Supplementary Table S1 | **Cannabinoid activity in animal models of cancer**

MODEL	TUMOUR TYPE	EXPERIMENTAL SYSTEM	EFFECT	CANNABINOID	RECEPTOR	REFS
			ANTI-TUMOUR ACTIONS			
SYNGENEIC TUMOURS						
Ectopic isografts	Lung carcinoma*	IM injection of cancer cells; IC mice	Decreased tumour size, increased survival time	Δ^9-THC, Δ^8-THC, CBN	n.d.	1
	Lymphoma	IP injection of cancer cells; IC mice	Decreased viable IP tumour cells, increased survival time (apoptosis)	Δ^9-THC, CBD	CB2	2, 3
	Skin carcinoma*	SC injection of cancer cells; ID mice	Decreased tumour size (apoptosis and angiogenesis)	WIN 55212-2, JWH-133	CB1, CB2	4
	Melanoma	SC injection of cancer cells; ID and IC mice	Decreased tumour size (apoptosis, inhibition of proliferation and angiogenesis)	WIN 55212-2, JWH-133	CB1, CB2	5
	Breast carcinoma	SC injection of cancer cells; ID mice	Decreased tumour size (inhibition of proliferation, apoptosis)	Δ^9-THC, JWH-133	CB2	6
Orthotopic isografts	Breast carcinoma	IMG injection of cancer cells; IC mice	Decreased tumour size, reduced lung metastases (inhibition of proliferation and invasiveness)	CBD, JWH-015	n.d.	7, 8
ALLOGENIC TUMOURS						
Ectopic xenografts	Glioma	SC injection of cancer cells; ID mice	Decreased tumour size (apoptosis, inhibition of angiogenesis, migration and invasiveness)	Δ^9-THC, JWH-133, WIN 55212-2, CBD	CB1, CB2	9-19
	Thyroid epithelioma		Decreased tumour size (inhibition of proliferation, apoptosis)	MET-AEA, 2-AG, CBD	CB1, CB2	20-23
	Pancreatic carcinoma		Decreased tumour size	Δ^9-THC, JWH-133	CB2	24
	Breast carcinoma		Decreased tumour size (apoptosis, inhibition of proliferation and angiogenesis)	JWH-133, WIN 55212-2	CB1, CB2	25
	Lung carcinoma		Decreased tumour size (apoptosis, inhibition of proliferation, invasiveness and angiogenesis)	Δ^9-THC, JWH-133, WIN 55212-2, CBD	CB1, CB2, TRPV1	26-29
	Lymphoma		Decreased tumour size (inhibition of proliferation, apoptosis)	MET-AEA	CB1, CB2	30
	Cholangio-carcinoma		Decreased tumour size (inhibition of proliferation, apoptosis)	AEA	GPR55	31-33
	Colon carcinoma		Decreased tumour size (apoptosis)	CB-13	CB1, CB2	34
	Rhabdomyo-sarcoma		Decreased tumour size (apoptosis)	HU-210	CB1	35
	Prostate carcinoma		Decreased tumour size (inihibition of proliferation, apoptosis)	JWH-015	CB2	36
	Oral carcinoma		Decreased tumour size (inhibition of proliferation)	AM-1241	CB2	37
	Hepatocellular carcinoma		Decreased tumour growth (apoptosis)	Δ^9-THC, JWH-015	CB2	38
	Transformed MEFs	SC injection of transformed cells; ID mice	Decreased tumour size (apoptosis)	Δ^9-THC	CB1, CB2	11, 13
Orthotopic xenografts	Glioma	Intracerebral injection of cancer cells; rats	Decreased tumour size, increased survival (apoptosis)	Δ^9-THC, WIN 55212-2	CB1, CB2	12
	Pancreatic carcinoma	Intrapancreatic injection of cancer cells; ID mice	Decreased tumour growth, reduced metastases (apoptosis)	WIN 55212-2	CB2	24
	Hepatocellular carcinoma	Intrahepatic injection of cancer cells; ID mice	Reduced hepatomegaly and ascites (apoptosis)	Δ^9-THC, JWH-015	CB2	38

