

Figure S1. Characterization of mouse ES neural differentiation. (A)

Representative immunofluorescence images at NS and ND cell stages for neural progenitor (nestin), neuronal (TUJ1 and NeuN) and astroglial (GFAP) markers. (B) Gene expression analysis by qPCR of projection neuronal markers (Tbr1, Bcl11b, Er81, Cux2, Uchl1 and Satb2 was performed from NS stage (12) DIV) to ND cells (18 DIV and 21 DIV). (C) Representative images for vGLUT1 and vGAT1 immunofluorescence and quantification of glutamatergic and GABAergic cells referred to total DAPI counterstained cells. (D) Representative image of TUJ1 and vGLUT1 immunofluorescence. (E) BCL11B+ and SATB2+ neurons were quantified after immunofluorescence in ND cells and referred to the total number of cells counterstained with DAPI. (F) Electrophysiological characterization of ES-derived neurons was performed by patch-clamp recordings in current- and voltage-clamp mode. (G) Representative biocytinlabelled cell during patch-clamp analysis, after immunofluorescence with an anti-ER81 antibody. The analyses were done in mRNA extracts and ES-derived cultures from n = 4 independent experiments. Scale bar, 50 µm (A, C, E) and 10  $\mu$ m (D, G). Statistics: \*\*\* p < 0.001.

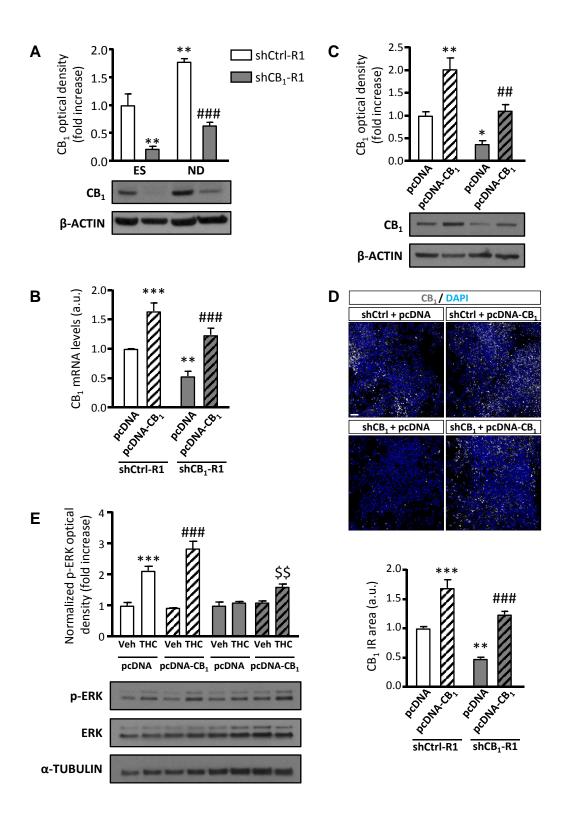
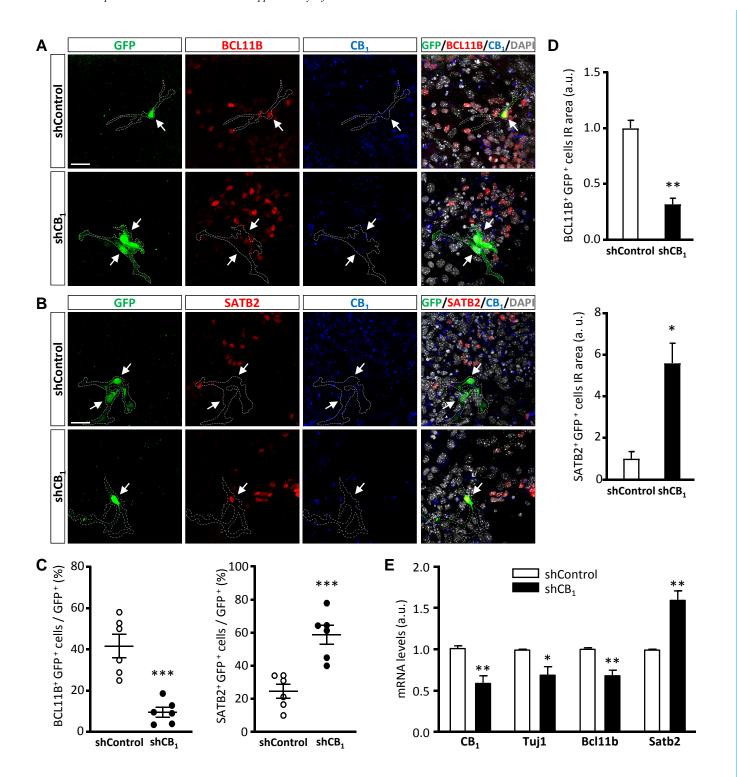


