

Fig. S1. Maternal blood THC levels.

The level of THC plus THC metabolites (11-hydroxy-THC and 11-nor-9-carboxy-THC) was measured over a 60-hour time course after IP administration of 15 mg/kg THC. Serum was collected and analyzed by ELISA. Values are means \pm SD, N=4-10 mice per time point.

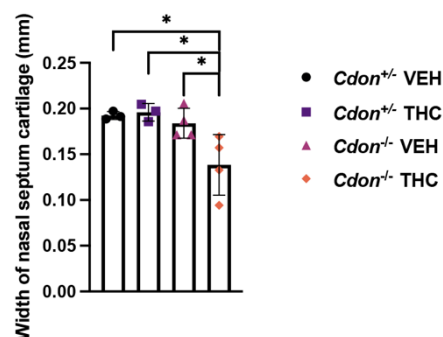


Fig. S2. Reduced width of the nasal septum cartilage in THC-treated *Cdon*^{-/-} embryos.

The width of nasal septum of embryos was quantified by measuring the widest point in H&E sections taken at level A" in Figure 1. Three or four serial sections per embryo at this level were measured and each point represents the mean \pm SD, N=3-4 embryos. Pregnant females were administered 15 mg/kg THC or VEH at E7.5 and analyzed at E14. *, p<0.05 with ordinary one-way ANOVA with Tukey's multiple comparison test.

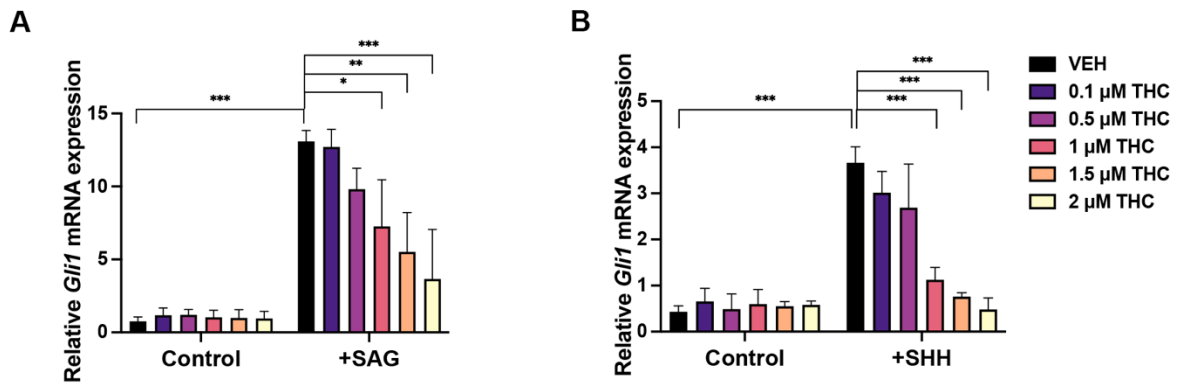


Fig. S3. THC suppresses SHH-induced *Gli1* expression in MEFs.

A. NIH3T3 cells were treated with 50 nM SAG and the indicated concentrations of THC for 24 hr.

B. MEFs were treated with 5 ng/ml SHH and the indicated concentrations of THC for 24 hr.

Relative *Gli1* mRNA expression was analyzed by qRT-PCR. Values are means \pm SD, N=3. *, **, ***, $p < 0.05$, $p < 0.01$, $p < 0.001$ with ordinary one-way ANOVA with Tukey's multiple comparison test.

