An adult-based genetic risk score for hepatic fat associates with liver and lipid traits in Danish children and adolescents

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FR104
An adult-based genetic risk score for hepatic fat associates with liver and lipid traits in Danish children and adolescents
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Results: was calculated to evaluate model performance. Analysis was performed on models based on risk factors for hepatic steatosis, defined as hepatic fat content measured by magnetic resonance spectroscopy in 539 individuals. We calculated a weighted GRS based on 10 variants known to associate with hepatic fat in adults, individually and combined as a genetic risk score (GRS), with cardiometabolic traits. The GRS was associated with higher liver fat content, liver enzymes and lipid profiles, but was not associated with adiposity and other metabolic traits in children and adolescents. The GRS could serve as a predictor of the risk for hepatic steatosis in addition to clinical risk factors and could be used for early preventative initiatives.

Conclusion: The adult-based GRS for hepatic fat was associated with liver fat content, liver enzymes and lipid profiles, but was not associated with adiposity and other metabolic traits in children and adolescents. The GRS could serve as a predictor of the risk for hepatic steatosis in addition to clinical risk factors and could be used for early preventative initiatives.

FR105
Identification of new potential biomarkers to follow steatohepatitis in patients with non-alcoholic/metabolic-associated fatty liver disease
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Background and aims: To integrate different liver gene-expression datasets to identify novel potential serological biomarkers to follow-up steatohepatitis in NAFLD patients.

Method: Initial candidates were obtained by comparing the gene expression of paired liver biopsies coming from NAFLD patients that were able (n = 20) or not (n = 17) to resolve steatohepatitis at the end of a dietary or a surgical intervention of 1 year (section 1). Association of candidates to steatohepatitis was initially explored in 6 microarray gene expression datasets (n = 317) in which patients were classified as NASH or No NASH according to the SAF score and analysed as a single cohort after batch normalization. Selected candidates were filtered through a series of public datasets to retain exclusively secreted proteins able to reach the bloodstream. Candidates were validated independently in three additional RNA-seq additional datasets in which patients with Bland Steatosis (SS) were compared against patients with steatohepatitis (NASH (Cohort 1: N = 31 SS/16 NASH) (Cohort 2 N = 67 23 SS/44 NASH) (Cohort 3 N = 99 51 SS/47 NASH)) introducing age (Cohorts 2 and 3) and sex as covariables in the analysis (3). These candidates were further explored in a recently published gene expression (Govaere et al. 2020) in which 163 NASH patients were stratified by fibrosis stage (F0–F1 n = 34; F2 n = 53; F3 n = 54; F4 n = 12) and compared against patients with bland steatosis with no or mild fibrosis (SS n = 51).

Results: Paired liver biopsy analysis identified 1363 genes that significantly change their behaviour specifically in patients achieving NASH resolution. 61 or them showed a positive or a negative association to steatohepatitis in the integrative multiarray comparison in the microarray microchord set. 22 of them are secreted and can reach the bloodstream. Only one of them, IL-29, replicated its behaviour in the microarray cohort (Fold Change: FC: 1.43, p-value 1.3 × 10−5, FDR:1.3 × 10−6) and in all three RNA-seq analysis (Cohort 1 FC: 2.47, p-value 6.2 × 10−4 FDR 1.0 × 10−2; Cohort 2: FC: 1.59, p-value 8.3 × 10−5, FDR: 9.7 × 10−2; Cohort 3 FC: 2.11, p-value 1.15 × 10−5, FDR: 3.2 × 10−6). This protein also replicated its behaviour in the last dataset independently from fibrosis stage (NASH F0–F1 vs NAFL FC: 1.64, p-value: 3.78 × 10−4, q-value: 9.99 × 10−4) (NASH F2 vs NAFL FC: 1.69, p-value: 5.62 × 10−5, q-value: 2.90 × 10−2) (NASH F3 vs NAFL FC: 2.03, p-value: 4.81 × 10−3, q-value: 8.52 × 10−4) (NASH F4 vs NAFL FC: 2.16, p-value: 4.80 × 10−3, q-value: 1.83 × 10−3).