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A Case of *SHOX* Gene Deletion Diagnosed By Microarray

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SHOX (Short Stature Homeobox) which is located at Xp22.33 is evolutionary well-conserved developmental gene expressed in osteogenic cells. *SHOX* is one of the suspected components of the short stature in Turner syndrome cases. Also functional homolog of *SHOX* gene is located at Y chromosome. Haploinsufficiency of genes on the X chromosome results in Turner syndrome.

Here, we present a 26-month-old female referred to genetic counseling because of short stature and developmental delay. Her height was 71 cm (< 3 percentile), weight 9.5 kg (< 3 percentile). She had frontal bossing, hypertelorism, and bilateral mesomelic short upper extremities. Her motor and mental developments were normal. Bone X-ray survey revealed a thickness of long bones and delayed bone age.

Karyotype showed an extra genomic material at the p arm of the X chromosome. We performed chromosomal microarray. Approximately 18 Mb gain at the short arm of chromosome 6 and 680 Kb deletion at the p arm of X chromosome were detected.

Three genes including *SHOX* were deleted from the involved region of X chromosome. A gain of 63 genes located at chromosome 6p was observed, which resulted in partial trisomy of 6p. Effects of partial trisomy 6p in our case is not clear, but the deleted *SHOX* is suspected to be the reason for short stature and delayed bone age.

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HOXC4 Gene is Possibly Responsible for Lin-Gettig Syndrome

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Lin-Gettig syndrome, described by Lin and Gettig in 1990, is a very rare autosomal recessive disease. The syndrome is characterized by craniosynostosis, severe mental retardation, absence of corpus callosum, dysmorphic facial features, camptodactyly, and hypogonadism. The molecular etiology of the syndrome has not yet been identified. In this report, we present a patient diagnosed as having Lin-Gettig syndrome via clinical findings. Molecular genetic studies have revealed that *HOXC4* may be the responsible gene for this syndrome.

Due to motor-mental retardation and abnormal facial features, a 15-month-old boy was referred to our department for genetic counselling and differential diagnosis. On physical examination, his weight, height, and head circumference were measured to be 9.4 kg (10^{th}-25^{th} centile), 74 cm (3^{th}-10^{th} centile), and 43 cm (< 3^{th} centile), respectively. He had microcephaly and trigonocephaly, proptosis, downslanting palpebral fissures, midface hypoplasia, depressed nasal bridge, short columella, micrognathia, and low-set dysplastic ears. His genital examination showed micropenis, bifid scrotum, and cryptorchidism. Craniosynostosis was diagnosed using 3D computed tomography. Brain magnetic resonance imaging revealed a Chiari I malformation.

Exome sequencing of the proband showed a homozygous c. 410C > G (p.P137R) mutation in *HOXC4* gene. The parents carried this mutation heterozygously. It has been considered that mutations in *HOXC4* gene are the most probable candidate responsible for the underlying molecular etiology in the syndrome.

This is the first study in the literature defining a gene considered to be responsible for Lin-Gettig syndrome.

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POU1F1 and *PROP1* Gene Mutations in 4 Cases of Combined Pituitary Hormone Deficiency

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Combined pituitary hormone deficiency (CPHD) is characterized by the impaired production of GH together with one or more of other pituitary hormones. The most commonly recognized genetic defects associated with CPHD include mutations within *PROP1*, *POU1F1*, *HESX1*, *LHX3*, *LHX4*, *OTX2*, *GLI2*, and *SOX3*.