Genome-wide association study

Genome-wide association study (GWA study, or GWAS), also known as whole genome association study (WGA study, or WGAS), is an observational study of a genome-wide set of genetic variants in different individuals to see if any variant is associated with a trait. GWASs typically focus on associations between single-nucleotide polymorphisms (SNPs) and traits like major human diseases, but can equally be applied to any other organism.

When applied to human data, GWA studies compare the DNA of participants having varying phenotypes for a particular trait or disease. These participants may be people with a disease (cases) and similar people without (controls), or they may be people with different phenotypes for a particular trait, for example blood pressure. This approach is known as phenotype-first, in which the participants are classified first by their clinical manifestation(s), as opposed to genotype-first. Each person gives a sample of DNA, from which millions of genetic variants are read using SNP arrays. If one type of the variant (one allele) is more frequent in people with the disease, the variant is said to be associated with the disease. The associated SNPs are then considered to mark a region of the human genome that may influence the risk of disease.

A GWAS data set of 250 intracranial aneurysms (IAs) and 294 controls was used to analyze the genetic link between matrix metalloproteinases (MMPs) and IAs via single-nucleotide polymorphisms (SNPs), MMP gene families, and in silico functional analyses of gene ontology (GO) enrichment and protein-protein interaction (PPI).

Forty-eight SNPs and 1 indel out of 342 markers of MMP genes were related to IAs. The rs2425024 SNP located on MMP24 was the most strongly associated with IAs (OR=0.43, CI=0.30-0.61, p=2.4×10-6), suggesting a protective effect. The 16938619 SNP of MMP26 significantly increased the risk of an IA (OR=3.12, 95% CI=1.76-5.50, p=8.85×10-5). Five MMP genes (MMP24, MMP13, MMP2, MMP17, and MMP1) increased the susceptibility to an IA. MMP24 was the gene most closely related to IAs (p=7.96×10-7). GO analysis showed that collagen catabolism was the most-enhanced biological process. Further, metalloendopeptidase activity and ECM were predominantly detected in the cellular component and molecular function, respectively. PPI provided evidence that MMP2, TIMP2 (tissue inhibitor of metalloproteinase 2), and TIMP3 genes constitute a network for predicting IA formation.

The present results provide comprehensive insight into the occurrence of IAs associated with MMPs [1].

GWASs have implicated several loci and genes that confer susceptibility to intracranial aneurysm [2] [3] [4] [5]. [6]. A meta-analysis of GWASs identified 19 genetic variants associated with intracranial aneurysm [7].

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