Supplemental Figures

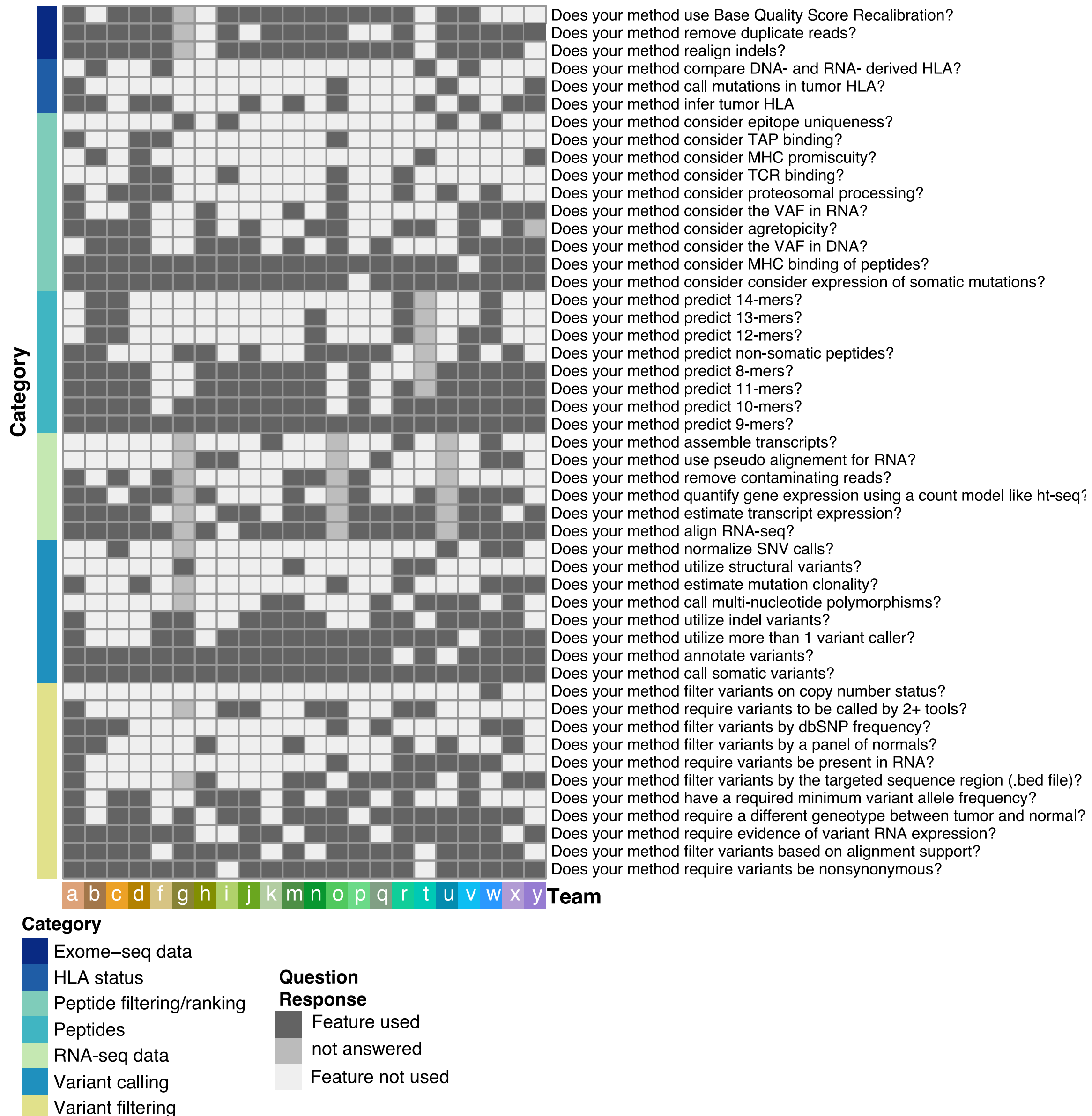

Figure S1. Pipeline Traits of Each TESLA Team, Related to Figure 1
Each team responded to a 49-question survey with yes/no questions about their pipeline. 22/25 teams responded to the survey (88% response rate).

