Excluding Treg epitopes and integrating CD8 and CD4 effector neoepitope content improves prognostic biomarker tool in bladder cancer

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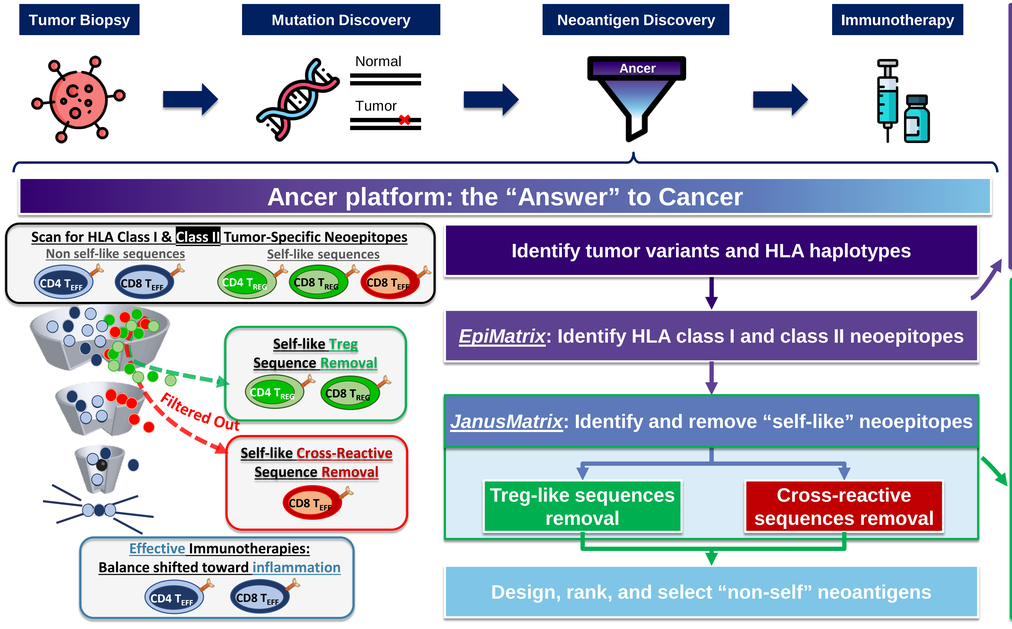
Overview

- **Hypothesis**: Accurately defining effector (Teff) and excluding **regulatory (Treg) neo-epitopes** will help **identify patients with improved prognosis**.
- **Approach**: TCGA bladder mutanomes (n=412) were analyzed with **Ancer, an advanced neo-epitope screening platform** that combines proprietary machine learning-based **CD8 and CD4** epitope mapping tools with removal of **inhibitory Treg** epitopes.
- **Results**: **Improved stratification of patients is obtained with Ancer** compared to public epitope prediction tools or TMB.
- **Improved prediction of 5-year survival is obtained with Ancer** compared to public epitope prediction tools or TMB.
- **Summary**: Precise identification of neoepitopes with EpiMatrix and their careful triaging with JanusMatrix improves our ability to predict patient outcomes.
- Ancer may represent a novel tool for defining new **prognostic or predictive biomarkers**.

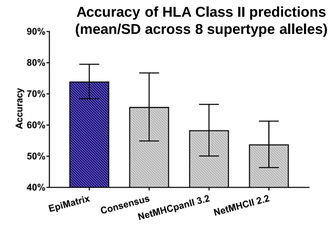
Mutanome-Directed Cancer Immunotherapy Based on 20 Years of Experience in Epitope Mapping



Accurate identification of epitopes using EpiMatrix

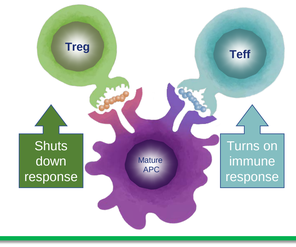
CD4 T cell epitopes. EpiMatrix Class II predictions are **74% accurate** when prospectively tested [1].

Between 175 and 251 peptides were tested per HLA in *in vitro* binding assays.

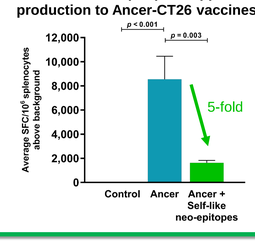


Identification and removal of Treg epitopes using JanusMatrix

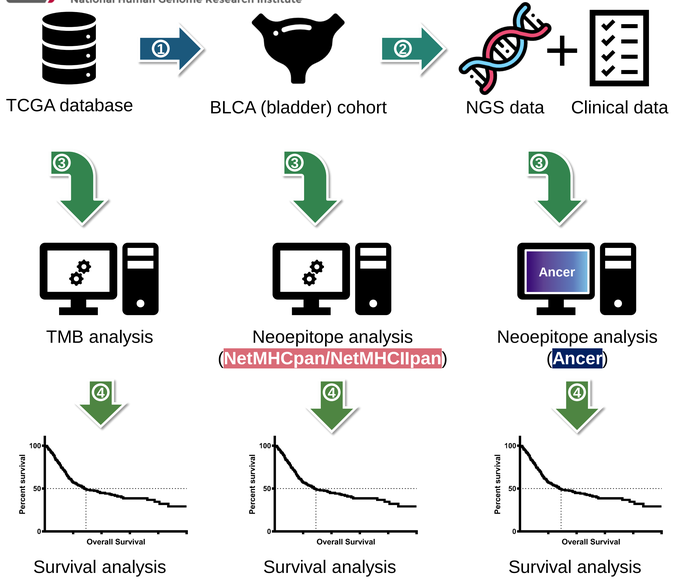
Epitopes can be either effector (Teff) or regulatory (Treg). JanusMatrix has identified **immunosuppressive epitopes** in pathogens [2, 3, 4] and **cancer mutanomes** [5].



