Complex Genetic Disorders, Genetic Susceptibility to Infections

AB070. Association of genome-wide significant single-nucleotide polymorphisms with coronary artery disease in Pakistani population: a case-control study

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Background: Genome wide association studies (GWAS) have successfully revealed >40 genetic risk loci associated with coronary artery disease (CAD) in Europeans. Only five loci have been replicated in South Asians.

Methods: We assessed the association of 47 genome-wide significant single-nucleotide polymorphisms (SNPs) with CAD in a Pakistani sample comprising of 663 clinically ascertained and angiographically confirmed cases and controls. Genotypes were performed using Sequenom's iPLEX assay. The association of selected SNPs with coronary stenosis was initially determined by chi-square and additive genetic model. We selected 12 SNPs based on additive model and their association was also analyzed by using dominant model. All statistical analyses were performed by R software. Linkage disequilibrium (LD) of significant SNPs was determined by SNAP web portal and functional annotation of SNPs was determined by RegulomeDB.

Results: We had five significant SNPs out of 47 variants (rs4252120; P=0.003, rs2505083; P=0.006, rs2048327; P=0.04, rs602633; P=0.02 & rs46522; P=0.02) under dominant model and two, *PLG*/rs4252120 (P=0.003) and *KIAA*1462/rs2505083 (P=0.006), showed significant association with CAD in our sample after correcting for multiple testing (q<0.05). The odds ratio (OR) in cases *vs.* controls for two significant SNPs were; [*PLG*/rs4252120 (OR =1.83; P=0.003, FDR =0.02)] and [*KIAA*1462/rs2505083 (OR =1.65, P=0.006, FDR =0.03)]. *PLG*/rs4252120 was in LD with two other functional *PLG* variants (rs4252126 and rs4252135) having RegulomeDB score of 1f. Likewise, *KIAA*1462/rs2505083 was in LD with a functional SNP *KIAA*1462/rs3739998 having RegulomeDB score of 2b (likely affects TF binding).

Conclusions: We have successfully replicated two previously reported genome-wide significant SNPs in our Pakistani sample. *KIAA*1462/rs2505083 appears to be functional by itself as well as proxy of a functional SNP (*KIAA*1462/rs3739998). *PLG*/rs4252120 is proxy of two functional SNPs. Further association studies in other non-European populations and future functional studies are warranted to assess the impact of these two variants on risk of CAD.

Keywords: Coronary artery disease (CAD); *KIAA*1462; *PLG*; rs4252120; rs2505083

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