

Identification of epitopes that pose as attractive targets for vaccination and other T-cell therapies with Klickmer™

Greenshields-Watson *et al.* CD4⁺ T cells recognize conserved influenza A epitopes through shared patterns of V-gene usage and complementary biochemical features. *Cell Reports* 2020 Jul 14;32(2):107885

BACKGROUND

CD4⁺ T cells orchestrate protection from severe influenza. However, knowledge of epitopes and the molecular patterns associated with recognition across the population is lacking.

In this study, researchers identified several influenza epitopes from internal virus proteins using customized Klickmer™ and applied this knowledge to explore the biochemical features that underpin CD4⁺ T-cell responses to influenza.

STUDY DESCRIPTION

Human peptide-HLA monomers were biotinylated and multimerized onto the Klickmer™ backbone. The peptide-HLA Klickmer™ reagents were then used to identify HLA-restricted epitopes within three internal Influenza A Viral proteins, including M1, NP, and PB-1 in peptide expanded cell cultures from five HLA-DR1⁺ donors.

RESULTS

To quantify and compare the recognition of selected epitopes, peptide-HLA Klickmer™ reagents were used to identify epitope-specific responses in five HLA-DR1⁺ donors (**Fig. 1A**).

Robust epitope-specific responses were detected in all donors to the control epitope HA³⁰⁶⁻³¹⁸-PKY, with natural donor-specific variation in response magnitude (range, 6.9%–26.2% CD4⁺). Of the five internal epitopes tested, 24 out of 25 possible responses were positive for Klickmer™ staining. Positive responses were defined as Klickmer™ staining/total CD4⁺ T cells 100 > 0.5%; donor-4 DPF was negative).

The largest responses, whether measured in terms of size of CD4⁺ T-cell expansion or of the median fluorescence intensity (MFI) of Klickmer™ positive cells, were consistent to M₁₁₂₉₋₁₄₂-GLI followed closely by HA₃₀₆₋₃₁₈-PKY (**Fig. 1B** and **1C**)

CONCLUSIONS

- HLA Klickmer™ was successfully applied to characterize CD4⁺ T cell responses to influenza A virus
- Five internal epitopes commonly recognized by CD4⁺ T cells in five HLA-DR1⁺ subjects correlated with protective immunity were identified

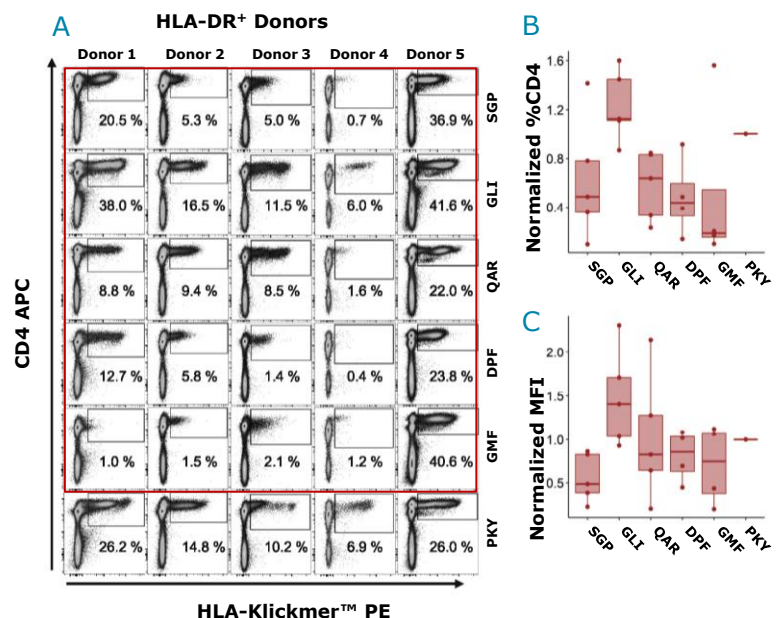


Fig. 1: Epitope recognition. A) Staining with peptide-HLA Klickmer in five HLA-DR1⁺ donors for identification of epitope responses. Responses were measured as B) CD4⁺ T cell expansion or C) median fluorescence intensity (MFI)