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CORRECTION

Genotypic and phenotypic spectrum of infantile liver failure due to pathogenic *TRMU* variants

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In the article "Genotypic and phenotypic spectrum of infantile liver failure due to pathogenic *TRMU* variants" by Vogel et al there were inaccuracies in variant classification in the published article. This article is not retracted. It has been withdrawn and republished at the request of the authors. These inaccuracies did not substantially change the results or conclusions of the original paper. See the updates made to the article listed below. The variant classification has been corrected and the article has been corrected online and republished at https://www.sciencedirect.com/science/article/pii/S1098360022009534?via%3Dihub.

ABSTRACT

Original

In 62 individuals, including 30 previously unreported cases, we describe 48 (likely) pathogenic *TRMU* variants, of which, 18 were novel

Corrected to

In 62 individuals, including 30 previously unreported cases, we describe 47 (likely) pathogenic *TRMU* variants, of which 17 were novel, and 1 intragenic deletion.

Material and Methods

Added

American College of Medical Genetics and Genomics classification

The meta tool REVEL that combines SIFT, PolyPhen-2, HVAR and HDIV, LRT, Mutation Taster, Mutation Assessor, FATHMM v2.3, and VEST 3.0 was used for PP3 scoring. If the result of the REVEL prediction was pathogenic, 4 points in PP3 were given. All analyzed variants were identified to be either pathogenic or uncertain using REVEL. PP4 was applied to

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all variants because of the highly specific clinical features, with exception of p.(Gly272Asp) in patient 52 (no liver involvement reported). Four points were given for PS3 if tRNA metabolism was analyzed and altered. Two points for PS3 were given if OXPHOS enzyme activity was reduced. Criteria for PP5 were not met. For all variants the following reference sequences were used: NM_018006.5, NP_060476.2 and NC_000022.11.

Results

Genetics

Original

A total of 48 different variants were identified, of these, 18 have not been reported previously (Table 1, Figure 1A). In 2 siblings (TRMU-12 and TRUM-13), a deletion encompassing more than 1 exon in phase with a recognized missense *TRMU* variant was detected.

[...] The most frequent variants were the missense variants c.835A>G, p.(Val279Met) and c.229T>C, p.(Tyr77His), which were detected in 15 and 13 individuals, respectively.

[...] The 18 loss-of-function (LoF) variants and the intragenic deletion predicted to lead to loss of protein were detected at least in monoallelic state in 24 individuals. Presence of a LoF variant strongly affected on overall individual survival ($P = .016$) (Figure 1D).

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A total of 47 different variants were identified; of these, 17 have not been reported previously (Table 1, Figure 1A). In 2 siblings (TRMU-12 and TRUM-13), a deletion encompassing more than 1 exon in phase with a recognized missense *TRMU* variant was detected.

[...] The most frequent variants were the missense variants c.835A>G, p.(Val279Met) and C.229T>C, p.(Tyr77His) detected in 16 and 13 individuals, respectively.

[...] The 17 loss-of-function (LoF) variants and the intragenic deletion predicted to lead to loss of protein were detected at least in monoallelic state in 23 individuals. Presence of a LoF variant strongly affected on overall individual survival ($P = .0089$) (Figure 1D).

Discussion

Added

TRMU deficiency was shown to have a specific clinical phenotype of an infantile onset (when survived) reversible, isolated ALF and can be distinguished from its differential diagnoses that encompass several other IMDs. In contrast to TRMU deficiency, individuals with DGUOK deficiency often already have liver cirrhosis upon presentation and do not show a reversible phenotype. In individuals with NBAS deficiency, the reversible ALF periods are related to febrile infections.[29] Individuals with LARS1 deficiency are characterized by recurrent elevation of liver transaminases up to liver failure and multisystem involvement (abnormalities of growth, blood, nervous system, muscles).[25] Furthermore, biallelic RINT1 variants have been associated to infantile ALF in association again with multisystem involvement in 1 family.[30]

LEGENDS

Added to legend Table 1

Four points for PP4 were given for all cases except patient 52 (no liver involvement reported) because the clinical features were highly characteristic for all patients included in the study. Four points were given for PS3 if transfer RNA metabolism was analyzed and altered. Two points for PS3 were given if OXPHOS enzyme activity was reduced. If the result of the REVEL prediction was pathogenic, 4 points were given in PP3.

TABLES

Table 1

- updated details ACMG rating for all variants
- the variant of TRMU-29 was corrected to c.835G>A p.(Val279Met)

Original

TRMU-29 was wrongly annotated as c.493C>A, p.Gln165Ter

Corrected to

genomic position: hg38_update for all variants

Added

footnote: The version number for each transcript is omitted, however it can be cross referenced from Table 2

Table 2

Original

the variant of TRMU-29 was wrongly annotated as c.493C>A, p.Gln165Ter

Corrected to

the variant of TRMU-29 was corrected to c.835G>A p.(Val279Met)

Original

the variant of TRMU-32 was wrongly annotated as 711_712insG; p.Gln238AlafsX14

Corrected to

the variant of TRMU-32 was corrected to c.711dup; p.Gln238AlafsTer14

FIGURES

Figure 1

- Figure 1D was updated according to the changed number of LoF variants

Supplementary Figure 1

- Supplementary Figure 1A was updated according to the changed number of LoF variants