Ironing out the genetic cause of hemoglobin problems

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The researchers say the enzyme produced by the TMPRSS6 gene is a good target for new drugs to maintain normal hemoglobin levels

(PhysOrg.com) -- A gene with a significant effect on regulating hemoglobin in the body has been identified as part of a genome-wide association study, which looked at the link between genes and hemoglobin level in 16,000 people. The research was carried out by scientists from Imperial College London and published in *Nature Genetics* today. It shows a strong association between a gene known as TMPRSS6 and the regulation of hemoglobin.

Hemoglobin is contained within red blood cells and is essential for transporting oxygen around the body. Problems with hemoglobin production cause common diseases, such as anaemia, which comes from low levels of hemoglobin and is found in 25% of the world's population.

"This new finding is critical: understanding how hemoglobin levels are controlled at a genetic level has significant public health implications for people of all ages in developing and developed countries", explains Dr John Chambers, from the Department of Epidemiology and Public Health at Imperial College London and one of the lead authors of the study.

"Abnormally high or low levels are associated with a range of serious health problems, such as poor growth (low levels) and increased risk of stroke (high levels). Changes in hemoglobin levels can also affect our susceptibility to diseases like malaria, which infect the red blood cells" says Professor Kooner, from the National Heart and Lung Institute at Imperial College London and the study's chief investigator.

The new research adds to our understanding of the multiple causes of problems with hemoglobin levels, which include an iron-deficient diet, chronic diseases such as cancer, and genetic associations, such as the one described in this paper. In the future, the finding could lead to new treatments for people suffering from chronic problems with hemoglobin levels not linked to iron in the diet.

"The enzyme protein produced by the TMPRSS6 gene is a good target for drug development. Designing a drug that enhances TMPRSS6 activity could augment hemoglobin in people such as cancer and kidney failure patients, who suffer from chronically low levels. A different drug that blocked TMPRSS6 enzyme production might bring down high hemoglobin levels", adds Dr Chambers.

The new paper is published as part of a series of new findings on links between genes and regulation of blood cell characteristics. The Imperial research focuses on two unique aspects in particular.

First, the genomic analysis is based on individuals of European and

Indian Asian ancestry, and shows a strong link in both populations, emphasising the global relevance of the finding, by showing it is not confined to individual ancestries.

Second, the paper includes evidence for how the genetic variant affects TMPRSS6 function at a molecular level, and shows that the genetic variation causes an amino acid change near the enzyme's active site, that is likely to affects the way TMPRSS6 reacts with target molecules.

More information:

1. "Genome-wide association study identifies variants in TMPRSS6 associated with hemoglobin levels" *Nature Genetics*, Sunday 11 October 2009.

2. "EpiCollect: Linking Smartphones to Web Applications for Epidemiology, Ecology and Community data collection." *PLoS One*, 16 September 2009. Lead author: John C Chambers, Imperial College London

Source: Imperial College London (news : web)