

Press Release

Genetic research identifies novel pathway leading to myocardial infarction

Starting with a severely affected family, a research team led by Jeanette Erdmann, Christian Hengstenberg and Heribert Schunkert (Institut für Integrative und Experimentelle Genomik, University of Lübeck and Deutsches Herzzentrum München) identified a novel mechanism leading to myocardial infarction. Specifically, the scientists detected two mutations that jointly blocked nitric oxide signalling in platelets leading to accelerated thrombus formation. Another variant of the same enzyme, affecting a large proportion of the population, was also found to affect coronary risk, albeit to a much lesser extent. Scientists from the Berliner Age Study II (BASE-II) participated with recent data from the BASE-II study. Co-authors are the speaker of the BASE-II consortium, Elisabeth Steinhagen-Thiessen as well as Lars Bertram from the Max Planck Institute for Molecular Genetics and Shu-Chen Li from the Technical University Dresden, who is working as a visiting scientist at the Max Planck Institute for Human Development. The work was published on November 10th in the prestigious journal *Nature*.

Background

The family was identified as part of the German Myocardial Infarction Family Study (GerMIFS). The aim of the GerMIFS was to analyse MI families to unravel the genetic components of this life-threatening disease. Until today the GerMIFS includes more than 7,500 probands with follow-up data of more than 10 years.

Interestingly, genetic data of more than 30.000 MI patients and 80.000 controls pulled together from the international consortium CARDIoGRAM provide evidence that not only very rare mutations in *GUCY1A3* lead to MI but also common variants in this gene increases MI risk substantially (cf. *Nature Genetics* 2013; 45:25-33).

Among others the Berlin Age Study II (BASE-II) provided data for the controls. Within BASE-II a great variety of datasets of ca. 2.200 Berlin citizens is collected, not only genetic data. The Berlin Aging Study II follows an interdisciplinary approach. The scientists involved assume that many different factors contribute to the way aging proceeds. For example, it may play a role where and how people live, what they eat,

or whether they carry certain genetic traits that influence aging. In order to obtain an overview that is as complete as possible, physicians, psychologists, nutritionists, social scientists as well as biologists are involved in BASE-II.

BASE-II is carried out in a common project by 5 research groups: The “Geriatrics Research Group (FGG)” of Charité - Universitätsmedizin Berlin (Prof. Dr. Elisabeth Steinhagen-Thiessen), the Max Planck Institute for Human Development (Prof. Dr. Ulman Lindenberger), the Socio-oeconomic Panel (SOEP) (Prof. Dr. Gert Wagner) at the German Institute for Economic Research (DIW) in Berlin, the Max Planck Institute for Molecular Genetics (Dr. Lars Bertram) und the “Tuebingen Ageing and Tumour Immunology Group (TATI)” at the Universität Tübingen (Prof. Dr. Graham Pawelec) .

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Dysfunctional nitric oxide signalling increases risk of myocardial infarction

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