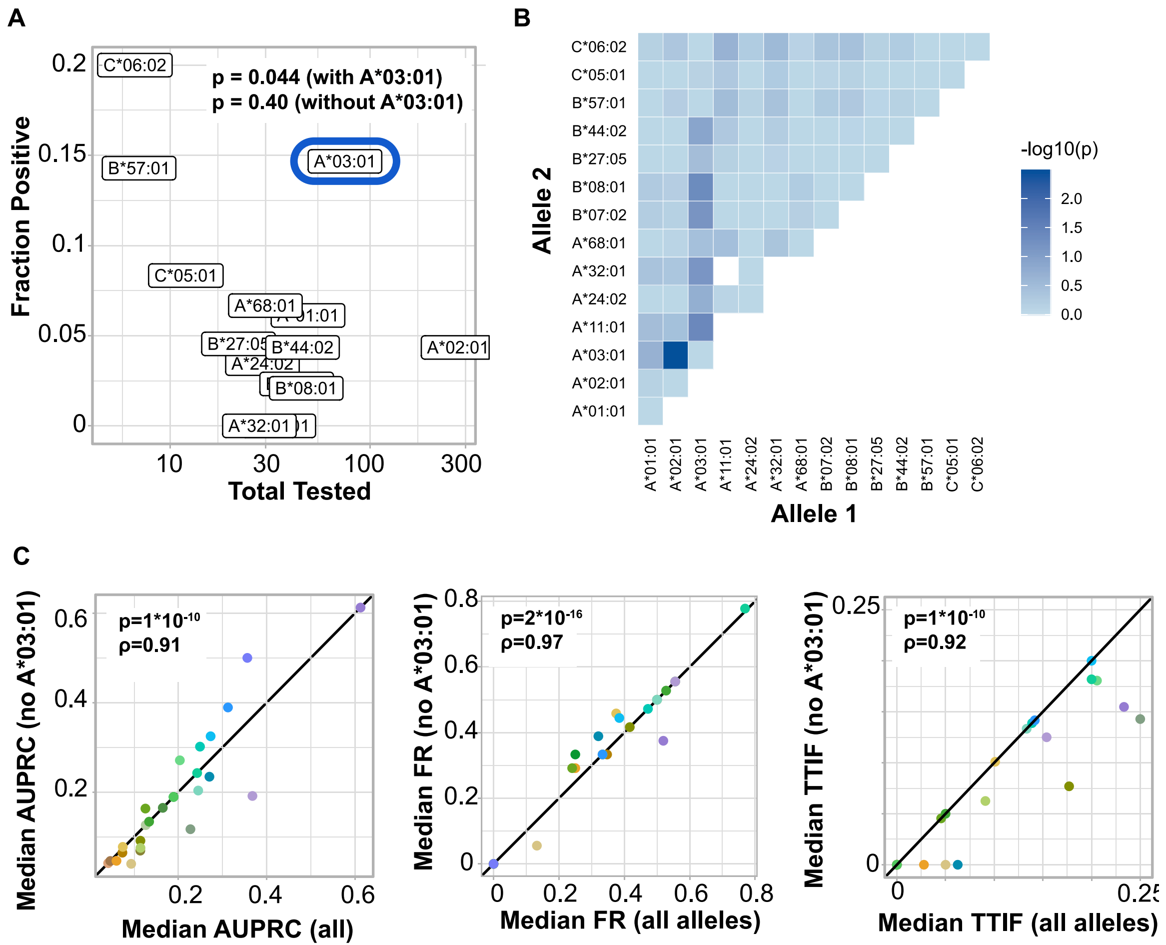

Figure S2. Immunogenicity of Peptides by MHC Allele, Related to Figure 3

(A) Scatterplot of median number of peptides tested for immunogenicity (x axis) versus median number of peptides with validated immunogenicity, by allele. p: Fisher exact test. (B) Transformed p value for Fisher exact test between validation counts of each allele pair. (C) *Left:* Median AUPRC for each team, including A*03:01 (x axis) versus excluding A*03:01 (y axis). Correlation: Spearman rho. *Center:* Median FR for each team, including A*03:01 (x axis) versus excluding A*03:01 (y axis). Correlation: Spearman rho. *Right:* Median TTIF for each team, including A*03:01 (x axis) versus excluding A*03:01 (y axis). Correlation: Spearman rho.

