

Extended Data

Table 1: The sequence of IL-2 β mimics

β agonist	Amino Acid Sequence
B0	MEEKLEELKKKLAELDGKYIYEKCYGTEEEAKKALEELKAALEELAKAEKEAAAAAA
B1	SEERRRREERREERREERREERLEKMRERDEEIREEEEEEEEEEEEEEEEEEEEEEE
B2	SLEEALRAELRRRAAEECGALLREAERAAAAFRAATPSEEEAAAFLEAARAEARAACEARFAAL
B3	EELEKKLKELEKAEAREKAKKEYSAKAVKYLADPSKKEEAEECLKKEELIKEERKYIEEAKKL
B4	MLEELKKKLEKLEKEEEERKKRWEARREEAKAAALAARKAEFEARAAAEAAAAAA
B5	AEELARRAAEFLARAKELDLEMAKKIEVRKKTGNEEETEKARKELLEELRKEIKRLKEEL
B6	EEERKKKIEEYKTKAEAHKLDAEQLEAKAAAAASPEAAKLYKKLAEKEKELAAEYKKAKELEEA
B7	SLLEELKRKLECEKRANECSEKLKKKREEEKEKKKKLEEEEEKLEEEEELEEEEEEEEEEE
B8	SLEKILEELKKKEEKKLEESLKKLEEEAKKFEEERKAAAAEAAKAAAE
B9	ELEEKAKKEAKEKEREERSKRLREERERRLEEEERRRREEEERRERERRRREEEEA
B10	SLEELLKRLRELKREECLARMRAKAEERAAEAAAAAAAAAAAEELARRLAELA
B11	SLAAEKAAKIAALTAEAEEKKAKELLAKAAAAASPEERKKYMEEAEKYLAEIRAEIAAIL
B12	SLEELLKELEKKKKKEEKKLKKAKENWEKYQKELAEERLAAALAAALAAAAALAAALAEAAAAAA
B13	SELKELEEKREEEKKLEETEKRLEEEERRFLEERARREARRAEERRRRREELERRR
B14	MSERIKTLREALELVRQGVENPATQAELIARGRALAEAATGEAGRALFERELARLEAQKAA
B15	EEEVKALLEELAKLEYEYLKAAKEDKKLAEYLLKAEAEKKLLEAKKALEEKKAKE
B16	EEERKAAEEAARKAAHLKEATERFRERRRRREEEEREREEREEREEREEREEREERE
B17	AAAAAAREAAALKARRAAGDEDAARDRAACEALYAEDPAKGAELAKVEAEKAFRAEIDAALAA
B18	SLEELRREEEERRREEEERLEELWKKNKEKAEELAKKREKELEEKKEKERKELEELKKELE
B19	MSEELKKLLEEQKKKIEQLRKEGEAKAAALRAAARAAAAALAAAAAA
B20	MTLEEKLANLQAGKAASLAALAEALAAEAAAESPEKAALVRELARRVRAQYDKEIAAVAAELA
B21	EEKEKEKKKKKEEKKKKEREKEKEYIEKVKKVKEREKEKAEKKEAKKKA
B22	SLEEVKATYEEISIAAKKLGAERVAKAAAEGPEAAEKAAALSKEAIELLEKKKEELAKL
B23	MEEKEKEKEKEELKKKAEAEKKAKELKEKMAKSSAEAEKLAKERELEKKRVELKKELE
B24	SLAAELAKKKEREKALEERKKKAEIEKEEEERKRKAAEAAAAAAAAAAAAAAAAAAAA
B25	AAALAAALAAAAAAAAAAAAAAAAARAAEAEKRAAELRRRREELARRLAA
B26	SLEEEKKRKEEKKRKKRLEEARREWEERLEARRRAEEERLEEEERRR
B27	SLLEELRRALEERELEERELEAKRYEEALKKLKEEKEKEEEERKRKEE
B28	MEEERKEERKREEEKERERRRAAGRAAREAAAAAAAAAAAAARAEERRR
B29	SAAAKAELAALEKRAKEAAALAEAAKKDKKKAKRYKADRDILEKEAKALKAAL
B30	AAAAEAAAAAAAAALRARQAEREARAREMAAIAAADGEEGKRKAALLHYAAVVRARVEAEVAA
B31	SEERERAEAAAAAAEAARAAARAKAKERYKEELEIKKKREEEKKKKEELK
B32	SLEALAAAAAAAAAAAAAAAAEAAALEEYRKRLEEEAELEEELEEEEEEEEEEELE
B33	AEERERAEAAAAAAAAEAEARLARMRAEDERIRAAKREAAAAAAAEAAAEERRRAE
B34	AAEAARRAARAFDARLTAAERKYLAQQDDPEAAAWLAIEAIEAERTAAERAWAA
B35	AAAAAAEIAEAARKAEERYKELEKEAEALKKDKEGTKKRKEALEESLKLAKELLELRKRLEA
B36	SLAEALAAAAAAAAAAEAARRARIEADIAEARRRLEEEEREKEEEEEKR
B37	SLLEELLRRRLREEEERRREKSREEGRRRREARAALAAAAEAAAAEAAAREAAEREA
B38	EEKRRKAELLKQIEEDLKKAEEALALGAATPKHDYIEGLAKSYLARAEEELKAILK
B39	EEERREENRKRKRAEKEIKESKEEEEARRRKEEEERRRREER
B40	EEEEKRRLEEEERAKREAEERAERIKAEIEAERARRAALEALRRELEEL
B41	EEKREKELKELQEEAERLAKELLEHALPKLLAALLAAAAALAAAAALLAALA
B42	SLLDALLEALFRALVTAHFQAAAAATDRETAVEQARAFAAALRAALAAAAAAAAALAAALA
B43	SELEELRRLEEEESRRQDEEARRRIREREAEAEARKRLEELLRKLLS

