

Network based analysis of genome wide association data provides novel candidate genes for lipoprotein traits

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Presently genome wide association studies (GWASs) have generated plethora of data that need to be interpreted with diverse biological dimensions. Here, we have designed a network-based approach to predict additional candidate genes using GWAS meta-analysis data of >100,000 individuals for lipid- and lipoprotein traits (Global Lipids Genetics Consortium, GLGC). Starting with seed genes located near SNPs with $p < 5 \times 10^{-8}$ in GLGC GWAS, we applied a multi-step prioritization scheme to identify candidate genes that have moderate p-values but nevertheless might play a role in lipid and lipoprotein metabolism. The method involved selecting candidate genes from the human interactome that cluster, co-express and share comorbidity patterns with seed genes. Furthermore, we assumed that addition of population-based comorbidity data with molecular- and genetic information provides additional power to uncover the other disease relations to the GWAS findings. The final candidate genes harbour SNPs with $p\text{-value} < 0.05$ in GWAS meta-analysis data. We selected four SNPs for validation in Malmö Diet and Cancer Cardiovascular Cohort based on their location and conservation status, and found significant association of a synonymous SNP rs234706 in cystathionine beta-synthase gene (*CBS*) with total cholesterol ($p=0.003$) and LDL cholesterol ($p=0.00001$) levels. Further, the minor allele of rs234706 associated significantly with mRNA level of *CBS* in liver samples of 206 subjects ($p=0.04$). Despite *CBS* known biological role in lipid metabolism, SNPs in this locus have not yet been identified as associated with lipoprotein traits by GWAS.

Biography

Amitabh Sharma has completed his Ph.D at the age of 30 years from Pune University and postdoctoral studies from Department of Clinical Sciences, CRC, Lund University, Malmö University Hospital, S-205 02 Malmö, Sweden. He is working as Research associate at Center for complex network research, Dept. of Physics, Northeastern University, Boston, USA-02115, a premier center for Network research. He has published more than 13 papers in reputed journals and involved in implementing the network medicine approach for understanding the complex diseases.