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Abstracts

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A Constitutional Balanced 1;17 Neuroblastoma Translocation

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One of the main genetic aberrations in neuroblastoma is deletion of the short arm of chromosome 1 (1p), which is found in approximately 30% of the cases. There is evidence for at least 2 neuroblastoma suppressor genes on 1p. Deletions of chromosome 1p in neuroblastoma are typically large which makes cloning of the genes difficult. We are studying a neuroblastoma patient with a constitutional balanced translocation between 1p36 and 17q11.2-12.1. As probably no chromosome 1 material is lost in the constitutional translocation, the 1p36 breakpoint is likely to have disturbed a tumour suppressor gene. This breakpoint was analysed in hybrids of the patient's fibroblasts with hamster A3 cells. It was localised in a cluster of at least 2 Mb of tRNA and small nuclear RNA U1 genes and many other locally repetitive sequences. Markers *D1S170* and *NN1.3* are proximal to the breakpoint and marker *PND* is distal to the breakpoint. We isolated many YACs from this region, which all hybridise at both sides of the breakpoint because of these local repeats. One YAC however probably crosses the breakpoint. CpG-island probes and corresponding cDNAs are currently under analysis.

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Chromosome 1p in Neuroblastoma: Suppressors and Prognosis

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Differences in tumour behaviour and prognosis suggest that neuroblastoma can be divided into several biological subgroups. We evaluated the most frequent genetic abnormalities (*MYC*N amplification, LOH 1p, 4p, 11q, 14q, additional 17q) occurring in neuroblastoma for their prognostic value. In a series of 89 clinically detected neuroblastoma we found allelic loss of chromosome 1p, *MYC*N amplification and gain of chromosome 17q to be significantly associated with an unfavourable outcome. Loss of 1p was demonstrated in all *MYC*N amplified cases. In multivariate analysis, loss of 1p was the most powerful prognostic factor of all clinical and genetic parameters. Loss of 1p in *MYC*N single copy cases mainly occurs in stage I/II/IVs patients, among whom it reliably identifies high risk cases. Loss of 1p with *MYC*N amplification is mostly found in stage III/IV cases, all of whom do badly. Recently, we found evidence for the existence of 2 suppressor loci on 1p. A 1p36.2-3 imprinted suppressor inactivated in the *MYC*N single copy cases and a 1p35-36.1 suppressor associated with *MYC*N amplification. Both suppressors correlate with an unfavourable outcome, the proximal especially in stage III/IV cases, the distal more in stage I/II/IVs cases.