B44	SKEEEEKLKKEKRKEELEKRLKEAEEIWKKYIELLKAKENEENKEKYLEEAKKLKEELEK
B45	AALREALEAEEAACRAALAALIAATRAAPRAERIAALTALVKECAARRAAVLA
B46	AAEIEALLAAADAEIAELRAAGVAEARAAPREERPAIVLETDRRALELRAAARAAAAALAAALA
B47	EEEERRRLEEERRAELERRLAEEREREELRRREEEREREELERELREEEERRRREA
B48	EEEEKRKLEERKKAEEKSKELIEKRKKEREERKRRREEEEEEEEEEEEEEEEEEEEELEEELEE
B49	SLLEELERLAAKAAEAARKAARLAAGEAALKARLAAEAAAREAEERRRRREEE
B50	AAAAEAAAAAAAAAAAAAAAAARAAREAEAAAEARAIAAARKAAEEAAAAAAAAAAAAAAAAEAAAAAA
B51	EEERRRQIEALKRAAAAAEYAYALAKELAAKDPAYAPLAEALKAELERLKAELAALEAA
B52	SLEDIEKKIAELKRLKLFEECKKIAEERLKKDPEKGKKHKEELEKLNELRKKVEAIEALLA
B53	PLLAALRELADRLHREAVRERERARREAERAARAAAAAEARAAAAAA
B54	MSPEQKELQAQRDKYDDEALKLNELALKDPEKAEYNAQAKKYIEKAYEIRKQIEA
B55	MEAVKKLEAKGEEYFALGKANPEKREYERLGKLYFESAKLAKERLEKAKAEKLA
B56	EEEEEEELRRLEEEERELEKRREERIAARAAEEAARRAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
B57	AEERREEEERREEEERRRREEEERLEEEERRRIEATKERREKLKKEKEKKKEEEEEKKEKE
B58	ALLEALREAAAAEAARLAALEAENRAKYAALTAALKALCAALAEAL
B59	SLLEALKALLEALKALVEKAKKEAEKKKAEKKKKKEEEKAKKELEELK
B60	EEEAARAAAAAAAAAAAAAAAAIAARAAEDAKRERERRKAEKERKELEELRKK
B61	SEEEERRRREEEERRRRSEEAGAEARAREKAELERRELEELLREL
B62	EEEEERERREEEERERLEKLRRDEEIMEKLREERRREEEERREREELERLR
B63	EEEEELERERERRRAAEAAAFRAEAAARRAALEAARAAAAAAAAAAAAAA
B64	SEELRRRLEELAAAAAAAAAAEAAARAARKAESEKIAAERREKAKKEK
B65	KELEEEKAKREKEREKLLAEAKAEGEKRLKAEEEARRREEEERE
B66	SEEREREEEEERARRAAEHREAVRRRAREELERRRAAAAAAAAAAEARAAA
B67	LPLLLLLLLLLLALLAALLAALAEQAAREKKLREESEKYEEELRKKKEEERRKEEEE
B68	SEKEALIAALKEKAALKALAELEEKAKEDPEAAAAAAAAALKAAATERLVARIKA
B69	KEKEEEEEKKKEKEKAEEEERKRKAELKARAAALAAERAAAAAAAAAAAA
B70	SAAELAAAAAEAAARAKALAEAMRAEEEAEREREAEAEARRRREEEERLR
B71	SLLAALAALLAAAAAAAAAAAAAAAAAGEARSRALHEEKQKKVLEEKLEEEKEKLEEELEKLL
B72	SLEELLEERRRAAEEEERERRREDIEEAREEALKRAEERKKKAE
B73	SPADALWEAELAAIREAVVAVGAASKLSPEEAARRWAAATAEAAARMAAAKARRDALLAAA
B74	MEEEEEKKKEEEKAKKEKEKEIEEIKKKGLESAKKSAAEASLAASLAYCLAAAAAAA
B75	EEELERRREEAERRIAELGRACLRAPEAERPACRAALRAEDRRLREELRREEAR
B76	SLEELLRALAAAAEAAEARRAEARARGAALRAEREARRAEERRRAEEEAARRAEEEAA
B77	AALAAALAALAAAAAAAAAAAAAAAAAAEAGEARLAAHRAEYEALLAARAAEAAAAA
B78	DAHLARARAEAAALAAELAAAGKAACGAAAAALLAAAKALAAANAAAAAAA
B79	AELEEKAAKAAAEAAKAAALEELKKKSEEFAKKRREEKKKEEEKK
B80	EEELQEYRERLQALAEAAKKGWSPPEVKEAAKKLQEELQERKER
B81	MEEKKKKKEEEKKRLEELKKEIAKATDEAERAKKNASDPANKAKMAEAKAKKEAAEKELK
B82	SEEEERRRRLAEELAAQRAREEALKRESEALAEARRRLRELAALLAALLAELA
B83	AEEEAERAAREIKAKTNELDAKCTAAANEVAKTEGPEAAEKVRAECEAQRAAEAAAIRAAA
B84	SLLEELLRRLLLEELERRRRLEEMEREREEAEARAAAQLAAEAAALA
B85	MAEEAAAAAAAAALRAEAAAAEAAWAEERRAAAAERERAEAEERRRREEELLE
B86	EEEEERRRREEEARREAEALRAWRERIERETAELRARNEEERRRREEEERRRRE
B87	GLAALAAEALRRALAEFARDRARLERLRDHYAGDPEKAARVDAALARLEAQRAEALA
B88	SLLAALAEAAAAAAAAEALRKAVREAAEEERKRRREEEERERREEEERERE
B89	SLEELLEELLEARRAAEELERLRREEREEDERERERLLRERREEEERR
B90	AAKEAEEARLARANAIIYAAAAARAAREAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
B91	AEAAALAEAAAAAAAAAAAAAEERRRRAEDIERAKKEREEKREKEEEERKRR

