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.
(296) The invention also provides host cells comprising the vectors described herein.
(297) The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells. Suitable insect cells include, but are not limited to, Sf9 cells.
(298) Uses
(299) Methods described herein include treating a disorder, e.g., a cancer, an autoimmune or inflammatory disorder, or an infectious disorder, in a subject by using an anti-NKp30 antibody molecule, e.g., a multispecific molecule, described herein, e.g., using a pharmaceutical composition described herein. Also provided are methods for reducing or ameliorating a symptom of a disorder, e.g., a cancer, an autoimmune or inflammatory disorder, or an infectious disorder, in a subject, as well as methods for inhibiting the growth of a diseased cell, e.g., cancer cell, and/or killing or depleting one or more diseased cells, e.g., cancer cells. In embodiments, the methods described herein decrease the size of a tumor and/or decrease the number of cancer cells in a subject administered with a described herein or a pharmaceutical composition described herein.
(300) In embodiments, the antibody molecule, e.g., multispecific molecules or pharmaceutical composition, is administered to the subject parenterally. In embodiments, the antibody molecule or pharmaceutical composition is administered to the subject intravenously, subcutaneously, intratumorally, intranodally, intramuscularly, intradermally, or intraperitoneally. In embodiments, the cells are administered, e.g., injected, directly into a tumor or lymph node. In embodiments, the cells are administered as an infusion (e.g., as described in Rosenberg et al., New Eng. J. of Med. 319:1676, 1988) or an intravenous push. In embodiments, the cells are administered as an injectable depot formulation.
(301) In embodiments, the subject is a mammal. In embodiments, the subject is a human, monkey, pig, dog, cat, cow, sheep, goat, rabbit, rat, or mouse. In embodiments, the subject is a human. In embodiments, the subject is a pediatric subject, e.g., less than 18 years of age, e.g., less than 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 or less years of age. In embodiments, the subject is an adult, e.g., at least 18 years of age, e.g., at least 19, 20, 21, 22, 23, 24, 25, 25-30, 30-35, 35-40, 40-50, 50-60, 60-70, 70-80, or 80-90 years of age.
(302) Cancers
(303) In embodiments, the cancer is a hematological cancer, a solid tumor or a metastatic lesion thereof. In some embodiments, the anti-NKp30 antibody molecule used to treat the cancer further comprises a tumor targeting moiety, e.g., a tumor targeting moiety as described herein.
(304) In embodiments, the hematological cancer is a leukemia or a lymphoma. As used herein, a “hematologic cancer” refers to a tumor of the hematopoietic or lymphoid tissues, e.g., a tumor that affects blood, bone marrow, or lymph nodes. Exemplary hematologic malignancies include, but are not limited to, leukemia (e.g., acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CIVIL), hairy cell leukemia, acute monocytic leukemia (AMoL), chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia (JMML), or large granular lymphocytic leukemia), lymphoma (e.g., AIDS-related lymphoma, cutaneous T-cell lymphoma, Hodgkin lymphoma (e.g., classical Hodgkin lymphoma or nodular lymphocyte-predominant Hodgkin lymphoma), mycosis fungoides, non-Hodgkin lymphoma (e.g., B-cell non-Hodgkin lymphoma (e.g., Burkitt lymphoma, small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, or mantle cell lymphoma) or T-cell non-Hodgkin lymphoma (mycosis fungoides, anaplastic large cell lymphoma, or precursor T-lymphoblastic lymphoma)), primary central nervous system lymphoma, Sezary syndrome, Waldenström macroglobulinemia), chronic myeloproliferative neoplasm, Langerhans cell histiocytosis, multiple myeloma/plasma cell neoplasm, myelodysplastic syndrome, or myelodysplastic/myeloproliferative neoplasm.
(305) In embodiments, the cancer is a solid cancer. Exemplary solid cancers include, but are not limited to, ovarian cancer, rectal cancer, stomach cancer, testicular cancer, cancer of the anal region, uterine cancer, colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, Kaposi's sarcoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, brain stem glioma, pituitary adenoma, epidermoid cancer, carcinoma of the cervix squamous cell cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the vagina, sarcoma of soft tissue, cancer of the urethra, carcinoma of the vulva, cancer of the penis, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, spinal axis tumor, neoplasm of the central nervous system

(CNS), primary CNS lymphoma, tumor angiogenesis, metastatic lesions of said cancers, or combinations thereof.

