Human-SARS-CoV-2 interactome and human genetic diversity: TMPRSS2-rs2070788, associated with severe influenza, and its population genetics caveats in Native Americans

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Abstract

The current search for host-susceptibility variants for COVID-19 contrasts with the fact that the study of the genetic architecture of Severe Acute Respiratory Syndrome (SARS) has been neglected. For human/SARS-CoV-2 interactome genes ACE2, TMPRSS2 and BSG, there is only one convincing evidence of association in Asians with influenza-induced SARS for TMPRSS2-rs2070788, tag-SNP of the eQTL rs383510. This case illustrates the importance of population genetics and of sequencing data in the design of genetic association studies in different human populations: the high linkage disequilibrium (LD) between rs2070788 and rs383510 is Asian-specific. Leveraging on a combination of genotyping and sequencing data for Native Americans (neglected in genetic studies), we show that while their frequencies of the Asian tag-SNP rs2070788 is, surprisingly, the highest worldwide, it is not in LD with the eQTL rs383510, that therefore, should be directly genotyped in genetic association studies of SARS in populations with Native American ancestry.

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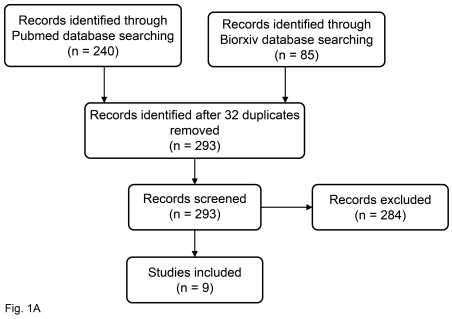

Fig. 1A

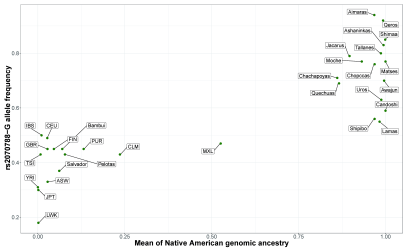

Fig. 1B

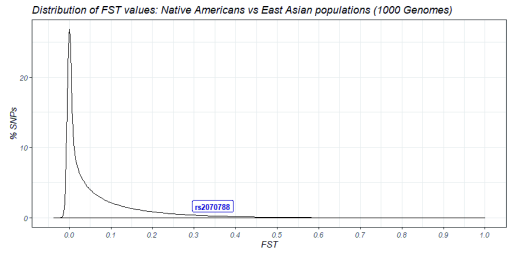

Fig. 1C

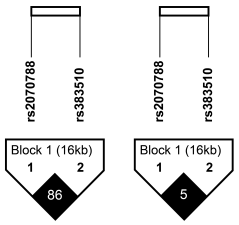

Fig. 1D