CHEMICALLY-INDUCED CARCINOGENESIS						
	Colon cancer	Azoxymethane treatment; C57BL/6 mice	Decreased aberrant crypt foci (apoptosis)	HU-210	n.d.	39
GENETICALLY-ENGINEERED MICE						
	Colorectal cancer	$Apc^{Min/+}$ mice	Reduced number of tumours (apoptosis)	R-1	CB1	40
	Breast cancer	Heterozygous PyMT mice	Increased tumour latency, decreased tumour size (apoptosis, inhibition of proliferation, angiogenesis, migration and invasiveness)	JWH-133	CB2	8, 25
		MMTV-neu mice	Inhibition of tumour generation, decreased tumour size, reduced lung metastases (apoptosis, inhibition of proliferation and angiogenesis)	Δ^9-THC, JWH-133	CB2	6
MODELS OF METASTASIS						
Intravenous injection of tumour cells	Lung carcinoma	Mouse cells: paw injection, IC mice Human cells: tail vein injection, ID mice	Reduced lung metastases (inhibition of invasiveness)	Δ^9-THC, JWH-133, WIN 55212-2, CBD, MET-AEA	CB1, CB2, TRPV1	21, 26, 27, 41
	Breast carcinoma	Mouse cells: paw and tail vein injection, IC mice Human cells: paw and tail vein injection; IC mice	Reduced lung metastases (inhibition of proliferation, adhesion, migration and invasion)	JWH-133, WIN 55212-2, MET-AEA, CBD	CB1, CB2	7, 23, 25, 42, 43
	Melanoma	Mouse cells: paw injection, IC mice	Reduced lung and liver metastases	WIN 55212-2	n.d.	5
Originated from an orthotopic xenograft	Pancreatic cancer	Orthotopic xenograft; ID mice	Reduced spleen, liver, diaphragm, intestine and stomach metastases (apoptosis)	Δ^9-THC, JWH-133	CB2	24
Derived from a primary tumour	Breast cancer	MMTV-neu mice, Orthotopic isograft	Reduced lung metastases (inhibition of proliferation and invasiveness)	Δ^9-THC, JWH-133, CBD	CB2	6, 7
			PRO-TUMOUR ACTIONS			
SYNGENEIC TUMOURS						
Ectopic isografts	Lung carcinoma*	SC injection of cancer cells; IC mice	Increased tumour size (inhibition of anti-tumour immune response)	Δ^9-THC, MET-AEA	CB2	44, 45
	Breast carcinoma		Increased tumour size (inhibition of anti-tumour immune response)	Δ^9-THC	CB2	46
MODELS OF METASTASIS						
Originated from an ectopic isograft	Breast carcinoma	Ectopic isograft; IC mice	Increased number and size of lung metastases (inhibition of anti-tumour immune response)	Δ^9-THC	CB2	24, 46

The table shows the different animal models of cancer in which the indicated cannabinoids have been proved to have pro- or anti-tumour effects. The membrane receptors involved in these actions are also specified. Note, nonetheless, that not all the indicated effects are produced by all the agonists, and that not all the indicated agonists are capable of activating (all) the indicated receptor(s).

*Although the cancer cell line used was of mouse origin, it was not injected in strictly syngeneic mice but in a different mouse strain.

IM, intramuscular; SC, subcutaneous; IMG, intramammary gland; IC, immunocompetent; ID, immunodeficient; MEFs, mouse embryonic fibroblasts; n.d., not determined. CB_1, cannabinoid receptor 1; CB2, cannabinoid receptor 2; TRPV1, transient receptor potential cation channel 1; GPR55, G protein-coupled receptor 55. Δ^9-THC (Δ^9-tetrahydrocannabinol), Δ^8-THC (Δ^8-tetrahydrocannabinol), CBN (cannabinol), WIN 55212-2, MET-AEA (methanandamide), 2-AG (2-arachidonoylglicerol), CB-13 and HU-210 are CB1/CB2-mixed agonists; JWH-133, JWH-015 and AM-1241 are CB2-selective agonists and R-1 is a CB_1-selective agonist. CBD (cannabidiol) does not bind to either CB1 or CB2 receptors with significant affinity.

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