CT26 self-like neo-epitopes suppress IFNγ production to Ancer-CT26 vaccines

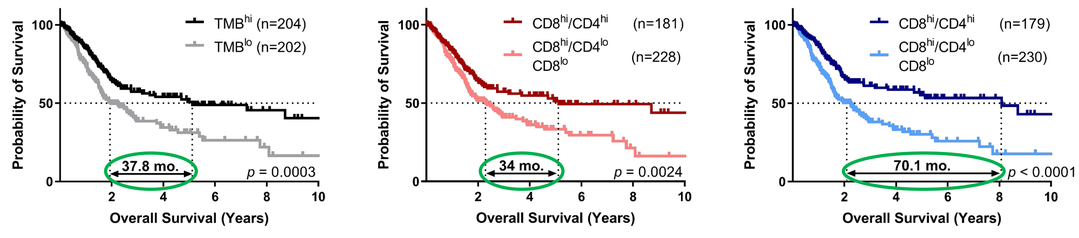


Methods – TCGA analysis of bladder cancer data



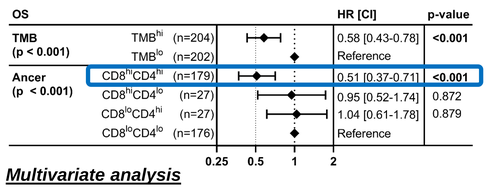
- High/low mutational or neoepitope burdens are defined by medians.
- Association between Ancer and outcome evaluated in both univariate and multivariate survival analyses.

Stratification of TCGA bladder cancer patients is better achieved with Ancer



Improved stratification of patients when analyzing their tumors with Ancer.

Univariate analysis

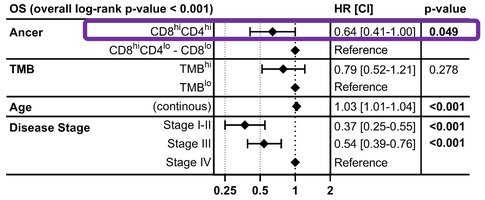


Only patients with **both** high numbers of CD8 and CD4 neoepitopes benefit from significantly improved outcomes.

Will vaccines generating balanced and robust CD8 and CD4 responses be more effective?

Will vaccines "rescue" patients with low numbers of effector neoepitopes?

Multivariate analysis

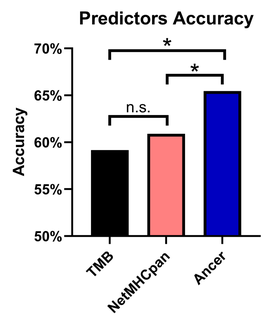


Ancer neoepitope counts remain significantly associated with outcomes in multivariate survival analysis.

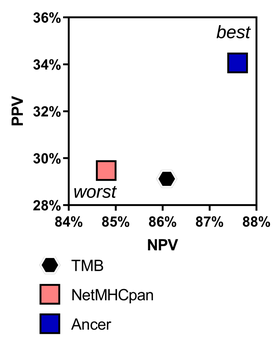
(PD-L1 expression was not significantly associated with outcomes in univariate analyses)

Predicting 5-year survival is better achieved with Ancer

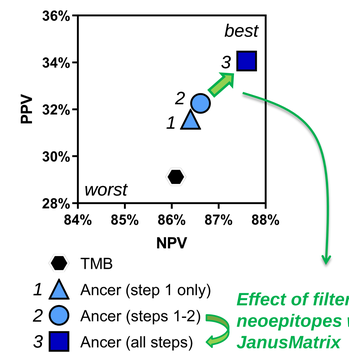
- **Hypothesis**: BLCA patients with "high"/"low" (mutational or neoepitope) burden will survive more/less than 5 years.
- **Ancer achieves a higher accuracy, PPV, and NPV than other predictors.**
- **Filtering out non-immunogenic or inhibitory neoepitopes improves survival predictions.**



Predictors PPV and NPV



Effect of Ancer filters on PPV and NPV



Conclusions

- **EpiVax's immunogenicity screening tools are integrated into the Ancer platform for streamlined designs of personalized cancer vaccines.**
- **Improved stratification of TCGA bladder cancer patients was obtained with Ancer compared to other analyses. These results highlight the importance of identifying neoepitopes with high-quality epitope prediction tools and of evaluating their phenotype (effector or regulatory) using specialized homology tools.**
- **Ancer may help understand patients' survival based on an in-depth analysis of their mutanome, including an evaluation of their CD8 and CD4 effector neoepitope contents.**
- **Follow-up studies include extension of this analysis to other cohorts of patients treated with a checkpoint modulator.**

References & Acknowledgments

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The results shown here are in part based upon data generated by the TCGA Research Network: http://cancergenome.nih.gov/.
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