(306) In certain embodiments, the cancer is an epithelial, mesenchymal or hematologic malignancy. In certain embodiments, the cancer treated is a solid tumor (e.g., carcinoid, carcinoma or sarcoma), a soft tissue tumor (e.g., a heme malignancy), and a metastatic lesion, e.g., a metastatic lesion of any of the cancers disclosed herein. In one embodiment, the cancer treated is a fibrotic or desmoplastic solid tumor, e.g., a tumor having one or more of: limited tumor perfusion, compressed blood vessels, fibrotic tumor interstitium, or increased interstitial fluid pressure. In one embodiment, the solid tumor is chosen from one or more of pancreatic (e.g., pancreatic adenocarcinoma or pancreatic ductal adenocarcinoma), breast, colon, colorectal, lung (e.g., small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC)), skin, ovarian, liver cancer, esophageal cancer, endometrial cancer, gastric cancer, head and neck cancer, kidney, or prostate cancer.

(307) Examples of cancer include, but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia or lymphoid malignancies. More particular examples of such cancers are noted below and include: squamous cell cancer (e.g. epithelial squamous cell cancer), lung cancer including small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung and squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial cancer or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, as well as head and neck cancer. The term “cancer” includes primary malignant cells or tumors (e.g., those whose cells have not migrated to sites in the subject's body other than the site of the original malignancy or tumor) and secondary malignant cells or tumors (e.g., those arising from metastasis, the migration of malignant cells or tumor cells to secondary sites that are different from the site of the original tumor).

(308) Other examples of cancers or malignancies include, but are not limited to: Acute Childhood Lymphoblastic Leukemia, Acute Lymphoblastic Leukemia, Acute Lymphocytic Leukemia, Acute Myeloid Leukemia, Adrenocortical Carcinoma, Adult (Primary) Hepatocellular Cancer, Adult (Primary) Liver Cancer, Adult Acute Lymphocytic Leukemia, Adult Acute Myeloid Leukemia, Adult Hodgkin's Disease, Adult Hodgkin's Lymphoma, Adult Lymphocytic Leukemia, Adult Non-Hodgkin's Lymphoma, Adult Primary Liver Cancer, Adult Soft Tissue Sarcoma, AIDS-Related Lymphoma, AIDS-Related Malignancies, Anal Cancer, Astrocytoma, Bile Duct Cancer, Bladder Cancer, Bone Cancer, Brain Stem Glioma, Brain Tumors, Breast Cancer, Cancer of the Renal Pelvis and Ureter, Central Nervous System (Primary) Lymphoma, Central Nervous System Lymphoma, Cerebellar Astrocytoma, Cerebral Astrocytoma, Cervical Cancer, Childhood (Primary) Hepatocellular Cancer, Childhood (Primary) Liver Cancer, Childhood Acute Lymphoblastic Leukemia, Childhood Acute Myeloid Leukemia, Childhood Brain Stem Glioma, Childhood Cerebellar Astrocytoma, Childhood Cerebral Astrocytoma, Childhood Extracranial Germ Cell Tumors, Childhood Hodgkin's Disease, Childhood Hodgkin's Lymphoma, Childhood Hypothalamic and Visual Pathway Glioma, Childhood Lymphoblastic Leukemia, Childhood Medulloblastoma, Childhood Non-Hodgkin's Lymphoma, Childhood Pineal and Supratentorial Primitive Neuroectodermal Tumors, Childhood Primary Liver Cancer, Childhood Rhabdomyosarcoma, Childhood Soft Tissue Sarcoma, Childhood Visual Pathway and Hypothalamic Glioma, Chronic Lymphocytic Leukemia, Chronic Myelogenous Leukemia, Colon Cancer, Cutaneous T-Cell Lymphoma, Endocrine Pancreas Islet Cell Carcinoma, Endometrial Cancer, Ependymoma, Epithelial Cancer, Esophageal Cancer, Ewing's Sarcoma and Related Tumors, Exocrine Pancreatic Cancer, Extracranial Germ Cell Tumor, Extragonadal Germ Cell Tumor, Extrahepatic Bile Duct Cancer, Eye Cancer, Female Breast Cancer, Gaucher's Disease, Gallbladder Cancer, Gastric Cancer, Gastrointestinal Carcinoid Tumor, Gastrointestinal Tumors, Germ Cell Tumors, Gestational Trophoblastic Tumor, Hairy Cell Leukemia, Head and Neck Cancer, Hepatocellular Cancer, Hodgkin's Disease, Hodgkin's Lymphoma, Hypergammaglobulinemia, Hypopharyngeal Cancer, Intestinal Cancers, Intraocular Melanoma, Islet Cell Carcinoma, Islet Cell Pancreatic Cancer, Kaposi's Sarcoma, Kidney Cancer, Laryngeal Cancer, Lip and Oral Cavity Cancer, Liver Cancer, Lung Cancer, Lymphoproliferative Disorders, Macroglobulinemia, Male Breast Cancer, Malignant Mesothelioma, Malignant Thymoma, Medulloblastoma, Melanoma, Mesothelioma, Metastatic Occult Primary Squamous Neck Cancer, Metastatic Primary Squamous Neck Cancer, Metastatic Squamous Neck Cancer, Multiple Myeloma, Multiple Myeloma/Plasma Cell Neoplasm, Myelodysplastic Syndrome, Myelogenous Leukemia, Myeloid Leukemia, Myeloproliferative Disorders, Nasal Cavity and Paranasal Sinus Cancer, Nasopharyngeal Cancer, Neuroblastoma, Non-Hodgkin's Lymphoma During Pregnancy, Nonmelanoma Skin Cancer, Non-Small Cell Lung Cancer, Occult Primary Metastatic Squamous Neck Cancer, Oropharyngeal Cancer, Osteo-/Malignant

