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Kirk Haltaufderhyde

Christine M. Boyle

Andres H. Gutierrez

Mayara Grizotte-Lake

Frances Terry

See next page for additional authors

Authors

Kirk Haltaufderhyde, Christine M. Boyle, Andres H. Gutierrez, Mayara Grizotte-Lake, Frances Terry, Bethany G. McGonnigal, Nicole Ruggiero, Leonard Moise, William D. Martin, and Anne S. De Groot

A NOVEL SARS-COV-2 (T CELL) VACCINE CANDIDATE DESIGNED USING THE I-VAX PLATFORM

Kirk Haltaufderhyde, EpiVax, Inc., Providence, RI, USA
khaltaufderhyde@epivax.com
Christine M. Boyle, EpiVax, Inc., Providence, RI, USA
Andres H. Gutierrez, EpiVax, Inc., Providence, RI, USA
Mayara Grizotte-Lake, EpiVax, Inc., Providence, RI, USA
Frances Terry, EpiVax, Inc., Providence, RI, USA
Bethany G. McGonnigal, EpiVax, Inc., Providence, RI, USA
Nicole Ruggiero, EpiVax Therapeutics, Inc., Providence, RI, USA
Leonard Moise, EpiVax, Inc., Providence, RI, USA
William D. Martin, EpiVax, Inc., Providence, RI, USA
Anne S. De Groot, EpiVax, Inc., Providence, RI, USA

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EpiVax, Inc., a Rhode Island-based Biotechnology company, develops vaccines that exploit T cell immunity using the innovative iVAX vaccine antigen design platform. The premise of our strategy is the crucial role T cells play in development of protective antibody and cell-mediated immunity in natural infection. Because vaccines aim to recapitulate protective immune responses in infection, a vaccine should effectively harness T cell immunity to be protective. The significance of T cell immunity is underscored by COVID-19. Efficacy trial and real-world COVID-19 vaccine data for different vaccine modalities show a single vaccine dose is as much as 90% effective starting 14 days post-administration, when 100% of vaccinees have functional CD4 and CD8 T cells but no detectable neutralizing antibodies. As T cells support the SARS-CoV-2 antibody response, clear virus-infected cells, and may be required to block transmission, we set out to develop a vaccine designed by iVAX to enhance T cell immunity and provide long lasting protection.

Using the iVAX platform, we identified conserved peptide epitopes associated with SARS-CoV-2 T cell immunity and assessed their immunogenicity in an HLA transgenic mouse model to support development of a T cell-directed COVID-19 vaccine. SARS-CoV-2 spike, membrane and envelope sequences were analyzed for potential binding to HLA class I and class II supertype alleles using EpiMatrix. JanusMatrix was used to identify SARS-CoV-2 epitopes that share TCR-face conservation with epitopes restricted by the same alleles, but found in the human proteome, and related alpha- and beta-coronaviruses. Conservation of epitopes with circulating SARS-CoV-2 was assessed using the Epitope Content Comparison (EpiCC) algorithm and showed the vaccine epitopes match >90% of the corresponding sequences in representative B.1.1.7, B.1.351, P.1, B.1.617.2, and B.1.1.529 variants. Epitopes were assayed for antigenicity and 66% of 32 predicted epitopes were recognized in direct ex vivo assays by individuals who mounted a protective immune response to SARS-CoV-2 infection. T cell responses correlated with total spike-specific IgG and neutralizing antibody responses ($p<0.01$). Individuals with no SARS-CoV-2 experience demonstrated ex vivo responses to only 9% of epitopes. However, following a period of epitope-specific T cell expansion in culture, these individuals demonstrated robust T cell responses to 97% of SARS-CoV-2 epitopes, similar to convalescents. These data suggest that pre-existing immunity, potentially to common cold coronaviruses, may contribute to natural immunity and enhance vaccine efficacy. Intradermal immunization of HLA-DR3 transgenic mice with 20 candidate peptides co-formulated with poly-ICLC demonstrated robust type 1 immunity skewing (>100-fold over type 2; $p<0.05$). This alleviates concern that the vaccine may enhance respiratory disease commonly associated with Th2 responses. Taken together, this work improves our understanding of natural vaccine-induced immunity and informs the development of our EPV-Cov19 vaccine.

Unlike currently available SARS-CoV-2 vaccines, EPV-Cov19 is being developed as a T cell-targeted vaccine and it is fully synthetic, requiring no cell culture expression. EPV-Cov19 consists of 15 peptides with over 200 T cell epitopes (CD8 and CD4) from SARS-CoV-2 spike and membrane proteins. In a planned Phase 1 trial, we intend to show that the peptides selected by EpiVax can boost the immunity of individuals previously vaccinated. In addition, EPV-Cov19 is versatile and can be formulated in peptide, RNA, DNA or viral-vectored formats. The iVAX platform used to design EPV-Cov19 may advance the development of SARS-CoV-2 vaccines and is adaptable to vaccine discovery against other infectious diseases.