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MICRODELETION AT Xq21 IN A PATIENT WITH NONSYNDROMIC MENTAL RETARDATION VALIDATES THE NOVEL XLMR GENE *ZNF711*

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Approximately 5-10% of X-linked mental retardation (XLMR) in males is due to copy number variations (CNV). The use of X-chromosome specific array-CGH (comparative genomic hybridization) enables identification of such defects with high resolution. However, most of the deletions and duplications involve more than one gene, and therefore it is difficult to decide which of them is causative.

We have analyzed a cohort of Polish male patients with X-linked mental retardation by X chromosome-specific BAC array-CGH. We identified a submicroscopic deletion at Xq21.1 in one patient. The deletion involves 5 genes: *RPS6KA6*, *HDX*, *APOOL*, *SATL1* and *ZNF711*. Previously, a partial deletion of *RPS6KA6* was reported in a patient without MR, showing that absence of this gene does not result in a cognitive phenotype. However, a recent study of large-scale resequencing of X chromosome coding exons in MR patients discovered two truncating mutations within the previously unknown gene (*ZNF711*), confirming its function in etiopathology of mental retardation. *ZNF711* encodes a zinc-finger protein of unknown function and is highly expressed in brain. Further qPCR analyses confirmed the *ZNF711* deletion in the patient and his carrier mother.

Clinical features of our patient include moderate intellectual impairment with significant speech, psychomotor delay (walking at the age of 22 months), and subtle dysmorphic features (high forehead, strabismus, large and prominent ears). Autistic spectrum behavioral abnormalities (hyperactivity, aggressiveness, poor attention span and eye contact) were also observed in early childhood. The two reported families with *ZNF711* mutations had moderate MR without consistent additional features. Therefore, the additional features observed in our patient could be due to nullisomy of one of the other genes within the deletion.

This study adds further evidence that *ZNF711* is an important gene in development or maintenance of cognition.