Study of Single Nucleotide Polymorphisms Associated with HIV-1 Set-Point Viral Load in Antiretroviral Therapy-Naïve HIV-Positive Participants of the START study

C Ekenberg1, MH Tang1, DD Murray1, C MacPherson1, BT Sherman2, M Losso3, R Wood4, R Paredes5, JM Molina6, M Helleberg1, N Jina7, CM Kityo8, E Florence9, MN Polizotto10, JD Neaton11, HC Lane12 and JD Lundgren1 for the INSIGHT START Study Group

BACKGROUND

- HIV 1-set point viral load (spVL) is predictive of disease progression and shows variability across HIV-1-positive (HIV+) persons.
- Various factors may influence spVL including viral features, environmental exposure and host genetics.
- To identify single nucleotide polymorphisms (SNPs) associated with spVL, we performed a genome-wide association study (GWAS) on a subset of participants from the Strategic Timing of Antiretroviral Treatment (START) study covering a demographically diverse population.

METHODS

- 4,864 HIV+ participants were included in the START trial, of which 2,547 consented to genomics and were genotyped. 2,544 had an HIV RNA (copies/mL) taken at study entry and were included in analysis. Participants were antiretroviral therapy (ART)-naïve and spVL was taken as log10(HIV RNA) at study entry.
- Genotypic data was generated on a custom content Affymetrix Axiom SNP array covering 770,558 probes, and the Ensembl Gene database, assembly GRCh37.p13, was used for annotation.
- To identify single nucleotide polymorphisms (SNPs) associated with spVL, we performed a genome-wide association study (GWAS) on a subset of participants from the Strategic Timing of Antiretroviral Treatment (START) study covering a demographically diverse population.

RESULTS

- Among the 2,544 participants, PCA showed distinct population structures with strong separation between Black (n=578) and non-Black (n=1966) participants, Figure 1. ANOVA was performed independently on both subsets.
- Two SNPs located in the Major Histocompatibility Complex (MHC) class I region of chromosome 6 reached genome-wide significance (P<5 x 10^-8) in the non-Black population; rs4418214 (P = 1.74 x 10^-8), and rs7356880 (P = 9.69 x 10^-8), in the same region approached significance. Two additional SNPs, rs9264942 (P = 5.99 x 10^-8) and rs73969216 (P = 9.09 x 10^-8), in the same region approached significance.

CONCLUSIONS

- In this study, we confirm the association of a previously reported SNP (rs4418214) and identify a novel candidate SNP (rs7356880) associated with lower spVL in a population of non-Black, ART-naïve HIV+ persons.
- Current findings suggest that the effects of these SNPs are consistent across race groups, but further studies are required to confirm this.
- Our results support previous findings that variation in the MHC class I region is a major host determinant of HIV-1 control.

REFERENCES:


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