FUNCTIONAL STUDIES OF PAX8 GENE VARIANTS IN PATIENTS AFFECTED BY CONGENITAL HYPOTHYROIDISM WITH EUTOPIC THYROID GLAND

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INTRODUCTION

Thyroid dyshormonogenesis is a heterogeneous group of hereditary diseases produced by a total/partial blockage of the biochemical processes of thyroid hormone synthesis and secretion. PAX8 is a transcription factor essential for thyroid morphogenesis and thyroid hormone synthesis. More than 50 PAX8 variants were reported, but most not functionally tested. We identified 52 PAX8 variants in 9 patients with congenital hypothyroidism (CH).

AIM

We aimed to determine if these PAX8 variants are pathogenic with in-vitro functional studies.

PATIENTS

Patients: 3 girls and 6 boys with CH, eutopic thyroid gland and a detected PAX8 variant. Catalan CH Neonatal Screening Programme (N=93).

RESULTS

In-silico analysis:
- Alignment of human and 9-orthologous PAX8 peptide sequences (NCBI database) by Clustal Omega webtool [EMBL-EBI, Hinxton, UK].
- Construction of PAX8 domains from literature.
- In-silico prediction studies with SpliceSiteFinder-like, MaxEntScan and NNSPLICE.

METHODS

In vitro analysis:
1. Production of PAX8 and TG promoter vector
2. Study of PAX8 transactivation of TG promoter

REFERENCE


CONCLUSIONS

Nine CH patients, with eutopic thyroid gland, presented PAX8 candidate variants. PAX8 functional studies have shown that six PAX8 variants are deleterious. Our studies have proven their effectiveness in evaluating these variants.

CONTACT INFORMATION

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