BRPF1-related disorder

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Background:

Over 500 epigenetic regulators have been identified throughout the human genome. Of these, approximately 30 chromatin modifiers have been implicated thus far in human disease. Recently, variants in BRPF1, encoding a chromatin reader, have been associated with a previously unrecognized autosomal dominant syndrome manifesting with intellectual disability (ID), hypotonia, dysmorphic facial features, ptosis, and/or blepharophimosis in 22 individuals.

Patients and methods:

We report a multiply affected nonconsanguineous family of mixed Jewish descent who presented due to ID in three male siblings. Molecular analysis of the family was pursued using whole exome sequencing (WES) and subsequent Sanger sequencing.

Results:

Whole exome sequencing analysis brought to the identification of a novel heterozygous truncating mutation (c.556C>T, p.Q186*) in the BRPF1 gene in the affected siblings and their mother. The four affected individuals showed varying degrees of intellectual disability, distinct facial features including downslanted palpebral fissures, ptosis, and/or blepharophimosis. Their clinical characteristics are discussed in the context of previously reported patients with the BRPF1-related phenotype.

Conclusion:

The reported family contributes to the current knowledge regarding this unique and newly recognized genetic disorder, and further implicates the role of BRPF1 in human brain development.