

## **Abstract**

### **Background:**

One major challenge in the development of an HIV-1 vaccine is the extreme genetic diversity of the virus. A more cross-reactive T-cell response would be beneficial in circumventing this issue, but many aspects of the variant-epitope CD8<sup>+</sup> T-cell response remain poorly defined. Here, we characterize CD8<sup>+</sup> T-cells specific to 4 immunodominant HIV-1 epitopes, and their common variants, to better understand their cross-reactivity and how this changes over time with progression to AIDS.

### **Methods:**

Blood samples were collected from HIV + female commercial sex workers from Nairobi, Kenya. Samples were stimulated for 6 hours with HIV-1 Gag and Envelope peptides, and IL2, IFN $\gamma$ , TNF, and MIP1B were measured via intracellular flow cytometry. Each sample was stained with tetramers specific to each peptide to assess which cells were actively secreting cytokines. Multiple samples were collected from the same patients over 1–6 years when available.

### **Results:**

This study revealed that the majority of cytokine production was by CD8<sup>+</sup> T-cells specific to the stimulating peptide. Cross-reactivity existed between epitopes and their variants, particularly with Gag IW9/LW9 epitopes, indicating that those regions may be better targets for future therapeutic agents. Cytokine production in response to Gag KF11 and KGF peptides were positively correlated to CD4 count. Production of IL2 was low or absent in all patients, and more likely produced by CD8<sup>lo</sup> cells in response to PMA stimulation.

### **Conclusion:**

Considering the ease with which HIV-1 mutates, it is important to consider how effective CD8<sup>+</sup>T cell responses are to these common HIV variants, and how they may change as disease progresses. This study provides unique insight into not only how responses to these variants differ, but how but how they change throughout long-term HIV infection. A better understanding of the dynamics of these important responses will be essential in guiding future vaccine or therapeutic candidates.