Fibrous Sarcoma, Osteosarcoma/Malignant Fibrous Histiocytoma, Osteosarcoma/Malignant Fibrous Histiocytoma of Bone, Ovarian Epithelial Cancer, Ovarian Germ Cell Tumor, Ovarian Low Malignant Potential Tumor, Pancreatic Cancer, Paraproteinemias, Purpura, Parathyroid Cancer, Penile Cancer, Pheochromocytoma, Pituitary Tumor, Plasma Cell Neoplasm/Multiple Myeloma, Primary Central Nervous System Lymphoma, Primary Liver Cancer, Prostate Cancer, Rectal Cancer, Renal Cell Cancer, Renal Pelvis and Ureter Cancer, Retinoblastoma, Rhabdomyosarcoma, Salivary Gland Cancer, Sarcoidosis Sarcomas, Sezary Syndrome, Skin Cancer, Small Cell Lung Cancer, Small Intestine Cancer, Soft Tissue Sarcoma, Squamous Neck Cancer, Stomach Cancer, Supratentorial Primitive Neuroectodermal and Pineal Tumors, T-Cell Lymphoma, Testicular Cancer, Thymoma, Thyroid Cancer, Transitional Cell Cancer of the Renal Pelvis and Ureter, Transitional Renal Pelvis and Ureter Cancer, Trophoblastic Tumors, Ureter and Renal Pelvis Cell Cancer, Urethral Cancer, Uterine Cancer, Uterine Sarcoma, Vaginal Cancer, Visual Pathway and Hypothalamic Glioma, Vulvar Cancer, Waldenstrom's Macroglobulinemia, Wilms' Tumor, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

(309) In other embodiments, the multispecific molecule, as described above and herein, is used to treat a hyperproliferative disorder, e.g., a hyperproliferative connective tissue disorder (e.g., a hyperproliferative fibrotic disease). In one embodiment, the hyperproliferative fibrotic disease is multisystemic or organ-specific. Exemplary hyperproliferative fibrotic diseases include, but are not limited to, multisystemic (e.g., systemic sclerosis, multifocal fibrosclerosis, sclerodermatous graft-versus-host disease in bone marrow transplant recipients, nephrogenic systemic fibrosis, scleroderma), and organ-specific disorders (e.g., fibrosis of the eye, lung, liver, heart, kidney, pancreas, skin and other organs). In other embodiments, the disorder is chosen from liver cirrhosis or tuberculosis. In other embodiments, the disorder is leprosy.

