A Constitutional Translocation t(1;17)(p36.2;q11.2) in a Neuroblastoma Patient Disrupts *NBPF1*, a novel putative tumor suppressor gene

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Neuroblastoma (NB) is the most common extracranial solid tumor in children and is characterized by a number of recurrent genetic alterations: gain of chromosome 17q, amplification of *MYCN*, and deletion of 1p36. We found that a constitutional translocation t(1;17)(p36.2;q11.2) in a neuroblastoma patient (Laureys et al., 1995) resulted in the disruption of a novel gene, *NBPF1* (Neuroblastoma Breakpoint Family, member 1). This gene is built of repetitive elements and is subject of structural variation in the human population. Thorough analysis of genomic sequences revealed that *NBPF1* is a member of a recently expanded gene family, with gene copies located on segmental duplications of chromosome 1 (Vandepoele et al., 2005). Both *in silico* and *in vitro* analysis failed to identify any rodent orthologs for the human *NBPF* genes. The members of the *NBPF* gene family are widely expressed, both in normal and cancerous tissues, including neuroblastoma cells. Our identification of NBPF-interacting proteins may link these genes to important signalling pathways such as the Wnt and NF-kappaB signalling pathways. The high sequence identity between different *NBPF* paralogs has thus far disabled the analysis of gene-specific expression patterns, but the development of an *NBPF1*-specific qRT-PCR assay is in progress. Transfection experiments revealed a cytoplasmic localization of the different NBPF proteins. Constitutive overexpression of different NBPF paralogs resulted in cell death in a variety of cell lines, including MCF7/AZ, HEK293T, and the neuroblastoma cell line IMR-32. We use now a conditional expression system to circumvent the detrimental properties of the overexpressed NBPF proteins and to investigate the process leading to NBPF1-induced cell death. Also, the development of transgenic mice with stable integration of the human *NBPF1* gene, will be undertaken in order to analyze the function of this intricate gene in both normal development and tumor pathology.

***References*:**

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