Novel KIAA1109 gene mutation in surviving patients with Alkuraya-Kučinskas syndrome and a review of literature

Babylakshmi Muthusamy[1], Kishore Kumar[1], Anikha Bellad[1], Pramada Prasad[2], and Satish Chandra Girimaji[2]

[1]Institute of Bioinformatics
[2]NIMHANS

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Abstract

Alkuraya-Kučinskas syndrome is an autosomal recessive disorder characterized by brain abnormalities associated with cerebral parenchymal underdevelopment, arthrogryposis, club foot and global developmental delay. Mutations in KIAA1109, a functionally uncharacterized gene causes Alkuraya-Kučinskas syndrome. Most of these mutations result in premature termination of pregnancies or neonatal deaths in addition to few surviving patients with global developmental delay and intellectual disability. Up until recently, only three surviving patients from two families have been reported with missense variants in KIAA1109. Here, we describe four additional surviving patients from two related families (a multiplex family) with global developmental delay and mild to severe intellectual disability, with no other systemic manifestations. There were no miscarriages or neonatal deaths reported in these families. Whole exome sequencing revealed a homozygous missense mutation in a highly conserved region of KIAA1109 protein. Sanger sequencing confirms the segregation of the mutation in both the families in autosomal recessive fashion. Our study is the second study reporting a KIAA1109 variant in surviving patients with Alkuraya-Kučinskas syndrome. Our study expands the spectrum of clinical phenotypic features and mutations associated with Alkuraya-Kučinskas syndrome.

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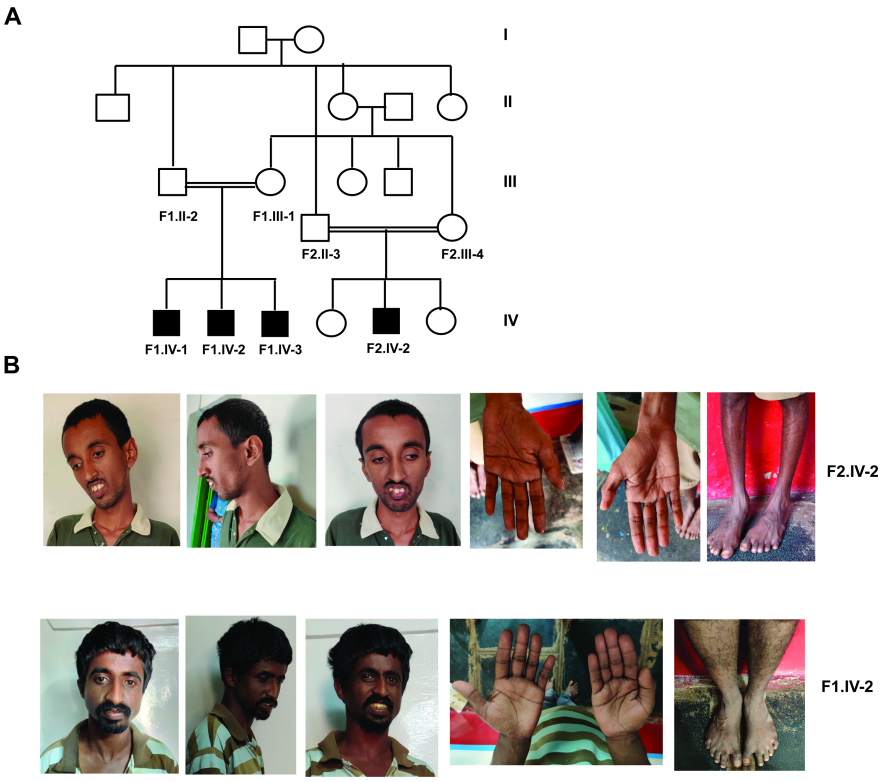

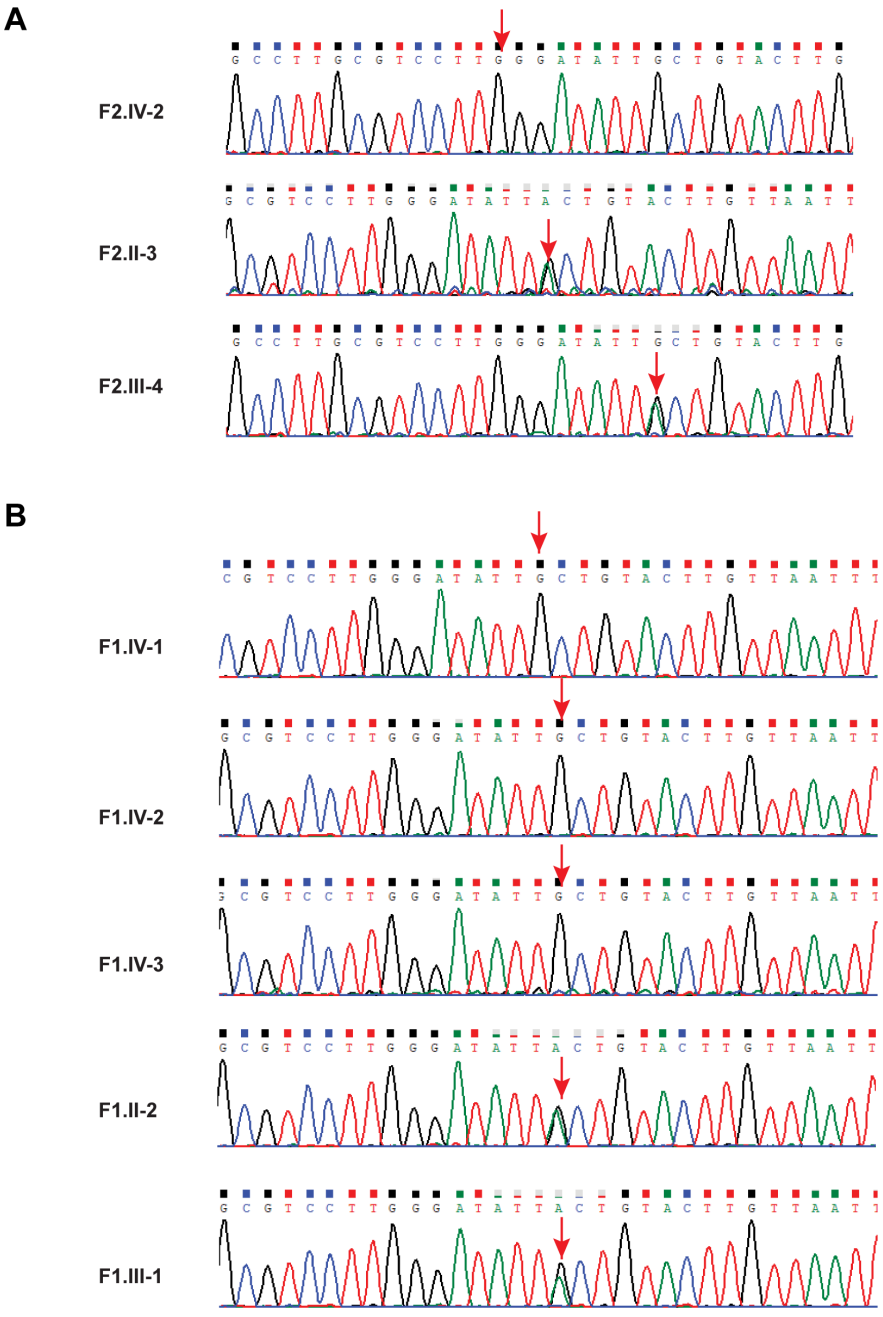

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