(310) In embodiments, the multispecific molecules (or pharmaceutical composition) are administered in a manner appropriate to the disease to be treated or prevented. The quantity and frequency of administration will be determined by such factors as the condition of the patient, and the type and severity of the patient's disease. Appropriate dosages may be determined by clinical trials. For example, when “an effective amount” or “a therapeutic amount” is indicated, the precise amount of the pharmaceutical composition (or multispecific molecules) to be administered can be determined by a physician with consideration of individual differences in tumor size, extent of infection or metastasis, age, weight, and condition of the subject. In embodiments, the pharmaceutical composition described herein can be administered at a dosage of 10.sup.4 to 10.sup.9 cells/kg body weight, e.g., 10.sup.5 to 10.sup.6 cells/kg body weight, including all integer values within those ranges. In embodiments, the pharmaceutical composition described herein can be administered multiple times at these dosages. In embodiments, the pharmaceutical composition described herein can be administered using infusion techniques described in immunotherapy (see, e.g., Rosenberg et al., New Eng. J. of Med. 319:1676, 1988).

(311) In embodiments, the cancer is a myeloproliferative neoplasm, e.g., primary or idiopathic myelofibrosis (MF), essential thrombocytosis (ET), polycythemia vera (PV), or chronic myelogenous leukemia (CIVIL). In embodiments, the cancer is myelofibrosis. In embodiments, the subject has myelofibrosis. In embodiments, the subject has a calreticulin mutation, e.g., a calreticulin mutation disclosed herein. In embodiments, the subject does not have the JAK2-V617F mutation. In embodiments, the subject has the JAK2-V617F mutation. In embodiments, the subject has a MPL mutation. In embodiments, the subject does not have a MPL mutation.

(312) In embodiments, the cancer is a solid cancer. Exemplary solid cancers include, but are not limited to, ovarian cancer, rectal cancer, stomach cancer, testicular cancer, cancer of the anal region, uterine cancer, colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, Kaposi's sarcoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, brain stem glioma, pituitary adenoma, epidermoid cancer, carcinoma of the cervix squamous cell cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the vagina, sarcoma of soft tissue, cancer of the urethra, carcinoma of the vulva, cancer of the penis, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, spinal axis tumor, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, metastatic lesions of said cancers, or combinations thereof.

(313) Inflammatory and Autoimmune Disorders

(314) In some embodiments, the anti-NKp30 antibody molecules, e.g., the multispecific antibody molecules, disclosed herein can be used to treat inflammatory and autoimmune diseases, and graft vs. host disease (GvHD). In some embodiments, the antibody molecules, e.g., the multispecific antibody molecules, disclosed herein deplete autoreactive T cells, e.g., by directing an NK cell, e.g., an NKp30-expressing cell, to an

autoreactive T cell. In some embodiments, the anti-NKp30 antibody molecule further comprises a binding specificity that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.

(315) As used herein, the term “autoimmune” disease, disorder, or condition refers to a disease where the body's immune system attacks its own cells or tissues. An autoimmune disease can result in the production of autoantibodies that are inappropriately produced and/or excessively produced to a self-antigen or autoantigen. Autoimmune diseases include, but are not limited to, cardiovascular diseases, rheumatoid diseases, glandular diseases, gastrointestinal diseases, cutaneous diseases, hepatic diseases, neurological diseases, muscular diseases, nephric diseases, diseases related to reproduction, connective tissue diseases and systemic diseases. In some embodiments, the autoimmune disease is mediated by T cells, B cells, innate immune cells (e.g., macrophages, eosinophils, or natural killer cells), or complement-mediated pathways.