B92	NEEKLKEEEKAKKEYKAKYEAACKAKAAEEKANGSPEEAAWQREANLYLGKYLVAEKKAKELKEK
B93	SREELEREAREAAEAARRAAEEARRAALGAAIEAARAAAEAAAAAAAAAAAEAEARAAA
B94	EEEEELRREEEAEERREERRRLLLEERLREGEEVEREREEELREREELEELERR
B95	SLKEEAERLKEEEENLRKAAEAYEAAGNKEKAKEAKEKAEAEAKKKAEAKKKLEEA
B96	EEEEEEERRRREERREERREAEERRAREEALREERRRRSEEEARRRREERRRREEREEERRR
B97	EEEEEEERRRREERKEKEREAEKEAKELREKADAEAAARAAAREAAAAAEELRRALE
B98	VKEKAEKEIEELLKEARAVLKEAAATAAADPATAAAAARAEAAKRLAELAKKIREVKKKMKEELA
B99	EAEELAAAAIAAAAAAAAAAAAAAAAAAARREIDAARAAREAAAAAAAAAAAAAAAAAAAA

Table 2: The sequence of IL-2 γ mimics

γ agonist	Amino Acid Sequence
G0	ALEEEERRKAEAAWLAEVKAKRAELTAAAEARAAGDSEADAAREKIRALVEEAIKRDRE
G1	AAAAEAAREAAAAAALARRAAALEARARARREAEEREEREKEEREREEER
G2	EEEEKEFEIEIRKKTQEMQEKIRELQRLEWEAKNGSKEKAEELRKKREEVLKELEELRKKRS
G3	DELEKEIEETEELLKKAKEEQAKTGKTEEYGKLIAELQARLEELKAALAAKAAEAAA
G4	AEVERKVAELKALNAECAARIAAAAEAGPEAAAAAERECNEELRRLVE
G5	MTDKELMKELKAKAEYKAAAAAAAAAGGDPECVATQQARADKYNELLAKLEAS
G6	EEKKREERKEIQEYVEIADKAGKGEEFLKLLSENKESKEKAKKLAEMKKKLKEEEKKKKA
G7	STVEELEANIAANRAAAALTAAFPETAAAAARAEAAAREARNQALIAKEKA
G8	EEERAKKLEELKELEKLVEKIKEEGKDPKAAELAEKLKKELEKLKAE
G9	SAAAKEAAKALATALRLAGTRLFTAGAVAAKIDPAAGAALFAAGAAFAAAAALEKALA
G10	DAVAAALAEVTAQCRAIVAASEDPEAALAEATALATAFFAQFVGPEEARRLGEEHARAVLAEV
G11	AAAAAELAAAAEAEEAAALARRAARAAALAEERERRREERREERREERR
G12	ELEEEEEEERRRFEEARRREEKRRREREERLRERIRRELEELRRLLE
G13	LEAELKALLAELTALAAAAAAAAAAAAAGDAELAAIWKAQAACLNALAAKVAAALA
G14	STLALARALRAIGRAVAAALFGLGYAALKAGNVALAALLYALGAAVLAATTAIRALLAA
G15	SAKLKEEYKAKAEAEKAKALAKEAAKHPEAGKAYQKYADRLEKLAKAIEKQI
G16	MSLAEAIRDAGVAAALASGDPAPHLDAAKAAIAAAVSPEEAARWAAVLDEDYARAAAA
G17	MIEQLENATKLAKIEYKLTGTPEEAKLAKIEYKYEKLEEKAKKKEKEEALKKLLEEL
G18	LLLLLLALLALAALAAAKVAAMRARRAAAAAARAAAEARAAAEAAAREAAAA
G19	SLAEAAALAAARAAREARAREARLEAEREARRREEKEEERRRELE
G20	SKQEALAKARELYEKARELIREGKFEEAEKLIEELEKTEQGKALAKALREELKKEKELLK
G21	LLELELKAKEEEAKKEYEERKKEREEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEE
G22	EKLKKLQELADKAKKREELAKARAAEAKAKGDAVAACEATAAKYKETAENLQKEIEKLK
G23	MTPEELAAALRAAIAANKARLAAEEARRAAREAAALLAEAAAALAAALAEALAA
G24	ALEELRRAAEELIREIRENGESKETKERLIAARRLREELGEEGARVVEELDREIERAYEEFKA
G25	KEEEAEKKREELLAKLKELAERNKKLAKEGIAPEEAKKIAEELEKKRKELE
G26	SREEEMERLEEEAKREVEEALRTGIEAAKAVAERLAAFEALGYLRVARRVRNYAESLILKAK
G27	MKEKAEEKKEAIALAKEGEEELAKKVEAANPAEQYRMLKKLKKEKAEK
G28	GLLLALLALLLLALLRAAIAAKGAAARAAAAASAAYRAAKAAA
G29	SEEERREREELKREEERKAKLKAEGKAKREALKKAGEEYKKEREEKKEEEERKKKEEE
G30	SDADRCAAAAARLRARAAQTEALAAQGLSPECRAAAAAEAARLRALAAELEARRAA
G31	LEEVIDVITRITDAIAQALIAANPVVGGAIAAAIRAASALLALIK

