

A Novel Missense Mutation in NALCN Cause CLIFAHDD Syndrome and Prenatal Diagnosis in China

Yuping Li

Jiangmen Maternity and Child Health Care Hospital

Chenglong Zhou

Jiangmen Maternity and Child Health Care Hospital

Yangran Chen

Jiangmen Maternity and Child Health Care Hospital

Haihong shi

Jiangmen Maternity and Child Health Care Hospital

Qiang Chen

Jiangmen Maternity and Child Health Care Hospital

Ning Li

Halo genetics

Qinlong Zeng

Jiangmen maternity and child health care hospital

Yan Hong

Jiangmen Maternity and Child Health Care Hospital

Qing Li

Jiangmen Maternity and Child Health Care Hospital

Choufen Deng

Jiangmen Maternity and Child Health Care Hospital

Feng Zhou

Jiangmen Maternity and Child Health Care Hospital

Jieliang Tan

Jiangmen Maternity and Child Health Care Hospital

Mei Yang

Jiangmen Maternity and Child Health Care Hospital

Qiuli Li

Jiangmen Maternity and Child Health Care Hospital

Yingsong Yang

Jiangmen Maternity and Child Health Care Hospital

Jianjiang Feng

Jiangmen Maternity and Child Health Care Hospital

Shuxiang Sun

Jiangmen Maternity and Child Health Care Hospital

Ziqian Tang

Zhuzhou Central Hospital

Liangping Luo

The First Affiliated Hospital of Jinan University

Jia Tang (✉ tony2081129@163.com)

Department of Medical Imaging Center, The First Affiliated 21 Hospital of Jinan University, Jinan University and Medical Genetics Center, Jiangmen 22 Maternity and Child health Care Hospital

<https://orcid.org/0000-0002-2000-934X>

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Abstract

Background: CLIFAHDD is caused by mutation in NALCN and characterized by facial malformation, hypotonia, and developmental delay. Recently rare mutations in NALCN associated with CLIFAHDD syndrome have been reported.

Methods: Whole exome sequencing (WES) was applied to a diagnosis suspected CLIFAHDD syndrome proband based on clinical symptoms. Blood samples were taken from the parents of the proband for co-segregation analysis using Sanger sequencing. In addition, prenatal gene diagnosis was performed to the family. Finally bioinformatics analysis was utilized to predict the pathogenesis of novel variant.

Result: We reported a 24-hour-old proband with a novel missense variant c.3016G>T (p.Val1006Phe) in NALCN by WES. The proband showed clinical symptoms of head abnormalities, neck shortage, thumbs adduction, positional foot deformities and elbows contracture. Prenatal diagnosis revealed that the proband's sibling did not carry c.3016G>T.

Conclusion: Our findings indicate c.3016G>T is a novel pathogenic mutation, while extending new phenotype CLIFAHDD syndrome and enriching the mutation spectrum of the NALCN gene.

Full Text

This preprint is available for [download as a PDF](#).

