Antigen presenting cell targeted T cell DNA vaccine candidate inducing strong and specific cellular responses across multiple T cell epitopes of SARS-COV-2

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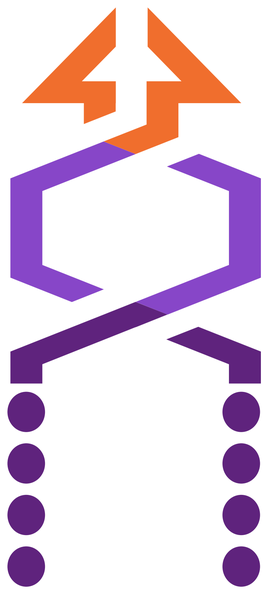
INTRODUCTION

The severe respiratory syndrome coronavirus 2 (SARS-CoV-2) causing COVID-19 has continuously evolved with successive new virus variants of concern (VOC). A key challenge that COVID-19 vaccine developers face is the need to develop vaccines that can prevent infection and/or protect against severe disease caused by these VOCs, known to evade vaccine induced Spike neutralizing antibodies. Cross-reactive T cell responses are less susceptible to immune escape and likely contribute to the efficacy of approved vaccines against VOCs, thus provide the rationale for the development of T-cell based vaccines.

VB10.2210 is a T-cell based vaccine that was developed using Nykode's easily adaptable DNA plasmid (pDNA) vaccine platform. VB10.2210 pDNA encodes homodimers consisting of i) a targeting unit that binds chemokine receptors on antigen-presenting cells, ii) a dimerization unit, and iii) an antigenic unit consisting of a selection of validated immunogenic SARS-CoV-2-specific T cells epitopes. The T cell epitopes were identified by Adaptive using T cell receptor sequencing of more than 6500 samples from COVID-19 individuals representing diverse geographies. The vaccine candidate was designed with broad HLA coverage and contains a diversity of both MHCI and MHCII T-cell epitopes across multiple viral proteins and known VOCs.

In vitro characterization of the VB10.2210 pDNA showed that intact protein was expressed and secreted in human cell culture. The immunogenicity of the vaccine candidate was evaluated in vivo in transgenic HLA-A2.1, C57BL/6 and BALB/c mice. Preclinical data in these three mouse models demonstrate that VB10.2210 consistently induced strong, broad, dose-dependent, and persistent T cell responses across multiple T cell epitopes.

VB10.2210 vaccine candidate

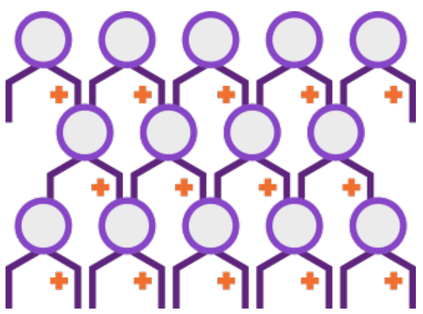


TARGETING UNIT
CCL3L1 chemokine that binds receptors on antigen presenting cells (APCs) and attracts immune cells

DIMERIZATION UNIT
Dimerization unit for crosslinking targeted receptor on the APC

ANTIGENIC UNIT
96+ Validated T cell epitopes from 8 antigens of SARS-CoV-2 identified by Adaptive Biotechnologies

SARS-CoV-2 T cell epitopes selection



Sequenced TCRs and identified expanded COVID-19 specific T cell clones in more than 6500 samples from COVID-19 patients

immunoSEQ®

Adaptive mapped TCRs to corresponding SARS-CoV-2 T cell epitopes using its proprietary functional, cell-based MIRA™ approach

Adaptive biotechnologies™

Adaptive launched T-Detect™ COVID, which is the first-in-class T-cell-based clinical test for Covid-19 with FDA Emergency Use Authorization

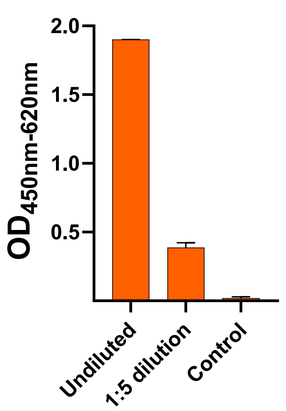
Optimized combination of conserved and immuno-dominant MHCI and MHCII T-cell epitope hotspots with broad HLA coverage across 8 SARS-CoV-2 antigens were used for vaccine design