G32	EKEKAILKQEAERAKKRAAGYNALAAEQAANGNTAAAAAAKAKAAAALKAKAAEYEEKAK
G33	EEEEERRKREEELRARIAALEAEAAAARALGAAIPALAAAAEGAAEAARRQAARIREYLAR
G34	AAAAAAEAAAAAAAAAAAAAAAAAAAAAARAVEALKAAALAEKLLKELLS
G35	AAEEEEERLRRAAAEALERLARAALLAALRAALARLANALKIAAAAAALAAAAA
G36	EEEELERELERLREERERFKEEEEKRRAALEAEAAAARRAAAEAAEEARRLAE
G37	MTPEERARALLEAALHTQARLAEKARTAESPEYAAEAEAAAARLARLQAALAA
G38	DKLEKELAEETTAEAEALAAAAAKAAEDPEKAKEYAHRLAVAQRRRDNIEKELEKKK
G39	MEREREERRRAEEEEAERARRAAERLEEKLAARKKEREKLLKERLEKELEELKKELE
G40	SVKEAIEEAIKEIKETEELSAGLSSTERAERIEETRKRAEERIREVIEKKKKKE
G41	SLEEVKQEAARIARLRAEAERICAASSPEECAEQRAIVEAREARIKALVE
G42	YLEEAVAALKKLRRDDLAAQLAKAKAAADTPEMKALAAETQALLELATKQLEKAEAKLK
G43	SLEELLKELEELKKKLLLEALALALALRRANQAPPELREKLLALADALKKLYLSLLK
G44	SLAEALRALAAAAGKALGNIAAGAAFLKALLAALAAAAAAAAAAAAA
G45	MTEEEKEREEKKKEAAKREARALAEARLLAAAAAALALLAALA
G46	SEAEKLVEKMREVRKEYRELAACKGEEEAKKVKEEMEKELKKLKEEREKVIKEKEEK
G47	ELEKKEELKKKKAEEAAKAAAALLAYALAKALAELEALAKALA
G48	EEEEAARKKLQEEVEKLEKETKERVKELEEKAKESTPEEAKEYKKEAEVVEETVKKIEEICKS
G49	LLALAARLAELARRAAIEARRAEVAARRAARAAAAAEAAAAA
G50	DLAELLRAVDAAIRAAAEALAAAAATEEEKLAVLQAGRLAIRLFRLLALLRALLS
G51	SPEALREACRAELEAVNKEYEKAKEEAKKLTPEEAKKVLAEQNKRLREAVERCRAAEA
G52	EEKKAKEKELLIAALKRKAEETARLKAEKGAEAEAFRAECEAKIAAAK
G53	EEEELKKAEAKKKLAEKKEERERRERAARLEEERRRREEEERRRRE
G54	MMEELKELVERLLELIDELLKNKELQPFAEELIKRFKEASKLSLEEFYKKVKELLEEAEEKLKEL
G55	SEEEKLKELAKKRKEELEAAKARREAEVARVLAEESEAAAKAKAAELTAAIVAKHKEFLKKLEE
G56	KEEKIKELEEKAKELEEEFKKAAKELIEAEKAGDKEKAEKYKEKAKELLKKKKEAEKKRKELE
G57	EELARLAEELAAARREALRAELEALRREQEERLREEEEERRRREEEEK
G58	ELEELAKKLREEREALKARAAALRAAAEAERAARAERAAAAARAAKAEERERLA
G59	LTEEEIKKLREQALQLREEINRLKSKAALASPEEKAKLEEEIKEKEAEREELIKKIK
G60	AALAAALQAALAAIDAAIAAAAAAARAAAAAEALKKLLEELAK
G61	SLAEIAARLAANKARAALFKALAAKLAKLTTPELAKKLAAKIVAK
G62	MEKELEELKKKKEEKKKEAEERKKAKEKAKELEKKKKKEKELKELE
G63	LPLAELLALLAALAAQLAAKAAYAACKAAIKAAGEARKAAEAAAAAEAEELL
G64	AQAELEAKRAAAAALAEELLEKRREEEEEEEEEEEEEEEEEEEEE
G65	SSLAKKILELRKKALEGLKAGK RTPETKRFQDIVEKTLKEEA EKAAKKALEELK
