

Table S1: IC50 concentrations of the different cell lines after treatment with CBD 10 nM – 20 µM.

Cell lines	IC50 concentration (µM)	
	72h incubation	144h incubation
MPC	17.6	12.3
MTT	11.7	11.3
BON1	23.2	10.4
GOT1	n/a	27.5
NCI-H727	15.7	13.3
QGP-1	n/a	27.5

Abbreviations: Cannabidiol (CBD), not available (n/a)

Table S2: NET patient cohort (n=11): listed in numerical order.

Patient ID	Sex	Age (yrs.)	Grading (WHO)	Tumor type	Meta static	Tumor characteristics, histology	Ki-67	Patient characteristics	Functionally active	Cell viability responsivity to CBD 5 µM	Cell viability responsivity to CBD 10 µM
1.1	F	56	NET G1	Small intestinal NET	Yes	Primary tumor (ileum), max 1.6 cm, ulceration of mucosa, muscularis propria invasion	<2%	Metastatic (liver, ovaries, peritoneal, lymph node), no clinical symptoms	Non-functional	Neutral	Significant decrease
1.2						Metastasis (peritoneal), max 1.7 cm				Neutral	Significant decrease
2	M	80	NET G1	Pancreatic NET	No	Primary tumor, 1 cm, SSTR2 IHC positive	<1%		Insulinoma	Neutral	Neutral
3	F	38	NET G2	Pancreatic NET	No	Primary tumor, max 3.4 cm	3-4%	No clinical symptoms	Non-functional	Neutral	Neutral
4	M	58	NET G2	Small intestinal NET	Yes	Metastasis (liver), max 7.5 cm, SSTR2 IHC negative	4%	Metastatic (liver, lymph node), no clinical symptoms	Non-functional	Neutral	Neutral
5	F	64	NET G2	Pancreatic NET	Yes	Metastasis (lymph node), max. 2.9 cm, capsular infiltration, ISLET1 positivity	15%	Metastatic (lymph nodes), chronic diarrhea	Non-functional	Neutral	Neutral
6	F	55	NET G1	Pancreatic NET	Yes	Primary tumor, max 9.2 cm, angioinvasion, infiltration of spleen and stomach to mucosa, lymphatic infiltration	2%	Metastatic (liver, lymph node), upper abdominal pain, no other clinical symptoms	Non-functional	Neutral	Neutral
7	M	72	NET G2	Pancreatic NET	Yes	Metastasis (liver), max 2.3 cm	5-10%	Metastatic (liver, lymph node)	Non-functional	Neutral	Neutral

8	F	63	NET G1	Small intestinal NET	Yes	Metastasis (liver), max 7.5 cm, lymphatic infiltration	<1%	Metastatic (liver, lymph node), chronic diarrhea, flush, hot flashes, weight loss, lipedema/lymphedema	Carcinoid syndrome	Neutral	Significant increase
9	M	64	NET G1	Small intestinal NET	Yes	Primary tumor, max 1.4 cm, lymphatic infiltration, perineural sheath infiltration	2%	Metastatic (lymph node, bone), no nausea/diarrhea/flush	Non-functional	Neutral	Neutral
10	M	81	NET G2	Small intestinal NET	Yes	Primary tumor (ileum/cecum) max 1.5 cm	4%	Metastatic (lymph node, liver)	Carcinoid syndrome	Significant increase	Significant increase
11	M	76	NET G2	Pancreatic NET	Yes	Primary tumor, max 8 mm	3%	Metastatic (liver), bilateral renal cell carcinoma suspected, germline testing: <i>VHL</i> negative	Non-functional	Neutral	Significant decrease

Abbreviations: Neuroendocrine tumor (NET), cannabidiol (CBD), immunohistochemistry (IHC), F (female), M (male), not available (n/a), variant of unknown significance (VUS)

Table S3: PPGL patient cohort (n=35): listed in numerical order.

Patient ID	Sex	Age (yrs.)	Tumor type	Metastatic	Biochemical phenotype	Histology and tumor characteristics	Ki-67	Germline sequencing	Somatic sequencing	Cell viability responsivity to CBD 5 μ M	Cell viability responsivity to CBD 10 μ M
1	F	27	HNPGL	No	Silent	2.7 cm, immunohistochemical <i>SDHB</i> -loss	n/a	<i>SDHB</i>	n/a	Neutral	Neutral
2	F	47	HNPGL	Yes	Silent	primary tumor, 1.2 cm, metastatic (bone)	n/a	<i>SDHB</i> (VUS <i>EPAS1</i>)	n/a	Neutral	Neutral
3	M	36	HNPGL	No	Silent	2.1 cm	n/a	Negative	<i>NFI</i>	Significant decrease	Significant decrease
4	M	44	PCC	No	Noradrenergic	2.5 cm, infiltration of periadrenal fatty tissue	2-3%	VUS in <i>NFI</i>	VUS in <i>NFI</i> likely pathogenic	Significant decrease	Significant decrease
5	M	52	PCC	No	Noradrenergic	max. 3 cm, GAPP 2, PASS 1	2%	Negative	n/a	Significant increase	Significant increase
6	M	42	PCC	No	Adrenergic	3.6 cm	1-2%	<i>NFI</i>	n/a	Significant decrease	Significant decrease
7	M	50	PCC	No	Adrenergic	bifocal, max. 1.2 cm and max. 0.5 cm, SSTR2 expression neg.	2%	<i>NFI</i>	n/a	Significant decrease	n/a
8	F	61	HNPGL	No	Dopaminergic	max. 8.5 cm	n/a	Negative	Negative	Neutral	Significant decrease

