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Background

Previous Genome Wide Association Studies performed on Elite Controllers and control HIV-1 infected individuals have shown that the MHC locus is predominantly responsible for containing plasma viremia below a threshold of detection. Here we performed a GWAS on a cohort of 160 HIV-1 infected Caucasian Long Term Non Progressors (LTNP) from the EC-funded European-African "GISHEAL" Consortium in order to explore whether novel genetic factors could account for the LTNP phenotype (i.e. maintenance of CD4 T cell counts >500 cells/μl and good health conditions without therapy).

Results

Frequencies of the SNPs found in LTNP were challenged vs. those of seroconverters of the French "PRIMO" cohort. Most of the SNPs strongly associated to LTNP phenotype were found in the MHC region (figure 1), especially encompassing class I and class III genes. Since 6 of the 10 top SNPs are in the HLA-B region, we confirm previous studies showing that class I HLA-B27 and HLA-B57 alleles are strongly correlated to the LTNP condition. In addition, about 65% of our LTNP naturally resist to HIV disease progression independently of HLA-B27/B57; in this regard, quite strikingly, 11 over 32 SNPs with a Q-value < 0.05 are located in MHC class III region in GISHEAL LTNP cohort.

Conclusion

Thus, our findings support the concept that different MHC loci significantly contribute to long-term control of HIV disease progression in the absence of antiretroviral therapy and provide novel evidence of a seminal role of MHC class III gene polymorphisms in determining the LTNP phenotype.