Figure S2. Characterization of CB<sub>1</sub> receptor expression in knockdown and control ES cells. (A) Western blot analysis of CB<sub>1</sub> receptor transcripts and levels after ES nucleofection with shCB<sub>1</sub> receptor and shControl and analysed at ES and ND stages. (B) qPCR quantification of CB<sub>1</sub> mRNA levels in shCB<sub>1</sub>-R1 and shCtrl-R1 cells transfected with pcDNA-Control or pcDNA-CB<sub>1</sub> expression vectors. (C) Western blot analyses of CB<sub>1</sub> protein levels in cell extracts as

above. (D) CB<sub>1</sub> receptor immunoreactivity determined in ND cells after immunofluorescence from shCtrl- and shCB<sub>1</sub>-R1 cells and transfection with pcDNA-Control or pcDNA-CB<sub>1</sub> expression vectors. Representative images are shown. (E) Western blot analyses of phosphor-ERK and ERK in the shCtrl-R1 and shCB<sub>1</sub>-R1 cells, at 21 DIV, as above, after 15 min stimulation with THC. The analyses were done in cells from n = 3 and mRNA extracts from n = 4 independent ES-differentiations. Statistics: \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001 (vs shCtrl-R1 at ES stage or shCtrl-R1+pcDNA or shCtrl-R1+pcDNA - Veh); ## p < 0.01, ### p < 0.001 (vs shCtrl-R1 at ND stage or shCB<sub>1</sub>+pcDNA or shCtrl-R1+pcDNA-CB<sub>1</sub> - Veh); \$\$ p < 0.01 (vs shCB<sub>1</sub>-R1+pcDNA-CB<sub>1</sub> - Veh). Scale bar, 15 µm (A), 25 µm (C).



**Figure S3.** Genetic ablation of the CB<sub>1</sub> receptor at NS stage interferes with deep cortical neuronal generation. (A, B) Representative immunofluorescence images of BCL11B<sup>+</sup> and SATB2<sup>+</sup> cells at ND stage in shCB<sub>1</sub> and shControl cells. (C, D) Quantification of BCL11B<sup>+</sup> and SATB2<sup>+</sup> cells in GFP<sup>+</sup> nucleofected cells and quantification of neuronal marker BCL11B and SATB2 immunoreactivity in the same cells. (E) qPCR quantification of  $CB_1$ , Tuj1, Bcl11b and Satb2 mRNA levels in ND differentiated cells. The analyses were done from n = 3-6 independent ES-differentiations. Statistics: \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001 (vs shControl). Scale bar, 25 μm.

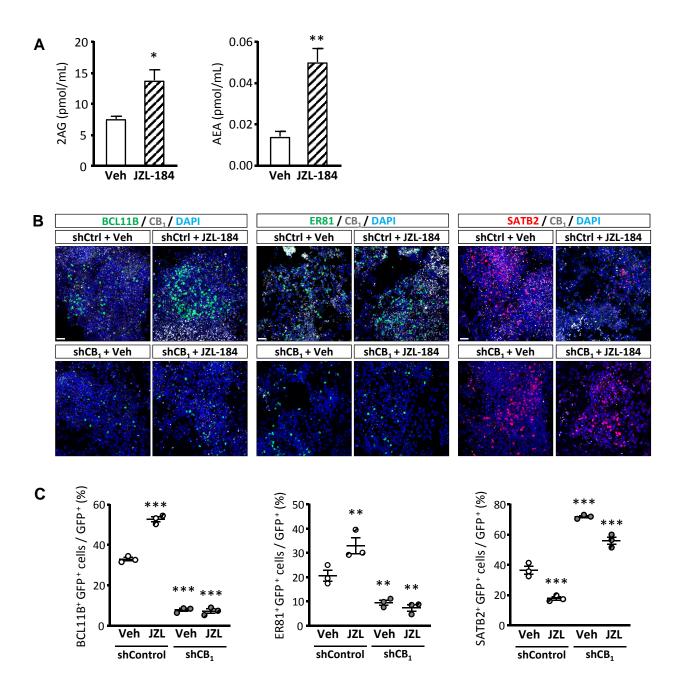
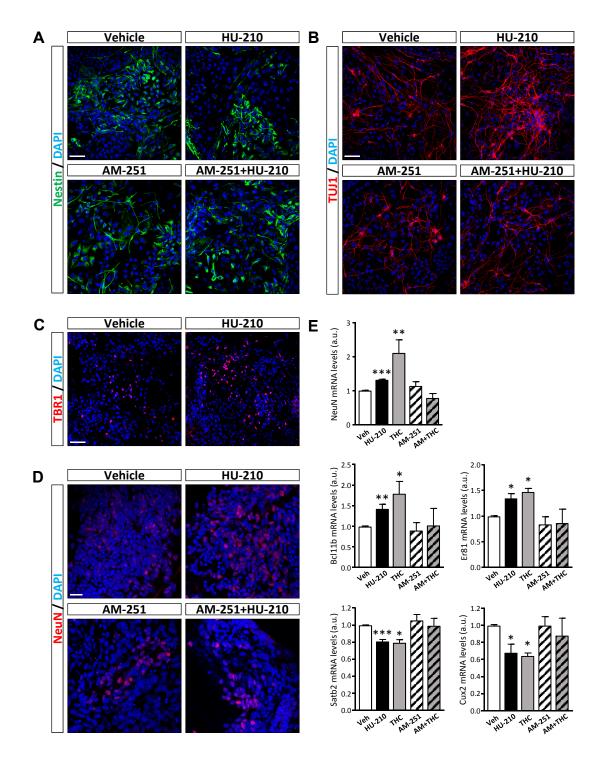


