Supplementary Material: The Role of Cannabinoids as Anti-Cancer Agents in Paediatric Oncology

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Table S1. Summary of selected studies that have investigated the anti-cancer efficacy of THC and/or CBD in pre-clinical mouse models used to generate Figure 2. Colours correspond to the symbols in Figure 2.

Model type		Cancer type	Compound Tested	References
Immune-Competent Models	Ectopic	Lung carcinoma	THC	[7]
		Breast carcinoma	THC	[8]
		Lymphoma	THC	[9]
		Melanoma	CBD	[10]
		Leukaemia (paediatric)	CBD	[1]
	Orthotopic	Breast carcinoma	CBD	[11]
		Melanoma	THC	[12]
		Colorectal (carcinogen-induced tumours)	CBD	[13]
Immune-Deficient Models	Ectopic	Melanoma	THC, CBD	[14]
		Colorectal cancer	CBD	[15–17]
		Prostate cancer	CBD	[18]
		Gastric cancer	CBD	[19]
		Glioblastoma	THC, CBD	[20,21]
		Lung cancer	THC, CBD	[22,23]
		Hepatocellular carcinoma	THC	[2]
		Pancreatic cancer	THC	[4]
		Neuroblastoma	THC, CBD	[5]
		Rhabdomyosarcoma	THC	[3]
	Orthotopic	Breast cancer	THC, CBD	[8,11]
		Glioblastoma	THC, CBD	[6,21]
		Hepatocellular carcinoma	THC	[2]
		Pancreatic cancer	THC	[4]
Genetically Modified Mice		Breast cancer	THC	[8]
		Pancreatic cancer	CBD	[24]

Table S2. Table of published sources used to generate Figure 3. Shown are drug metabolising enzymes reported to be affected by THC and CBD, with a list of other drugs used in childhood cancer treatment that are also affected by those enzymes. The reported effects of each cannabinoid are shown with matching citations which have been crosschecked with [106].

Enzyme	Possible Drug Interactions		Reported Effect of Cannabinoids on Each Enzyme	
			CBD	THC
CYP1A2	Antipsychotics	Olanzapine	• Substrate [26] • Inhibits [27]	• Likely inhibitor [28] • Possible inducer [27,29]
CYP2B6	Anti-cancer agents	Cyclophosphamide	• Inhibits [27]	• Inhibits [27]
CYP2C8	Anti-cancer agents	Dabrafenib	• Inhibits [27]	• n/a
CYP2C9	Anaesthetics Anti-cancer agents: Anticonvulsants Cannabinoids	Ketamine, Propofol Imatinib Phenytoin Dronabinol	• Substrate [26] • Inhibits [27]	• Substrate [30] • Inhibits [27]
CYP2C19	Anaesthetics Antibiotics Anti-cancer agents Anticonvulsants Anxiolytics	Propofol Voriconazole Ifosamide Phenytoin Diazepam	• Substrate [26] • Inhibits [27]	• Substrate [31] • potential inhibitor [28]
CYP2D6	Analgesics: Antipsychotics:	Hydromorphone, Morphine, Oxycodone Chlorpromazine	• Substrate [26] • Inhibits [27]	• Substrate [29] • Inhibits [27]
CYP3A4	Antibiotics Anti-cancer agents Anticonvulsants Antiemetic Anxiolytics Sedatives Steroids	Voriconazole Ceritinib, Crizotinib, Dabrafenib, Dasatinib, Everolimus, Imatinib, Lapatinib, Nilotinib, Sirolimus, Tacrolimus, Tazemetostat, Temsirolimus, Vinblastine, Vincristine Phenytoin Aprepitant Diazepam Midazolam Hydrocortisone	• Substrate [26] • Inhibits [27]	• Metabolites are substrates [29] • Inhibits [27]
UGT1A9	Anaesthetics	Propofol	• Inhibits [27]	• Metabolites are substrates [29] • Inhibited by CBN (THC metabolite) [28]
UGT2B7	Anxiolytics	Lorazepam	• Inhibits [27]	• Metabolites are substrates [111] • Inhibited by CBN (THC metabolite) [28]

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