

**Analysis of the isochromosome 17q breakpoint in medulloblastomas**

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**Aims:** Medulloblastomas are the most common malignant brain tumours of childhood. Despite the consistent identification of isochromosome 17q (i(17q)) as a frequent finding in these tumours, little attention has been paid to the genes involved in the isochromosome breakpoint. We have previously identified 2 isochromosome breakpoint cluster regions, both on 17p11.2, in a series of 34 classic medulloblastomas. Our aim was to map these breakpoints and to identify their effects on nearby genes.

**Procedures:** We have used custom chromosome 17 arrays to analyse 34 classic medulloblastomas and 3 medulloblastoma cell lines. The arrays consist of overlapping BAC clones (n=736) covering 90.6% of chromosome 17 and overlapping fosmids (n=79) to increase resolution at breakpoint regions. Transcriptomal analysis has been performed using Affymetrix Genechips®.

**Findings:** Changes consistent with i(17q) were seen in 10 of 34 cases. Analysis of the BAC array showed 2 breakpoints: at Ch17: 18863800-19132640 (n=6) and Ch17: 21119127-21822899 (n=4). These regions were further defined using the fosmid array which showed breakpoints to cluster around particular regions. More detailed mapping is underway using Southern blotting, PCR and sequencing to define them at a sequence level and to identify the effects on nearby genes. In addition, transcriptomal analysis has identified genes differentially expressed between cases with different breakpoints.

**Significance and Conclusions:** Using high-resolution array CGH we have identified several breakpoint clusters in medulloblastomas with i(17q). Analysis currently underway will further define these breakpoints and their functional impact on tumour biology.