Figures

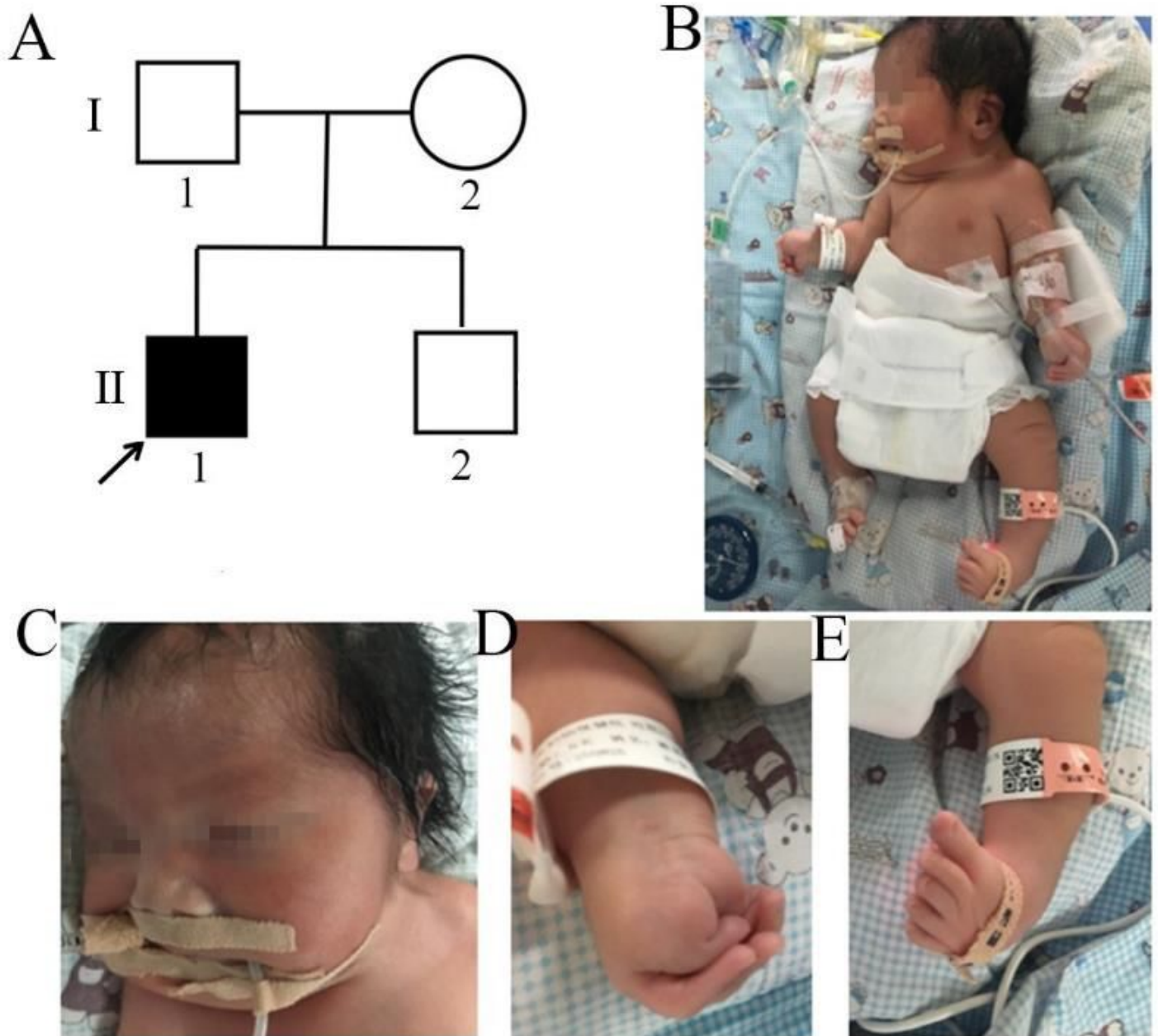


Figure 1

(A) Pedigree of the present family. (B) The overall abnormality of the proband's face and limbs. (C) The head and neck abnormality of the proband which including broad nasal bridge with an anteverted nasal tip, micrognathia, full cheeks, short columella, long philtrum, pursed lips, and short neck. (D) The thumb adduction deformity. (E) Foot deformities and knees contractures of the proband.

