BCB 731:

Defense Against the Dark Arts

Critic: Key Parameters of Tumor Epitope Immunogenicity Revealed Through a Consortium Approach Improve Neoantigen Prediction

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Resource

Key Parameters of Tumor Epitope Immunogenicity Revealed Through a Consortium Approach Improve Neoantigen Prediction

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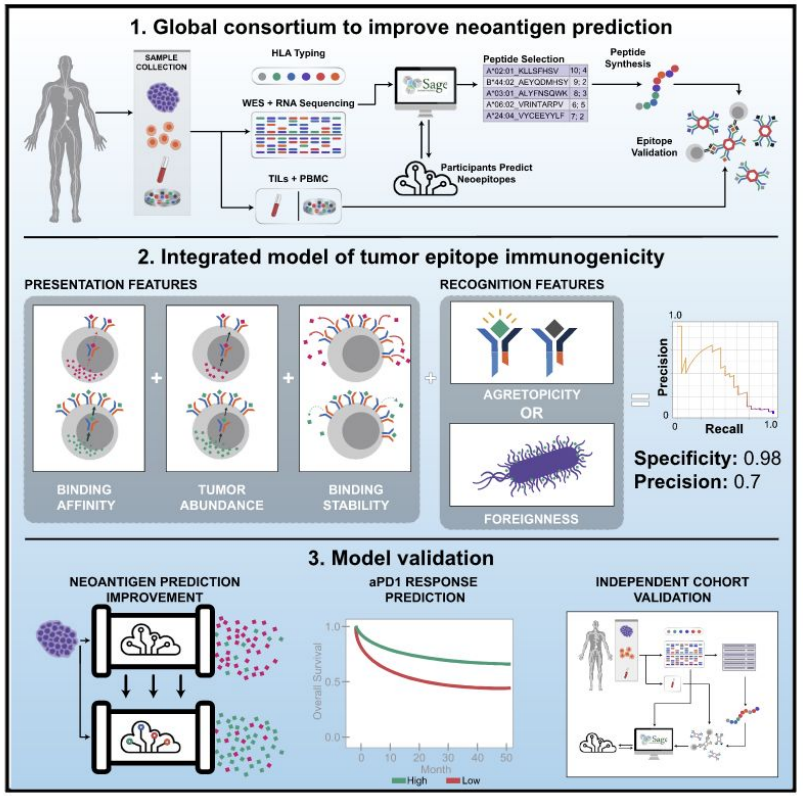


Summary

Many approaches to identify therapeutically relevant neoantigens couple tumor sequencing with bioinformatic algorithms and inferred rules of tumor epitope immunogenicity. However, there are no reference data to compare these approaches, and the parameters governing tumor epitope immunogenicity remain unclear. Here, we assembled a global consortium wherein each participant predicted immunogenic epitopes from shared tumor sequencing data. 608 epitopes were subsequently assessed for T cell binding in patient-matched samples. By integrating peptide features associated with presentation and recognition, we developed a model of tumor epitope immunogenicity that filtered out 98% of non-immunogenic peptides with a precision above 0.70. Pipelines prioritizing model features had superior performance, and pipeline alterations leveraging them improved prediction performance. These findings were validated in an independent cohort of 310 epitopes prioritized from tumor sequencing data and assessed for T cell binding. This data resource enables identification of parameters underlying effective anti-tumor immunity and is available to the research community.

TESLA contest

Many approaches to identify therapeutically relevant neoantigens couple tumor sequencing with bioinformatic algorithms and inferred rules of tumor epitope immunogenicity. However, there are no reference data to compare these approaches, and the parameters governing tumor epitope immunogenicity remain unclear. Here, we assembled a global consortium wherein each participant predicted immunogenic epitopes from shared tumor sequencing data. 608 epitopes were subsequently assessed for T cell binding in patient-matched samples. By integrating peptide features associated with presentation and recognition, we developed a model of tumor epitope immunogenicity that filtered out 98% of non-immunogenic peptides with a precision above 0.70. Pipelines prioritizing model features had superior performance, and pipeline alterations leveraging them improved prediction performance. These findings were validated in an independent cohort of 310 epitopes prioritized from tumor sequencing data and assessed for T cell binding. This data resource enables identification of parameters underlying effective anti-tumor immunity and is available to the research community.

Immunogenicity model from TESLA data

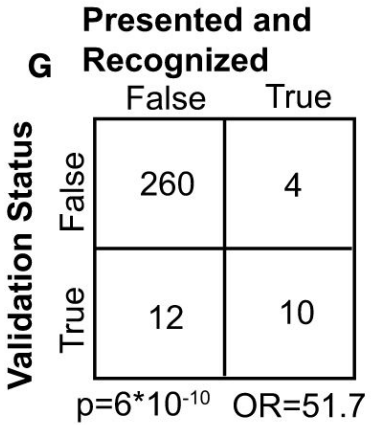
Many approaches to identify therapeutically relevant neoantigens couple tumor sequencing with bioinformatic algorithms and inferred rules of tumor epitope immunogenicity. However, there are no reference data to compare these approaches, and the parameters governing tumor epitope immunogenicity remain unclear. Here, we assembled a global consortium wherein each participant predicted immunogenic epitopes from shared tumor sequencing data. 608 epitopes were subsequently assessed for T cell binding in patient-matched samples. By integrating peptide features associated with presentation and recognition, we developed a model of tumor epitope immunogenicity that filtered out 98% of non-immunogenic peptides with a precision above 0.70. Pipelines prioritizing model features had superior performance, and pipeline alterations leveraging them improved prediction performance. These findings were validated in an independent cohort of 310 epitopes prioritized from tumor sequencing data and assessed for T cell binding. This data resource enables identification of parameters underlying effective anti-tumor immunity and is available to the research community.