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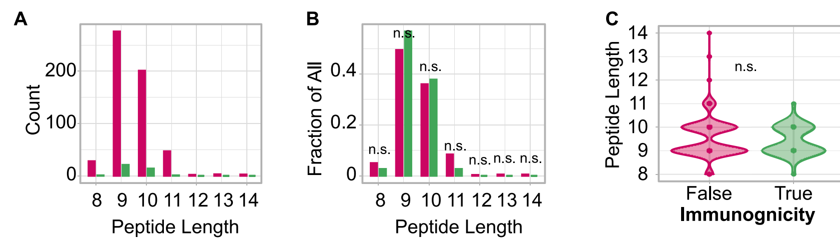

Figure S3. Peptide Length and Immunogenicity, Related to Figure 3

(A) Counts of each peptide length by immunogenic (green) and non-immunogenic (red) status. (B) Normalized fraction of peptides of each length for immunogenic and non-immunogenic peptides separately. No significant difference in fraction immunogenic is seen in any peptide length (Fisher exact test). (C) Violin plot of peptide length stratified by immunogenicity. Difference not significant (Mann-Whitney U).

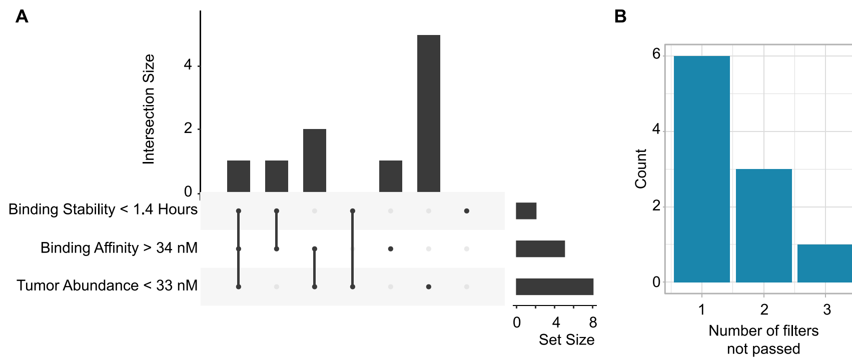

Figure S4. Features of Immunogenic Peptides that Do Not Pass Presented Criteria, Related to Figure 3

(A) Upset plot of the three ways to fail the presented criteria and the overlap between each of those groups. (B) The number of filters not passed for each immunogenic peptide.

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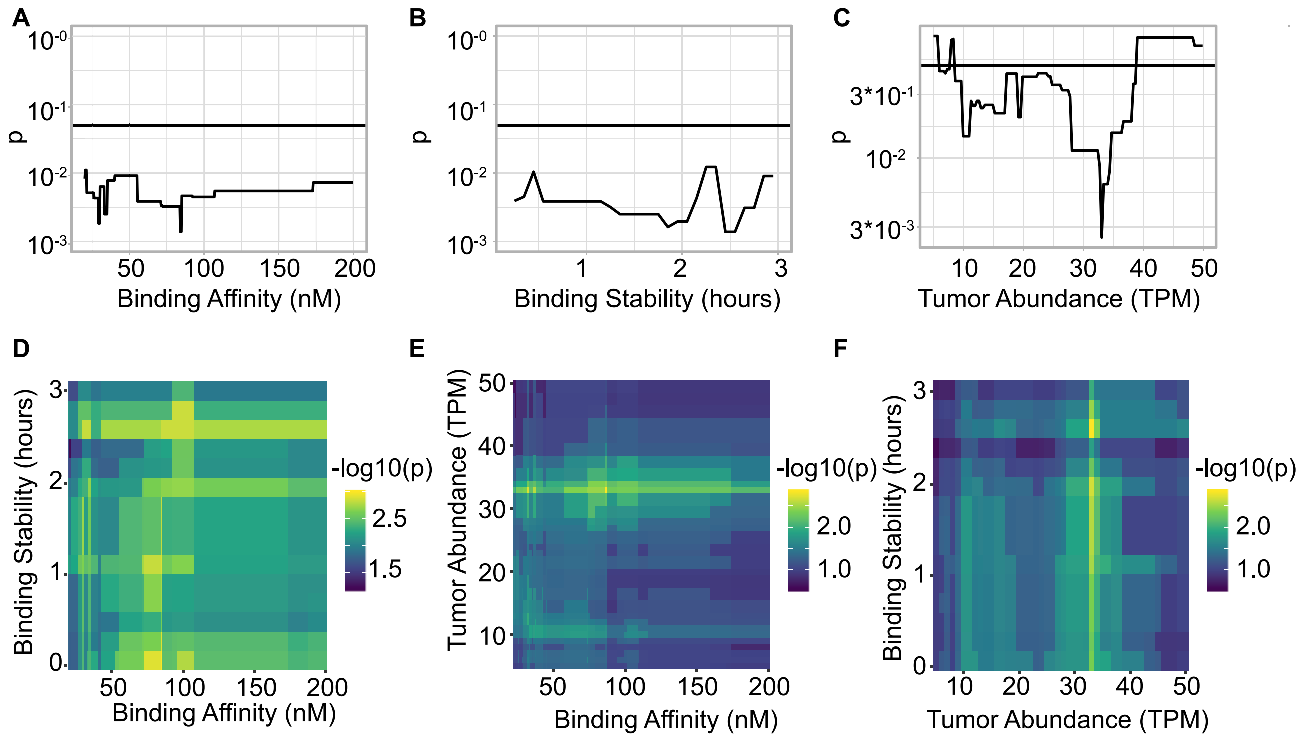

