Bioinformatics-Driven Identification and Examination of Candidate Genes for Non-Alcoholic Fatty Liver Disease - DTU Orbit (03/01/2019)

Bioinformatics-Driven Identification and Examination of Candidate Genes for Non-Alcoholic Fatty Liver Disease

Objective: Candidate genes for non-alcoholic fatty liver disease (NAFLD) identified by a bioinformatics approach were examined for variant associations to quantitative traits of NAFLD-related phenotypes. Research Design and Methods: By integrating public database text mining, trans-organism protein-protein interaction transferal, and information on liver protein expression a protein-protein interaction network was constructed and from this a smaller isolated interactome was identified. Five genes from this interactome were selected for genetic analysis. Twenty-one tag single-nucleotide polymorphisms (SNPs) which captured all common variation in these genes were genotyped in 10,196 Danes, and analyzed for association with NAFLD-related quantitative traits, type 2 diabetes (T2D), central obesity, and WHO-defined metabolic syndrome (MetS). Results: 273 genes were included in the protein-protein interaction analysis and EHHADH, ECHS1, HADHA, HADHB, and ACADL were selected for further examination. A total of 10 nominal statistical significant associations (P <0.05) to quantitative metabolic traits were identified. Also, the case-control study showed associations between variation in the five genes and T2D, central obesity, and MetS, respectively. Bonferroni adjustments for multiple testing negated all associations. Conclusions: Using a bioinformatics approach we identified five candidate genes for NAFLD. However, we failed to provide evidence of associations with major effects between SNPs in these five genes and NAFLD-related quantitative traits, T2D, central obesity, and MetS.