SARC - Sarcoma

Subtype	Biology & Expression	Genomic Alterations	Clinical Features
UPS (Undifferentiated Pleomorphic Sarcoma)	Enriched in immune-related and mesenchymal signatures; highly heterogeneous	TP53 mutations (~50%); RB1 deletions; chromosomal instability	Most common subtype; aggressive; variable prognosis; immune-infiltrated subtype may respond to immunotherapy
DDLPS (Dedifferentiated Liposarcoma)	High expression of adipogenic regulators and cell cycle genes	**MDM2 and CDK4 amplifications** (hallmarks); HMGA2 overexpression	Intermediate behavior; retroperitoneal location common; surgery often difficult
LMS (Leiomyosarcoma)	Smooth muscle–like transcriptional programs; immune desert	TP53 and RB1 co-inactivation (~90%); frequent PTEN loss	Aggressive clinical behavior; poor response to chemo; limited targeted options
Synovial Sarcoma	Stem-like transcriptional profile; high proliferation and low immune infiltration	**SS18–SSX1/2 fusion** from t(X;18) translocation	Typically affects young adults; chemosensitive; better prognosis than other high-grade sarcomas
Myxofibrosarcoma	Mesenchymal program with ECM remodeling; angiogenic signaling	Frequent CNAs; TP53 mutations; NF1 alterations	Often extremity tumors; locally aggressive; intermediate prognosis
Malignant Peripheral Nerve Sheath Tumor (MPNST)	Schwann cell–like gene expression; loss of neurofibromin and polycomb regulators	NF1 mutations/loss; SUZ12, EED (PRC2 complex) loss	Often NF1-associated; highly aggressive; poor response to current therapies