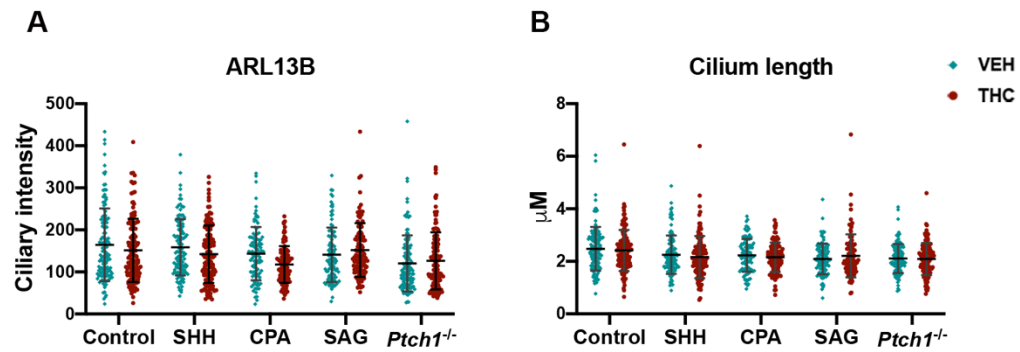
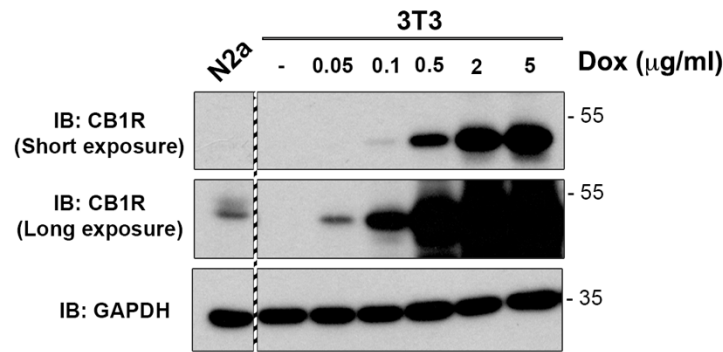
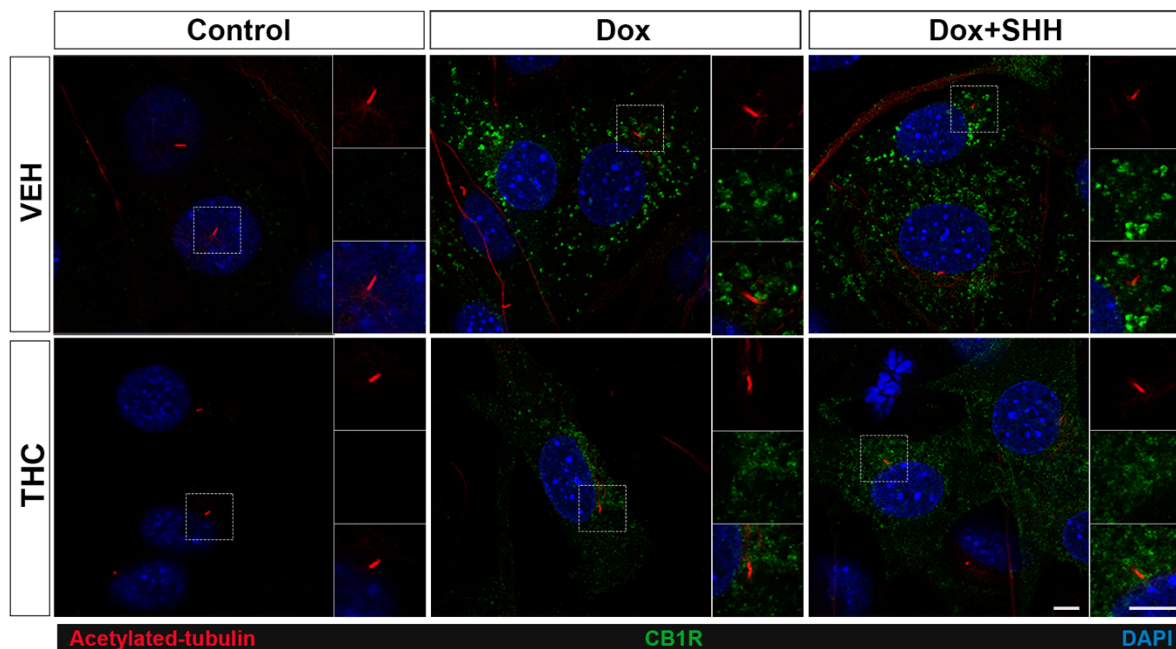


Fig. S4. THC does not grossly affect primary cilia.

A. Fluorescence intensity for the primary cilia marker, ARL13B.

B. Primary cilia length.

Each point represents an individual cell collated from at least 3 independent experiments.

A**B****Fig. S5. NIH3T3 cells with inducible expression of CB1R.**

A. NIH3T3 cells were infected with a lentiviral vector encoding doxycycline-inducible expression of CB1R. Cells were treated with the indicated doses of doxycycline (Dox) and harvested for western blot analysis 24 hours later. N2a, Neuro-2a cells, a cell line that expresses CB1R endogenously. The samples are from the same gel and membrane. The dashed region indicates lanes not shown. B. Exogenously expressed CB1R does not localize to primary cilia in NIH3T3 cells, with or without SHH stimulation. Primary cilia are marked by acetylated tubulin. Scale bars, 5 μm.

Table S1. Frequency of THC-induced HPE in *Cdon*^{-/-} embryos. Related to Figure 1.

Treatment	# <i>Cdon</i> ^{+/-} or <i>Cdon</i> ^{+/-} embryos	# <i>Cdon</i> ^{+/-} or <i>Cdon</i> ^{+/-} embryos with HPE	# <i>Cdon</i> ^{+/-} embryos	# <i>Cdon</i> ^{-/-} embryos with HPE (%)	P value, Fisher's exact test (vs.VEH)
Vehicle	29	0	15	0	
THC (5 mg/kg)	33	0	12	2 (16.7)	>0.05
THC (10 mg/kg)	32	0	13	4 (30.8)	0.03
THC (15 mg/kg)	27	0	11	4 (36.4)	0.02

Table S2. Numbers of FOXA2⁺, NKX2.2⁺ and OLIG2⁺ cells in the VNT. Related to Figure 2.

E9.5	<i>Cdon</i> ^{+/-} VEH	<i>Cdon</i> ^{+/-} THC	<i>Cdon</i> ^{-/-} VEH	<i>Cdon</i> ^{-/-} THC
FOXA2 ⁺ cells	24.5 ± 2.7	23.5 ± 2.8	24.1 ± 4.7	12 ± 2.1
NKX2.2 ⁺ cells	32.2 ± 4.5	32.8 ± 4.1	32.7 ± 7.1	20.4 ± 3.6
OLIG2 ⁺ cells	98.9 ± 15.4	106.3 ± 26.5	97.8 ± 18.5	77.7 ± 20.7
Whole neural tube	317.8 ± 18.7	327.1 ± 8.4	320.5 ± 14.1	307.4 ± 32.5

N=5 embryos for each group, 3-6 sections per mouse