

Familial testicular germ cell tumors in adults: 2010 summary of genetic risk factors and clinical phenotype - Abstract

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Familial aggregations of testicular germ cell tumor (FTGCT) have been well described, suggesting the existence of a hereditary TGCT subset. Approximately 1.4% of newly diagnosed TGCT patients report a positive family history of TGCT. Sons and siblings of TGCT patients have four- to sixfold and eight- to tenfold increases in TGCT risk respectively. Segregation analyses suggest an autosomal recessive mode of inheritance. Linkage analyses have identified several genomic regions of modest interest, although no high-penetrance cancer susceptibility gene has been mapped yet. These data suggest that the combined effects of multiple common alleles, each conferring modest risk, might underlie familial testicular cancer. Families display a mild phenotype: the most common number of affected families is 2. Age at diagnosis is 2-3 years younger for familial versus sporadic cases. The ratio of familial seminoma to nonseminoma is 1.0. FTGCT is more likely to be bilateral than sporadic TGCT. This syndrome is cancer site specific. Testicular microlithiasis is a newly recognized FTGCT component. Candidate gene-association studies have implicated the Y chromosome gr/gr deletion and PDE11A gene mutations as genetic modifiers of FTGCT risk. Two genomewide association studies of predominantly sporadic but also familial cases of TGCT have implicated the KIT-ligand, SPRY4, and BAK1 genes as TGCT risk modifiers. All five loci are involved in normal testicular development and/or male infertility. These genetic data provide a novel insight into the genetic basis of FTGCT, and an invaluable guide to future TGCT research.

Written by:

Greene MH, Kratz CP, Mai PL, Mueller C, Peters JA, Bratslavsky G, Ling A, Choyke PM, Premkumar A, Bracci J, Watkins RJ, McMaster ML, Korde LA. Are you the author?

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