(316) Examples of autoimmune disorders that may be treated by administering the antibodies of the present invention include, but are not limited to, alopecia greata, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison's disease, autoimmune diseases of the adrenal gland, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune oophoritis and orchitis, autoimmune thrombocytopenia, Behcet's disease, bullous pemphigoid, cardiomyopathy, celiac sprue-dermatitis, chronic fatigue immune dysfunction syndrome (CFIDS), chronic inflammatory demyelinating polyneuropathy, Churg-Strauss syndrome, cicatrical pemphigoid, CREST syndrome, cold agglutinin disease, Crohn's disease, discoid lupus, essential mixed cryoglobulinemia, fibromyalgia-fibromyositis, glomerulonephritis, Graves' disease, Guillain-Barre, Hashimoto's thyroiditis, idiopathic pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA neuropathy, juvenile arthritis, lichen planus, lupus erthematosus, Meniere's disease, mixed connective tissue disease, multiple sclerosis, Neuromyelitis optica (NMO), type 1 or immune-mediated diabetes mellitus, myasthenia gravis, pemphigus vulgaris, pernicious anemia, polyarteritis nodosa, polychrondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, Raynauld's phenomenon, Reiter's syndrome, Rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren's syndrome, stiff-man syndrome, systemic lupus erythematosus, lupus erythematosus, takayasu arteritis, temporal arteristis/giant cell arteritis, transverse myelitis, ulcerative colitis, uveitis, vasculitides such as dermatitis herpetiformis vasculitis, vitiligo, and Wegener's granulomatosis. In some embodiments, the autoimmune disorder is SLE or Type-1 diabetes.

(317) Examples of inflammatory disorders which can be prevented, treated or managed in accordance with the methods of the invention include, but are not limited to, asthma, encephilitis, inflammatory bowel disease, chronic obstructive pulmonary disease (COPD), allergic disorders, septic shock, pulmonary fibrosis, undifferentiated spondyloarthropathy, undifferentiated arthropathy, arthritis, inflammatory osteolysis, and chronic inflammation resulting from chronic viral or bacterial infections.

(318) Thus, the anti-NKp30 antibody molecules, e.g., multispecific molecules, of the present invention have utility in the treatment of inflammatory and autoimmune diseases.

(319) Infectious Diseases

(320) In some embodiments, the anti-NKp30 antibody molecules, e.g., the multispecific antibody molecules, disclosed herein can be used to treat infectious diseases. In some embodiments, the antibody molecules, e.g., the multispecific antibody molecules, disclosed herein deplete cells expressing a viral or bacterial antigen. In some embodiments, the anti-NKp30 antibody molecule further comprises a binding specificity that binds to an antigen present on the surface of an infected cell, e.g., a viral infected cell.

(321) Some examples of pathogenic viruses causing infections treatable by methods include HIV, hepatitis (A, B, or C), herpes virus (e.g., VZV, HSV-1, HAV-6, HSV-II, and CMV, Epstein Barr virus), adenovirus, influenza virus, flaviviruses, echovirus, rhinovirus, coxsackie virus, cornovirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus and arboviral encephalitis virus. In one embodiment, the infection is an influenza infection.

(322) In another embodiment, the infection is a hepatitis infection, e.g., a Hepatitis B or C infection.

(323) Exemplary viral disorders that can be treated include, but are not limited to, Epstein Bar Virus (EBV), influenza virus, HIV, SIV, tuberculosis, malaria and HCMV.

(324) Some examples of pathogenic bacteria causing infections treatable by methods of the invention include syphilis, chlamydia, rickettsial bacteria, mycobacteria, staphylococci, streptococci, pneumonococci, meningococci and conococci, klebsiella, proteus, serratia, pseudomonas, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lymes disease bacteria. The anti-NKp30 antibody molecules can be used in combination with existing treatment modalities for the aforesaid infections.

For example, Treatments for syphilis include penicillin (e.g., penicillin G.), tetracycline, doxycycline, ceftriaxone and azithromycin.