Figure S4. JZL-184 induced eCB levels and promoted ES-derived deep layer neuronal differentiation. (A) Levels of the eCBs 2AG and AEA were determined in JZL-184- and vehicle-treated ND cells. (B) Representative images of BCL11B<sup>+</sup>, ER81<sup>+</sup> and SATB2<sup>+</sup> cells derived from JZL-184- and vehicle-treated shCB<sub>1</sub>-R1 or shCtrl-R1 cells. (C) Quantification of BCL11B<sup>+</sup>, ER81<sup>+</sup> and SATB2<sup>+</sup> cells in GFP<sup>+</sup> neurons derived from shControl or shCB<sub>1</sub> transfected R1-derived NS cells. The analyses were done in mRNA extracts and immunofluorescence experiments from n = 3 independent ES-differentiations.



**Figure S5. HU-210-induced CB**<sub>1</sub> receptor activation promotes ES neuronal differentiation. (A-D) mES cells were differentiated in the presence of HU-210 (100 nM) in the presence or absence of AM-251 (1 μM) or vehicle, and neuronal differentiation was characterized by the analysis of nestin, TUJ1, TBR1 and NeuN immunofluorescence. Quantification is shown in Table S1. (E) Cannabinoid induced changes in *NeuN, Bcl11b, Er81, Satb2* and *Cux2* transcript levels determined by real-time PCR as compared to vehicle treated ES cells. ES cells were treated with HU-210, THC combined or not with AM-251 as above. The analyses were done in mRNA extracts and ES-derived cultures from n = 3-5 independent experiments. Statistics: \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001 (vs vehicle). Scale bar, 50 μm.

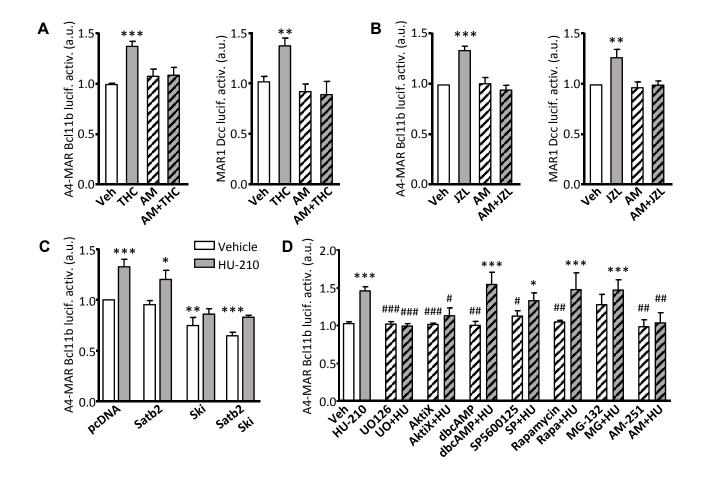


Figure S6. Characterization of CB₁ receptor-mediated regulation of Bcl11b transcriptional activity. (A, B) R1 mES cells were treated during neuronal differentiation with the CB₁ receptor agonist THC (2 μM) or JZL-184 (1μM) in the presence and absence of AM-251 (1 μM), and luciferase activity of MAR-A4 Bcl11b and MAR1-Dcc constructs were determined. (C) HiB5 cells were transfected with 500 ng of pCAG-Satb2, 2 μg of pCMV-Ski and pSatb2, 1 μg MAR-A4-pfosluc of Bcl11b and 40 ng Renilla vectors and luciferase activity determined 24h after vehicle and HU-210 (100 nM) treatment. (D) Luciferase activity of the MAR-A4 Bcl11b reporter in vehicle and HU-210 treated cells in the presence of different pharmacological modulators UO126 (1 μM), AktiX (2.5 μM), rapamycin (100 nM), SP600125 (12.5 μM) and dibutiryl cyclic AMP (2.5 μM), MG-132 (5 μM). The analyses were done in ES-derived cultures from n = 3-6 independent experiments. Statistics: \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001 (vs vehicle), # p < 0.05, ## p < 0.01, ### p < 0.001 (vs HU-210).

