RAB3IP and DGCR8 as a potentially pathogenic novel candidate gene involving in growth disorders

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Introduction

The majority of children with short stature are classified as idiopathic short stature. Whole exome sequencing can help identify genetic causes of short stature.

Objectives

To identify the genetic aetiology of some idiopathic short stature by exome sequencing (WES).

Methods

- Prenatal proportional short stature
- Neonatal hypoglycemia and jaundice
- Mild neurodevelopment delay
- Echocardiogram: Pulmonary atresia
- Low IGF-1; normal GH peak
- Good response to rhGH therapy

Results

The mean coverage of the captured regions was 170x (99.6% of target region with more than 10x). Each patient had an average of 64,490 allelic variants. All pedigrees suggested an autosomal dominant pattern of inheritance. We identified two novel candidate genes with loss of function (LoF) mutations.

- Prenatal short stature
- Consanguineous family
- Microcephalic (normal intelligence)
- Seizure during the childhood
- Low IGF-1/IGFBP-3, normal GH peak
- MRI – small intrasellar rathe pouch cyst
- Elevated TSH, normal/mild elevated FT4
- Small testis (10mL), normal testosterone levels, elevated LH (38U/L), FSH (18.4U/L)
- Normal spermogram at the age of 24
- Normal karyotype and CGH-array

Conclusions

It is possible that RAB3IP and DGCR8 genes have a relationship with a dysmorphic features and short stature in these patients. The identification of other patient with similar phenotype and genetic findings is important to prove this relationship.

References