Targeted/exome sequencing identified mutations in 55 Chinese children diagnosed with Noonan syndrome and a autosomal recessive form associated with LZTR1 variants

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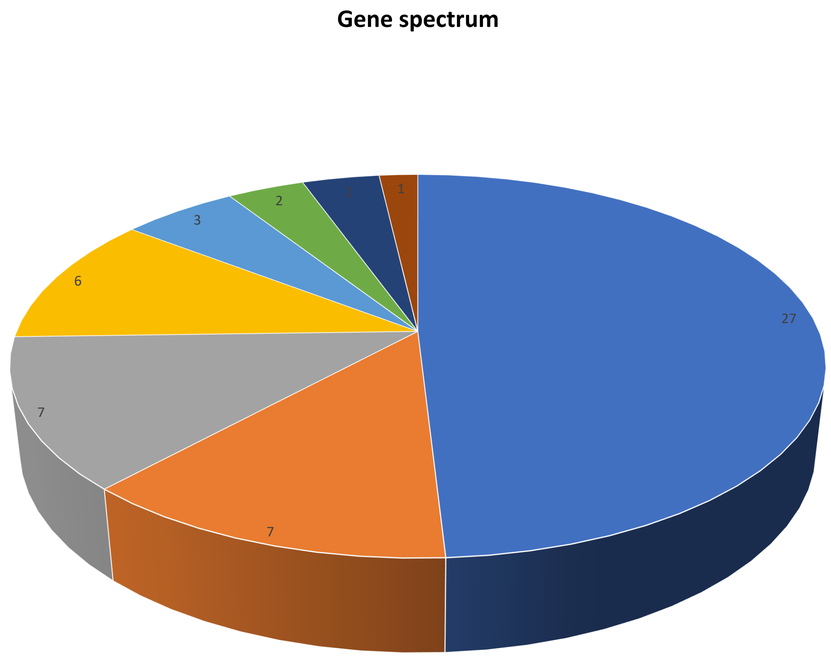
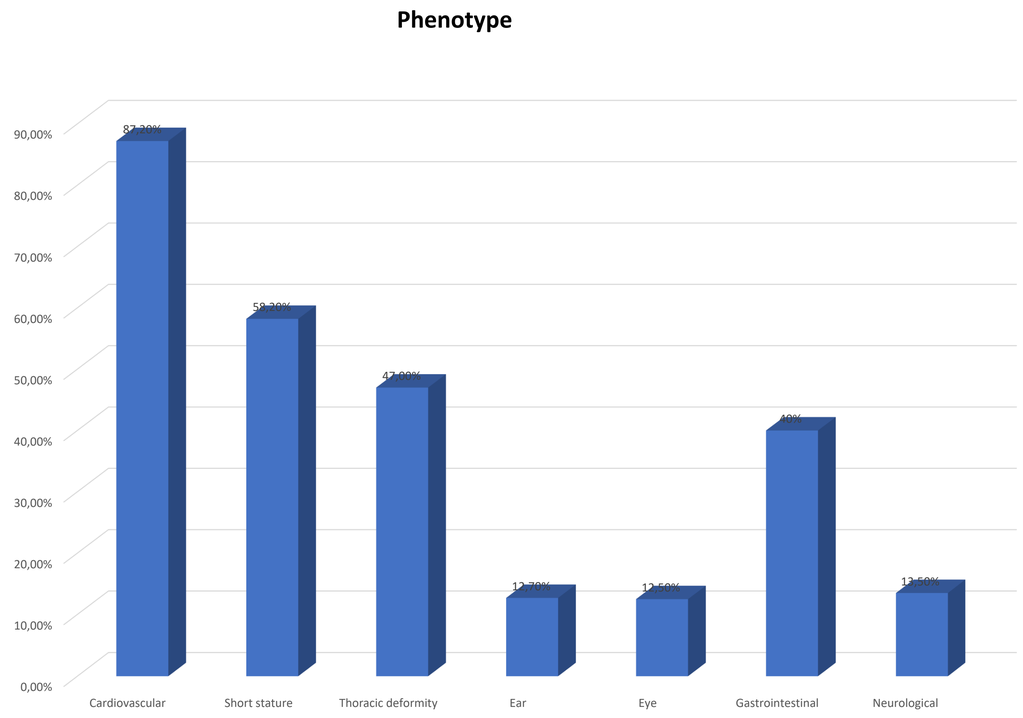
Objectives: Noonan syndrome (NS) is generally considered an autosomal dominant, multisystemic disorder caused by dysregulation of the RAS/mitogen activated protein kinase (MAPK) pathway. The latest research confirmed the existence of a form of Noonan syndrome that is inherited in an autosomal recessive pattern and identify biallelic mutations in *LZTR1*. In this study, we diagnosed 55 Chinese NS Children via targeted sequencing or whole exome sequencing (TS/WES).

Methods: TS/WES was performed to identify mutations in 55 Chinese Children who exhibited the following manifestations: potential NS facial dysmorphisms, short stature, congenital heart defects, and developmental delay. Sanger sequencing was used to confirm the suspected pathological variants in the patients and their family members.

Results:

- 55 Patients
- 28 Male ; 27 Female
- 3 months ~ 15years
- Include 8 gene; 50 *de novo*





- Cardiovascular defect
  PVS 58.3%
  HCM 25%
- Cryptorchidism
  in 35.7% boys

Conclusions: TS/WES has emerged as a useful tool for definitive diagnosis and accurate genetic counseling of atypical cases. This is a large sample study using TS/WES to diagnose Chinese patients with Noonan syndrome, and helping to reveal gene spectrum of Chinese NS patients. Our study also identified an autosomal recessive pattern in NS Patients with novel mutations in *LZTR1*. And it is the first report about a Chineses NS Patient with mutations in *LZTR1* and Changed our traditional understanding about the inherited pattern of Noonan syndrome.

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Growth and syndromes (to include Turner syndrome)

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