(325) Diagnostic Uses

(326) In one aspect, the present invention provides a diagnostic method for detecting the presence of a NKp30 protein in vitro (e.g., in a biological sample, such as a tissue biopsy, e.g., from a cancerous tissue) or in vivo (e.g., in vivo imaging in a subject). The method includes: (i) contacting the sample with an antibody molecule described herein, or administering to the subject, the antibody molecule; (optionally) (ii) contacting a reference sample, e.g., a control sample (e.g., a control biological sample, such as plasma, tissue, biopsy) or a control subject)); and (iii) detecting formation of a complex between the antibody molecule, and the sample or subject, or the control sample or subject, wherein a change, e.g., a statistically significant change, in the formation of the complex in the sample or subject relative to the control sample or subject is indicative of the presence of NKp30 in the sample. The antibody molecule can be directly or indirectly labeled with a detectable substance to facilitate detection of the bound or unbound antibody. Suitable detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials and radioactive materials, as described above and described in more detail below.

(327) The term “sample,” as it refers to samples used for detecting polypeptides includes, but is not limited to, cells, cell lysates, proteins or membrane extracts of cells, body fluids, or tissue samples.

(328) Complex formation between the antibody molecule and NKp30 can be detected by measuring or visualizing either the binding molecule bound to the NKp30 antigen or unbound binding molecule. Conventional detection assays can be used, e.g., an enzyme-linked immunosorbent assays (ELISA), a radioimmunoassay (RIA) or tissue immunohistochemistry. Alternative to labeling the antibody molecule, the presence of NKp30 can be assayed in a sample by a competition immunoassay utilizing standards labeled with a detectable substance and an unlabeled antibody molecule. In this assay, the biological sample, the labeled standards and the antibody molecule are combined and the amount of labeled standard bound to the unlabeled binding molecule is determined. The amount of NKp30 in the sample is inversely proportional to the amount of labeled standard bound to the antibody molecule.

EXAMPLES

(329) The Examples below are set forth to aid in the understanding of the inventions but are not intended to, and should not be construed to, limit its scope in any way.

Example 1: Immunization of Armenian Hamster to Generate Anti-NKp30 Antibodies

(330) Briefly, armenian hamster were immunized with the extracellular domain of human NKp30 protein in complete Freund's adjuvant and boosted twice on day 14 and day 28 with NKp30 in incomplete Freund's adjuvant (IFA). On day 56 one more boost in IFA was given and the animals harvested three days later. Spleens were collected and fused with P3X63Ag8.653 murine myeloma cell line. 0.9×10{circumflex over ( )}5 cells/well in 125 ul were seated in 96 well plate and fed with 125 μl of I-20+2ME+HAT (IMDM (4 g/L glucose) supplemented with 20% fetal bovine serum, 4 mM L-glutamine, 1 mM sodium pyruvate, 50 U penicillin, 50 μg streptomycin and 50 μM 2-ME in the absence or presence of HAT or HT for selection, and Hybridoma Cloning Factor (1% final) on days 7, 11 and thereafter as needed. At approximately 2 weeks after fusion (cells are about 50% confluent), supernatant was collected and assayed for binding.

Example 2: Hybridoma Screen for NKp30 mAbs

(331) Expi293 cells were transfected with BG160 (hNKp30 cell antigen) 18 hours prior to screening. The day of screening, transfected cells were diluted to 0.05×10{circumflex over ( )}.sup.6/mL and anti-Armenian hamster Fc Alexa Fluor 488 added to a final concentration of 0.4 ug/mL. 50 uL (2,500 cells) of this mixture was added to each well of a 384 well plate. The same density of untransfected 293 cells with secondary were used as a negative control. 5 uL of hybridoma supernatant was added to the cell mixture and the plate incubated for 1 hour at 37° C. The plates were then imaged on Mirrorball. Positive clones were identified and subcloned by serial dilution to obtain clonal selected hybridoma. After reconfirmation using the same protocols the hybridoma cells were harvested and the corresponding heavy and light chain sequences recovered. The DNA was subcloned into pcDNA3.4 for subsequent expression of the corresponding antibodies and further validation.