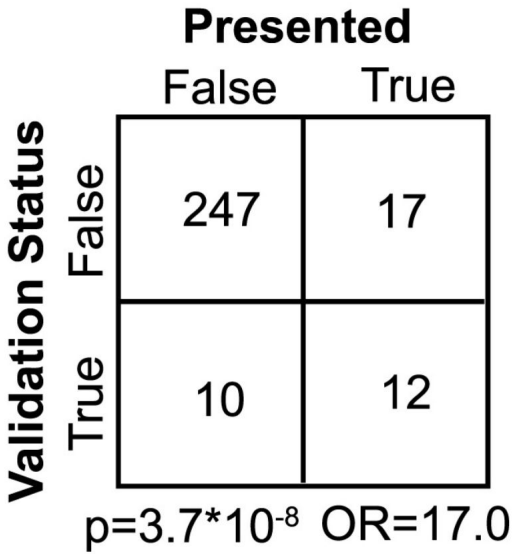
Validation of new model

Many approaches to identify therapeutically relevant neoantigens couple tumor sequencing with bioinformatic algorithms and inferred rules of tumor epitope immunogenicity. However, there are no reference data to compare these approaches, and the parameters governing tumor epitope immunogenicity remain unclear. Here, we assembled a global consortium wherein each participant predicted immunogenic epitopes from shared tumor sequencing data. 608 epitopes were subsequently assessed for T cell binding in patient-matched samples. By integrating peptide features associated with presentation and recognition, we developed a model of tumor epitope immunogenicity that filtered out 98% of non-immunogenic peptides with a precision above 0.70. Pipelines prioritizing model features had superior performance, and pipeline alterations leveraging them improved prediction performance. These findings were validated in an independent cohort of 310 epitopes prioritized from tumor sequencing data and assessed for T cell binding. This data resource enables identification of parameters underlying effective anti-tumor immunity and is available to the research community.

Funny numbers (286 vs. 608 pMHCs)

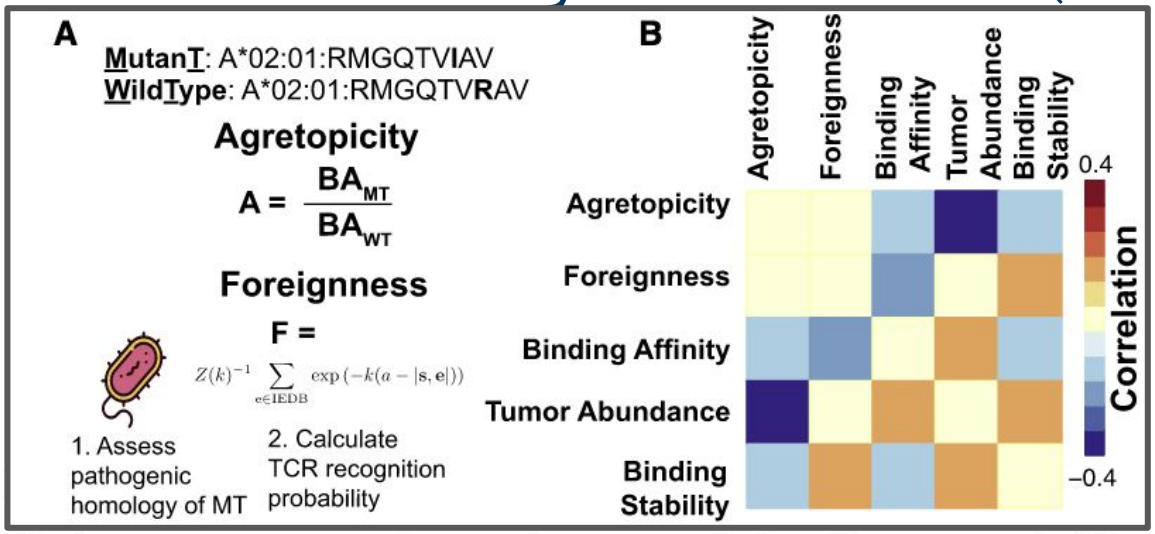
ranked pMHC per tumor sample (median: 204). From these submitted predictions, 608 peptides selected from among the top-ranked peptides from all groups (median, 97/subject; range, 73–144, see Table S4 for complete list of tested peptides) were tested for immunogenicity by pMHC multimer-based assays and 37 (6%) of those were found to be immunogenic, a validation





