

New discovered biomarkers as useful molecular targets in testicular germ cell tumors

Testicular germ cell tumors (TGCTs) are histologically classified as seminomas and non-seminomas according to the international classification of oncological diseases. Both these tumors display an invasive phenotype and are believed to be derived from a common ancestor, intratubular germ cell neoplasia unclassified (IGCNU) and gonadoblastoma, where the generation and expansion of tumor cells are limited to within the seminiferous tubules. Intra-tubular non-seminomas (ITNS), including embryonal carcinoma and teratoma, contain stem cells as well as cells that have differentiated toward somatic lineages to various degrees, thus giving rise to a morphologically pleiotropic appearance. In contrast, seminomas have a rather uniform appearance, at least at the histological level. Due to this apparently homogenous cell composition, seminomas are particularly suitable for investigations of tumor-associated alterations in gene expression. In addition, the cells that constitute seminomas resemble the primordial germ cells and/or the cells in the IGCNU. Thus, the gene expression profile in seminomas is interesting not only with regard to understanding their oncogenesis, but it also may be useful for research into primordial germ cells (PGCs).

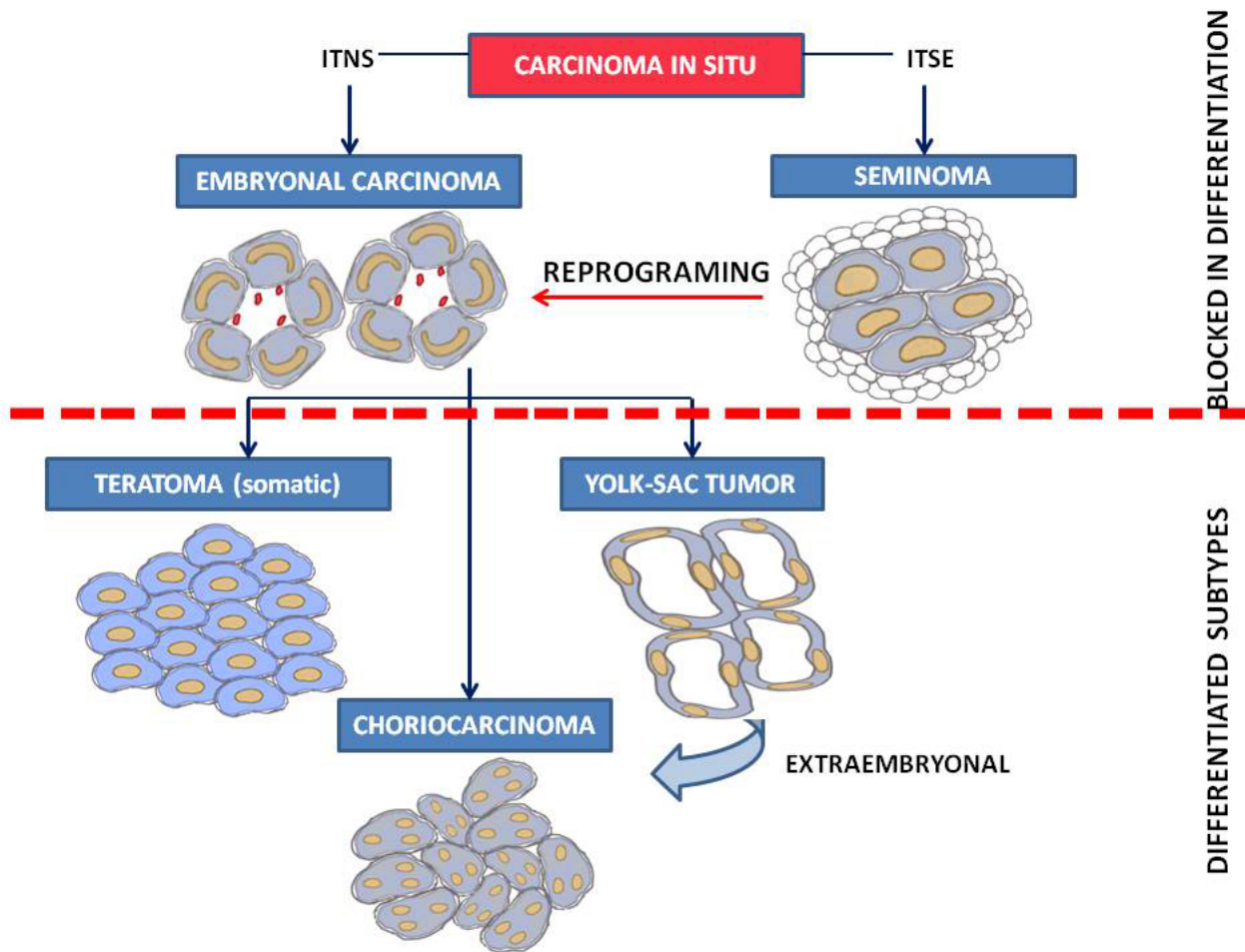


Fig. 1. Differentiative relations between Testicular Germ Cell tumors histotypes. ITNS, intratubular non seminoma; ITSE, intratubular seminoma.

A substantial increase in cure rates of the medical treatment of advanced testicular cancer has raised from approximately 25% in the mid-1970s to nearly 90% today. This is the highest cure rate in solid tumor. Improved survival is primarily due to effective chemotherapy. A great advance in chemotherapy for TGCT was the introduction of cisplatin in association with vinblastine, and bleomycin. The response rate increased to more than 80% with the use of this regimen in combination with surgery.

The International Germ Cell Cancer Collaborative Group (IGCCCG) was formed and a universal classification scheme was developed. In this stratification system, patients are separated into good-, intermediate-, and poor prognostic groups according to predicted outcome to cisplatin-combination

chemotherapy, based on histology, but also on primary site, sites of metastasis, and serum tumor marker elevation.

Although most patients with testicular cancer will be cured and can expect decades of additional life, thousands of men around the world will still die from testicular cancer every year, and many challenges remain. Cytotoxic chemotherapy remains the mainstay of therapy for advanced disease. A deeper understanding of the molecular mechanisms underlying the development of TGCTs may provide new tools to specifically target neoplastic cells and could contribute to overcome acquired and intrinsic chemotherapy resistance.

Both clinical and epidemiological evidence strongly suggest that genetic and environmental factors play an important role in the genesis and development of TGCTs. Several genes are implicated in the pathogenesis of TGCTs, but the involvement of other genetic factors remains unknown. Susceptibility genes and environmental factors may deregulate normal differentiation processes of PGCs. In fact, TGCT have an invasive phenotype and are believed to be derived from a common ancestor, IGCNU, where the generation and expansion of tumor cells are limited to within the seminiferous tubules. A number of environmental factors have been investigated to explain the possible links. Some evidence suggests association of increased TGCTs risk and maternal smoking during pregnancy, adult height, body mass index, diet rich in cheese, and others. However, the biological mechanisms remain to be elucidated. The incidence of seminomas has been increasing over the last decades. Diagnosis is usually based on identification of histological subgroups. In last years, many potential biomarkers useful as therapeutic targets have been discovered, including OCT3/4, SOX2, SOX17, NEK2, HMGA1, and HMGA 2, Aurora B, PATZ1, GPR30 and others. Promising molecules capable to selectively target neoplastic cells, that are, serine–threonine kinases, tyrosine kinases, HMGAs, GPR30 antagonists, proangiogenic factors inhibitors, and micro-RNAs already under clinical evaluation will open a new scenario for TGCTs treatment.

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Publication

[An Overview on Predictive Biomarkers of Testicular Germ Cell Tumors.](#)

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