Example 3: Binding of NKp30 Antibodies to NK92 Cells

(332) NK-92 cells were washed with PBS containing 0.5% BSA and 0.1% sodium azide (staining buffer) and added to 96-well V-bottom plates with 200,000 cells/well. Hamster NKp30 antibodies were added to the cells in 2.0 fold serial dilutions and incubated for 1 hour at room temperature. The plates were washed twice with staining buffer. The secondary antibody against hamster Fe conjugated to AF647 (Jackson, 127-605-160) was added at 1:100 dilution (1.4 mg/ml stock) and incubated with the cells for 30 minutes at 4° C. followed by

washing with staining buffer. Cells were subsequently were fixed for 10 minutes with 4% paraformaldehyde at room temperature. The plates were read on CytoFLEX LS (Beckman Coulter). Data was calculated as the percent-AF747 positive population (FIG. **1**).

Example 4: Bioassay to Measure Activity of NKp30 Antibodies Using NK92 Cell Line

(333) NKp30 antibodies were three-fold serially diluted in PBS and incubated at 2-8° C. overnight in flat bottom 96 well plates. Plates were washed twice in PBS and 40,000 NK-92 cells were added in growth medium containing IL-2. Plates were incubated at 37° C., 5% CO.sub.2, humidified incubator for 16-24 hours before supernatants were collected. IFNγ levels in supernatants was measured following MSD assay instructions (FIG. **2**). Supernatant collected from cells incubated with hamster isotype IgG was used as negative control and supernatants from cells incubated with NKp30 monoclonal antibody (R&D, clone 210847) was utilized as a positive control. Data were generated using hamster anti-NKp30 mABs.

Example 5: Generation and Characterization of Humanized Anti-NKp30 Antibodies

(334) A series of hamster anti-NKp30 antibodies were selected. These antibodies were shown to bind to human NKp30 and cynomolgus NKp30 and induce IFNγ production from NK-90 cells (data not shown). The VH and VL sequences of exemplary hamster anti-NKp30 antibodies 15E1, 9G1, 15H6, 9D9, 3A12, and 12D10 are disclosed in Table 9. The VH and VL sequences of exemplary humanized anti-NKp30 antibodies based on 15E1, 9G1, and 15H6 are also disclosed in Table 9. The Kabat CDRs of these antibodies are disclosed in Table 18 and Table 8.

(335) Two humanized constructs based on 15E1 were selected. The first construct BJM0407 is a Fab comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7302 and a lambda light chain variable region comprising the amino acid sequence of SEQ ID NO: 7305. Its corresponding scFv construct BJM0859 comprises the amino acid sequence of SEQ ID NO: 7310. The second construct BJM0411 is a Fab comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7302 and a kappa light chain variable region comprising the amino acid sequence of SEQ ID NO: 7309. Its corresponding scFv construct BJM0860 comprises the amino acid sequence of SEQ ID NO: 7311. BJM0407 and BJM0411 showed comparable biophysical characteristics, e.g., binding affinity to NKp30 and thermal stability. The scFv constructs BJM0859 and BJM0860 also showed comparable biophysical properties.

INCORPORATION BY REFERENCE

(336) All publications, patents, and Accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference.

EQUIVALENTS

(337) While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

Claims

1. An antibody or an antigen-binding portion thereof that binds to NKp30 comprising: (a) a heavy chain variable region (VH) comprising (i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313, (ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and (iii) a VHCDR3 amino acid sequence of SEQ ID NO: 7315; and (b) a light chain variable region (VL) comprising (i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326, (ii) a VLCDR2 amino acid sequence of SEQ ID NO: 7327, and (iii) a VLCDR3 amino acid sequence of SEQ ID NO: 7329.

2. The antibody or an antigen-binding portion thereof of claim 1, wherein (a) the VH comprises an amino acid sequence with at least 75% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 7298 and 7300-7304; and (b) the VL comprises an amino acid sequence with at least 75% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 7299 and 7305-7309.