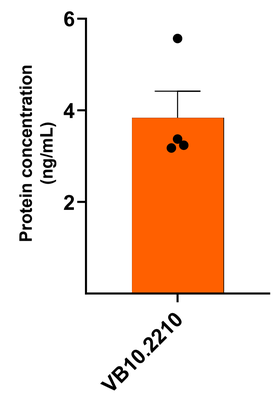
Protein secretion *in vitro*

plasmid DNA Expi293 cells

Expi293 cells were transiently transfected with plasmid DNA and supernatant harvested at day 3 post transfection

Sandwich ELISA using antibodies detecting the human IgG CH3 domain and human CCL3L1

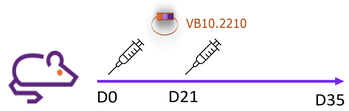




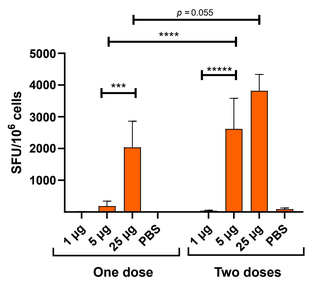
Vaccine protein is expressed and secreted

T cell responses in transgenic HLA-A2.1 mice

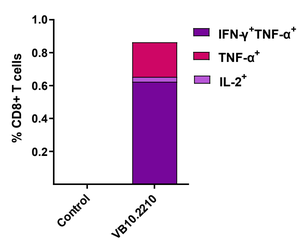
Transgenic mice expressing human HLA-A2.1 molecules



IFN-γ ELISpot



Flow cytometry

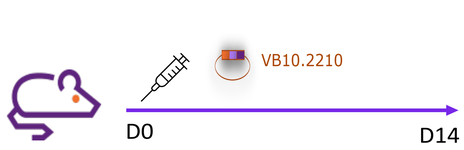


Strong CD8 T cell responses against HLA-A2.1 specific epitopes in transgenic HLA-A2.1 mice

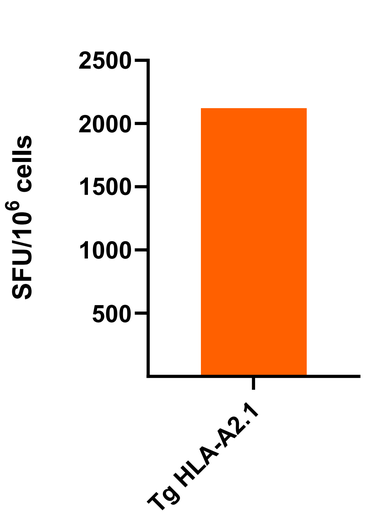
Dose response and second dose effect analyzed by ex-vivo IFN-γ ELISpot

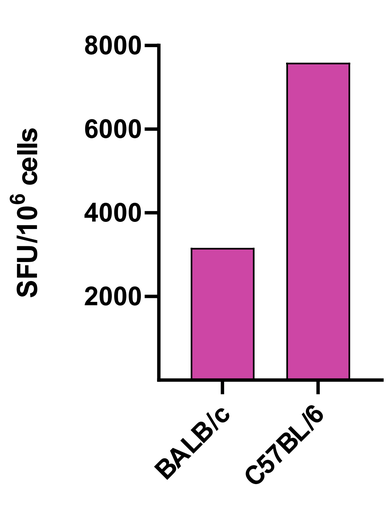
Pro-inflammatory cytokine profile analyzed by multicolor Flow cytometry

Strong immunogenicity in 3 mouse models

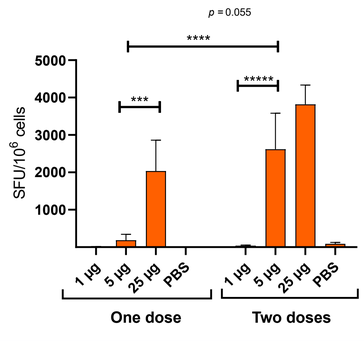


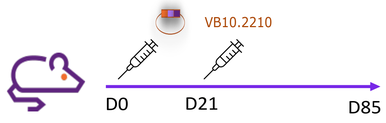
T cell responses across diverse MHC haplotypes in three mouse models of different genetic backgrounds





Long-term T cell immunity in C57BL/6 mice





Persistent and dose-dependent T cell responses observed independent of HLA selection, at day 85 post prime vaccination

CONCLUSIONS:

- Nykode has developed a COVID-19 vaccine candidate, VB10.2210, encoding clinically validated T cell epitopes based on Adaptive's unique TCR and epitope matching technology
- VB10.2210 consistently induced strong and persistent T cell immunity across three mouse models
- VB10.2210 could serve as a potential booster vaccine for inducing T cell based protection against current and future SARS-CoV-2 VoC

Download our poster!

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