

Disease-specific eQTL screening reveals an anti-fibrotic effect of AGXT2 in nonalcoholic fatty liver disease

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The Manuscript Microscope Sentence Audit is a research paper introspection system that parses the text of your manuscript into minimal sentence components for faster, more accurate, enhanced proofreading.

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- **Accelerated Proofreading:** Examine long technical texts in a fraction of the usual time.
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Manuscript Authors: Taekyeong Yoo, Sae Kyung Joo, Hyo Jung Kim, Hyun Young Kim, Hyungtai Sim, Jieun Lee, Hee-Hoon Kim, Sunhee Jung, Youngha Lee, Oveis Jamialahmadi, Stefano Romeo, Won-Il Jeong, Geum-Sook Hwang, Keon Wook Kang, Jae Woo Kim, Won Kim & Murim Choi

Features of the Sentence Audit:

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1. Each sentence of your text is parsed and displayed in isolation for focused inspection.
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The combined approaches ensure easier, faster, more effective proofreading.

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
- Always consult the original research paper as the true reference source for the text.

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title **Disease-specific eQTL screening reveals an anti-fibrotic effect of AGXT2 in nonalcoholic fatty liver disease**

S1 [001] Abstract

S1 [002] Background & Aims

Background & Aims

S1 [003] Nonalcoholic fatty liver disease (NAFLD) poses an impending clinical burden.

Nonalcoholic fatty liver disease ...

... (NAFLD) ...

... poses an impending clinical burden.

S1 [004] Genome-wide association studies have revealed a limited contribution of genomic variants to the disease, requiring alternative but robust approaches to identify disease-associated variants and genes.

Genome-wide association studies have revealed a limited contribution ...

... of genomic variants ...

... to the disease, ...

... requiring alternative ...

... but robust approaches ...

... to identify disease-associated variants ...

... and genes.

S1 [005] We carried out a disease-specific expression quantitative trait loci (eQTL) screen to identify novel genetic factors that specifically act on NAFLD progression on the basis of genotype.

We carried out a disease-specific expression quantitative trait loci ...

... (eQTL) ...

... screen ...

... to identify novel genetic factors ...

... that specifically act ...

... on NAFLD progression ...

... on the basis ...

... of genotype.

S1 [006] Methods

Methods

S1 [007] We recruited 125 Korean biopsy-proven NAFLD patients and healthy individuals and performed eQTL analyses using 21,272 transcripts and 3,234,941 genotyped and imputed SNPs.

We recruited 125 Korean biopsy-proven NAFLD patients ...

... and healthy individuals ...

... and performed eQTL analyses ...
... using 21,272 transcripts ...
... and 3,234,941 genotyped ...
... and imputed SNPs.

S1 [008] We then selected eQTLs that were detected only in the NAFLD group, but not in the control group (i.e., NAFLD-eQTLs).

We then selected eQTLs ...
... that were detected ...
... only in the NAFLD group, ...
... but not ...
... in the control group ...
... (i.e., NAFLD-eQTLs).

S1 [009] An additional cohort of 162 Korean NAFLD individuals was used for replication.

An additional cohort ...
... of 162 Korean NAFLD individuals was used ...
... for replication.

S1 [010] The function of the selected eQTL toward NAFLD development was validated using HepG2, primary hepatocytes and NAFLD mouse models.

The function ...
... of the selected eQTL toward NAFLD development was validated ...
... using HepG2, ...
... primary hepatocytes ...
... and NAFLD mouse models.

S1 [011] Results

Results

S1 [012] The NAFLD-specific eQTL screening yielded 242 loci.

The NAFLD-specific eQTL screening yielded 242 loci.

S1 [013] Among them, AGXT2, encoding alanine-glyoxylate aminotransferase 2, displayed decreased expression in NAFLD patients homozygous for the non-reference allele of rs2291702, compared to no-NAFLD subjects with the same genotype ($P = 4.79 \times 10^{-6}$).

Among them, ...
... AGXT2, ...
... encoding alanine-glyoxylate aminotransferase 2, ...
... displayed decreased expression ...
... in NAFLD patients homozygous ...
... for the non-reference allele ...
... of rs2291702, ...
... compared ...
... to no-NAFLD subjects ...
... with the same genotype ...
... ($P = 4.79 \times 10^{-6}$).

S1 [014] This change was replicated in an additional 162 individuals, yielding a combined P-value of 8.05×10^{-8} from a total of 245 NAFLD patients and 48 controls.

This change was replicated ...
... in an additional 162 individuals, ...
... yielding a combined P-value ...
... of 8.05×10^{-8} ...
... from a total ...
... of 245 NAFLD patients ...
... and 48 controls.

S1 [015] Knockdown of AGXT2 induced palmitate-overloaded hepatocyte death by increasing ER stress, and exacerbated NAFLD diet-induced liver fibrosis in mice.

Knockdown ...
... of AGXT2 induced palmitate-overloaded hepatocyte death ...
... by increasing ER stress, ...
... and exacerbated NAFLD diet-induced liver fibrosis ...
... in mice.

S1 [016] However, overexpression of AGXT2 reversely attenuated liver fibrosis and steatosis as well.

However, ...
... overexpression ...
... of AGXT2 reversely attenuated liver fibrosis ...
... and steatosis ...
... as well.

S1 [017] Conclusions

Conclusions

S1 [018] We implicate a new molecular role of AGXT2 in NAFLD.

We implicate a new molecular role ...
... of AGXT2 ...
... in NAFLD.

S1 [019] Our overall approach will serve as an efficient tool for uncovering novel genetic factors that contribute to liver steatosis and fibrosis in patients with NAFLD.

Our overall approach will serve ...
... as an efficient tool ...
... for uncovering novel genetic factors ...
... that contribute ...
... to liver steatosis ...
... and fibrosis ...
... in patients ...
... with NAFLD.

S1 [020] Lay summary

Lay summary

S1 [021] Elucidating causal genes for NAFLD has been challenging due to limited tissue availability and the polygenic nature of the disease.

Elucidating causal genes ...
... for NAFLD has been challenging ...
... due to limited tissue availability ...
... and the polygenic nature ...
... of the disease.

S1 [022] Using liver and blood samples from 125 biopsy-proven NAFLD and no-NAFLD Korean individuals and an additional 162 individuals for replication, we devised a new analytic method to identify causal genes.

Using liver ...
... and blood samples ...
... from 125 biopsy-proven NAFLD ...
... and no-NAFLD Korean individuals ...
... and an additional 162 individuals ...
... for replication, ...
... we devised a new analytic method ...
... to identify causal genes.

S1 [023] Among the candidates, we found that AGXT2-rs2291702 protects against liver fibrosis in a genotype-dependent manner with the potential for therapeutic interventions.

Among the candidates, ...
... we found ...
... that AGXT2-rs2291702 protects ...
... against liver fibrosis ...
... in a genotype-dependent manner ...
... with the potential ...
... for therapeutic interventions.

S1 [024] Our approach enables the discovery of NAFLD causal genes that act on the basis of genotype.

Our approach enables the discovery ...
... of NAFLD causal genes ...
... that act ...
... on the basis ...
... of genotype.

S2 [025] Introduction

S2 [026] Nonalcoholic fatty liver disease (NAFLD) is a growing burden that affects approximately a quarter of the world's population and contributes to liver-related morbidity.

Nonalcoholic fatty liver disease ...
... (NAFLD) ...

End of Sample Audit

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