9	F	76	PCC	No	Adrenergic	max. 2 cm, SSTR2 expression pos.	1-2%	Negative	Negative	Significant increase	n/a
10	M	65	PCC	No	Silent	1.3 cm, GAPP 1, PASS 2	<1%	n/a	n/a	Neutral	Neutral
11	M	25	HNPGL	No	Noradrenergic	max. 3.8 cm, SSTR2 pos.	n/a	<i>SDHD</i>	n/a	Neutral	n/a
12	F	74	PCC	No	Noradrenergic	max. 2.2 cm, PASS 2	n/a	VUS in <i>VHL</i>	n/a	Neutral	Neutral
13.1	M	49	PCC	No	Adrenergic	bilateral, right side, max. 4.5 cm, GAPP 3, PASS <4	1%	<i>RET</i>	n/a	Neutral	Significant decrease
13.2						bilateral, left side, max. 2.7 cm, GAPP 2, PASS <4	<1%			Neutral	Neutral
14	F	56	PCC	No	Adrenergic	2.2 cm, GAPP 1, PASS 2	<1%	Negative	n/a	Neutral	Neutral
15	M	66	HNPGL	No	Adrenergic	max. 2.1 cm, reduced <i>SDHB</i> expression	5%	Negative	<i>SDHD</i>	Significant increase	Neutral
16	F	39	PCC	No	Adrenergic	max. 3.5 cm, PASS 0	n/a	Negative	n/a	Significant decrease	Significant decrease
17	F	27	PCC	No	Silent	recurrence, right side 2.6 cm, status post resection PCC left, multiple neurofibromas of tongue, medullary thyroid carcinoma	n/a	MEN2B (<i>RET</i>)	n/a	Neutral	Significant decrease
18	M	42	PGL	No	Adrenergic	periadrenal, 5.3 cm, lymphatic invasion	1%	Negative	<i>HRAS</i>	Neutral	Neutral
19	M	51	PCC	No	Noradrenergic	4.0 cm	<1%	Negative	Negative	Neutral	Significant increase
20	F	41	PCC	No	Noradrenergic	6.0 cm	1%	n/a	n/a	Neutral	Significant increase
21	F	65	PCC	No	Adrenergic	4.3 cm	n/a	Negative	<i>NFI</i>	Neutral	Neutral
22	F	57	PCC	No	Adrenergic	2.2 cm, PASS 2	n/a	n/a	n/a	Significant increase	Neutral
23	M	57	PCC	No	Adrenergic	4.7 cm	<1%	n/a	n/a	Neutral	Neutral
24	F	30	PGL	No	Noradrenergic	abdominal, 6.5 cm, capsule infiltration, angioinvasion	<5%	<i>SDHC</i>	n/a	Neutral	Neutral
25	F	55	PCC	No	Noradrenergic	3.1 cm	1-2%	Negative	n/a	Neutral	Neutral
26	F	27	PCC	No	Noradrenergic	7.5 cm, angioinvasion, lymphatic invasion, necrotic	5%	Negative	n/a	Neutral	Neutral
27	M	55	PCC	No	Noradrenergic	3.8 cm	1%	n/a	n/a	Neutral	Neutral
28	M	68	PCC	No	Adrenergic	max. 3.8 cm, angioinvasion, capsule infiltration, GAPP 3	2%	n/a	n/a	Neutral	Neutral
39	F	66	PCC	No	Adrenergic	2.5 cm, GAPP 3, PASS 2	1%	n/a	n/a	Neutral	Significant increase

30	F	37	PCC	No	Noradrenergic	recurrence, 1.7 cm, GAPP 3	<2%	<i>MAX</i>	n/a	Neutral	Neutral
31	F	53	PCC	No	Noradrenergic	composite PCC (with ganglioneuroma portion), max. 4.9 cm, GAPP 3	<3%	n/a	n/a	Significant increase	Significant increase
32	F	39	PGL	No	Noradrenergic	4.1 cm	<1%	<i>SDHB</i>	n/a	Significant increase	Neutral
33	M	58	PGL	No	Adrenergic	cystic extraadrenal, 4.2 cm	n/a	n/a	n/a	n/a	Significant decrease
34	M	52	PCC	No	Adrenergic	max. 5cm, GAPP 1	1-2%	<i>BRCA</i>	n/a	Neutral	Neutral
35	M	53	PCC	Yes	Noradrenergic	pulmonary metastasis, 1.2 cm, metastatic (lung, lymph node), SSTR2 IHC expression positive	10-20%	Negative	<i>ATRX</i>	Neutral	Significant decrease

Abbreviations: Pheochromocytoma and paraganglioma (PPGL), pheochromocytoma (PCC), paraganglioma (PGL), head and neck paraganglioma (HNPG), cannabidiol (CBD), immunohistochemistry (IHC), F (female), M (male), not available (n/a), variant of unknown significance (VUS)