Molecular and phenotypic spectrum of Noonan syndrome in Chinese patients

Xin Li¹, RuenYao², Xin Tan³⁴, Niu Li², Yu Ding¹, Juan Li¹, Guoying Chang¹, Yao Chen¹, Lizhuang Ma³⁴⁵, Jian Wang², Lijun Fu⁶, Xiumin Wang¹

¹Department of Endocrinology and Metabolism, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China
²Department of Medical Genetics and Molecular Diagnostic Laboratory, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China
³Department of Computer Science and Engineering, Shanghai Jiao Tong University, Shanghai, China
⁴MoE Key Lab of Artificial Intelligence, AI Institute, Shanghai Jiao Tong University, Shanghai, China
⁵School of Computer Science and Software Engineering, East China Normal University, Shanghai, China
⁶Department of Cardiology, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Introduction

- Noonan syndrome (NS) is a common autosomal dominant/recessive disorder. No large-scale study has been conducted on NS in China, which is the most populous country in the world.

Methods

- Next-generation sequencing (NGS) was used to identify pathogenic variants in patients that exhibited NS-related phenotypes.
- We assessed the facial features and clinical manifestations of patients with pathogenic or likely pathogenic variants in the RAS-MAPK signaling pathway.
- Gene-related Chinese NS facial features were described using artificial intelligence (AI).

Results

- NGS identified pathogenic variants in 103 Chinese patients in eight NS-related genes: PTPN11 (48.5%), SOS1, SHOC2, KRAS, RAF1, RIT1, CBL, NRAS, and LZTR1.
- Gene-related facial representations showed that each gene was associated with different facial details.
- Eight novel pathogenic variants were detected and clinical features because of specific genetic variants were reported, including hearing loss, cancer risk due to a PTPN11 pathogenic variant, and ubiquitous abnormal intracranial structure due to SHOC2 pathogenic variants.

Conclusion

- NGS facilitates the diagnosis of NS, especially for patients with mild/moderate and atypical symptoms. Our study describes the genotypic and phenotypic spectra of NS in China, providing new insights into distinctive clinical features due to specific pathogenic variants.