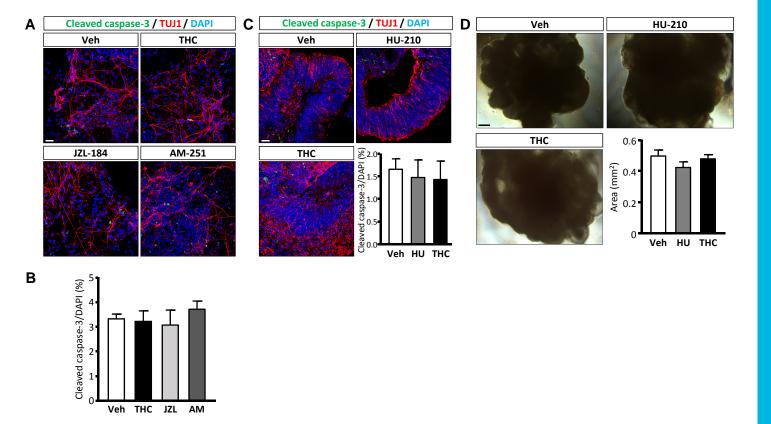


Figure S7. Lack of toxicity in mES-derived cells and hiPS-derived organoids at the usage concentrations. (A,B) Representative images and quantification of Cleaved caspase-3 on ND cells derived from mES in the presence of THC (2 μM), JZL-184 (1 μM) and AM-251 (1 μM). (C) Representative images and quantification of Cleaved caspase-3 on human iPS cell-derived organoids in the presence of THC (2 μM), JZL-184 (1 μM) and AM-251 (1 μM). (D) Representative images and quantification of organoid area in the presence of HU-210 (100 nM) and THC (2 μM). Scale bar: 25 μm (A,C); 0.3 mm (D).

	Positive cells/DAPI (± SEM)					
	Vehicle	HU-210	AM-251	AM-251+HU-210		
Nestin	38.24 ± 1.57	30.47 ± 2.59	39.42 ± 2.28	37.83 ± 2.90		
TUJ1	42.82 ± 3.20	$55.20 \pm 4.90$	41.80 ± 2.37	39.87 ± 4.48		
NeuN	36.33 ± 1.90	47.95 ± 1.27	37.45 ± 2.25	25.50 ± 5.37		
TBR1	8.31 ± 0.34	18.47 ± 2.30	ND	ND		

**Table S1.** Quantification of neuronal cell population changes determined after immunofluorescence for the indicated antibodies in ES-differentiated neurons in the presence of HU-210 (100 nM) in the presence or absence of AM-251 (1 $\mu$ M) and vehicle treated cells. Representative images are shown in Supplementary Fig. 2. (ND) not determined. The analyses were done in cells from n= 4 independent ES-differentiations.

Antigen	Species reactivity	Clonality	Dilution (IF/WB)	Reference
α-TUBULIN	Mouse	Monoclonal	Sigma (n.e./1:5000)	T9026
β-ACTIN	Mouse	Monoclonal	Sigma (n.e./1:5000)	A5441
CB <sub>1</sub>	Guinea pig	Polyclonal	Frontier Institute (1:500/n.e)	CB1-GP-Af530-1
CB <sub>1</sub>	Rabbit	Polyclonal	Frontier Institute (n.e./1:500)	CB1-Rb-Af380-1
CTIP2	Rat	Monoclonal	Abcam (1:500/n.e.)	ab18465
DAGL	Guinea pig	Polyclonal	Frontier Institute (1:200/n.e.)	DGLα-GP-Af380
ER81	Rabbit	Polyclonal	Abcam (1:500/n.e.)	ab184120
ERK 1/2	Mouse	Monoclonal	Cell Signalling (n.e./1:1000)	4696
FAAH	Rabbit	Polyclonal	Chemicon (1:50/n.e.)	AB5644P
GFAP	Mouse	Polyclonal	Invitrogen (1:400/n.e.)	PA5-16291
GFP	Rabbit	Polyclonal	Abcam (1:1000/n.e.)	ab290
MAP2	Mouse	Monoclonal	Sigma (1:500/n.e.)	M9942
MGL	Rabbit	Polyclonal	Cayman Chem (1:100/n.e.)	100035
NAPE-PLD	Guinea pig	Polyclonal	Frontier Institute (1:200/n.e.)	NAPE-PLD-GP-Af720
Nestin	Mouse	Monoclonal	Chemicon (1:500/n.e.)	MAB353
Nestin	Rabbit	Polyclonal	Covance (1:200/n.e.)	839801
NeuN	Mouse	Monoclonal	Chemicon (1:500/n.e.)	MAB377
OCT4	Rabbit	Polyclonal	Abcam (1:500/n.e.)	ab19857
p-ERK 1/2	Rabbit	Polyclonal	Cell Signalling (n.e./1:1000)	9101
SATB2	Mouse	Monoclonal	Abcam (1:50/n.e.)	ab51502
TBR1	Rabbit	Polyclonal	Abcam (1:500/n.e.)	ab23345
TUJ1	Mouse	Monoclonal	Chemicon (1:500/n.e.)	MAB1637
TUJ1	Rabbit	Polyclonal	BioLegend (1:500/n.e.)	802001
vGLUT1	Rabbit	Polyclonal	Synaptic Systems (1:250/n.e.)	135303
vGAT1	Rabbit	Polyclonal	Synaptic Systems (1:250/n.e.)	131003

**Table S2.** Primary antibodies used in this study. Dilution employed for immunofluorescence (IF) and western blot (WB) are indicated, (n.e.) application not employed.

