PRINT: ISSN 0972-3757 ONLINE: ISSN 2456-6330
International Journal of
HUMAN GENETICS

Full text open access online (Since 2001)

PRINT: ISSN 0972-3757 ONLINE: ISSN 2456-6330
Int J Hum Genet, 26(3): 160-168 (2026)
DOI: 10.31901/24566330.2026/25.03.939

Novel Homozygous Large Deletion Mutation in the *PKLR* Causes Transfusion-Dependent Severe Pyruvate Kinase Deficiency: A Case Report

Qiuyu Liutang[1], Weijie Zhang[1], Chuanming Huang[1], Xiao-Mei Zheng[1], Chuan Tian[2], Guoda Ma[3], Muhammad Wasim[3*], and Riling Chen[1*]

[1]Department of Pediatric Hemato-oncology, Shunde Women and Children's Hospital of Guangdong Medical University, Foshan 528300, China
[2]Department of Pediatrics, Affiliated Hospital of Guangdong Medical University, Zhanjiang 524001, China
[3]Institute of Pediatric Hemato-oncology, Shunde Women and Children's Hospital of Guangdong Medical University, Foshan 528300,China

KEYWORDS Autosomal Recessive Disease. Copy Number Variation. Genetic Diagnosis. Haemolytic Anaemia. PKLR Mutation. Pyruvate Kinase Deficiency

ABSTRACT Pyruvate kinase deficiency (PKD) is an autosomal recessive erythrocytic enzymopathy driven by biallelic PKLR defects, classically presenting as congenital non-spherocytic haemolytic anaemia. This report details the molecular and clinical characterisation of a previously unannotated homozygous structural rearrangement affecting PKLR. The proband, a 7-month-old male with sustained transfusion dependence since birth, underwent targeted sequencing coupled with multiplex copy-number variation profiling, which identified a complete homozygous excision spanning exons 3 to 9 (NM_000298.6). Parental genotyping confirmed trans-inheritance of this allele from each heterozygous carrier. This ~70-kb genomic deletion, removing seven coding exons, represents a mutational mechanism absent from current PKD variant databases. Currently, the patient remains transfusion-committed and is scheduled for allogeneic haematopoietic stem cell engraftment. This case unequivocally demonstrates that comprehensive deletion-detection assays are non-negotiable for accurate PKD subtyping, as standard exon-limited panels would miss this lesion, thereby directly informing prognosis, transplantation timing, and cascade carrier screening across affected kindreds