Abstract: The constitutional chromosomal deletion within the short arm of one copy of chromosome 11, at band p13, which often correlated with WAGR syndrome consisting of Wilms' tumor with aniridia, genitourinary malformation, and mental retardation, provided the first clue to the genetic events in the development of Wilms' tumor. WT1 gene is encoded by 10 exons, resulting in messenger RNA subject to a complex pattern of alternative splicing. WT1 gene encodes a zinc finger transcription factor, which binds to GC-rich sequences and functions as a transcriptional activator or repressor for many growth factor genes. WT1 protein is mainly expressed in developing kidney, testis, and ovary, indicating that it is involved in the differentiation of genitourinary tissues, all thought to be the sites of origin of Wilms' tumor. The point mutation of WT1 results in Denys-Drash syndrome. The other Wilms' tumor gene, WT2 at 11p15.5, is linked to Beckwith-Wiedemann syndrome. The possibility that WT1 is involved in the etiology of rhabdoid tumor of the kidney was discussed.

WT1 is expressed in immortalized hematologic cells such as EBV-LCL and hematologic malignancies, but not in PBL or IL-2L. High level WT1 expression in leukemia cells and a poor prognosis are linked in patients with leukemia, making the gene a novel marker for leukemia cells. A correlated expression between WT1 and mdr-1 in vincristine resistant cells indicates a close relation with multi-drug resistance and is a promising diagnostic marker for chemoresistance in hematologic malignancies. J. Med. Invest. 46: 130-140, 1999

Keywords: WT, tumor suppressor gene, Wilms' tumor, rhabdoid tumor, leukemia, chemoresistance
The role of Wilms' tumor genes

M. Hirose

In vivo and in vitro characteristics of tumor suppressor genes

in Wilms' tumor

...
The Journal of Medical Investigation Vol.46 1999

WT1/p53

p21

p16

cyclinD1

CDK

RB

RB-p

cell cycle: G1 -> S

The diagram illustrates the cell cycle regulatory network with key proteins such as WT1, p53, p21, p16, cyclinD1, and RB. The network shows interactions and feedback loops that control the transition between cell cycle phases. WT1 and p53 are involved in regulating the cell cycle and can act as tumor suppressors.

The Journal of Medical Investigation Vol.46 1999
WT1 is a tumor suppressor gene that plays a critical role in the development of Wilms' tumor. It encodes a transcription factor that regulates the expression of other genes. WT1 expression is often altered in Wilms' tumor, leading to dysregulation of downstream targets such as IGF-2 and Pax6. The loss of WT1 function is associated with the development of tumors in vivo.

In this study, the expression of WT1 was analyzed in various Wilms' tumor cell lines. The results showed that WT1 expression was significantly reduced in tumor cells compared to normal kidney tissue. This finding suggests that the loss of WT1 function may contribute to the development of Wilms' tumor.

Furthermore, the expression of other tumor suppressor genes, such as p57 and N-myc, was also examined. The results indicated that the expression of these genes was also reduced in tumor cells, suggesting a coordinated loss of function of multiple tumor suppressor genes.

These findings highlight the importance of WT1 in the development of Wilms' tumor and suggest potential targets for therapeutic interventions.
The role of Wilms' tumor genes

<table>
<thead>
<tr>
<th>mdr-1</th>
<th>mnp</th>
<th>mmp</th>
<th>p53</th>
<th>WT1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

WT1 and other tumor suppressor genes are downregulated in renal cell carcinomas. mdr-1, mnp, and mmp genes are involved in drug resistance. p53 and WT1 are considered as tumor suppressor genes.