G66	MELEKKIEELAKMKELAAKGPEYRPELEKAGAKAREYREKLREELKKEEEE
G67	ELLKKLILLIKIGRGLNELGKKLRKAGLKKLANKFFKIGRKLYEIAEKL
G68	AEALEDLARRLIAKVREEAEKRAKAGTPEEAKEAWKEAAELRARIEALRAALLAA
G69	AATIAAYAAKLAHAAQCRALGAHPEIKAAAEKNAAAIEAARDKALANAAA
G70	SAAEAFAELAAAKAAYAAERDAAAAYKDNLEKREAALREWHRKEAETIAALKAKHAAEKAAA
G71	DVATLKALAAQYRAARAARVREEAARLAAAEPERAAEILAEGAALAAAFDAKAAAAAAAAAAAA
G72	TEEELRRELEARRAAAEEEARREAAARKEQAEKQAKAAALEAALKAAA
G73	EEEEERRRREEEREARLALREENERRRAERQAKIAAALALLAALLAA
G74	SLEENKKQWEKLQEETEKEVAKLKAEGDARRAALAAEAAARAAAEALAALAL
G75	SEIKEEAERRRREEEEERARRIAEAEARAAAAAAAAAAAAALAAAAAEELARA

G76	AEEELRAAEERAAALAEAAAARKAAREARKAAEEAAKAAAEAEELERKRAE
G77	EEEEKERLKEELREKLKKLLEEASKLENPQEVSEEAKKVYEEYLAL
G78	SAECTKLKVETHKKYQELAKKSKPEDLPVLVKKKEELKKIEEKCK
G79	EEEIRKRKEELEKKIAEAKEELEKAKSNPEMAKIAQELLEKLKAWAAEEIAKLEK
G80	AEEKEKRLEELKKEAARLEEEAARYKELAPETGLEARKKAGEAEREREKALEEIRCLEAE
G81	GYAELAKRYEEIAAKLKEQAKKNKEKGISEEKAKYLEEKAAEFEAKAKEAKAIYEA
G82	ETLAQLRAERDRAEARRAALLALPPEERAANAAAAIAAAAAAAAEAGIKKLEEEK
G83	LLEQLATLAALAAALAERAAREARRERLRREERERREERREERREERREERREER
G84	EEEEKKRKEELEKLKAEKEAERAALKAAEEAYRAAREAARREAEERERRER
G85	LSPEELEARRAALRAAEEARRAAERAAREEARAAAAAAEAEARARLEAELEAAAA
G86	DPEELKKEAEELAKKAEIYKKLAEEAAAKYSQSAADRLKAKAAEYEA KRKAVEAKLKALE
G87	EALRAAIDALADALLAATDALAAASTPEAAARLRAATAAAIRALYALAE
G88	SEVERLKAEAAARLTERIVELAEKAMELAKKSTPEEAKKIMEEAKKERDRLRAERERALAEAEALE
G89	SKEEIEALEKKLAEKALAEKAAENPVLAAQYRAQALEAEAQLEKLKKEA
G90	LSDLASALAQALGLELLADPETKEEGLKLIAEALARLAAALEQLARLLAGLAAKAAEEAA
G91	AEVAKLKAEAAAAKAKAAAAAAGNLAADAARKKALEYEAKANKALEE
G92	EEELAKAALEAERAALKAAREAERAAREAAAAERAEEEEARRAAEAEERERAA
G93	SEEEIEKIEEAIKKLKEVKAEAEKKKATSSPEEREKIEKEAKEKMDIEILREEREKIEKLKKE
G94	EEEELEEKLKKLLEEKEKKLKELEERKKRKEKLEKAEEKELKKKLE
G95	LDEAVAAAAREAIRAAVEEAKKLYKEDPEKGKELLKAAQAALAALRAARAAEAAAAAA
G96	SALEELAKAKAEAEKLAETKTGDEETAKKTLEARAKALKLEEL
G97	SLRELLRLLASLALRLFRALRAAAGAFMAADPALGAALLAAVEALEEAFRALVLAILLS
G98	LAELYKKQAEKQAQAAAAAQAAADPANAAELQAQAQAKLQAQAELQKKAAEALA
G99	EEEKEVEKKIKELLEKGKKSTPEEAAKYNAAEYLKIEAEAKKRKEEAEKAKKLKEELEKL

