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High expressions of neuronatin isoforms in favorable neuroblastoma.

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Abstract

Neuroblastoma is a malignant solid tumor of children, which derives from the embryonal sympathoadrenal lineage. Clinical cases can vary widely from a favorable to an unfavorable prognosis according to the presence of genetic aberrations, such as MYCN amplification. Our cDNA microarray analysis which compared the gene expressions between favorable and unfavorable neuroblastomas showed a high expression of the **neuronatin** (Nnat) gene in favorable neuroblastomas. Nnat is highly conserved in mammalian species, and its expression appears in nervous systems from the hindbrain to the peripherals during the prenatal periods. The Nnat mRNA expression, investigated in 63 of neuroblastoma samples by quantitative reverse-transcription polymerase chain reaction, was found to be significantly higher in the favorable prognosis groups than in the unfavorable groups. Nnat is an imprinted gene, and its expression in IMR32 neuroblastoma cell line was up-regulated by treatment with a demethylating agent. High expressions of Nnat isoforms induced in an IMR32 neuroblastoma cell line changed the cell morphology to the extension of the neural processes, which thus indicated the occurrence of cell differentiation. In conclusion, the high expressions of Nnat were found to be associated with good prognoses in neuroblastoma, which might indicate tumor differentiation, and its suppressions in unfavorable tumors are considered to be under epigenetic control.

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MeSH Terms, Substances

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