Genetic diagnosis of congenital growth hormone deficiency by massive parallel sequencing using a target gene panel

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* Nothing to disclose

Background
Congenital GH deficiency (GHD) can be isolated (IGHD) or combined with other pituitary hormone deficiencies (CPHD). The identification of mutations has clinical implications for the management of patients and genetic counseling.

Objective
To prospectively conduct a molecular-genetic analysis in selected target genes in patients with congenital IGHD or CPHD.

Methods
Casuistic

<table>
<thead>
<tr>
<th>Topic Posterior Lobe</th>
<th>Data analysis</th>
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</thead>
<tbody>
<tr>
<td>N = 2 (42%)</td>
<td>1 Consanguineous</td>
</tr>
<tr>
<td>Ectopic Posterior Lobe</td>
<td>N = 5 (13%)</td>
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<tr>
<td>N = 17 (42%)</td>
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<tr>
<td>Non Visualized</td>
<td>N = 11 (33%)</td>
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</tbody>
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Sequencing

- Design technology: Agilent Sure Design
- Genes included: 27 genes associated with GHD + 57 genes associated with growth disorders without GHD
- Coverage: 1000X
- Exomes: 1000X
- Targeted: 1000X
- Whole exome: 1000X

Data analysis
- Minor allele frequency: < 1%
- Data basis: EVAC, ESP5000
- Location: Exonic or splice site
- In silico: Polyphen, Mutation Taster, SIFT, GERP
- Evaluation of gains or losses: copy number analysis for targeted resequencing method

Results

99.9% of the targeted genes presented > 20 reads

Summary and Conclusions
The panel provided good coverage of the known genes previously associated to GHD and exclusion of mutations in many patients. The panel established the diagnosis of 3 patients. Low rate of diagnoses could be due to incomplete penetrance, digenic or environmental conditions or mutations in genes not previously associated with GHD.

The patients with negative results are candidates for whole exome sequencing.