Presented:
Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours

Funny numbers (286 vs. 608 pMHCs)



feature (i.e., binding affinity, tumor abundance, binding stability, fraction hydrophobic, and mutational position)—shown in Figure 3L. 286 (out of the 608) peptides had measurements of all 5 of these variables, and it is this set we analyzed. Using our approach, we identified

Missing entries in validated epitopes

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINITY	NETMHC_PAN_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	FRAC_HYDROPHOBIC	AGRETOPICITY	FOREIGNNESS	MUTATION_POSITION	NUMBER_PREDICTING	VALIDATED
A*01:01_FTNESYLELY	3	PBMC	A*01:01	FTNESYLELY	10	2	7.5	62.9918092	2.83	0.3	2.29119253	6.95E-09	3	11	TRUE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13	7	12	TRUE
A*01:01_LSDGPSMGRY	3	PBMC	A*01:01	LSDGPSMGR'	10	6	15.6	73.9485217	2.41	0.2	1.398413287	0	4	10	TRUE
A*02:01_ALDHMFMYFL	1	PBMC	A*02:01	ALDHMFMYF	10	10	32.4	50.383842	5.06	0.6	0.586219548	6.15E-13	3	9	TRUE
A*02:01_ALPPTVYEV	2	PBMC	A*02:01	ALPPTVYEV	9	7	6.8	83.895846	11.82	0.333333333	0.162908109	0.007619771	9	15	TRUE
A*02:01_FLDPDLTNI	1	PBMC	A*02:01	FLDPDLTNI	9	5	4.2	8.3503516	5.09	0.444444444	0.148379071	0	1	5	TRUE
A*02:01_FLGSLLILV	1	PBMC	A*02:01	FLGSLLILV	9	9	6.2	52.051897	8.45	0.777777778	0.463529085	0.999999997	1	15	TRUE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0	4	2	TRUE
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13	3	12	TRUE
A*02:01_KAWENFPNV	1	PBMC	A*02:01	KAWENFPNV	9	14	34.7	110.0615949	2.42	0.333333333	0.443930005	0.007677829	6	17	TRUE
A*02:01_KLLSFHSV	16	TIL	A*02:01	KLLSFHSV	8	372	160	1.28079	20.01	0.5	0.339337413	0	8	7	TRUE
A*02:01_RVYDALNLL	1	PBMC	A*02:01	RVYDALNLL	9	85	79.6	97.944239	1.89	0.444444444	0.293871706	0	8	12	TRUE
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0	6	3	TRUE
A*02:01_YLYHRVDVI	1	PBMC	A*02:01	YLYHRVDVI	9	15	16.4	85.797266	6.46	0.444444444	0.005610301	0	1	14	TRUE
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298	1	5	TRUE
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0	3	8	TRUE
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0	6	10	TRUE
A*03:01_ATRYNYTSEK	3	PBMC	A*03:01	ATRYNYTSEK	10	14	16.7	36.6277262	1.89	0	0.002436715	0	10	10	TRUE
A*03:01_ATYKGVPYEVK	3	PBMC	A*03:01	ATYKGVPYEV	11	5	48.6	44.59235	4.48	0.181818182	0.762838237	9.05E-07	8	10	TRUE
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0	3	9	TRUE
A*03:01_ILFRTPSVAK	3	PBMC	A*03:01	ILFRTPSVAK	10	0	10.5	32.7431059	3.8	0.4	0.500936987	0	3	10	TRUE
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0	7	1	TRUE
A*03:01_KIYTGEKPYK	3	PBMC	A*03:01	KIYTGEKPYK	10	30	14.1	11.13847	6.71	0.1	0.218105535	1.36E-06	3	7	TRUE
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07	7	10	TRUE
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0	3	14	TRUE
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0	5	16	TRUE
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11	6	4	TRUE
A*68:01_DTIDVSKLNR	1	PBMC	A*68:01	DTIDVSKLNR	10	19	16.6	76.848704	2.43	0.3	1.80108118	0	7	13	TRUE
A*68:01_EIIPQCIAR	1	PBMC	A*68:01	EIIPQCIAR	9	29	24.1	69.68075	2.61	0.444444444	0.030952544	0	1	17	TRUE
B*07:02_RGRMQTASL	12	TIL	B*07:02	RGRMQTASL	9	1.7	57.7	2.87527	1.5	0.222222222	1.095658276	0	4	10	TRUE
B*08:01_HALRRHYHL	3	PBMC	B*08:01	HALRRHYHL	9	52	10.3	40.43526	0.47	0.222222222	0.021019138	0	9	15	TRUE
B*27:05_RRSMLFARH	16	TIL	B*27:05	RRSMLFARH	9	5.1	62.1	15.071688	3.97	0.333333333	0.582559182	0	5	10	TRUE
B*44:02_AEYQDMHSY	10	TIL	B*44:02	AEYQDMHSY	9	43	16.4	0.931241	3.28	0.111111111	0.53662253	0	3	6	TRUE
B*44:02_VEHINISQDW	10	TIL	B*44:02	VEHINISQDW	10	75	32.4	3.963	0.93	0.4	1.061775959	1.21E-17	3	8	TRUE
B*57:01_KSFKEIKLW	2	PBMC	B*57:01	KSFKEIKLW	9	26	6	51.16246263	49.34	0.444444444	0.7110974	0.5	5	16	TRUE
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA	4	6	TRUE
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0	9	10	TRUE

Only 22/37 have all five features!