Gene	Forward primer (5'-3')	Reverse primer (3'-5')	
Abhd4	GGGCTTGTTTACTATGGCTGA	CAAGTGGGGAGCCAGCTA	
Abhd6	CTCCTATGTCCGCTTCAAGG	GAATGCGAACATCGACAAGA	
Abhd12	GGATGATGTGACTATTGGAGTCTG	CACATCTGGTCCTTCCCTTG	
CB <sub>1</sub>	GGGCAAATTTCCTTGTAGCA	GGCTCAACGTGACTGAGAAA	
Ctip2	ACCCACGAAAGGCATCTGT	GCTGGAAGGCTCATCTTTACC	
Cux2	TCAGTCAACAGCTCCATTCG	GCCCTGAACACAGAGCAAAG	
Daglα	CTTTTCCTCTTGGGCATCAT	GCATCGTGCATTCCTTATCA	
Dcc	TGTCGAGGAGAGCCACAAG	CGCTCAAGTCATCCTGTTCA	
Er81	ATGGAGAAAAGTGCCTGTACAAT	GGTGTAGTGGGGACACTGGA	
Faah	GCAGGTGGGCTGTTCAGT	AAGCAGGGATCCACAAAGTC	
MgI	TGATGTCTGCAGCCTGTCTC	GCCGTTGTACAAAAGGATTGT	
Rbfox3 (NeuN)	AAGAAGCCTGGGAACCCATA	GGCCCATAGACTGTTCCTACC	
Satb2	TTTAGCCAGCTGGTGGAGAC	CACCTCCCTAGCTTGATTATTCC	
Tbr1	CAAGGGAGCATCAAACAACA	GTCCTCTGTGCCATCCTCAT	
Tuj1	GCGCATCAGCGTATACTACAA	CATGGTTCCAGGTTCCAAGT	
Uchl1	GCCCTTTCCAGTGAACCAT	TGAATTCTCTGCAGACCTTGG	
Unc5C TCCAAGAACTGCACTGATGG		CCACGTAGAGAGCCACATCAT	

