TGCT - Testicular Germ Cell Tumors

Subtype	Biology & Expression	Genomic & Epigenomic Alterations	Clinical Features
Seminoma	• Primordial-germ-cell–like expression; high POU5F1/NANOG; low proliferation	• Universal i(12p) • KIT mutations in ~35% of pure seminomas • Global CpG demethylation; decreased KRAS copy number in KIT-mutant subset • Very low point-mutation burden	• Median age ~34 y; indolent course • Highly sensitive to radiotherapy and platinum-based chemo • Excellent overall survival
Embryonal Carcinoma	• Embryonic-stem-cell–like; high SOX2/POU5F1; robust proliferation	• Universal i(12p) • "ESC-like" CpG and CpH methylation signature • Promoter hypermethylation of BRCA1, RAD51C, MGMT	• Younger onset (~26 y); aggressive behavior • Highly chemosensitive; key driver of nonseminoma mortality risk
Yolk Sac Tumor	• Endodermal differentiation; high AFP and GPC3; moderate proliferation	• Universal i(12p) • Promoter hypermethylation of DNA-repair genes (MGMT, RAD51C, BRCA1) • Imprinting alterations (e.g., NESP55 methylation)	• Presents in children and young adults; AFP elevation • Aggressive but generally chemosensitive
Teratoma	• Somatic-lineage differentiation across multiple tissue types; low proliferation	• Universal i(12p) • Promoter hypermethylation of DNA-repair genes • Imprinting alterations (e.g., XLαs methylation)	• Mature teratoma: chemoresistant, managed surgically • Immature/malignant teratoma: risk of malignant transformation