# Molecular and phenotypic spectrum of Noonan syndrome in Chinese patients

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## 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.

## 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.

## Methods

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

(A)


(B)

| Actual \ Predicted | PTPN11 | SOS1 | SHOC2 | KRAS | RAF1 | RIT1 |
|---|---|---|---|---|---|---|
| PTPN11 | 0.26 | 0.20 | 0.12 | 0.16 | 0.06 | 0.20 |
| SOS1 | 0.14 | 0.26 | 0.04 | 0.40 | 0.02 | 0.14 |
| SHOC2 | 0.06 | 0.24 | 0.54 | 0.10 | 0.02 | 0.04 |
| KRAS | 0.24 | 0.30 | 0.04 | 0.22 | 0.12 | 0.08 |
| RAF1 | 0.12 | 0.24 | 0.00 | 0.32 | 0.16 | 0.16 |
| RIT1 | 0.26 | 0.18 | 0.00 | 0.20 | 0.12 | 0.24 |

MEAN ACCURACY 28.00% STANDARD DEVIATION 15.18% RANDOM CHANCE FOR COMPARISON 16.67%

## 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.