Chitayat Syndrome (ERF Variant)

https://pubmed.ncbi.nlm.nih.gov/27738187/

Background:

In 1993, Chitayat et al., reported a newborn with hyperphalangism, facial anomalies, and bronchomalacia. We identified three additional families with similar findings. Features include bilateral accessory phalanx resulting in shortened index fingers; hallux valgus; distinctive face; respiratory compromise.

Objectives:

To identify the genetic aetiology of Chitayat syndrome and identify a unifying cause for this specific form of hyperphalangism.

Methods:

Through ongoing collaboration, we had collected patients with strikingly-similar phenotype. Trio-based exome sequencing was first performed in Patient 2 through Deciphering Developmental Disorders study. Proband-only exome sequencing had previously been independently performed in Patient 4. Following identification of a candidate gene variant in Patient 2, the same variant was subsequently confirmed from exome data in Patient 4. Sanger sequencing was used to validate this variant in Patients 1, 3; confirm paternal inheritance in Patient 5.

Results:

A recurrent, novel variant NM_006494.2:c.266A>G p.(Tyr89Cys) in

ERF

was identified in five affected individuals: de novo (patient 1, 2 and 3) and inherited from an affected father (patient 4 and 5). p.Tyr89Cys is an aromatic polar neutral to polar neutral amino acid

substitution, at a highly conserved position and lies within the functionally important ETS-domain of the protein. The recurrent

ERF

c.266A>C p.(Tyr89Cys) variant causes Chitayat syndrome.

Discussion:

ERF

variants have previously been associated with complex craniosynostosis. In contrast, none of the patients with the c.266A>G p.(Tyr89Cys) variant have craniosynostosis.

Conclusions:

We report the molecular aetiology of Chitayat syndrome and discuss potential mechanisms for this distinctive phenotype associated with the p.Tyr89Cys substitution in

ERF

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