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINITY	NETMHC_PAN_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	FRAC_HYDROPHOBIC	AGRETOPICITY	FOREIGNNESS	MUTATION_POSITION	NUMBER_PREDICTING	VALIDATED
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A*01:01_LSDGPSMGRY	3	PBMC	A*01:01	LSDGPSMGR	10	6	15.6	73.9485217	2.41	0.2	1.398413287	0	4	10	TRUE
A*02:01_ALDHMFMYFL	1	PBMC	A*02:01	ALDHMFMYF	10	10	32.4	50.383842	5.06	0.6	0.586219548	6.15E-13	3	9	TRUE
A*02:01_ALPPTVYEV	2	PBMC	A*02:01	ALPPTVYEV	9	7	6.8	83.895846	11.82	0.333333333	0.162908109	0.007619771	9	15	TRUE
A*02:01_FLDPDLTNI	1	PBMC	A*02:01	FLDPDLTNI	9	5	4.2	8.3503516	5.09	0.444444444	0.148379071	0	1	5	TRUE
A*02:01_FLGSLLILV	1	PBMC	A*02:01	FLGSLLILV	9	9	6.2	52.051897	8.45	0.777777778	0.463529085	0.999999997	1	15	TRUE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0	4	2	TRUE
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13	3	12	TRUE
A*02:01_KAWENFPNV	1	PBMC	A*02:01	KAWENFPNV	9	14	34.7	110.0615949	2.42	0.333333333	0.443930005	0.007677829	6	17	TRUE
A*02:01_KLLSFHSV	16	TIL	A*02:01	KLLSFHSV	8	372	160	1.28079	20.01	0.5	0.339337413	0	8	7	TRUE
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A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0	6	3	TRUE
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A*03:01_ATRYNYTSEK	3	PBMC	A*03:01	ATRYNYTSEK	10	14	16.7	36.6277262	1.89	0	0.002436715	0	10	10	TRUE
A*03:01_ATYKGVPYEVK	3	PBMC	A*03:01	ATYKGVPYEV	11	5	48.6	44.59235	4.48	0.181818182	0.762838237	9.05E-07	8	10	TRUE
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0	3	9	TRUE
A*03:01_ILFRTPSVAK	3	PBMC	A*03:01	ILFRTPSVAK	10	0	10.5	32.7431059	3.8	0.4	0.500936987	0	3	10	TRUE
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0	7	1	TRUE
A*03:01_KIYTGEKPYK	3	PBMC	A*03:01	KIYTGEKPYK	10	30	14.1	11.13847	6.71	0.1	0.218105535	1.36E-06	3	7	TRUE
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07	7	10	TRUE
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0	3	14	TRUE
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0	5	16	TRUE
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11	6	4	TRUE
A*68:01_DTIDVSKLNR	1	PBMC	A*68:01	DTIDVSKLNR	10	19	16.6	76.848704	2.43	0.3	1.80108118	0	7	13	TRUE
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B*44:02_AEYQDMHSY	10	TIL	B*44:02	AEYQDMHSY	9	43	16.4	0.931241	3.28	0.111111111	0.53662253	0	3	6	TRUE
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C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0	9	10	TRUE

34nM cutoff based on measured peptide-MHC binding affinity

and (3) a subset of highly ranked predicted pMHC from each team are tested *in vitro* to determine MHC binding and peptide immunogenicity, the latter determined via the detection of

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINITY	NETMHC_PAN_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	FRAC_HYDROPHOBIC	AGRETOPICITY	FOREIGNNESS	MUTATION_POSITION	NUMBER_PREDICTING	VALIDATED
A*01:01_FTNESYLELY	3	PBMC	A*01:01	FTNESYLELY	10	2	7.5	62.9918092	2.83	0.3	2.29119253	6.95E-09	3	11	TRUE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13	7	12	TRUE

Validation dataset only has predicted MHC binding affinity

and (3) a subset of highly ranked predicted pMHC from each team are tested *in vitro* to determine MHC binding and peptide immunogenicity, the latter determined via the detection of

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINITY	NETMHC_PAN_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	FRAC_HYDROPHOBIC	AGRETOPICITY	FOREIGNNESS	MUTATION_POSITION	NUMBER_PREDICTING	VALIDATED
A*01:01_FTNESYLELY	3	PBMC	A*01:01	FTNESYLELY	10	2	7.5	62.9918092	2.83	0.3	2.29119253	6.95E-09	3	11	TRUE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13	7	12	TRUE

VS.

