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Scientists find gene variant associated with reduced risk of hypertension and cardiovascular disease

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(PhysOrg.com) -- Hypertension is the leading contributor to global mortality, and is known to depend on the interaction of environmental and heritable factors. However, the genetic variations identified so far only explain 1-2% of the difference in blood pressure in the population, suggesting the presence of many more variations yet to be discovered.

A new genetic variation has just been identified by an international team of researchers, led by the University of Glasgow and Istituto Auxologico Italiano of Milano. This new genetic variation is associated with a reduced risk of hypertension, and also a reduced risk of cardiovascular disease events. Indeed, each copy of the variation – of which a person can have a maximum of two – was associated with a 7.7 per cent reduction of strokes, myocardial infarctions (heart attack) and coronary deaths.

Anna Dominiczak, Regius Professor of Medicine and Head of the College of Medical, Veterinary and Life Sciences at the University of Glasgow, and one of the leading investigators in the project said: “We believe the newly discovered variant gives doctors a valuable insight into the mechanisms of high blood pressure and may help identify possible targets for new drug therapies”.

The research was conducted as part of the InGenious HyperCare Project, a European Commission (EC) funded international

collaboration of 31 research groups (including an SME) in 13 European countries.

In order to identify which genetic variations play a part in a common disease, such as hypertension, a genome wide association study must be undertaken, which means that more than 500,000 variants (known as Single Nucleotide Polymorphisms, SNP) are analyzed throughout the spectrum of the human genome. While previous genome wide association studies on high blood pressure had investigated populations of individuals with a wide spectrum of blood pressures, the researchers of Glasgow and Milan investigated individuals with extremes of blood pressure,
comparing individuals with very high or with fully normal blood pressures.

Blood samples from these 'extreme' individuals were provided by collaboration with the University of Lund, Sweden, and replications of initial findings could be done through a wider collaboration with other researchers from the United Kingdom, Italy, the Netherlands, Switzerland, Ireland, Germany, as well as the United States: on the whole, genetic data were analysed in 39,706 individuals – 21,466 with hypertension and 18,240 with normotension.

The new variation found by the researchers is located in the UMOD gene in chromosome 16. This gene expresses a renal protein excreted in the urine, and called uromodulin. The researchers have also found less uromodulin is excreted in urines of the individuals carrying the variant. Uromodulin, also called Tamm Horsfall protein, is one of the major proteins in urines, but its functional role was until now largely unknown.

Professor Alberto Zanchetti, Scientific Director of Istituto Auxologico Italiano and coordinator of the InGenious HyperCare Project, was also one of the leading investigators of this genetic research. He commented:

"Our finding that variation in uromodulin promoter gene causing less uromodulin to be released, is associated with lower blood pressure and less risk of cardiovascular disease suggests that uromodulin may be related to blood pressure regulation. Uromodulin is exclusively produced in a specific part of the kidney, the thick portion of the ascending limb of Henle, which is known to be involved in sodium reabsorption. It appears reasonable to suggest uromodulin participates in blood pressure regulation and disregulation though a sodium linked mechanism".

Professors Dominiczak and Zanchetti concluded: "We need to carry out more studies to know just how important this UMOD gene and its protein are, but our findings seem to contribute strongly to the story of salt involvement in hypertension".

The results of the study are published in the *Public Library of Science Genetics* open-source journal. They will be presented and discussed on 4th November at a meeting on "How can medical innovation reduce the cardiovascular disease burden?", convened in Brussels by the Health Directorate of the European Commission. During this meeting experts from different European countries will discuss current and future trends of research in cardiovascular disease to help the Commission shape their strategic support to research in this area.

More information: www.plosgenetics.org/home.action

Provided by University of Glasgow

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