MS03-2-3 Molecular insights into the HLA-B35 molecules' classification associated with HIV control #MS03-2-3

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Abstract
Human leukocyte antigen (HLA) class I molecules have been shown to strongly influence the immune response to HIV infection and acquired immunodeficiency syndrome (AIDS) progression. Polymorphisms within the HLA-B35 molecules divide the family into 2 groups Px and Py. The Px group is associated with deleterious effects and an accelerated disease progression in HIV+ patients, while the Py group is not. The classification is based on the preferential binding of a Tyrosine at the C-terminal part of the peptide in the Py group, and a non-Tyrosine residue in the Px group. However, there is lack of knowledge on the molecular differences between the two groups. Here, we have investigated three HLA-B35 molecules, namely HLA-B*35:01 (Py), HLA-B*35:03 (Px), and HLA-B*35:05 (unclassified). We selected an HIV-derived peptide, NY9, and demonstrated that it can trigger a polyfunctional CD8+ T cell response in HLA-B*35:01+/HIV+ patients. We also provided the first αβTCR repertoire analysis of the NY9-specific T cells. We determined that in complex with the NY9 peptide, the Py molecule was more stable than the Px or the unclassified molecule. We solved the structures of the three HLA molecules in complex with the NY9 peptide, and structural similarities with HLA-B*35:01 would classify the HLA-B*35:05 within the Py group.

Graphical Abstract