A novel mutation of type insulin-like growth factor receptor (IGF1R) gene in a severe short stature pedigree identified by targeted Next-generation sequencing (NGS)

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Objectives:

To identify genetic mutations of a pedigree affected by severe short stature in Chinese populations for the first time.

Methods:

Auxological and endocrinological profiles were measured. Targeted next-generation sequencing (NGS) analyses comprising 277 shorted stature-associated candidate genes and 19 related copy number variation (CNV) regions were used to identify gene mutations in the proband. Three web-based software programs (SIFT, PolyPhen-2 and Align-GVGD) were used to evaluate the functionalsignificance of the mutation.

Results:

We identified a novel heterozygous missense mutation in exon3 (c.926C>T, p.S309L) of IGF1R in the Chinese proband, inherited from his mother. The proband and his mother had severe prenatal and postnatal growth failure. After recombinant human GH therapy, the growth rate increased in the patient. The missense mutation might affect the structure of the protein and was scored as deleterious according to the Align GVGD.

Conclusions:

Our results show a novel missense mutation in the IGF1R (c.926C>T, p.S309L) associated with severe short stature in Chinese populations for the first time. Targeted NGS provides a promising method for efficient diagnosis and genetic consultation of short stature children.