**Table S3.** Primers used for qPCR in this study.

Figure		Statistical analysis	Comparison	p-value (n experiments)
Figure 1	В	One-way ANOVA (Dagla, p = 0.085; Mgl, p < 0.0001; Abhd6, p = 0.0029; Abhd12, p = 0.019)	ES vs ND	Post-hoc: p = 0.039 (Daglα, n = 5), p < 0.001 (Mgl, n = 6), p = 0.0012 (Abhd6, n = 4) and p = 0.0092 (Abhd12, n = 4)
	С	One-way ANOVA (Nape-pld, p = 0.37; Faah, p < 0.0001; Abhd4, p = 0.002)	ES vs ND	Post-hoc: p = 0.77 (Nape-pld, n = 0.77), p < 0.0001 (Faah, n = 6) and p < 0.0001 (Abhd4, n = 4)
	Б	One-way ANOVA	ES vs NS	Post-hoc: p = 0.008 (CB <sub>1</sub> , n = 5)
	Ы	(p = 0.021)	ES vs ND	Post-hoc: p < 0.0001 (CB <sub>1</sub> , n = 5)
	E	One-way ANOVA (2AG, p = 0.0064; AEA, p = 0.0015; OEA, p = 0.0074;	ES vs NS ES vs ND	Post-hoc: p = 0.039 (2AG, n = 3), p = 0.0005 (AEA, n = 3), p = 0.0025 (OEA, n = 3) and p = 0.0007 (PEA, n = 3)  Post-hoc: p = 0.0021 (2AG, n = 3), p = 0.027 (AEA, n = 3), p = 0.076 (OEA, n=3) and p = 0.0014 (PEA, n = 3)
	Н	PEA, p = 0.0014) One-way ANOVA	shCtrl+pcDNA vs shCtrl+pcDNA-CB <sub>1</sub>	Post-hoc: p = 0.0018 (BCL11B, n = 3), p < 0.0001 (ER81, n = 3) and p = 0.0004 (SATB2, n = 3)
	В	(BCL11B, p = 0.0003;	shCtrl+pcDNA vs shCB <sub>1</sub> +pcDNA	Post-hoc: p = 0.031 (BCL11B, n = 3), p = 0.0014 (ER81, n = 3) and p = 0.0025 (SATB2, n = 3)
		ER81, p < 0.0001;	shCtrl+pcDNA vs shCB1+pcDNA-CB <sub>1</sub>	Post-hoc: p = 0.0036 (BCL118, n = 3), p = 0.0021 (ER81, n = 3) and p = 0.0003 (SATB2, n = 3)
Figure 3	Н	SATB2 p < 0.0001)	shCB <sub>1</sub> +pcDNA vs shCB1+pcDNA-CB <sub>1</sub>	Post-hoc: p = 0.0002 (BCL11B, n = 3), p < 0.0001 (ER81, n = 3) and p < 0.0001 (SATB2, n = 3)
		One-way ANOVA (Bcl11b, p = 0.0002;	shCtrl+pcDNA vs shCtrl+pcDNA-CB <sub>1</sub>	Post-hoc: p = 0.0019 (Bcl11b, n = 4), p = 0.0011 (Er81, n = 4), p = 0.0014 (Satb2, n = 4) and p = 0.030 (Cux2, n = 4)
	c	Er81, p = 0.0002;	shCtrl+pcDNA vs shCB <sub>1</sub> +pcDNA	Post-hoc: p = 0.019 (Bcl11b, n = 4), p = 0.040 (Er81, n = 4), p < 0.0001 (Satb2, n = 4) and p = 0.0014 (Cux2, n = 4)
		Satb2, p < 0.0001; Cux2, p = 0.0002) One-way ANOVA	shCB <sub>1</sub> +pcDNA vs shCB1+pcDNA-CB <sub>1</sub>	Post-hoc: p = 0.012 (Bcl11b, n = 4), p = 0.011 (Er81, n = 4), p < 0.0001 (Satb2, n = 4) and p = 0.0011 (Cux2, n = 4)
	В	(BCL11B, p = 0.0064; ER81, p = 0.029; SATB2, p = 0.010)	Veh vs JZL-184	Post-hoc: p = 0.0023 (BCL11B, n = 3), p = 0.0075 (ER81, n = 3-4) and p = 0.0057 (SATB2, n = 3-4)
		One-way ANOVA (BCL11B, p < 0.0001;	Veh-shCtrl vs JZL-shCtrl	Post-hoc: p < 0.0001 (BCL11B, n = 3), p < 0.0001 (ER81, n = 3) and p < 0.0001 (SATB2, n = 3)
Figure 4	c	ER81, p < 0.0001;	Veh-shCtrl vs Veh-shCB <sub>1</sub>	Post-hoc: p = 0.0095 (BCL11B, n = 3), p = 0.0003 (ER81, n = 3) and p = 0.0002 (SATB2, n = 3)
	Н	SATB2, p < 0.0001) One-way ANOVA	Veh-shCtrl vs JZL-shCtrl	Post-hoc: p = 0.012 (BCL11B, n = 3), p = 0.0003 (ER81, n = 3) and p = 0.0012 (SATB2, n = 3)  Post-hoc: p < 0.0001 (BcL11B, n = 2), p = 0.0004 (Er81, n = 3), n = 0.0004 (Satb2, n = 3) and p = 0.0077 (Cuv2, n = 2)
