Wilms tumor gene 1 (WT1), TP53, RAS/BRAF and KIT aberrations in testicular germ cell tumors.

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Abstract

PURPOSE: Wilms tumor gene 1 (WT1), a zinc-finger transcription factor essential for testis development and function, along with other genes, was investigated for their role in the pathogenesis of testicular germ cell tumors (TGCT).

METHODS: In total, 284 TGCT and 100 control samples were investigated, including qPCR for WT1 expression and BRAF mutation, p53 immunohistochemistry detection, and massively parallel amplicon sequencing.

RESULTS: WT1 was significantly (p < 0.0001) under-expressed in TGCT, with an increased ratio of exon 5-lacking isoforms, reaching low levels in chemo-naïve relapsed TGCT patients vs. high levels in chemotherapy-pretreated relapsed patients. BRAF V600E mutation was identified in 1% of patients only. p53 protein
was lowly expressed in TGCT metastases compared to the matched primary
tumors. Of 9 selected TGCT-linked genes, RAS/BRAF and WT1 mutations were
frequent while significant TP53 and KIT variants were not detected (p = 0.0003).

CONCLUSIONS: WT1 has been identified as a novel factor involved in TGCT
pathogenesis, with a potential prognostic impact. Distinct biologic nature of the
two types of relapses occurring in TGCT has been demonstrated. Differential
mutation rate of the key TGCT-related genes has been documented.

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