Proteomic characterization of peripheral leukocytes in variant carriers of CDKAL1 associated with cholesterol efflux capacity

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Background: Genetic variations near CDKAL1 (CDK5 regulatory subunit-associated protein 1-like 1) gene recently showed association with individual’s cholesterol efflux capacity. The aim of this study was to compare the proteomes of peripheral leukocytes in CDKAL1 variant carriers and controls to identify evidence of biological impact caused by these variants.

Methods: Peripheral blood leukocytes were isolated from five individuals with any of four CDKAL1 variants (rs117835232, rs117252933, rs118064592, and rs150434350) and five controls. Cell lysates were digested to peptides and Q Exactive Orbitrap Plus mass spectrometry was applied for comparative proteomics analysis. Protein identification and quantification were performed with MaxQuant software.

Results: In total, 2,387 proteins were identified at false discovery rate 1% level, of which 176 proteins were differently abundant between CDKAL1 variant and control groups (p < 0.05, fold-difference > 1.5). Among them, 39 upregulated and 137 downregulated proteins were identified in the variant group (p < 0.05; fold change > 1.5) (Figure 1). The upregulated included docosahexaenoic acid omega hydroxylase, resistin, and apoA1, whereas the downregulated included NADH ubiquinone oxidoreductase. The functional enrichment and KEGG pathway analysis showed 20 associated pathways including carbon metabolism, synthesis of antibiotics, and RNA transport.

Conclusions: Differential expression of proteins regulating lipid metabolism and RNA transport in CDKAL1 variant carriers indicates differences in corresponding biological function in these individuals. Detailed contribution of the reported proteins remains to be clarified.