Supplemental Table S1. Selected References for Mitogenic Signaling and Cell Cycle Checkpoint Alterations in Osteosarcoma

Molecular Alteration	N	Key findings	Reference
TP53 alterations	765	< 30 years: 3.8% with germline mutations >30 years : 0% with germline mutations	Mirabello et al., 2015
	34	≤ 18 years: >90% with TP53 alterations No adults included in this study.	Chen et al., 2014
	25	18 samples with somatic alterations (ages included 8-79), not reported by age	Lorenz et al., 2016
	59	12% had germline TP53 variants 75% had TP3 inactivation	Perry et al. 2014
MDM2 / CDK4 amplification	207	16% osteosarcoma samples in pan-cancer study with MDM2 amplification, no specification of age of patients	Momand et al., 1998
	34	≤18 years: 3% with structural variant in MDM2 No adults included in this study.	Chen et al., 2014
	66	14% with MDM2 or CDK4 amplification	Suehara et al., 2019
RB1		Germline *RB1* mutations confers 400-500x risk of osteosarcoma over general population	Wong et al., 1997
	59 (ages 6-28)	3% with somatic RB1 mutations, 61% with RB1 deletion	Perry et al., 2014
	34	≤18 years: 29% with somatic RB1 alteration No adults included in this study.	Chen et al, 2014
	72 samples (from 67 total patients) n=33, age range 8–18 n=34, age range 19–80	19.4% of all samples with RB1 alterations, no difference between children or adults	Suehara et al, 2019
	30	43% with somatic RB1 alterations (8 patients 18 or older, oldest 42)	Toguchida et al, 1988
MYC	56	85.7% of all tumors with c-MYC expression by IHC	Wu et al., 2012
	25	Amplification in 7% adults	Ladanyi et al., 1993
	258	Amplification in 40% children and 5% adults	De Noon et al., 2021