		(Bcl11b, p < 0.0001;	Veh-shCtrl vs JZL-shCtrl Veh-shCtrl vs Veh-shCB <sub>1</sub>	Post-hoc: p < 0.0001 (Bcl11b, n = 3), p = 0.0004 (Er81, n = 3), p = 0.0004 (Satb2, n = 3) and p = 0.0077 (Cux2, n = 3)  Post-hoc: p = 0.0031 (Bcl11b, n = 3), p = 0.0046 (Er81, n = 3), p < 0.0001 (Satb2, n = 3) and p = 0.0058 (Cux2, n = 3)
	D	Er81, p < 0.0001; Satb2, p < 0.0001;		
		Cux2, p = 0.0002)	Veh-shCtrl vs JZL-shCB <sub>1</sub>	Post-hoc: p = 0.0096 (Bcl11b, n = 3), p = 0.015 (Er81, n = 3), p < 0.0001 (Satb2, n = 3) and p = 0.0063 (Cux2, n = 3)
Figure 5	В	One-way ANOVA (BCL11B, p = 0.0092; ER81, p = 0.0003; SATB2, p = 0.15)	Veh vs THC	Post-hoc: p = 0.0057 (BCL11B, n = 5), p = 0.0004 (ER81, n = 4) and p = 0.039 (SATB2, n = 4)
	С	One-way ANOVA (Dcc, p = 0.071; Unc5C, p = 0.10)	Veh vs THC	Post-hoc: p = 0.016 (Dcc, n = 5) and p = 0.038 (Unc5C, n = 4)
Figure C	С	Student's t test Welch's test	Veh vs THC	p = 0.0004 [AP threshold, n = 42 (Veh) and n = 44 (THC) cells] and p < 0.0001 [Inward current, n = 42 (Veh) and n = 44 (THC) cells] p < 0.0001 [AP amplitude, n = 42 (Veh) and n = 44 (THC) cells]
Figure 6	F	Student's t test	Veh vs JZL-184	p < 0.0001 [AP threshold, n = 9 (Veh) and n = 12 (JZL) cells] and p = 0.0047 [Inward current, n = 29 (Veh) and n = 41 (JZL) cells]
	H	Welch's test One-way ANOVA	Veh vs HU-210	p < 0.0001 [AP amplitude, n = 29 (Veh) and n = 41 (JZI) cells]
Figure 7	b	(BCL11B, p < 0.0001;		Post-hoc: p < 0.0001 [BCL11B, n = 13 (Veh) and n = 24 (HU-210) ventricles] and p = 0.0003 [SATB2, n = 12 (Veh) and n = 10 (HU-210) ventricles]
_	L	SATB2, p < 0.0001)	Veh vs THC	Post-hoc: p = 0.0003 [BCL11B, n = 13 (Veh) and n = 24 (THC) ventricles] and p < 0.0001 [SATB2, n = 12 (Veh) and n = 10 (THC) ventricles]
Figure S1	C	Student's t test	Glu vs GABA	p < 0.0001 (n = 4)
	A	One-way ANOVA (p < 0.0001)	-	Post-hoc: p = 0.0016 (ES-shCtrl vs ES-shCB <sub>1</sub> , n = 3), p = 0.0016 (ES-shCtrl vs ND-shCtrl, n = 3) and p = 0.0001 (ND-shCtrl vs ND-shCB <sub>1</sub> , n = 3)
	В	One-way ANOVA (p < 0.0001)	-	Post-hoc: $p = 0.0007$ (shCtrl+pcDNA vs shCtrl+pcDNA-CB <sub>1</sub> , $n = 4$ ), $p = 0.006$ (shCtrl+pcDNA vs shCB <sub>1</sub> +pcDNA, $n = 4$ ) and $p = 0.0003$ (shCB <sub>1</sub> +pcDNA vs shCB <sub>1</sub> +pcDNA-CB <sub>1</sub> , $n = 4$ )
Figure S2	С	One-way ANOVA (p = 0.0005)	-	Post-hoc: $p = 0.0015$ (shCtrl+pcDNA vs shCtrl+pcDNA-CB1, $p = 0.021$ (shCtrl+pcDNA vs shCB1+pcDNA, $p = 0.021$ (shCtrl+pcDNA vs shCB1+pcDNA, $p = 0.021$ (shCB1+pcDNA vs shCB1+pcDNA-CB1, $p = 0.021$ (shCB1+pcDNA vs shCB1+pcDNA-CB1, $p = 0.021$ (shCB1+pcDNA vs shCB1+pcDNA-CB1, $p = 0.021$ (shCB1+pcDNA vs shCB1+pcDNA vs shCB1+pcDNA-CB1, $p = 0.021$ (shCTrl+pcDNA vs shCB1+pcDNA, $p = 0.021$ (shCTrl+pcDNA, $p = 0.021$ (shCTrl+pcDNA, $p = 0.021$ (shCTrl+pcDNA, $p = 0.021$ (shCTrl+pcDNA, $p =$
	b	One-way ANOVA	-	Post-hoc: p = 0.0002 (shCtrl+pcDNA vs shCtrl+pcDNA-CB., n = 3), p = 0.0014 (shCtrl+pcDNA vs shCB <sub>1</sub> +pcDNA, n = 3)
	Н	(p < 0.0001) One-way ANOVA		and p = $0.0001$ (shCB <sub>1</sub> +pcDNA vs shCB <sub>1</sub> +pcDNA-CB <sub>1</sub> , n = 3) Post-hoc: p < $0.0001$ (Veh-shCtrl+pcDNA vs THC-shCtrl+pcDNA, n = 3), p < $0.0001$ (Veh-shCtrl+pcDNA-CB <sub>1</sub> vs THC-shCtrl+pcDNA-CB <sub>1</sub> , n = 3)
	E	(p < 0.0001)	-	and p = 0.0087 (Veh-shCB1+pcDNA-CB <sub>1</sub> vs THC-shCB1+pcDNA-CB <sub>1</sub> , n = 3)