PMHC	PATIENT_ID	TISSUE_TYPE	ALT_EPI_SEQ	PEP_LEN	PREDICTED_BINDING_AFFINITY	NETMHC_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	AGRETOPICITY	FOREIGNNESS	MUTATION_	VALIDATED
A*01:01_AISDSLLWKY	8	TIL	AISDSLLWKY	10	62.9	32.15	16.319886	1.65	0.16474594	0.5	8	0
A*01:01_ASSSGTRLY	8	TIL	ASSSGTRLY	9	218.7	334.79	3.024792	1.31	0.020217614	0	9	0
A*01:01_ATDTNNLNVNY	9	TIL	ATDTNNLNV	11	67.4	45.31	49.85	4.19	0.350858928	6.98E-09	7	1
A*01:01_CSFRGSGSLSY	8	TIL	CSFRGSGSLS	11	715.1	648.89	0.392	0.54	0.297983165	2.05E-13	9	0
A*01:01_CSTVKDFSY	8	TIL	CSTVKDFSY	9	186.7	251.42	4.834086	0.76	0.017516865	0	9	0
A*01:01_DTCQGAFMY	8	TIL	DTCQGAFMY	9	345.970754	119.99	7.097683935	1.26	0.44184962	0	7	0
A*01:01_DTERLPTSY	9	TIL	DTERLPTSY	9	193.0919777	28.56	13.66323041	0.42	0.013744542	0	9	0
A*01:01_ELESSNDSY	8	TIL	ELESSNDSY	9	526.8182007	175.56	0.5975109	0.34	0.752352409	5.34E-11	6	0
A*01:01_ESDKTPWFW	9	TIL	ESDKTPWFW	9	2683	1173.38	1.55	1.06	0.147516467	5.90E-05	3	0
A*01:01_ETDLQPEWEA	9	TIL	ETDLQPEWE	10	2542.6	1223.55	13.1979	0.24	0.637051513	6.95E-09	8	0

Checkpoint blockade cohort only has predicted peptide-MHC binding

Predicted Neoantigen Abundance

Potential immunogenic peptides were generated using a previously generated set of mutation calls (Liu et al., 2019) and predicted MHC binding affinity was assigned using NetMHCPan4.0. Predicted neoantigen abundance was taken as the sum of the normalized transcripts per million (TPM) of the mutations which passed all "presented" filters from Figure 3L (excluding the abundance filter) – specifically, MHC binding affinity stronger than 34 nM and MHC binding stability longer than 1.4 hours, and mutational position not 2.

Predicted and Recognized Neoantigen Abundance

Potential immunogenic p eptides were generated using a previously generated set of mutation calls (Liu et al., 2019) and predicted MHC binding affinity was assigned using NetMHCPan4.0. Predicted and recognized neoantigen abundance was taken as the sum of the normalized transcripts per million (TPM) of the mutations which passed all "presented" features (excluding the abundance filter, identical to predicted neoantigen abundance) and the "recognized' filters from Figure 4D – specifically, peptide agretopicity less than 0.1 or peptide foreignness greater than 10^{-16}.

Would “NA” validated epitopes be predicted as “recognized”?

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16}(Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

Would “NA” validated epitopes be predicted as “recognized”?

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16}(Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

Would “NA” validated epitopes be predicted as “recognized”?

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16}(Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

Would “NA” validated epitopes be predicted as “recognized”?

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

Would “NA” validated epitopes be predicted as “recognized”?

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

15 missing validated epitopes → 14 known prediction → 9 wrong!

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

What about presentation features?

Presented:
Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

What about presentation features?

Presented:
Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

What about presentation features?

Presented:

Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

What about presentation features?

Presented:

Binding Affinity < 34 nM;

Tumor Abundance > 33 TPM;

Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or

Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

15 validated epitopes w/ “NA”, 11+ wrong

Presented:

Binding Affinity < 34 nM;

Tumor Abundance > 33 TPM;

Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or

Foreignness > 10^{-16} (Group 2)

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*01:01_ILDTAGHEEY	2	PBMC	A*01:01	ILDTAGHEEY	10	NA	131.8	55.8579	1.8	0.2	0.939635593	2.05E-13
A*02:01_GLYGNLIVL	2	PBMC	A*02:01	GLYGNLIVL	9	NA	31.4	10.594267	3.15	0.555555556	0.263456745	4.10E-13
A*03:01_AINRPTVLK	3	PBMC	A*03:01	AINRPTVLK	9	NA	17.5	2.65461	5.14	0.333333333	2.67792685	0
A*03:01_HLFDIQGLPK	3	PBMC	A*03:01	HLFDIQGLPK	10	NA	16.7	17.71229827	3.6	0.4	0.351232197	0
A*03:01_KLRDEISLAK	3	PBMC	A*03:01	KLRDEISLAK	10	NA	18.7	41.438896	13.5	0.3	0.670289067	9.05E-07
C*05:01_KTDTGVHATL	16	TIL	C*05:01	KTDTGVHATL	10	NA	415.5	0.89626	0.24	0.2	2.167248023	NA
C*06:02_VRINTARPV	12	PBMC	C*06:02	VRINTARPV	9	NA	351.9	14.25145	0.14	0.333333333	0.110403328	0