Table 3: HDock scores for IL-2 mimics targeting IL-2R α and IL-2R β

IL-2 Mimetics and IL-2R α	HDock	IL-2 Mimetics and IL-2R β	HDock
B73	-266.18	B41	-283.09
B30	-262.99	B78	-274.87
B19	-259.94	B66	-271.51
B12	-256.36	B73	-268.54
B46	-256.1	B19	-266.05
B85	-254.93	B42	-264.04
B50	-254.4	B53	-262.29
B28	-253.48	B70	-249.3
B42	-252.07	B14	-248.62

B66	-247.32	B69	-248.6
B92	-244.83	B63	-245.8
B56	-241.86	B2	-244.07
B78	-240.6	B45	-243.82
B53	-240.58	B75	-243.7
B54	-240.03	B90	-243.13
B67	-239.77	B30	-242.64
B60	-239.71	B99	-241.69
B14	-238.68	B71	-240.88
B75	-238.26	B18	-240.85
B9	-236.76	B58	-240.04
B77	-235.83	B86	-237.62
B33	-234.25	B98	-237.13
B80	-232.22	B34	-233.13
B64	-232.13	B36	-233.12
B36	-232.1	B76	-233.09
B58	-231.73	B25	-232.64
B16	-230.57	B50	-232.58
B4	-230.56	B26	-232.26
B11	-229.48	B16	-231.97
B2	-228.91	B12	-229.92
B86	-228.15	B24	-228.96
B93	-228.03	B56	-228.32
B10	-227.84	B87	-227.6
B71	-227.61	B92	-225.01
B25	-226.9	B51	-223.91
B96	-226.73	B88	-222.72
B37	-226.47	B77	-221.42
B79	-226.42	B82	-220.4
B87	-226.02	B67	-220.16

B43	-225.68	B46	-219.73
B82	-225.21	B4	-218.47
B68	-224.88	B0	-218.14
B76	-224.12	B28	-216.02
B18	-223.68	B96	-215.17
B89	-223.59	B10	-214.62
B35	-222.33	B20	-213.94
B38	-222.26	B80	-212.86
B98	-221.76	B32	-212.4
B40	-221.54	B83	-211.39
B70	-221.54	B44	-210.94
B26	-221.29	B68	-210.78
B13	-220.32	B74	-209.05
B39	-219.83	B35	-209
B45	-219.81	B84	-208.86
B41	-219.33	B31	-207.51
B49	-217.12	B3	-207.22
B97	-217.1	B38	-206.82
B72	-216.79	B49	-205.16
B99	-216.48	B11	-204.37
B15	-215.88	B37	-204.01
B22	-215.35	B97	-203.77
B29	-215.22	B61	-203.35
B52	-215.13	B39	-203.2
B90	-214.74	B54	-201.1
B51	-214.42	B27	-200.1
B20	-214.39	B93	-199.98
B74	-213.96	B43	-199.63
B27	-213.23	B17	-199.02
B88	-212.92	B52	-198.86

B63	-211.11	B33	-198.72
B17	-210.81	B85	-198.55
B31	-210.55	B48	-198.42
B55	-209.91	B5	-198.4
B32	-209.14	B72	-196.92
B5	-206.15	B40	-196.5
B47	-206.07	B94	-195.94
B34	-205.46	B1	-193.57
B3	-205.42	B15	-193.53
B57	-205.28	B55	-190.82
B62	-204.36	B7	-189.85
B84	-203.91	B57	-189.79
B83	-201.54	B79	-189.54
B24	-200.87	B64	-189.35
B1	-200.44	B91	-189.31
B61	-200.07	B9	-189.02
B7	-199.55	B22	-188.94
B48	-197.47	B60	-186.98
B44	-196.46	B89	-185.69
B0	-195.97	B29	-184
B69	-195.65	B62	-182.49
B65	-195.24	B8	-181.75
B21	-195.03	B13	-180.98
B8	-192.53	B47	-179.07
B91	-188.54	B21	-177.55
B94	-185.84	B81	-176.32
B6	-183.34	B6	-172.16
B59	-180.23	B59	-167.59
B95	-174.85	B23	-167.13
B23	-167.66	B95	-161.25

