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Correlation between expression profile of Wilms tumor 1 gene isoforms and neuroblastoma grade malignancy

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Wilms tumor 1 gene (WT1) is expressed in neuroblastoma (NB) which represents the most aggressive extracranial pediatric tumor. This latter may transform into a more benign form such as ganglioneuroblastoma and ganglioneuroma or progress into a highly aggressive metastatic cancer with a poor survival rate. WT1 acts as tumor suppressor gene in NB by inducing the maturation in a less invasive mass. To date, it has been identified 13 mRNA WT1 variants encoding 13 proteins, however, most of the studies have focused their attention exclusively on isoform of ~49 kDa molecular weight (1, 2). In the present study, we have analyzed, the expression profile of WT1 isoforms, in undifferentiated and all-trans retinoic acid (RA) differentiated NB cells in order to evaluate their involvement in tumor malignancy. Results have shown that different isoforms are expressed both in untreated and RA treated NB cells. Their expression is significantly increased in RA treated cells, suggesting that WT1 isoforms are inversely related to NB malignancy grade. In accord to this hypothesis, WT1 isoforms and nestin expression are inversely related in undifferentiated and RA treated cells. Furthermore, the inhibition of the two signalling pathways specifically involved in differentiation of NB, PI3K/Akt and MAPK/ERK respectively, trigger an overexpression of all WT1 isoforms. In conclusion, these data suggest that overexpression of WT1 isoforms might promote trans-differentiation of NB into a more benign tumor such as ganglioneuroblastoma or ganglioneuroma.

References

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Keywords

Wilms tumor 1 gene; neuroblastoma; WT1 isoforms.

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