PMHC	PATIENT_ID	TISSUE_TYPE	MHC	ALT_EPI_SEQ	PEP_LEN	MEASURED_BINDING_AFFINI	NETMHC_PAN_BINDING_AFFINI	TUMOR_ABUNDANC	BINDING_STABILI	FRAC_HYDROPHOB	AGRETOPICI	FOREIGNNE
A*02:01_FLNCDIMLGV	1	PBMC	A*02:01	FLNCDIMLGV	10	11	6.2	NA	9.32	0.7	1.441860465	0
A*02:01_YLNEAVFNFV	16	TIL	A*02:01	YLNEAVFNFV	10	8.4	3.5	NA	20.22	0.5	0.714285714	0
A*02:01_YQANVVWKV	12	TIL	A*02:01	YQANVVWKV	9	7	4.1	NA	27.13	0.444444444	8.51E-05	0.015124298
A*03:01_ALYFNSQWK	12	TIL	A*03:01	ALYFNSQWK	9	12	21.9	NA	4.14	0.333333333	0.725591879	0
A*03:01_KIVEMSTSK	3	PBMC	A*03:01	KIVEMSTSK	9	122	61.2	NA	3.9	0.333333333	0.931506849	0
A*03:01_RLFPYALHK	3	PBMC	A*03:01	RLFPYALHK	9	15	3.5	NA	42.15	0.333333333	0.583839837	0
A*03:01_RTREFTAKK	3	PBMC	A*03:01	RTREFTAKK	9	36	35.7	NA	12.4	0.111111111	0.602166481	0
A*24:02_VYCEEYYLF	10	TIL	A*24:02	VYCEEYYLF	9	17	6.1	NA	82.53	0.444444444	0.198039324	2.67E-11

Closer look at that validation data...

Presented:
Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours

Recognized:
Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16}(Group 2)

Agretopicity

$$A = \frac{BA_{MT}}{BA_{WT}}$$

Foreignness

$$F = Z(k)^{-1} \sum_{e \in IEDB} \exp\left(-k(a - |\mathbf{s}, \mathbf{e}|)\right)$$

PREDICTED_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY
67.4	49.85	4.19
12	16.319886	7.29
128.6	28.887051	0.71
42.38742509	145.4920265	3.11

AGRETOPICITY	FOREIGNNESS
0.350858928	6.98E-09
0.224719101	2.67E-11
1.038772213	0
0.002893805	4.53E-07

Closer look at that validation data...

Presented:

Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or
Foreignness > 10^{-16}(Group 2)

Agretopicity

$$A = \frac{BA_{MT}}{BA_{WT}}$$

Foreignness

$$F = Z(k)^{-1} \sum_{e \in IEDB} \exp\left(-k(a - |\mathbf{s}, \mathbf{e}|)\right)$$

PREDICTED_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	AGRETOPICITY	FOREIGNNESS	
67.4	49.85	4.19	0.350858928	6.98E-09	✗
12	16.319886	7.29	0.224719101	2.67E-11	
128.6	28.887051	0.71	1.038772213	0	✗
42.38742509	145.4920265	3.11	0.002893805	4.53E-07	✗

Closer look at that validation data...

Presented:

Binding Affinity < 34 nM;

Tumor Abundance > 33 TPM;

Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or

Foreignness > 10^{-16}(Group 2)

Agretopicity

$$A = \frac{BA_{MT}}{BA_{WT}}$$

Foreignness

$$F = Z(k)^{-1} \sum_{e \in IEDB} \exp\left(-k(a - |\mathbf{s}, \mathbf{e}|)\right)$$

PREDICTED_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	AGRETOPICITY	FOREIGNNESS	
67.4	49.85	4.19	0.350858928	6.98E-09	✗
12	16.319886	7.29	0.224719101	2.67E-11	✗
128.6	28.887051	0.71	1.038772213	0	✗
42.38742509	145.4920265	3.11	0.002893805	4.53E-07	✗

Closer look at that validation data...

Presented:

Binding Affinity < 34 nM;

Tumor Abundance > 33 TPM;

Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or

Foreignness > 10^{-16}(Group 2)

Agretopicity

$$A = \frac{BA_{MT}}{BA_{WT}}$$

Foreignness

$$F = Z(k)^{-1} \sum_{e \in IEDB} \exp\left(-k(a - |\mathbf{s}, \mathbf{e}|)\right)$$

PREDICTED_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	AGRETOPICITY	FOREIGNNESS	
67.4	49.85	4.19	0.350858928	6.98E-09	✗
12	16.319886	7.29	0.224719101	2.67E-11	✗
128.6	28.887051	0.71	1.038772213	0	✗
42.38742509	145.4920265	3.11	0.002893805	4.53E-07	✗

Closer look at that validation data...

Presented:

Binding Affinity < 34 nM;

Tumor Abundance > 33 TPM;

Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or

Foreignness > 10^{-16} (Group 2)

Agretopicity

$$A = \frac{BA_{MT}}{BA_{WT}}$$

Foreignness

$$F = Z(k)^{-1} \sum_{e \in IEDB} \exp\left(-k(a - |\mathbf{s}, \mathbf{e}|)\right)$$

PREDICTED_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	AGRETOPICITY	FOREIGNNESS	
67.4	49.85	4.19	0.350858928	6.98E-09	✗
12	16.319886	7.29	0.224719101	2.67E-11	✗
128.6	28.887051	0.71	1.038772213	0	✗
42.38742509	145.4920265	3.11	0.002893805	4.53E-07	✗

Closer look at that validation data...