B81	-163.65	B65
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Table 4: HDock scores for IL-2 mimics targeting IL-2R α and IL-2R γ

IL-2 Mimetics and IL-2R α	HDock	IL-2 Mimetics and IL-2R γ	HDock
G14	-289.8	G14	-290.86
G50	-281.82	G35	-289.62
G97	-273.2	G71	-276.1
G2	-261.96	G9	-274.13
G33	-254.27	G83	-266.59
G70	-254.27	G2	-263.08
G37	-251.79	G63	-258.95
G66	-248.84	G61	-257.87
G83	-248.61	G97	-255.6
G71	-244.66	G50	-255.49
G51	-244.46	G26	-252.8
G18	-242.97	G70	-252.07
G28	-242.86	G30	-249.95
G61	-241.7	G90	-249.32
G35	-241.13	G57	-248.37
G23	-240.98	G36	-247.29
G65	-240.87	G37	-247.22
G44	-240.73	G42	-246.37
G69	-240.24	G44	-244.12
G30	-238.8	G12	-243.49
G56	-238.58	G16	-243.02
G43	-238.15	G18	-242.61
G92	-238.03	G28	-241.43
G11	-236.9	G32	-241.03
G98	-236.19	G88	-240.63

G67	-235.11	G23	-239.76
G36	-234.53	G43	-239.59
G15	-233.55	G68	-239.25
G85	-232.64	G11	-236.5
G90	-232.34	G1	-236.28
G74	-231.44	G66	-235.87
G95	-230.47	G19	-235.43
G1	-229.89	G76	-231.9
G9	-229.06	G15	-231.52
G73	-228.44	G39	-231.4
G63	-228.37	G69	-229.72
G19	-227.89	G77	-229.33
G8	-227.69	G7	-228.79
G39	-227.37	G67	-228.73
G76	-225.45	G87	-228.67
G58	-225.28	G85	-227.87
G57	-225.23	G98	-227.86
G49	-224.89	G58	-227.72
G84	-224.87	G73	-227.27
G46	-224.37	G0	-226.34
G13	-223.61	G53	-226.24
G0	-223.35	G75	-225.41
G31	-221.81	G60	-224.77
G68	-221.7	G92	-223.79
G47	-221.26	G49	-223.55
G78	-221.21	G45	-221.54
G88	-219.56	G10	-221.17
G55	-219.21	G31	-221.15
G29	-218.42	G38	-220.99
G75	-218.07	G95	-220.49

G41	-216.91	G33	-220.16
G77	-212.81	G51	-220.02
G87	-212.36	G41	-219.89
G24	-212.1	G84	-217.6
G45	-211.87	G4	-215
G42	-211.6	G82	-212.68
G5	-211.34	G29	-211.89
G81	-210.87	G47	-211.24
G32	-209.65	G6	-210.7
G94	-209.51	G13	-210.55
G54	-209.4	G74	-209.54
G52	-209.21	G86	-209.33
G7	-208.07	G55	-208.45
G53	-207.78	G54	-207.32
G25	-205.98	G20	-204.86
G10	-205.45	G34	-203.87
G59	-205.08	G99	-203.16
G60	-204.46	G59	-202.84
G89	-204.37	G25	-202.44
G17	-202.19	G24	-201.79
G79	-201.97	G81	-201.56
G27	-201.81	G3	-200.46
G64	-201.52	G72	-199.78
G22	-201.46	G27	-198.77
G20	-200.93	G52	-196.96
G40	-200.92	G5	-196.58
G34	-198.18	G78	-196.1
G72	-197.62	G40	-195.96
G99	-197.26	G21	-195.94
G38	-195.1	G46	-195.23

G91	-194.48	G22	-192.55
G16	-194.05	G17	-192.42
G4	-190.55	G64	-191.91
G86	-189.76	G79	-190.15
G26	-189.49	G91	-189.24
G48	-189.13	G48	-186.86
G21	-188.47	G89	-186.59
G82	-186.88	G65	-185.23
G93	-185.74	G80	-183.47
G80	-181.05	G94	-181.76
G96	-177.09	G56	-181.69
G6	-174.79	G8	-174.57
G62	-173.53	G96	-168.89
G3	-169.35	G93	-166.7
G12		G62	-154.13

