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Study identifies genetic variants giving rise to differences in metabolism

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Common genetic polymorphisms induce major differentiations in the metabolic make-up of the human population, according to a paper published November 28 in the open-access journal *PLoS Genetics*. An international team of researchers, led by Karsten Suhre, has conducted a genome-wide association study with metabolomics, identifying genetic variants in genes involved in the breakdown of fats. The resulting differences in metabolic capacity can affect individuals' susceptibility to complex diseases such as diabetes and hyperactivity.

In the rapidly evolving field of metabolomics, scientists aim to measure all endogenous metabolites in a cell or body fluid. These measurements provide a functional readout of the physiological state of the human body. Investigation into these so-called "genetically determined metabotypes" in their biochemical context may help determine the pathogenesis of common diseases and gene-environment interactions.

The team identified four single nucleotide polymorphisms (SNPs) located in genes coding for well-characterized enzymes of the lipid metabolism. Individuals with different genotypes in these genes have significantly different metabolic capacities with respect to the synthesis of some polyunsaturated fatty acids, the beta-oxidation of short- and medium-chain fatty acids and the breakdown of triglycerides. By simultaneous measurements of both SNPs and serum concentrations of endogenous metabolites, the researchers determined the metabolome of several hundred healthy individuals and compared it to their genetic inheritance.

The results suggest that most individuals carry one or more risk alleles in their genetic inheritance that may determine a certain medical phenotype, the response to a given drug treatment, or the reaction to a nutritional intervention or environmental challenge. These findings may lead to more targeted approaches to health care based on a combination of genotyping and metabolic characterization. To achieve this goal, it will be necessary to identify the major genetically determined metabotypes and their association to complex diseases.

Citation: Gieger C, Geistlinger L, Altmaier E, Hrabe´ de Angelis M, Kronenberg F, et al. (2008) Genetics Meets Metabolomics: A Genome-Wide Association Study of Metabolite Profiles in Human Serum. PLoS Genet 4(11): e1000282. doi:10.1371/journal.pgen.1000282
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