Presented:

Binding Affinity < 34 nM;

Tumor Abundance > 33 TPM;

Binding Stability > 1.4 hours

Recognized:

Agretopicity < 0.1 (Group 1) or

Foreignness > 10^{-16} (Group 2)

Agretopicity

$$A = \frac{BA_{MT}}{BA_{WT}}$$

Foreignness

$$F = Z(k)^{-1} \sum_{e \in IEDB} \exp\left(-k(a - |\mathbf{s}, \mathbf{e}|)\right)$$

PREDICTED_BINDING_AFFINITY	TUMOR_ABUNDANCE	BINDING_STABILITY	AGRETOPICITY	FOREIGNNESS	
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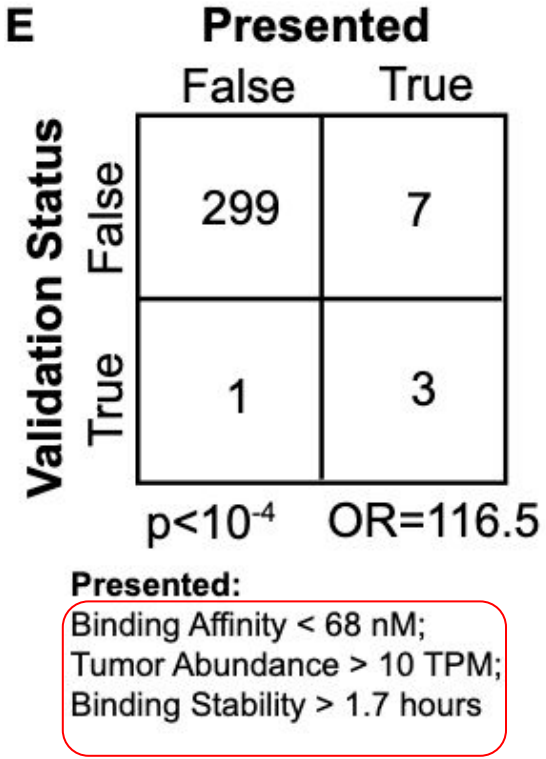
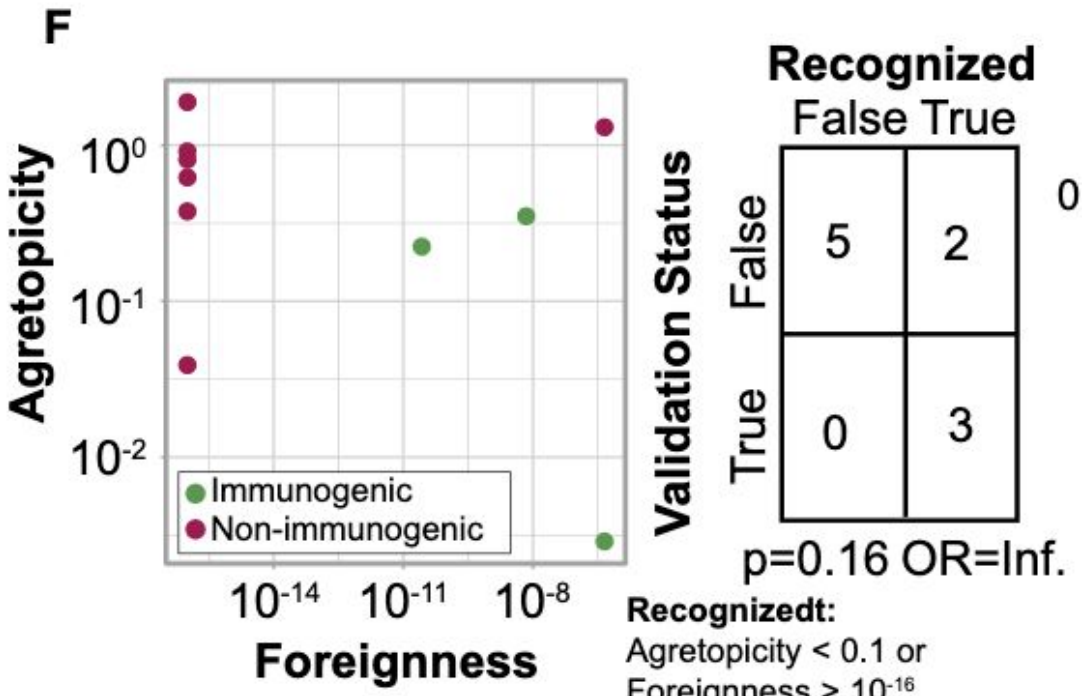
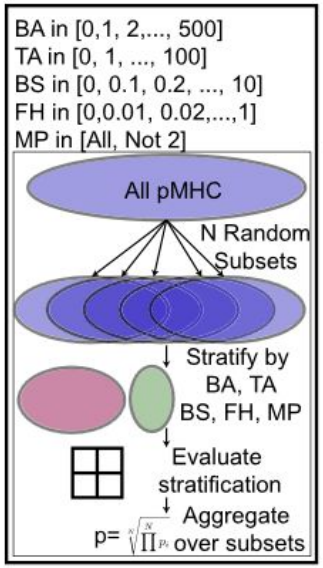
42.38742509	145.4920265	3.11	0.002893805	4.53E-07	✗

They re-estimated the model parameters!