	С	Student's t test	shControl vs shCB <sub>1</sub>	p = 0.0004 (BCL11B, n =6) and p = 0.0007 (SATB2, n =6)
Figure S3	Б	Student's t test	shControl vs shCB <sub>1</sub>	p = 0.0015 (BCL11B, n = 3) and p = 0.010 (SATB2, n = 3)
0	E	Student's t test	shControl vs shCB <sub>1</sub>	p = 0.003 (CB <sub>1</sub> , n = 4), p = 0.034 (Tuj1, n = 3), p = 0.0026 (Bcl11b, n = 4) and p = 0.0014 (Satb2, n = 4)
	-	Student's t test		
	Α	One-way ANOVA	Veh vs JZL-184  Veh-shControl vs JZL-shCtrl	p = 0.023 (2AG, n = 3) and p = 0.007 (AEA, n = 3)  Post-hoc: p < 0.0001 (BCL11b, n = 3), p = 0.004 (ER81, n = 3) and p = 0.0001 (SATB2, n = 3)
Figure S4		(BCL11B, p < 0.0001;	Ven-shControl vs J2L-shCtri Veh-shControl vs Veh-shCB <sub>1</sub>	Post-hoc: p < 0.0001 (BCL11B, n = 3), p = 0.004 (ER81, n = 3) and p = 0.0001 (SATB2, n = 3)  Post-hoc: p < 0.0001 (BCL11B, n = 3), p = 0.0068 (ER81, n = 3), and p < 0.0001 (SATB2, n = 3)
	c	ER81, p = 0.0001; SATB2, p < 0.0001)	Veh-shControl vs JZL-shCB <sub>1</sub>	Post-hoc: p < 0.0001 (BCL11B, n = 3), p = 0.0026 (ER81, n = 3) and p < 0.0001 (SATB2, n = 3)
Figure S5		Student's t test	Veh vs HU-210	p < 0.0001 [NeuN, n = 5 (Veh) and n = 4 (HU-210)], p = 0.0068 [Bcl11b, n = 5 (Veh) and n = 5 (HU-210)], p = 0.010 [Er81, n = 4 (Veh) and n = 4 (HU-210)], p < 0.0001 [Satb2, n = 5 (Veh) and n = 5 (HU-210)], and p = 0.010 [Cux2, n = 5 (Veh) and n = 4 (HU-210)]
	Ε	One-way ANOVA (NeuN, p = 0.0029; Bc111b, p = 0.10; Er81, p = 0.059; Satb2, p = 0.032; Cux2, p = 0.15)	Veh vs THC	Past-hac: p = 0.0024 [NeuN, n = 5 (Veh) and n = 5 (THC)], p = 0.043 [Bcl11b, n = 5 (Veh) and n = 4 (THC)], p = 0.046 [Er81, n = 4 (Veh) and n = 3 (THC)], p = 0.020 [Satb2, n = 5 (Veh) and n = 3 (THC)], and p = 0.020 [Satb2, n = 5 (Veh) and n = 4 (THC)] and p = 0.047 [Cux2, n = 5 (Veh) and n = 5 (THC)]
	А	One-way ANOVA (Bcl11b, p = 0.0008; Dcc, p = 0.0048)	Veh vs THC	Post-hoc: p = 0.0001 (Bcl11b, n = 6) and p = 0.0098 (Dcc, n = 4)
Figure S6	В	One-way ANOVA (Bcl11b, p < 0.0001; Dcc, p = 0.0034)	Veh vs JZL-184	Post-hoc: p < 0.0001 (Bcl11b, n = 6) and p = 0.0024 (Dcc, n = 4)
	С	One-way ANOVA (p < 0.0001)	-	Post-hoc: p = 0.0009 (pcDNA-Veh vs pcDNA-HU, n = 3), p = 0.018 (pcDNA-Veh vs Satb2-HU, n = 3), p = 0.0062 (pcDNA-Veh vs Ski-Veh, n = 3) and p = 0.0004 (pcDNA-Veh vs Satb2+Ski-Veh, n = 3)
	D	One-way ANOVA (p < 0.0001)		Post-hoc: p = 0.0003 (Veh vs HU, n = 6), p = 0.0003 [Veh vs dbAMPc+HU, n = 6 (Veh) and n = 3 (dbAMPc+HU]], p = 0.032 [Veh vs SP+HU, n = 6 (Veh) and n = 3 (SP+HU)], p = 0.0008 [Veh vs Rapa+HU, n = 6 (Veh) and n = 4 (Rapa+HU)], p = 0.0009 [Veh vs MG+HU, n = 6 (Veh) and n = 4 (MG+HU)], p = 0.0005 [HU-210 vs UO+HU, n = 6 (HU-210) and n = 4 (MG+HU)], p = 0.0005 [HU-210 vs UO+HU, n = 6 (HU-210) and n = 4 (UO+HU)], p = 0.0016 [HU-210 vs AKIX+HU, n = 6 (HU-210) and n = 4 (AKIX+HU)], p = 0.018 [HU-210 vs SP5600125, n = 6 (HU-210) and n = 3 (SP5600125)], p = 0.0011 [HU-210 vs AM-251, n = 6 (Veh) and n = 3 (AM-251)] and p = 0.0033 [HU-210 vs AM+HU, n = 6 (Veh) and n = 3 (AM+HU)],

**Table S4.** Detailed statistical analyses per figure, containing relevant test performed, p-values and number of experiments.