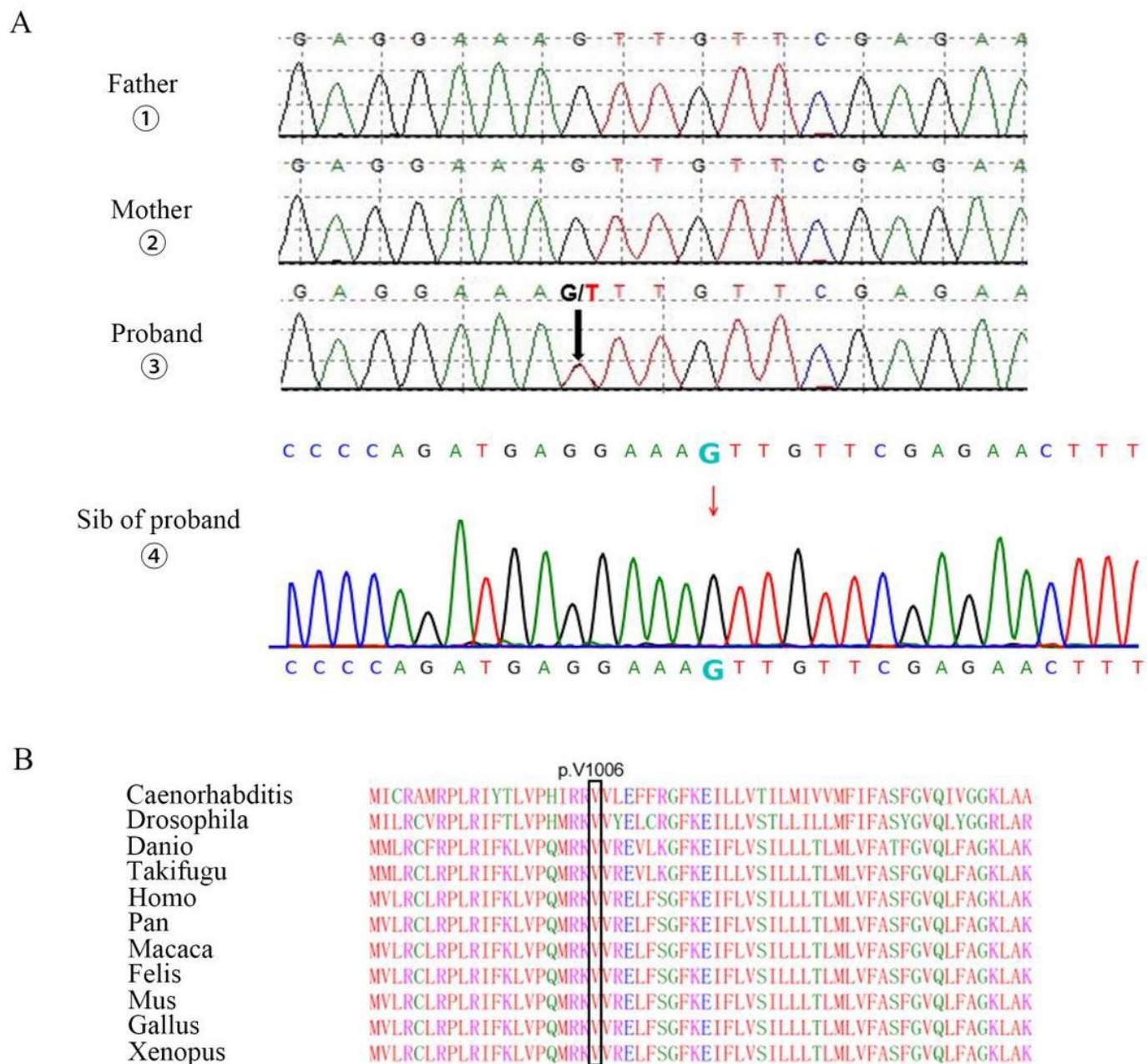


Figure 2

(A) Sanger sequencing of the c.3016 area of NALCN gene. ☐Father: G/G at c.3016; ☐Mother: G/G at c.3016; ☐Proband: G/T at c.3016; ☐The sibling of proband: G/G at c.3016. (B) Species conservation analysis of p.V1006. are highly conserved among cross-species.

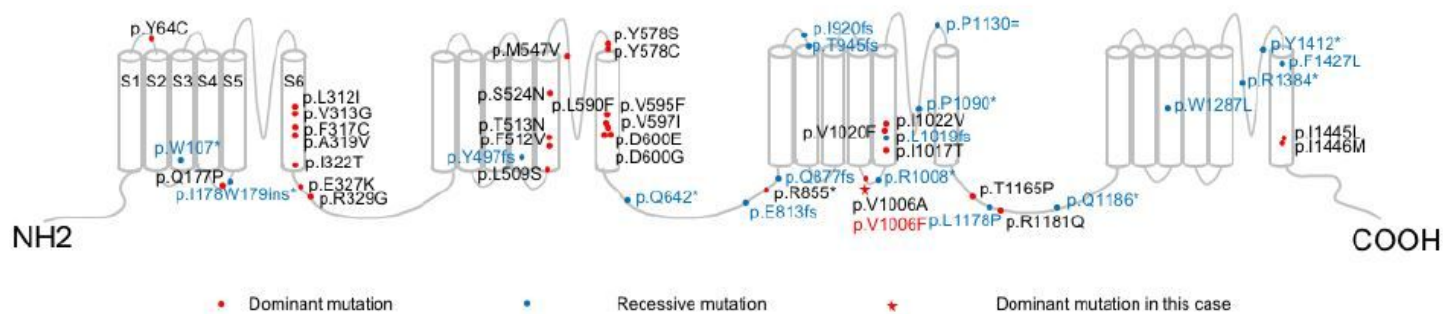


Figure 3

Mutations in NALCN found in current study (red five-pointed star) and the 433 dominant ones (red dots) and recessive ones (blue dots) in previous studies.