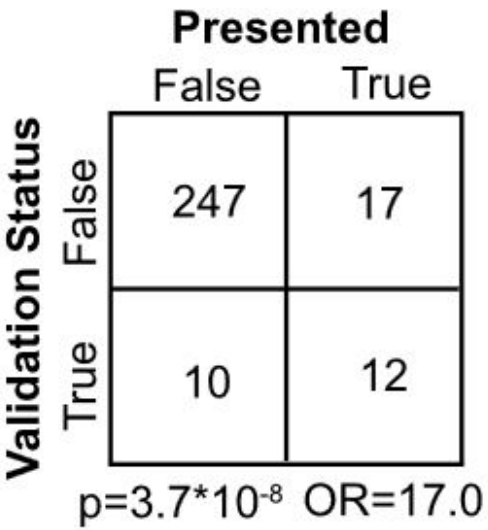
Threshold selection as p-hacking

Parameter Selection via Repeated Random Subsampling

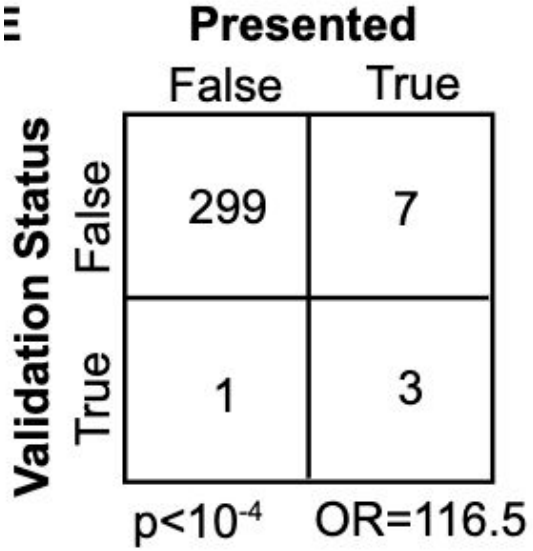
For each continuous parameter (MHC binding affinity, MHC binding stability, tumor abundance, hydrophobicity fraction) a range of values covering two orders in magnitude was generated while for binary features (mutation position) both levels were considered. For each unique parameter combination, 10 random subsets of 70% of tested peptides (with immunogenic/non-immunogenic ratio equal to the whole dataset) were selected and stratified using the given features. Immunogenicity stratification was calculated using a Fisher exact test. The parameter set with the smallest average p value over all random subsets was chosen to be the one with the best overall stratification ability.

For each of the three presentation associated parameters, we iterate over approximately an order of magnitude in parameter values: Specifically, we iterate over the following ranges: Binding Affinity: [15nM, 16nM, 17nM,… 200nM]; Binding Stability: [0.2 hours, 0.3 hours, … 3 hours]; Tumor Abundance: [5 TPM, 6TPM, …50 TPM]. For each single parameter value, we hold the other two parameters at their previously identified values (Binding Affinity: 34nM; Binding Stability: 1.4 hours; Tumor Abundance; 33 TPM). Peptides are stratified based on the updated threshold set and the relationship between peptide recognition and immunogenicity is tested on the reduced set of presented peptides (those that pass all three filters) using a Fisher exact test. A-C: Univariate sensitivity tests. Line plot of p value from

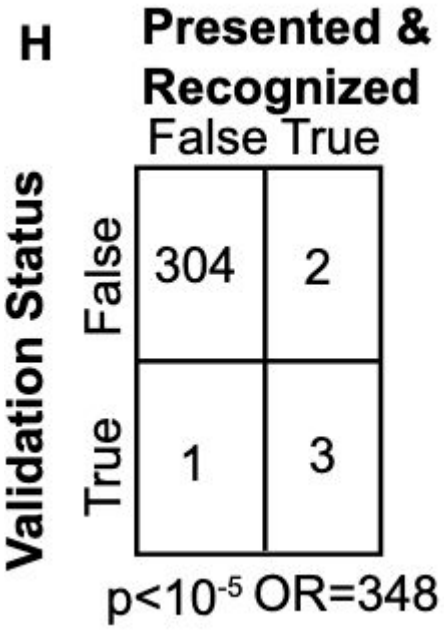
Then...they report the p-values!



Presented:
Binding Affinity < 34 nM;
Tumor Abundance > 33 TPM;
Binding Stability > 1.4 hours



Presented:
Binding Affinity < 68 nM;
Tumor Abundance > 10 TPM;
Binding Stability > 1.7 hours




Fin