Table 5: The sequence of IL-2R γ mimics

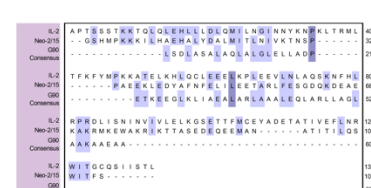
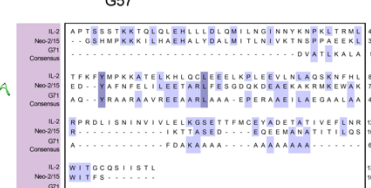
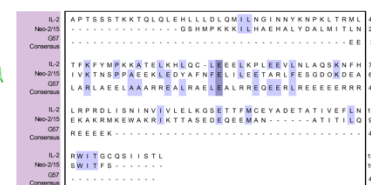
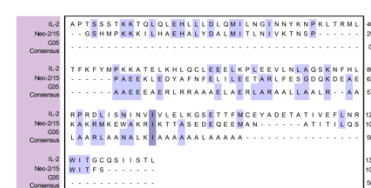
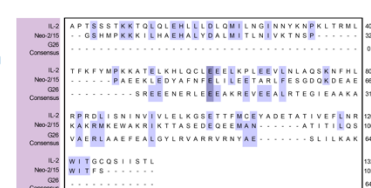
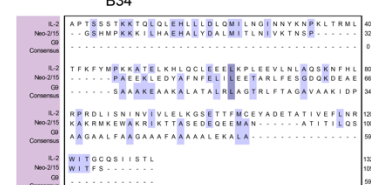
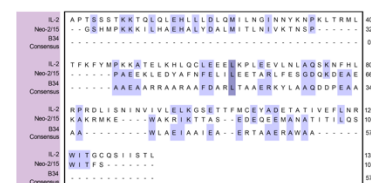
Complex design model	Sequence
G9	SAAAKEAAKALATALRLAGTRLFTAGAVAAKIDPAAGAALFAAGAAAFAAAAAL EKALA
G16	MSLAEAR DAGVAAALASGDPAHLDAAKAAIAAAVSPEEAARWAAVLDEDYARA RAAAA
G35	AAAAEAERLRRAAAELAERLARAALLAALRAALAARLAANALKIAAAAAALAAA AA
G42	YLEEAVAALKKKLRDDLAAQLAKAKAAAADTPEMKALAAETQALLELATKQLEKAE AKLK
G57	EELARLAEELAAARREALRAELEA LRREQEERLREEEEEERRRREEEEK
G71	DVATLKALAAQYRAARAAVREEAARLAAAEPERAAEILAEGAALAAAFDAKAAA AAAAAAAAA

Table 6: The sequence of IL-2R β mimics

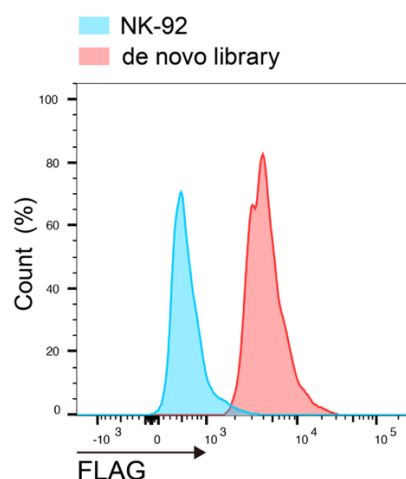
Complex design model	Sequence
B0	MEEKLEFLKKKLAELD ^D GKY ^I YEKCYGT ^E EEAKKALEELKA ^A LEELAKAEKEAAA AAA
B34	AAEAARRAARA ^A FDARLTAA ^E ERKYLA ^A QDDPEAAAAWLAEIAA ^I E ^E AERTAA ^E R ^R AWA ^A
B51	EEERRRQIEALKRA ^A AAEY ^E YALAKELAAK ^D PAYAP ^L AEALKAE ^E LERLKAELA ALEAA

Table 7: The ipTM and pTM score of IL-2 mimics

IL-2 mimics	ipTM	pTM
B34G35R-GALA4	0.63	0.7
B34G35R-GALA5	0.55	0.67
B34G35R-GALA6	0.46	0.61
B51G35R-GALA4	0.62	0.72
B51G35R-GALA5	0.66	0.75
B51G35R-GALA6	0.5	0.62
B51G9-GALA4	0.66	0.75
B51G9-GALA5	0.7	0.72
B51G9-GALA6	0.63	0.71



Extended Data Fig. 1 | Visual inspection for the de novo design protein. Multiple sequence alignment (MSA) via DNAMAN revealed low similarity between the synthetic sequence and native IL-2/neo-2-15 (de novo IL-2 mimic(*I*)) with IL-2R β and γ ; structural visualization of the binding sites (front and side views) generated using PyMOL; molecular docking scores were subsequently quantified using HDock.



Extended Data Fig. 2 | The verification of the library construction of de novo library. De novo library expression. At 72 h after retroviral transduction, the expression of de novo library on human NK-92 cells were measured by staining with anti-FLAG antibody, followed by flow cytometry analysis. NK-92 cells without transduction were used as negative controls. The wave peak shown in blue correspond to the isotype controls and the red histograms indicate positive fluorescence of de novo library expression.

Reference

- [1] SILVA D A, YU S, ULGE U Y, et al. De novo design of potent and selective mimics of IL-2 and IL-15 [J]. Nature, 2019, 565(7738): 186-91.