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Title: Keratin 8/18 variants involved in non-alcoholic fatty liver disease and their association with insulin resistance: a case-control study in Chinese cohort

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1 What did this study explore?

The study explored the hypothesis that keratin 8/18 variants predispose human to non-alcoholic fatty liver disease (NAFLD) progression and its metabolic phenotype.

2 How did the authors perform all experiments?

The subjects were selected from our Physical Examination Department, and diagnose of NAFLD were established according to ultrasonic sign of fatty liver. Each participant underwent a medical history, general examinations and laboratory examinations, at the same time, K8/K18 coding regions were analyzed.

3 How did the authors process all experimental data?

Messenger RNA sequences of K8 (NM002273) and K18 (NM000224) were used to localize coding variants, while genomic sequences (hKRT8 [M34482] and hKRT18 [AF179904]) were employed for noncoding variants. Statistical analyses were performed using SPSS statistical software, version 20.0 for Windows. For continuous variables, a two-tailed *t*-test was used for two group comparisons, whereas Kruskal-Wallis nonparametric one-way analysis of variance was used to compare qualitative variables.

K8/K18 variant frequencies in the NAFLD patient and control groups were compared with the two-tailed Fisher exact probability test.

4 How did the authors deal with the pre-study hypothesis?

K8/K18 proteins protect hepatocytes from various kinds of injury as major cytoskeletal proteins. There are studies showed that K8/K18 variants are expressed in a high percentage of the end-stage liver diseases, chronic hepatitis C infection, drug-induced liver injury and other liver diseases. Moreover, K8/K18 is also involved in blood glucose control and insulin response. A literature search was conducted and it turned out that none of the prior studies have evaluated about K8/K18 variants and NAFLD. Thus, this study was undertaken.

5 What are the novel findings of this study?

We found an increased frequency of variants in NAFLD patients versus controls. We also identified one novel amino-acid-altering heterozygous variant (K18 N193S) and three novel non-coding variants (K8 IVS5-9A→G, K8 IVS6+19G→A, K18 T195T). Moreover, the keratin variant was significantly associated with insulin resistance in NAFLD patients. The finding highlights the importance of K8/K18 gene variants in NAFLD.

Sincerely,

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