MS02-2-1 HLA-B*57-restricted immune response to HIV TW10 epitope drives for selection of specific TCR gene usages regardless of the viral load
#MS02-2-1

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Abstract
HIV infects and depletes $CD4^+$ T cells leading to severe immunosuppression. Currently almost 38 million people live with HIV worldwide[1]. Rare individuals, termed HIV controllers, can control viral load and remain healthy while infected. Despite Human Leukocyte Antigen (HLA) gene diversity in the population, almost 50% of HIV controllers express the HLA-B57 molecule which presents, among others, the Gag derived epitope, TW10[2]. Given the strong T-cell responses to this epitope and its presentation in early infection, TW10, could therefore shape the long-term control of HIV[3,4]. However, the mechanisms contributing to HIV control related to this epitope remain unclear. Here, we study the $CD8^+$ T cell responses to the TW10 epitope presented in HLA-B*57:01$^+$ HIV^+ individuals. We determine the αβ T cell receptor (TCR) repertoire in both HIV controller and non-controller individuals revealing similarities and the existence of a public TCR and public clonotypes in both groups. We further determine the polyfunctionality of selected T cell clones from each group that reveal strong $CD8^+$ T cell responses, shaped by the specific TCR repertoire biases regardless of the viral load. Furthermore, affinity measurements of selected TCRs and the first crystal structure of HLA-B*57:01-TW10 in complex with a $CD8^+$ TCR reveal the basis of the TW10 TCR repertoire biases and their impact on antigen recognition. The link between HIV viral load and T cell function driven by immunodominant epitopes may further our understanding of immunologic control of HIV.

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