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German Research Center for Environmental Health

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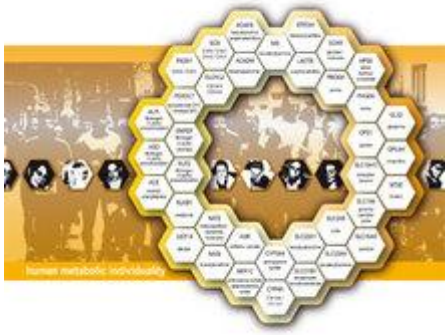
New Insights into the Etiology of Complex Common Diseases

Neuherberg, 01.09.2011. Scientists at Helmholtz Zentrum München, in cooperation with Wellcome Trust Sanger Institute and King's College London (KCL), have identified the association between genetic variants and specific metabolic changes. The study, published today in Nature, provides new functional insights regarding associations between risk factors and the development of complex common diseases.



37 genetic risk loci were discovered. Credit: Cornelia Kruppa

In the study appearing today in the journal Nature, the researchers identified 37 previously unknown genetic risk loci, elucidated their effect on the human metabolism and found clear associations to complex common diseases such as type 2 diabetes mellitus. Professor Karsten Suhre and Dr. Christian Gieger of Helmholtz Zentrum München, together with colleagues from Wellcome Trust Sanger Institute in the UK and King's College London under the lead of Nicole Soranzo, conducted this research to gain in-depth insight into the etiology of disease. In the study, the scientists present the most comprehensive evaluation of genetic variance in human metabolism so far, combining genome-wide association studies * (GWAS) with metabolomics*. Over 250 metabolytes were analyzed from 60 disease-relevant metabolic pathways.

"The advantage of our study design," Suhre and Gieger said, "is that we studied genetic variance in its biological context – and thus identified previously unknown risk loci." By

combining genetics and metabolomics, a method which already showed promising results in two previous studies, the scientists were able to evaluate the biological effect of the identified genetic risk loci. In stand-alone GWAS this is not possible.

Every individual is unique – a closer look at the individual's metabolites could enable a better evaluation of the risks for developing complex common diseases in the future. "We have made considerable advances in understanding complex diseases such as type 2 diabetes mellitus," the two scientists said. "The findings of the study will lead to new approaches for pharmaceutical research."

The aim of Helmholtz Zentrum München is to better understand the etiology of complex common diseases and to derive new targets for diagnosis, therapy and prevention.

Further information

Background
*Metabolomics is the study of the metabolic profile (= metabolome) of an organism. This profile adapts to the respective life circumstances. It sheds light on which metabolic pathways are active at a given time and under specific conditions. In genome-wide association studies (GWAS) scientists study the genome (= the entirety of the genes) of a large number of test subjects and correlate this data with diseases that the test subjects are known to have. In this way scientists identify genetic patterns that are associated with various diseases. The combination of genetics and metabolomics provides insights into the causes and course of specific diseases. Thus, new therapeutic approaches and drugs can be developed and, in addition, markers for the early detection of diseases such as diabetes can be found.

* Genome-wide association studies investigate large numbers of patients to determine at which loci there is a genetic variation. When just one locus is altered, the term used is single nucleotide polymorphism (SNP). Not all SNPs are distributed equally frequently in the population – besides frequent variations, there are also rare ones.

Original publication:
Suhre K. et al.(2011): Human metabolic individuality in biomedical and pharmaceutical research, Nature 477, 7362 (2011). doi:10.1038/nature10354
Link to journal publication

Previous studies:
Gieger C et al (2008). Genetics meets metabolomics: a genome-wide association study of metabolite profiles in human serum. PLoS Genet. 4(11):e1000282.

Illig T et al (2010) A genome-wide perspective of genetic variation in human metabolism. Nat Genet. 42(2):137

As German Research Center for Environmental Health, **Helmholtz Zentrum München** pursues the goal of developing personalized medical approaches for the diagnosis, therapy and prevention of major common diseases such as diabetes mellitus and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. Helmholtz Zentrum München has about 1,900 staff members and is headquartered in Neuherberg in the north of Munich. Helmholtz Zentrum München is a member of the Helmholtz Association, a community of 17 scientific-technical and medical-biological

research centers with a total of about 31,000 staff members. In addition, it is a partner in the German Center for Diabetes Research (DZD). www.helmholtz-muenchen.de

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