Combining plasma screening methods better identifies diagnostic and therapeutic targets

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For the first time, scientists have combined genomic and proteomic analysis of blood plasma to enhance identification of genetically regulated protein traits. This could be applied to any large association study of civilization diseases where blood plasma has been collected, vastly improving a clinician's ability to identify disease susceptibility in individuals and populations. This advance is published in the February 2013 issue of the journal *Genetics*.

"We hope that combining genome-wide with proteome-wide screening of blood plasma will aid in the identification of molecular disease mechanisms," said Daniel Teupser, M.D., a researcher involved in the work from the Institute of Laboratory Medicine at Ludwig-Maximilians-University, in Munich, Germany. "The methodology is applicable to many frequent diseases such as diabetes, cardiovascular disease or cancer and might accelerate identification of novel diagnostic and therapeutic targets."

To make this advance, Teupser and colleagues analyzed 455 plasma samples from the offspring of two different inbred mouse strains using mass spectrometry. This allows researchers to distinguish proteins based on differences in their molecular weight. The resulting protein phenotypes of all 455 F2 mice were associated with 177 genetic markers evenly distributed over the mouse genome. This led to the identification of genetically regulated plasma proteins. The strongest two associations were with the genes encoding hemoglobin and apolipoprotein 2. The responsible genetic variants were identified in additional functional

experiments.

Mass spectrometry has already been adapted for clinical applications, and plasma is often the target because of it easy accessibility. Since plasma comes in contact with most tissues, it often mirrors metabolism and disease. This study pioneers a promising approach to identify novel disease-associated proteins, which could provide novel diagnostic or therapeutic targets of disease.

"Gene variants are now easy to identify, so what's become limiting is the traits—the phenotype—to link to those variants. This study goes a long way to opening up that bottleneck. The high-throughput screening the authors describe holds tremendous promise for finding diagnostic markers and therapeutic targets of disease," said Mark Johnston, Editor-in-Chief of the journal *Genetics*.

More information: Holdt, Lesca M., Annette von Delft, Alexandros Nicolaou, Sven Baumann, Markus Kostrzewa, Joachim Thiery, and Daniel Teupser, Quantitative Trait Loci Mapping of the Mouse Plasma Proteome (pQTL) , *Genetics*, February 2013 193:601-608.

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