Hormonal clusters of testicular cancers

	#1	#2	#3	#4
Sex hormone-related gene expression	Pituitary hormone-related genes (*GNRH1*, *PRL*) Testosterone - DHT conversion (*SRD5A1*) Receptors: *FSHR*, *AR* Expression of ER-responsive genes	Testosterone - DHT conversion (*SRD5A3*) Receptors: *ESR2*, *AR* Expression of AR responsive genes	Gonadotropin (*CGA*) Estrogen/estradiol synthesis (*HSD17B1*, *HSD18B12*, *CYP19A1*) Sex hormone transport (*SHBG*) Receptors: *FSHR* Expression of ER-responsive genes	Steroid synthesis (*STAR*, *POMC*, *HSD3B2*, *CYP11A1*, *CYP17A1*) Testosterone synthesis (*HSD17B3*) Receptors: *LHCGR*, *ESR2*, *AR*
Histology	NSGCT, teratoma, mixed	Seminoma	NSGCT, embryonal carcinoma, mixed, yolk sac	NSGCT, embronal carcinoma, mixed, seminoma, yolk sac
Risk profile and prognosis	Younger patients Serum markers: S1/S2 Cancer marker expression: *AFP* Progression/relapse: intermediate - high risk	Older patients Serum markers: mostly S0/S1 Cancer marker expression: *LDHC* Progression/relapse: low risk	Older patients Serum markers: mostly S2 Cancer marker expression: *LDHA*, *AFP*, *CGA* Progression/relapse: high risk	Younger patients Serum markers: mostly S0/S1 Cancer marker expression: *LDHA*, *AFP* Progression/relapse: intermediate risk
Immunity, TME, ECM, and epithelial phenotype	Fibroblast-rich, immune desert Collagens, glycoproteins, and proteoglycans Keratins, mesenchymal cell features	T and B cell infiltration, immune checkpoint gene and cancer testis antigen expression ECM desert Cell adhesion	Fibroblasts, immune desert ECM regulators, fibrinogens, proteases, and protease inhibitors Mesenchymal cell features	Stroma- and immune desert ECM secreted factors
Transcriptome, biology, signaling, metabolism	FGFR, ERBB, EPH, TGF/BMP/SMAD, and SRC-YAP signaling Hypoxia, suppression of oxidative energy metabolism Nucleotide interconversion, arachidonic acid metabolism	JAK/STAT and c-Kit signaling Antigen processing, inflammation, apoptosis, DNA repair Transport reactions	FGFR, ERBB, WNT, and SRC/YAP signaling Hypoxia, AP1/JUN and ER-responsive transcriptome, supporession of oxidative energy metabolism Lipid metabolism, female steroid hormone turnover	EGFR, FGFR, and ER signaling CREB and POU5F1 transcriptome, RNA turonver, nucleotide metabolism Steroid and androgen production
Genetics	*GRID2* and *PDE4D* gene deletions 20q11 amplification (*BCL2L1*, *ID1*) High deletion count, high MSI	KIT and KRAS mutations Low deletion count, low MSI	GRID2 deletion 12q15 amplification (*MDM2*, *PTPRR*, *PTPRB*) High deletion count, high MSI	No strong genetic features
Predicted drug sensitivity	TKI inhibitors	BCL2 family-, cytoskeleton/microtubule-, epigenetic-interfering, and DNA-toxic drugs	TKI inhibitors	cytotoxic drugs, TKI inhibitors