Figure S5. Sensitivity Analysis of Immunogenicity Enrichment in Recognized Peptides by Presentation-Associated Parameter Values, Related to Figure 4

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 resulting Fisher test for each of the three presentation parameters considered. Black line is at p = 0.05. D-E: Bivariate sensitivity tests. In each panel, values of two parameters are iterated over and the resulting p value plotted.

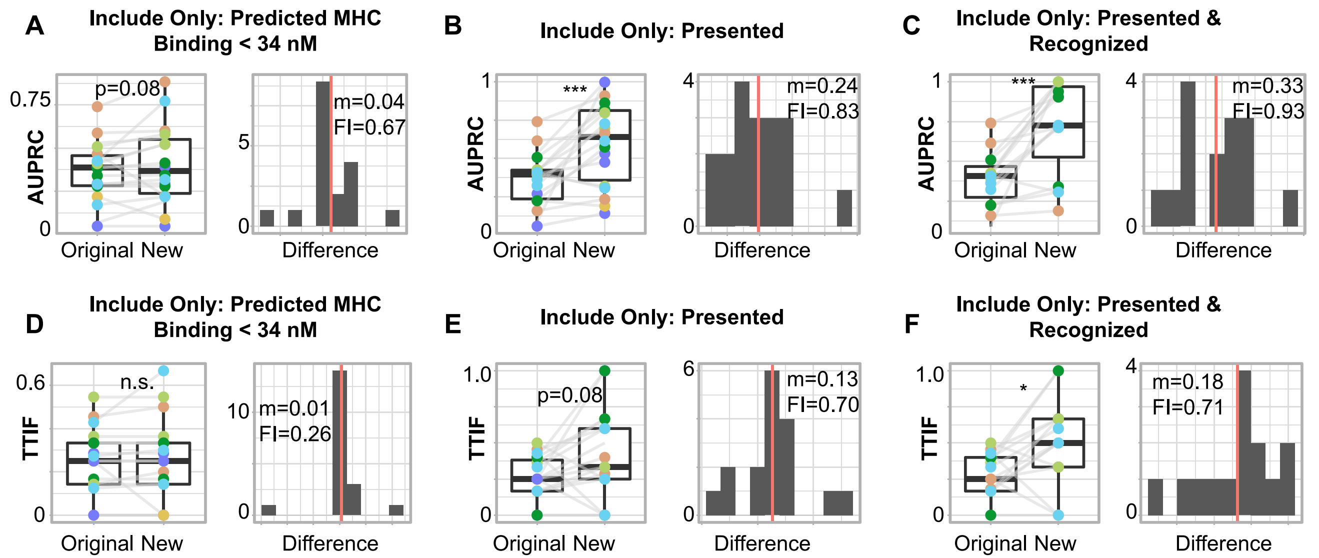

Figure S6. Directed Interventions on Submission Features Improves Neoantigen Pipeline Performance in a Separate Set of TESLA participants, Related to Figure 5

Two pipeline performance metrics are considered (AUPRC, panels A-C; TTIF, panels D-F), and for each metric three interventions are demonstrated. For each intervention, the boxplot (*Left*) shows the change in the performance metrics from the original prediction to the new prediction (post intervention). Significance values are calculated using a paired Mann-Whitney U test. *$p < 0.05$; ***$p < 10^{-3}$. The histogram (*Right*) shows the distribution of changes to the performance metric. Red line: median; m: median improvement; FI: fraction improved.

