Journal of Zhejiang University-SCIENCE B (Biomedicine & Biotechnology)

Cite this as: Nan Hong, Yan-hua Chen, Chen Xie, Bai-sheng Xu, Hui Huang, Xin Li, Yue-qing Yang, Ying-ping Huang, Jian-lian Deng, Ming Qi, Yang-shun Gu, 2014. Identification of a novel mutation in a Chinese family with Nance-Horan syndrome by whole exome sequencing. *Journal of Zhejiang University SCIENCE B (Biomedicine & Biotechnology),* **15**(8):727-734. [doi:10.1631/jzus.B1300321]

Identification of a novel mutation in a Chinese family with Nance-Horan syndrome by whole exome sequencing

Key words:

Nance-Horan syndrome (NHS), Exome sequencing, X-linked disorder

Nance-Horan syndrome (NHS) is a rare X-linked syndrome, affected male patients often manifest bilateral congenital dense nuclear cataracts, characteristic dental anomalies, craniofacial abnormalities, and, in some cases, mental retardation (MR).

Heterozygous females display similar, but milder clinical manifestations than affected males.

NHS is caused by mutations in the *NHS* gene, which comprises 10 coding exons and encodes at least 5 isoforms as a result of alternative splicing. To date, approximately 27 mutations in the NHS gene have been identified.

In this study, we identified a novel nonsense mutation c.322G>T (E108X) in the *NHS* gene's exon 1 in a family with NHS by a combination of exome sequencing and Sanger sequencing. The clinical features in all affected males and female carriers are described in detail.

Results

Table 1 Clinical Features of the affected males and the female carriers in the NHS family

Subject	Eye	BSCVA	Ocular feature	Dental anomaly	Craniofacial dysmorphism
Male patients					
II:1	OD	20/400	Underwent bilateral lensectomy due to congenital nuclear cataract, bilateral microcornea, strabismus, and nystagmus	Screwdriver-shaped left incisor* and diastema	Long and narrow face, broad base to nose, and thin nasal bridge
	OS	20/160			
II:2	OD	20/400	Underwent bilateral lensectomy due to congenital nuclear cataract, bilateral microcornea, strabismus, and nystagmus		Long and narrow face, broad base to nose, and thin nasal bridge
	OS	20/160			
III:1	OD	20/120	Underwent bilateral lensectomy due to congenital nuclear cataract, bilateral microcornea, strabismus, and nystagmus		Long and narrow face, broad base to nose, and thin nasal bridge
	OS	20/120			
Female carriers					
I:1	OD	20/60	Opacities in the Y-suture and contex of the lens in both eyes		Bitemporal retraction
	OS	20/40			
II:3	OD	20/20	Lens opacities in the posterior Y-suture		Bitemporal retraction
	OS	20/30	Lens opacities in the posterior Y-suture and cortical coralliform opacity		

BSCVA: best spectacle corrected visual acuity; OD: the right eye; OS: the left eye. * The right incisor of the patient was broken in his childhood

