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COMMENTARY

Commentary on 'Identification of a microdeletion at Xp22.13 in a Taiwanese family presenting with Nance–Horan syndrome'

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The article entitled 'Identification of a microdeletion at Xp22.13 in a Taiwanese family presenting with Nance–Horan syndrome' is an interesting article.[1] Nance–Horan syndrome (NHS) is a rare X-linked developmental disorder characterized by congenital cataract, dental anomalies, and facial dysmorphism. The NHS protein is a putative nuclear protein involved in the regulation of the development of eye, tooth, brain, face, and skull. Some patients show mental retardation. NHS may be classified as one of the X-linked mental retardation (XLMR) syndromes. Differential diagnosis of NHS is important in patients with congenital cataract and other anomalies. Mostly, protein truncation mutations in the *NHS* gene have been identified in patients with NHS.

The authors identified a microdeletion of ~0.92 Mb at Xp22.13 detected by array-based comparative genomic hybridization (array CGH) in two brothers presenting with congenital cataract, dental anomalies, facial dysmorphisms, and MR. The deleted region included the *REPS2*, *NHS*, *SCML1*, and *RAI2* genes. Their carrier mother showed only mild cataract. These findings further indicate that genomic rearrangement involving the *NHS* gene is an important genetic etiology underlying NHS.

Van Esch *et al.*[2] also reported a male patient with a deletion at Xp22, detected by high-resolution X-array CGH. The patient showed severe encephalopathy, congenital cataracts, and tetralogy of Fallot. The deleted segment included *NHS,* and *CDKL5*.

Mental retardation (MR) is a common and heterogeneous disorder affecting about 3% of the general population. More than 200 XLMR conditions have been described, and mutations have been identified near 90 different genes. Hayashi *et al.*[3] constructed a high-density and high-resolution human chromosome X array (X-tiling array) for CGH. They found novel copy-number aberrations and suggested that the results of X-tiling array are useful for the identification of cryptic copy-number aberrations containing novel genes responsible for diseases such as congenital disorders and X-linked MR. Recently, Honda *et al.*[4] screened copy-number variations (CNVs) in individuals with MR from 144 families by array CGH using a bacterial artificial chromosome-based X-tiling array. They detected 10 (6.9%) pathogenic CNVs. Five of the families had pCNVs involving known XLMR genes and new candidate pCNVs were detected in five families. They suggested that array CGH identified the novel XLMR genes and mechanisms leading to MR and revealed the clinical conditions and genomic background of XLMR. A number of different microarray platforms have emerged and are being used in clinical setting.

Consensus statement has been published that chromosomal microarray offers a much higher diagnostic yield (15–20%) for genetic testing of individuals with unexplained developmental delay/intellectual disability, autism spectrum disorders, or multiple congenital anomalies than G-banded karyotype analysis.[5] The use of chromosomal microarray is recommended as the first-tier cytogenetic diagnostic test for these patients.[5] G-banded karyotype analysis should be reserved for patients with apparent chromosomal aberration syndromes including Down's syndrome, a family history of chromosomal rearrangement, or a history of multiple miscarriages.[5] The application of array CGH to idiopathic mental retardation, autism spectrum disorder, or multiple congenital anomalies opens up a promising new field for finding the basic defect underlying these conditions. However, we should keep in mind that interpretation of array CGH data is sometimes difficult by the presence of CNVs of undermined significance.

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