iVAX for antigen discovery, vaccine design, diagnostics, and epidemiology

Frances Terry1, Sundos Khan1, Jacob Tivin1, Matthew Ardito1, Andres H. Gutierrez1, Leonard Moise1,2, William Martin1, and Anne S. De Groot1,2

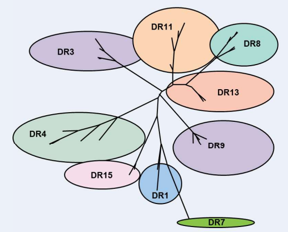
[1] EpiVax, Inc [2] EpiVax Therapeutics, Inc.

The process of designing and developing vaccines necessitates sophisticated analysis of data from multiple sources at multiple decision points in order to achieve protection against disease. EpiVax's in silico vaccine design platform, iVAX, has historically been applied in a genome-to-vaccine fashion to predict and optimize pathogen-specific T cell-dependent immune responses to establish long-lasting immune memory that protects upon exposure to the target pathogen. Beyond immunogen design, iVAX applications include antigen discovery, diagnostic tests, and epidemiological studies.

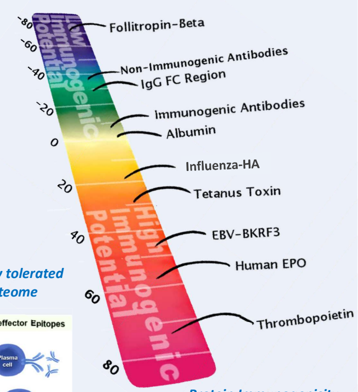
ANTIGEN DISCOVERY

EpiMatrix-supported antigen discovery identifies proteins in a pathogen genome with the highest predicted epitope density and immunogenic potential, suggesting the best candidates for vaccine antigen selection.

Predict T cell epitope content relevant to globally representative HLA supertype alleles that cover >95% of human populations worldwide

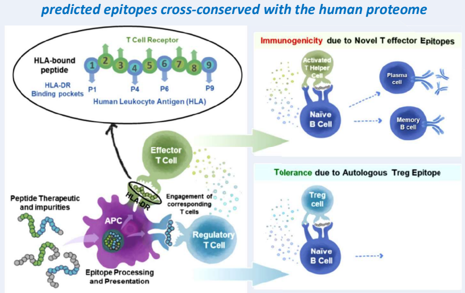


Rank potential antigens based on putative T cell epitope density. Higher density → more likely to drive an immunogenic response → more likely to develop protective immunological memory



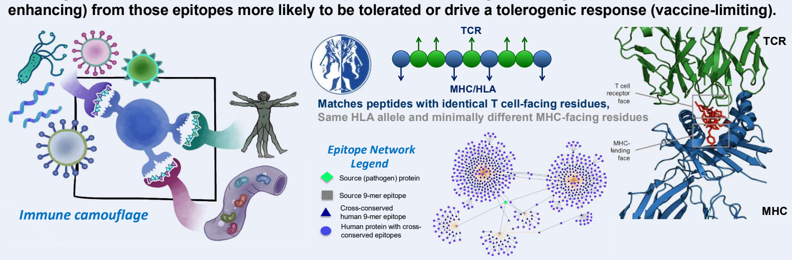
Protein Immunogenicity Scale

Exclude or modify antigens with high numbers of potentially tolerated predicted epitopes cross-conserved with the human proteome



VACCINE DESIGN

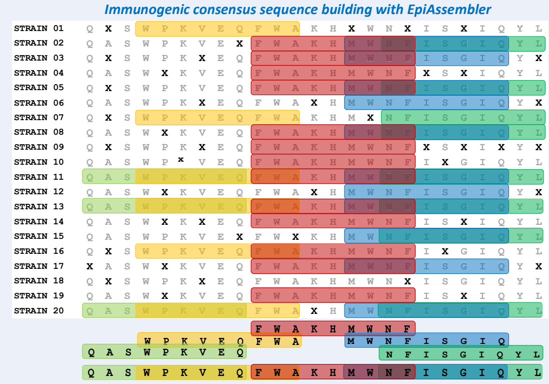
JanusMatrix predicts the extent of cross-conservation between a given T cell epitope and TCR-face homologous T cell epitopes in the human proteome to distinguish likely effector epitopes (vaccine-enhancing) from those epitopes more likely to be tolerated or drive a tolerogenic response (vaccine-limiting).



The least human-like, most highly pathogen-conserved and immunogenic peptide sequences from large sets of pathogenic variants can be determined by the Conservatrix and EpiAssembler algorithms.