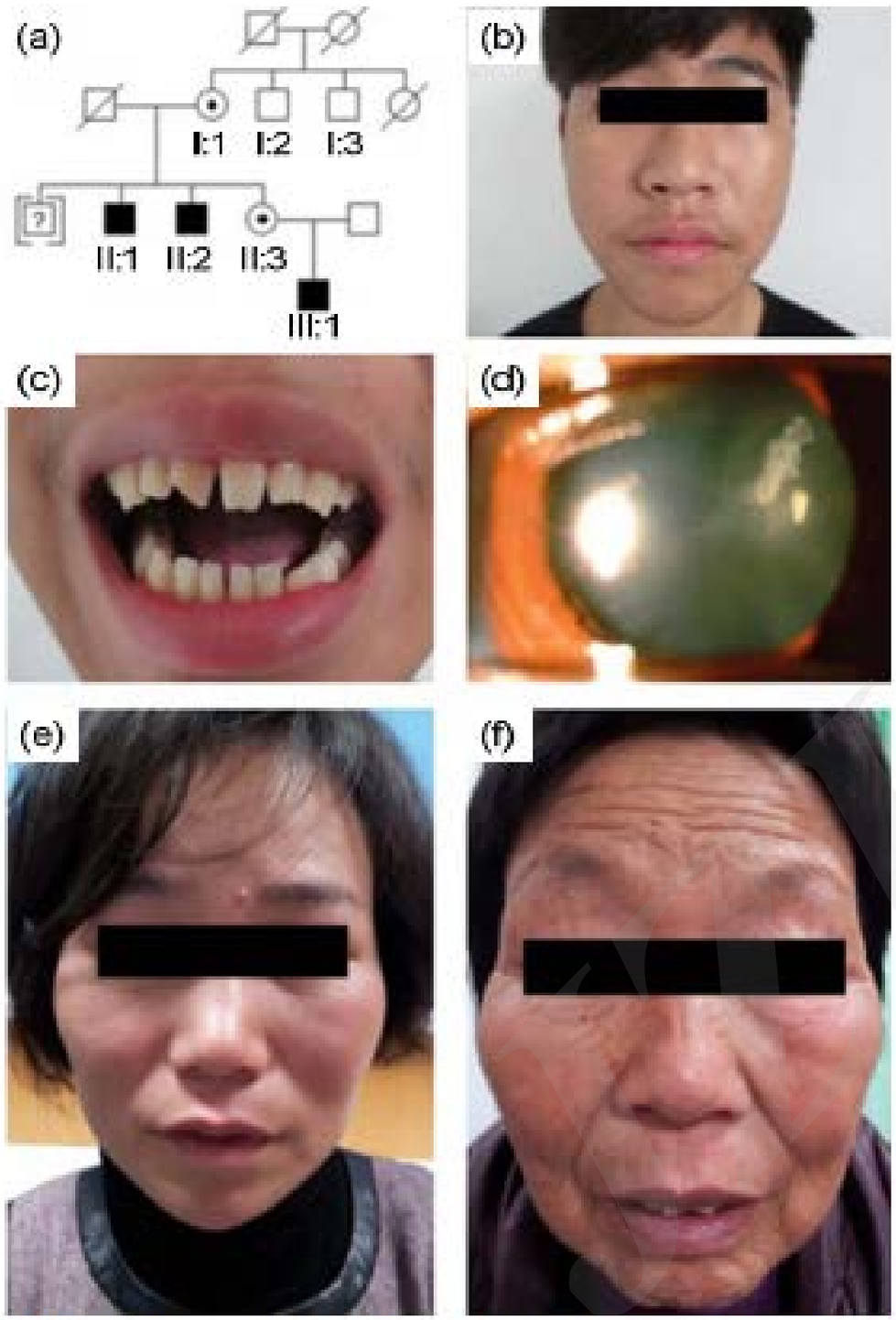

Fig. 1 Pedigree structure and patient phenotypes of the family

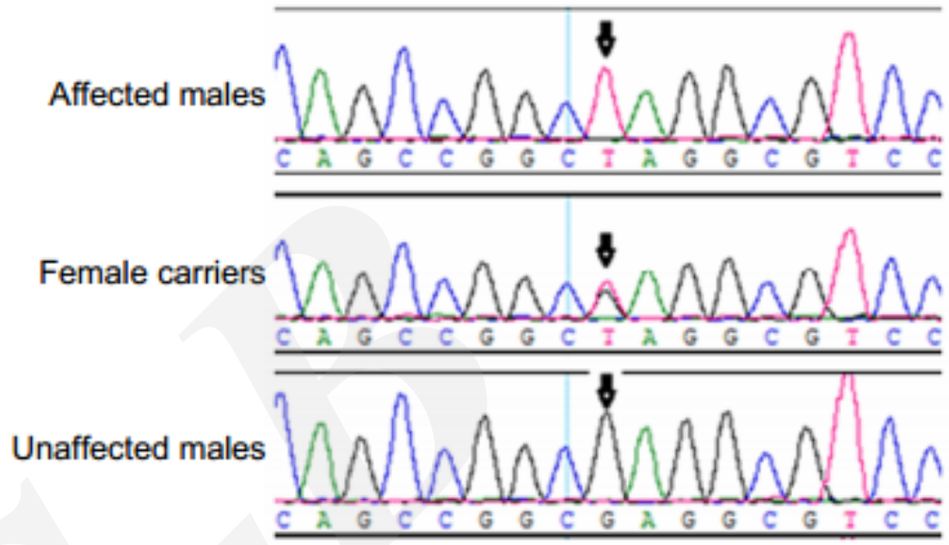

Fig. 2 DNA sequence chromatograms

A nonsense mutation in exon 1, c.322G>T, resulting in E108X in the three affected males and two female carriers, and the normal sequence from two unaffected males

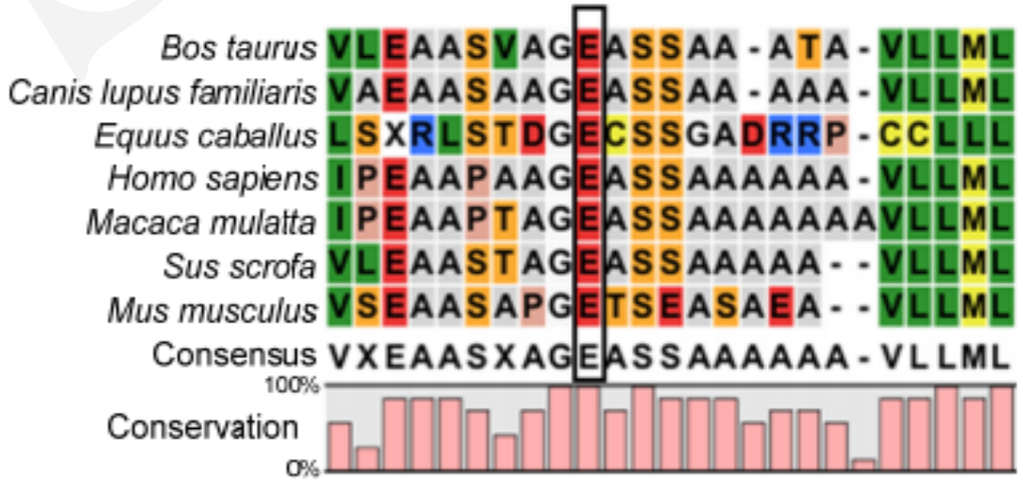

Fig. 3 Multiple-sequence alignment of NHS from different species

Multiple-sequence alignment of NHS from different species revealed that codon 108, where the mutation (E108X) occurred, was located within a highly conserved region

Conclusion

we identified a novel nonsense mutation (c.322G>T) in exon 1 of the *NHS* gene in a Chinese family, which leads to the conversion of glutamic acid to a stop codon (E108X).

Our study shows that whole-exome analysis in a single affected male from a family exhibiting X-linked inheritance could be used efficiently to identify causative mutations on the chromosome X, thus providing help to clinicians in making a definitive diagnosis of rare diseases.