3. The antibody or an antigen-binding portion thereof of claim 2, wherein (a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7302; and (b) the VL comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7305.

4. The antibody or an antigen-binding portion thereof of claim 2, wherein (a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7302; and (b) the VL comprises an amino acid

sequence with at least 75% sequence identity to SEQ ID NOs: 7305 or SEQ ID NO: 7309.
5. The antibody or antigen-binding portion thereof of claim 4, wherein (a) the VH comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 7302; and (b) the VL comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 7305 or SEQ ID NO: 7309.
6. The antibody or antigen-binding portion thereof of claim 5, wherein (a) the VH comprises the amino acid sequence of SEQ ID No: 7302; and (b) the VL comprises the amino acid sequence of SEQ ID No: 7305.
7. The antibody or antigen-binding portion thereof of claim 5, wherein (a) the VH comprises the amino acid sequence of SEQ ID No: 7302; and (b) the VL comprises the amino acid sequence of SEQ ID No: 7309.
8. The antibody or an antigen-binding portion thereof of claim 2, wherein the antibody or an antigen-binding portion thereof comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7310 or SEQ ID NO: 7311.
9. A multispecific molecule comprising the antibody or an antigen-binding portion thereof of claim 2.
10. The multispecific molecule of claim 9, wherein the multispecific molecule further comprises (a) a tumor targeting moiety; (b) a cytokine molecule; (c) a T cell engager; (d) a stromal modifying moiety; or (e) any combination thereof.
11. The multispecific molecule of claim 9, wherein the multispecific molecule further comprises (a) a T cell engager that binds to an antigen present on the surface of an autoreactive T cell that is associated with an inflammatory or autoimmune disorder, or (b) a binding moiety that binds to an antigen present on the surface of a cell infected by a virus or a bacteria.
12. The multispecific molecule of claim 10, wherein the multispecific molecule comprises a linker between one or more of: (a) the targeting moiety and the cytokine molecule or the stromal modifying moiety, (b) the targeting moiety and the immune cell engager, (c) the cytokine molecule or the stromal modifying moiety, (d) the immune cell engager, the cytokine molecule or the stromal modifying moiety and the immunoglobulin chain constant region, (e) the targeting moiety and the immunoglobulin chain constant region, and (f) the immune cell engager and the immunoglobulin chain constant region.
13. The antibody or the antigen-binding portion thereof of claim 1, wherein the antibody or the antigen-binding portion thereof comprises an immunoglobulin chain constant region.
14. The antibody or the antigen-binding portion thereof of claim 13, wherein the immunoglobulin chain constant region is an IgGI chain constant region that comprises an amino acid substitution at a position selected from the group consisting of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, 409, and any combination thereof.
15. The antibody or the antigen-binding portion thereof of claim 14, wherein the IgGI chain constant region comprises an amino acid substitution at a position selected from the group consisting of T366S, L368A, Y407V, T366W, and any combination thereof.
16. A polynucleotide comprising a sequence encoding the antibody or an antigen-binding portion thereof of claim 2.
17. A host cell comprising the polynucleotide of claim 16.
18. An expression vector comprising a polynucleotide sequence encoding the antibody or an antigen-binding portion thereof of claim 2.
19. A host cell comprising the expression vector of claim 18.
20. A method of making the antibody or an antigen-binding portion thereof of claim 2, comprising culturing the host cell of claim 17 under suitable conditions for gene expression and/or homo- or heterodimerization.
21. A pharmaceutical composition comprising the antibody or an antigen-binding portion thereof of claim 2; and a pharmaceutically acceptable carrier, excipient, or stabilizer.
22. A method of treating a disease or condition, wherein the disease or condition is cancer, an autoimmune or inflammatory disorder, an infectious disorder, or a hyperproliferative disorder, comprising administering to a subject in need thereof the antibody or an antigen-binding portion thereof of claim 2, wherein the antibody or antigen-binding portion thereof is administered in an amount effective to treat the disease or condition.
23. The method of claim 22, wherein the disease or condition is cancer, an autoimmune or inflammatory disorder, or an infectious disorder.