String-of-beads epitope designs with limited artifactual and non-specific immunogenicity at the junctions between individual peptides can be optimized using the VaccineCAD algorithm.

Immunogenic consensus sequence building with EpiAssembler

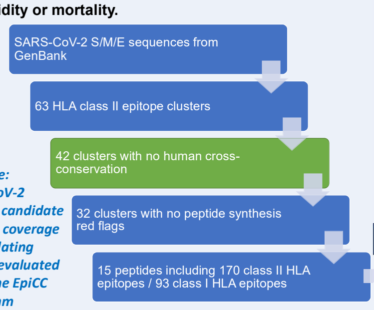


iVAX

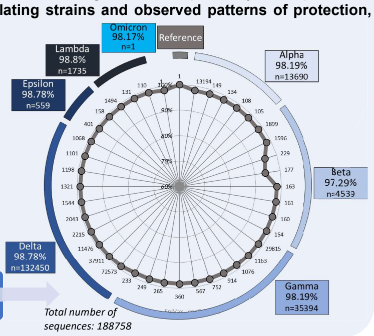
The iVAX toolkit, a web-based platform, includes an algorithm for predicting Class I and Class II HLA ligands in protein antigens that broadly cover HLA diversity of the world population (EpiMatrix).

EPIDEMIOLOGY

When epidemiological data are available, the EpiCC (epitope content comparison) algorithm can be applied prospectively to select an optimal vaccine for field strain coverage, or retrospectively to explore the relationship between vaccine epitope coverage of circulating strains and observed patterns of protection, morbidity or mortality.

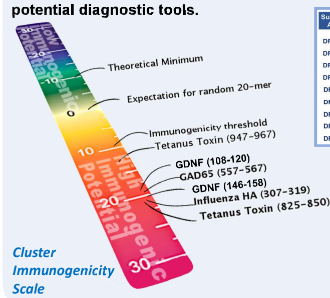


Example: SARS-CoV-2 vaccine candidate epitope coverage of circulating strains evaluated using the EpiCC algorithm

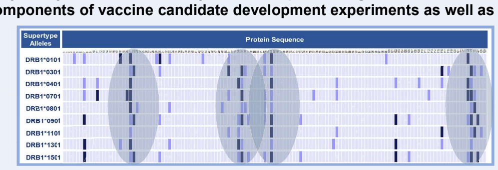


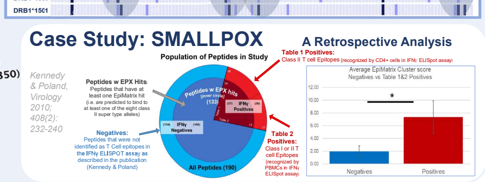
DIAGNOSTICS

Within any given antigen, the ClustiMer algorithm identifies "hot spots" of concentrated epitope density. Pathogen-exposed individuals are highly likely to mount memory T cell responses against such T cell epitope clusters, making them useful components of vaccine candidate development experiments as well as potential diagnostic tools.



Cluster Immunogenicity Scale





CONCLUSIONS

- Using iVAX, we have developed T cell epitope and whole antigen vaccines in nucleic acid and protein formats with demonstrated immunogenicity and efficacy against several pandemic pathogens and biothreat agents.
- The vaccines are based on identification of T cell epitopes that are recognized in natural infection and immunization and can be used to answer outstanding questions about T cell immunity in infectious disease and to generate diagnostic assays with high sensitivity and specificity.
- In an epidemiological application, we have assessed the vaccine T cell epitope coverage of circulating isolates of fast-evolving pathogens including SARS-CoV-2, human and swine influenza virus, and PCV2.
- Future studies will seek to refine thresholds for JanusMatrix that more accurately determine the T cell phenotype elicited by predicted epitopes and EpiCC thresholds that distinguish between vaccine outcomes.

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SUBMITTED ABSTRACT

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Using iVAX, we have developed T cell epitope and whole antigen vaccines in nucleic acid and protein formats with demonstrated immunogenicity and efficacy against several pandemic pathogens and biothreat agents. The vaccines are based on identification of T cell epitopes that are recognized in natural infection and immunization and can be used to answer outstanding questions about T cell immunity in infectious disease and to generate diagnostic assays with high sensitivity and specificity. In an epidemiological application, we have assessed the vaccine T cell epitope coverage of circulating isolates of fast-evolving pathogens including SARS-CoV-2, human and swine influenza virus, and porcine circovirus type 2. Future studies will seek to refine thresholds for JanusMatrix that more accurately determine the T cell phenotype elicited by predicted epitopes and EpiCC thresholds that distinguish between vaccine outcomes.