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CASK MUTATIONS CAUSE X-LINKED NYSTAGMUS AND VARIABLE XLMR PHENOTYPES

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Mutations and deletions of the calcium/calmodulin-dependent serine protein kinase (*CASK*) gene have recently been associated with X-linked mental retardation (XLMR) with microcephaly, optic atrophy and brainstem and cerebellar hypoplasia, as well as an X-linked syndrome with some FG-like features. Our group have recently identified four male probands from 358 probable XLMR families with missense mutations (p.D710G, p.Y268H, p.W919R and p.P396S) in the *CASK* gene. Nystagmus was present in two of these families. We screened an additional 38 probands with mental retardation (MR) and either nystagmus or microcephaly and identified a missense mutation (p.Y728C) and a splice mutation (c.2995-2A>T) in two small families with MR and nystagmus. Detailed clinical examinations of all six families, including ophthalmological review in 4 families, were undertaken to further characterise the phenotype. We report on the clinical features of 24 individuals from six families with *CASK* mutations. The phenotype was variable, ranging from non-syndromic mild MR to severe MR associated with microcephaly and dysmorphic facial features. Carrier females were variably affected. Nystagmus was present in four of the families. Our findings reinforce the *CASK* gene as a relatively frequent cause of XLMR.