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116.768 Mb, 87 kb from the *TRPS1* 5′ end. The breakpoint on chromosome 13 was localised within a gene-poor region at 65.101 Mb, and the nearest gene, 1.5 Mb distal from the breakpoint, is protocadherin 9 (*PCDH9*). Analysis of the three affected relatives by the 33K tiling BAC array and of the proband by 2.7-M high-resolution oligonucleotide array painting did not reveal additional genomic variation. Furthermore, mutation screening of the *TRPS1* also did not reveal any alteration. Finally, expression studies of *TRPS1* performed from LCLs indicate that inter-individual variation is higher than the expected gene expression changes induced by the translocation. Although the reason underlying the severe mental retardation observed in the proband is unknown, the available data indicate that this is not associated with the translocation. As far as we know, this is the first reported case of position effect or "*cis*-ruption" causing TRPS I. Finally, further studies are necessary to unveil the molecular pathogenic mechanisms of this "*cis*-ruption disorder" triggered by chromosome translocation.

Keywords: Balanced translocation, Tricho-rhino-phalangeal syndrome type I, Position effect, *cis*-ruption disorder

1.P91

A pathogenic breakpoint at 566.8 kb from the 3′ end of the SATB2 leads to a 2q33.1 microdeletion-like phenotype

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SATB2 is an AT-rich sequence-binding protein that binds to nuclear matrix attachment regions. It plays an important role in transcription regulation and chromatin loop remodelling. Deletions, chromosome translocations, as well as heterozygous nonsense mutations affecting this gene have been reported associated with overlapping conditions involving drome (OMIN 612313) and Toriello–Carey syndrome (OMIM 217980). The aim of this study was the identification of the breakpoint sequences and candidate gene/s of a de novo t(1;2)(q14.1;q35) associated with severe mental retardation, behaviour disturbance, dysmorphic facies, dental anomalies, convergent strabismus and high palate but without clefting. The chromosome 2 breakpoint is localised at position 199,567,382 of the current human genome assembly (hg19), within IVS1 of the processed transcript AC019330.1. This breakpoint disrupts an evolutionarily conserved non-coding genomic element localised 566.8 kb from the 3′ end of the *SATB2* gene. The chromosome 1 breakpoint is localised within IVS13 of the zyg-11 homolog A (*Caenorhabditis elegans*) *ZYG11A* gene, at position 53,355,744 (assembly hg19). Although the chromosome 1 breakpoint disrupts the *ZYG11A*, we consider that the *SATB*2 is the main candidate gene, which is substantiated by the overlap observed between the probands' phenotype with the pathologies associated with this gene. The characterization of the translocation breakpoints allowed us to establish an accurate clinical diagnosis. As pathogenic mechanism, we propose the disruption of the genomic architecture of evolutionary conserved long-range regulatory elements leading to a so-called *cis*-ruption disorder. The elucidation of the pathogenic mechanism by which disruption of such an evolutionarily conserved sequence element leads to the aforementioned condition will allow us to consider new therapeutic strategies that may hinder progressive deterioration of the clinical condition in such "*cis*-ruption disorders".

Keywords: SATB2, Position effect, Microdeletion-like phenotype, Toriello–Carey syndrome

1.P92

Characterization of a familial case with complex chromosome rearrangement involving chromosomes 1, 10, 11, 13 and 18

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