

The Genetic Link between NAFLD and Type 2 Diabetes: Comparing Disease Signatures

Jacob Leung¹, Masaki Kimura¹, Takanori Takebe¹

¹Division of Gastroenterology, Hepatology and Nutrition, Division of Developmental Biology, & Center for Stem Cell and Organoid Medicine (CuSTOM) Cincinnati Children's Hospital Medical Center and Department of Pediatrics, University of Cincinnati College of Medicine

Introduction: America is in the midst of an obesity epidemic and Type 2 diabetes mellitus (T2DM) and nonalcoholic fatty liver disease (NAFLD) are two of the most common comorbidities. Though the etiology of these diseases is not entirely understood, genetic factors are known to play a key role in pathogenesis. Here we compare the expression signatures and identify genes that may play a part in both T2DM and NAFLD.

Hypothesis: Using pre-existing data from published studies, we generated a list of genes that are differentially expressed (DE) in the same direction in both NAFLD and T2DM; these genes may underlie a link between the two conditions.

Methods: Gene expression data was gathered from Gene Expression Omnibus (GEO). Seven studies were selected for NAFLD: (all samples liver biopsies, 267 NAFLD, 120 control), and 5 studies for T2DM: 1 study in liver biopsies (9 T2DM, 9 control), 2 in muscle (19 T2DM, 35 control), and 2 in visceral adipose (11 T2DM, 11 control). Differential gene expression was determined for both conditions, cross-referenced with current literature, and compared. Differential gene expression analyses were performed with iGEAK. Enrichment analyses were performed with WebGestalt.

Results: Over 800 different genes were DE in both NAFLD and T2DM compared to the respective controls. Of those, 92 genes were DE in the same direction in both conditions, and only 6 were previously identified as candidate genes for either condition (5 in NASH, 1 in T2DM). Additionally, 75 of the 92 DE genes were expressed in the liver. Further analysis of these 75 genes revealed significant enrichment of numerous pathways, including several metabolic pathways, namely carbohydrate metabolism, as well as various mitochondrial processes.

Conclusions: Here we report the finding of 92 genes similarly regulated in both NAFLD and T2DM, including over 80 genes not previously considered in the context of either disease. These genes could represent a genetic link between NAFLD and T2DM. Further studies should confirm these findings and further exploration into these genes is needed.

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