Functional clustering and association of HLA class I alleles to viral load in HIV-positive and ART-naïve participants from the INSIGHT START study

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Results

• Two functional groups were associated with a lower VL, one composed of HLA-B*57:01, B*57:02, and B*57:03 (β -0.32, q-value 1.77E-07, Fig. 2 center) and a pair of HLA-C*08 alleles (β -0.29, q-value 0.043, Fig. 2 right).
• In contrast, an HLA-B*44 cluster showed an association with higher VL (β 0.15, q-value 0.005, Fig. 2 left).
• Among the 13 alleles implicated by these 3 functional clusters, only two (HLA-B*57:01 and B*57:03) were detected at individual allele level (Fig. 1).

Methods

• 1.03 million putative HIV-1 peptides (9-mers) were generated from HIV consensus sequences of 3785 HIV+ participants across 35 countries in the START study (3).
• Consensus clustering (4, 5) was implemented using predicted binding affinities of putative peptides to 259 HLA class I alleles by netMHCPan 4.0 (6).
• Associations of log(10)(VL) to each node were tested by linear regression using imputed HLA alleles from 2546 ART-naïve participants and adjusted by sex, self-reported race and country.
• Multiple testing was controlled by a false discovery rate (FDR)-based procedure using a q-value < 0.05 to identify associations.

Conclusions

• Consensus clustering of HLA alleles based on predicted epitopes provides functional groups to efficiently explore associations with VL.
• Three functional clusters associated with viral load were found containing both previously reported HLA alleles (HLA-B*57) and novel candidates that were not detected at individual allele level.

References

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