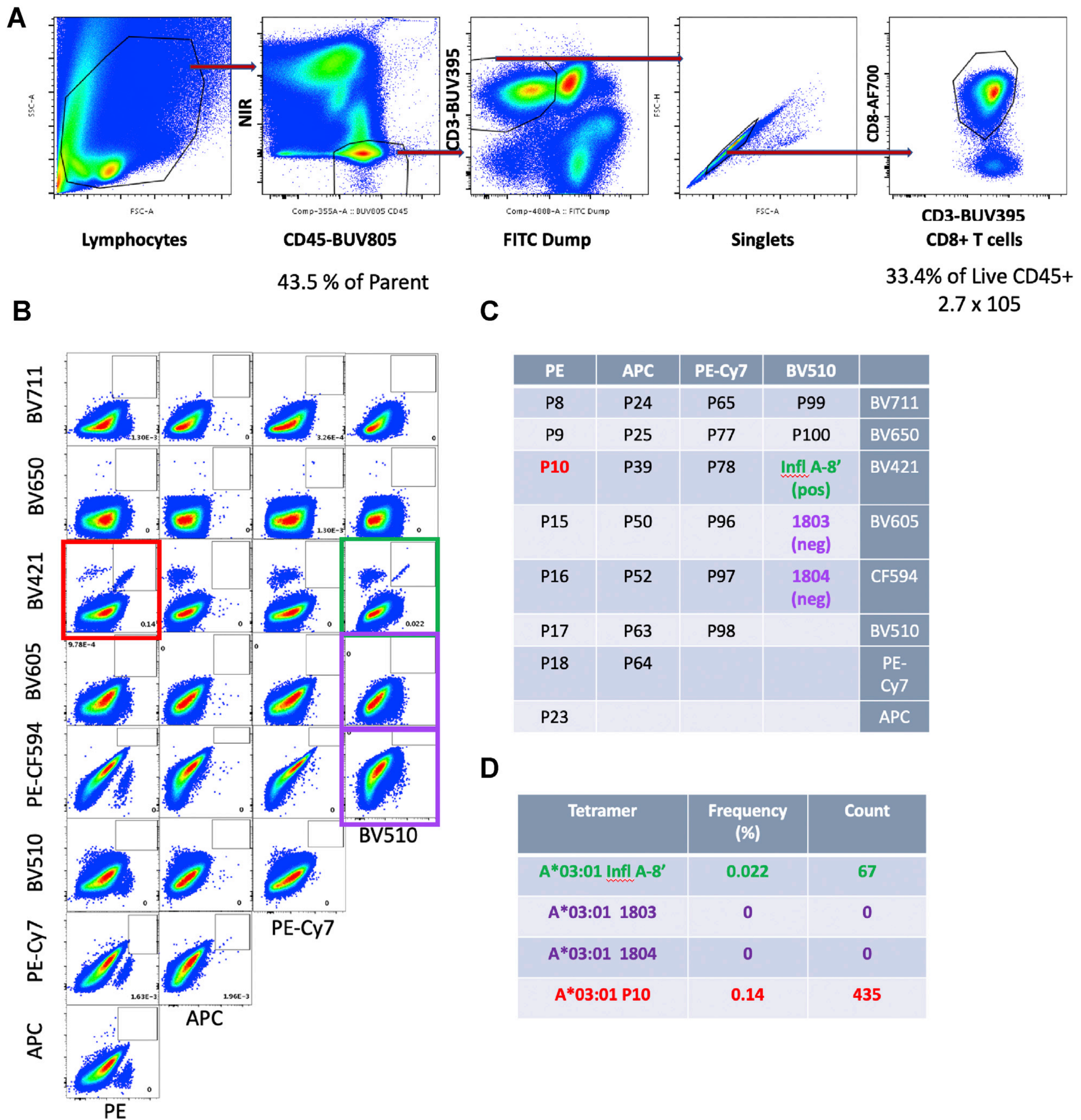

Figure S7. Representative Tetramer Staining, Related to STAR Methods

(A) Patient derived PBMC were stained with a cocktail of reagents to isolate CD45+ live cells. These were further gated positively for CD3 and negatively for CD4, CD14, CD16, CD19 and CD40. Singlets were further gated on CD3+CD8+ T cells. (B) Cells were stained with HLA-A*03:01 tetramers exchanged with a panel of 23 neoantigen peptides as well as positive control A*03:01 binding peptide Infl A-8' (green box) and negative control peptides 1803 and 1804 (purple box). All tetramers were barcoded and cells were stained with tetramers that displayed two distinct fluorochrome labels. Positive peptide P10 boxed in red. (C) Peptide staining map. (D) Frequency of gated positive cells and cell counts.