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Mutations in IL11RA: a genetic cause of scaphocephaly

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Introduction: The premature closure of calvarial sutures, particularly the corona sutures, can have a genetic cause. In approximately 24% of cases a genetic cause can be identified. With sagittal suture synosotosis, a genetic cause is rarely encountered. In this study, we present two such cases with a duplication in the *IL11RA* gene.

Methods: Both patients had non-consanguineous not-affected parents.
Patient(1) showed a scaphocephaly directly after birth. CT-scan confirmed synostosis of the sagittal suture. He underwent frontobiparietal remodellation at the age of 12 months. At the age of 9 a mild midface hypoplasia was noted. His older brother presented with skull growth retardation at the age of 8. He had pansynostosis, clinically diagnosed as Crouzon syndrome.
Patient(2) presented with scaphocephaly. Skull X-ray showed sagittal suture synostosis. At the age of 12 months, a frontobiparietal remodellation was performed. He also had delayed dental development, maxillary hypoplasia, class III malocclusion and exorbitism. A clinical suspicion of Crouzon syndrome was raised. He underwent a LeFort III monobloc osteotomy combined with external distraction at the age of 13. His oldest sister has comparable clinical features.
Genetic analysis of the *FGFR2*, *FGFR3* and *TWIST1* gene in both families was negative. Whole Genome Sequencing (WGS) was performed on family(1) and in patient(2) and his not-affected parents.

Results: An homozygous duplication was found (c.916_924dup, p.(Thr306_Ser308dup)) in *IL11RA* in the three patients. The parents were heterozygous for the duplication. The results were confirmed by targeted sequencing.

Conclusion: By WGS, a mutation was found in *IL11RA*, leading to Craniosynostosis and Dental Anomalies Syndrome. Two out of three Dutch patients with this syndrome presented with scaphocephaly. Although sagittal synostosis is usually isolated, this study illustrates that one should remain attentive for genetic causes; for example if craniosynostosis runs in the family, or if patients have secondary findings, like dental anomalies.