

**Table S1.** Oncostatic effects of melatonin (MEL) added to treatment with chosen pleiotropic drugs/chemotherapeutics in vivo and in human trials.

Species, strain/study	Tumor site	Initiating agent	Chemopreventive/chemotherapeutic agent	Effect on tumor growth: chemopreventive agent(s)	Effect on tumor growth: MEL	Effect of combination with MEL compared to single agent	Reference		
Female Sprague-Dawley rats	Mammary gland	DMBA	Indomethacin	↓ tumor incidence, frequency and volume ↑ latency	↓ tumor incidence and frequency	↓ tumor incidence (ns)	[208]		
				NMU	↑ tumor volume ↑ tumor incidence (ns) ↓ latency (ns)	↓ tumor volume ↓ tumor frequency (ns)	↑ latency (ns) ↓ tumor volume (ns)	[209]	
		DMBA	Nimesulide	≈	↓ tumor incidence and frequency ↓ tumor volume	↓ tumor incidence ↓ tumor frequency and volume (ns)	↓ tumor volume ↓ tumor frequency (ns)	[210]	
				NMU	↓ tumor incidence and frequency ↓ tumor volume	↑ tumor volume ↓ tumor incidence (ns)	↑ latency (ns)	[211]	
		Male Syrian hamsters	Pancreas	BOP	Celecoxib	↓ tumor frequency ↓ tumor incidence (ns)	↓ tumor frequency (ns) ↑ latency (ns)	↑ latency (ns)	[212]
						↓ tumor nodules ↑ survival ↓ oxidative stress	↓ tumor nodules ↑ survival ↓ lung metastases ↓ oxidative stress	↓ oxidative stress	[212]
Female Sprague-Dawley rats	Mammary gland	NMU	Pravastatin	↑ apoptosis ↓ tumor volume ↓ HG tumor proportion ↑ proliferation ↓ tumor frequency (ns)	-	↑ apoptosis ↓ proliferation ↓ tumor frequency and volume ↑ latency ↓ tumor incidence (ns)	[235]		
			Pitavastatin	↑ apoptosis ↓ proliferation ↓ tumor volume ↑ latency (ns)	-	↓ VEGF expression ↓ tumor frequency (ns)	[236]		
Male SHR mice	Skin	BP	Metformin	↓ tumor incidence, frequency and volume ↑ latency and survival	↓ tumor incidence, frequency and volume ↑ latency and survival	↓ tumor incidence, frequency and volume ↑ latency and survival	[273]		
Female SHR mice				↓ tumor frequency and volume	↓ tumor volume ↓ tumor incidence (ns) ↑ latency (ns)	↓ tumor incidence (ns)	[274]		

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Clinical study		Melanoma treated with dacarbazine				Delayed response to chemotherapy	-	[264]
Case-report	Adrenals	Adrenocortical carcinoma					7-year remission post diagnosis	[276]
Female FVB/N HER2/neu mice	Mammary gland	Spontaneous		↑ latency ↑ survival	↑ survival	≈		
Male FVB/N mice		HER2/neu transplants		≈	≈	↓ tumor volume ↑ survival		[272]
Male SHR mice		Ehrlich carcinoma transplants		-	-	↓ tumor volume ↑ survival (ns)		
	Mammary carcinoma			↓ tumor incidence ↑ survival (ns)		-		
Female FVB/N mice		HER2/neu transplants	Paclitaxel	↓ tumor incidence ↑ survival (ns)	≈	↓ tumor incidence ↑ survival (ns)		[275]
			Metformin + paclitaxel	↓ tumor incidence ↑ survival (ns)		↓ tumor incidence (ns) ↑ survival (ns)		
		NMU+high-fat diet		↓ HG tumor proportion ↓ tumor volume	↓ HG tumor proportion ↓ proliferation ↓ incidence (ns)	≈		[278]
		DMBA+high-fat diet	Metformin	↓ tumor volume ↑ apoptosis (ns) ↓ tumor incidence (ns)	↑ apoptosis ↓ tumor volume ↓ tumor incidence and frequency (ns) ↑ latency (ns) ↓ HG tumor proportion (ns)	↑ apoptosis ↓ tumor incidence and frequency (ns) ↓ HG tumor proportion (ns)		[277]
Female Sprague-Dawley rats	Mammary gland	NMU+high-fat diet	Pioglitazone	↑ apoptosis ↓ HG tumor proportion	↑ apoptosis ↑ latency (ns)	↓ tumor incidence and frequency (ns) ↓ HG tumor proportion (ns)		[325]
		DMBA		↓ tumor incidence and frequency ↑ latency	↓ tumor frequency ↑ latency (ns)	↓ tumor frequency (ns)		[331]
		NMU	Retinyl acetate	↑ latency (ns)	↑ latency ↓ tumor incidence (ns)	↓ tumor incidence and frequency		[332]

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				↓ tumor incidence, frequency and volume (ns)	-	↓ tumor incidence (ns)	[333]
			9-cis-retinoic acid	↓ tumor incidence, frequency and tumor area	↓ tumor incidence, frequency and tumor area	↓ tumor incidence, frequency and tumor area	[334]
				↓ ER $\alpha$ mRNA expression	↓ ER $\alpha$ mRNA expression	↓ tumor frequency and volume	
				↓ tumor frequency (ns)	↓ tumor frequency and volume (ns)	↑ apoptosis	[335]
						↓ ER $\alpha$ mRNA expression	
			Bexarotene	↓ tumor frequency ↓ HG tumor proportion ↓ tumor incidence (ns)	-	↓ tumor incidence ↓ frequency (ns)	[336]

Abbreviations: BOP, N-nitrosobis(2-oxopropyl)amine; BP, benz(a)pyrene; DMBA, 7,12-dimethylbenz(a)anthracene; ER, estrogen receptor; HG, high-grade; NMU, N-methyl, N-nitrosourea; ns, non-significant; -, no results;  $\approx$ , no effect; ↓, decrease in parameter; ↑, increase in parameter. Boldface indicate undesirable effect.