DREAM-PL

Shaheen et al., previously suggested that a single founder splicing variant in human CTU2 causes a novel multiple congenital anomalies syndrome consisting of dysmorphic facies, renal agenesis, ambiguous genitalia, microcephaly, polydactyly, and lissencephaly (DREAM-PL). In this work, we describe five new patients with DREAM-PL phenotype and whose molecular analysis expands the allelic heterogeneity of the syndrome to five different alleles; four of which predict protein truncation. Functional characterization using patient-derived cells for each of these alleles, as well as the original founder allele; revealed a specific impairment of wobble uridine thiolation in all known thiol-containing tRNAs. Our data establish a recognizable CTU2-linked autosomal recessive syndrome in humans characterized by defective thiolation of the wobble uridine. The potential deleterious consequences for the translational efficiency and fidelity during development as a mechanism for pathogenicity represent an attractive target of future investigations [1)].

1)
Shaheen R, Mark P, Prevost CT, AlKindi A, Alhag A, Estwani F, Al-Sheddi T, Alobeid E, Alenazi MM, Ewida N, Ibrahim N, Hashem M, Abdulwahab F, Bryant EM, Spinelli E, Millichap J, Barnett SS, Kearney HM, Accogli A, Scala M, Capra V, Nigro V, Fu D, Alkuraya FS. Biallelic Variants in CTU2 Cause DREAM-PL Syndrome and Impair Thiolation of tRNA Wobble U34. Hum Mutat. 2019 Jul 13. doi: 10.1002/humu.23870. [Epub ahead of print] PubMed PMID: 31301155.