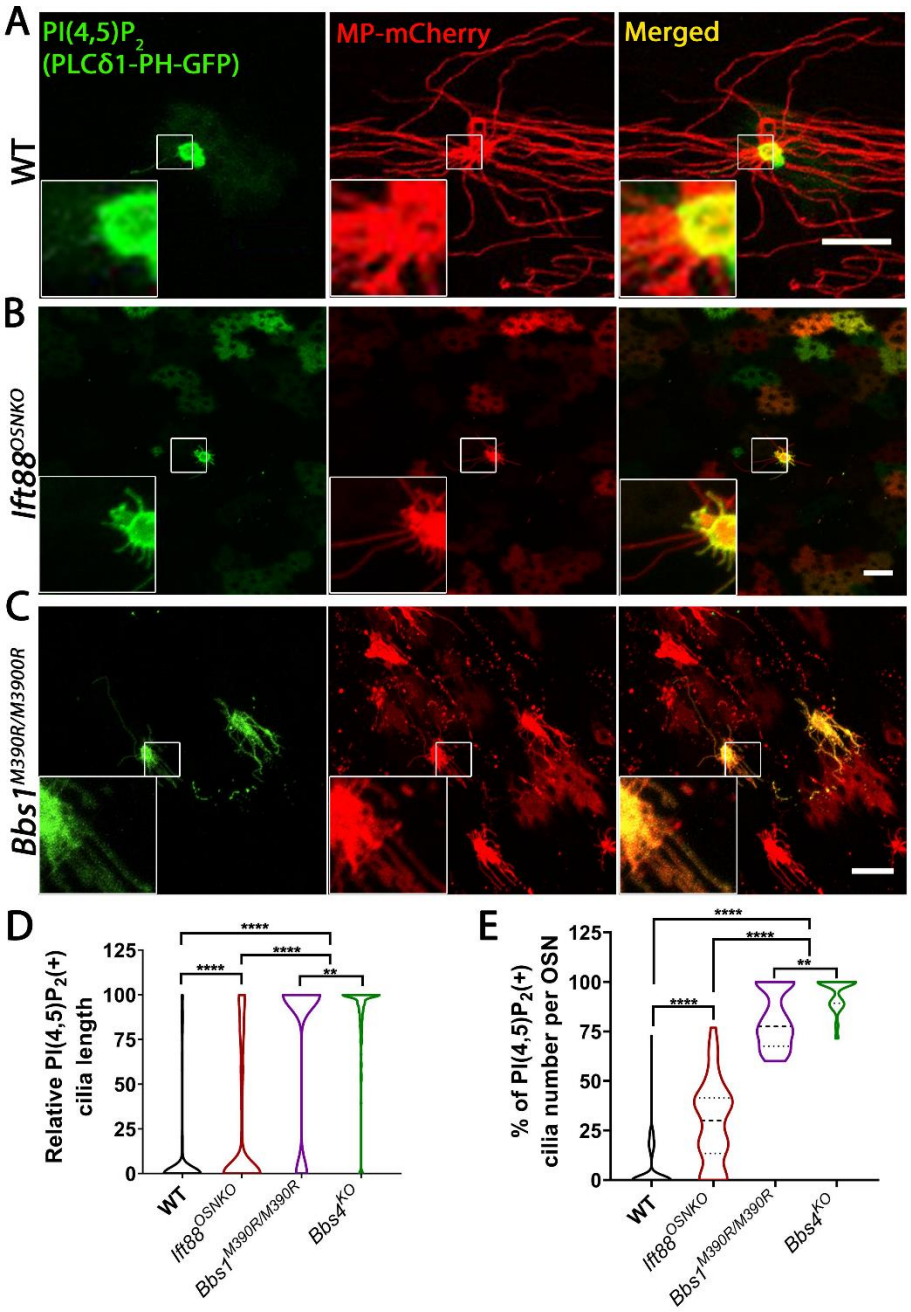
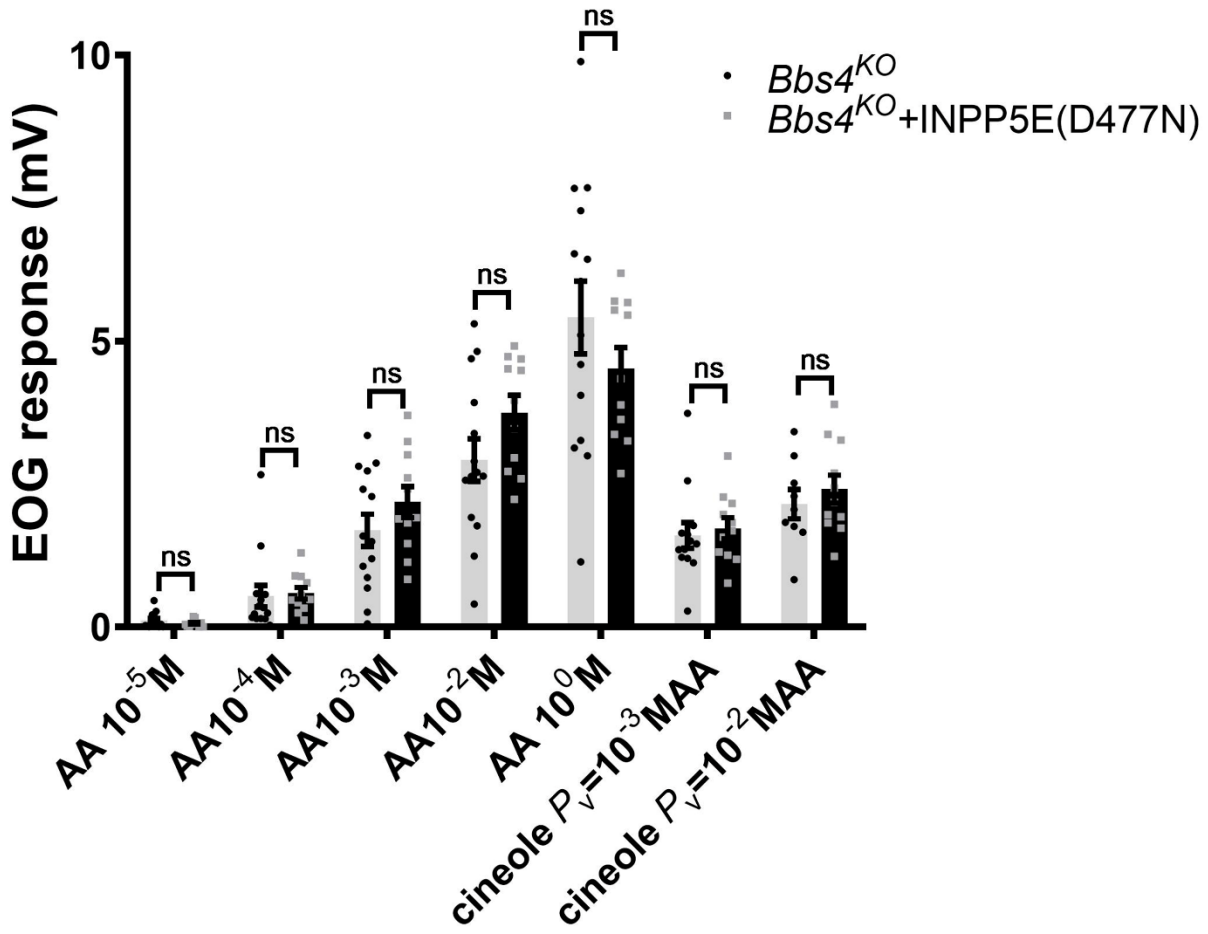
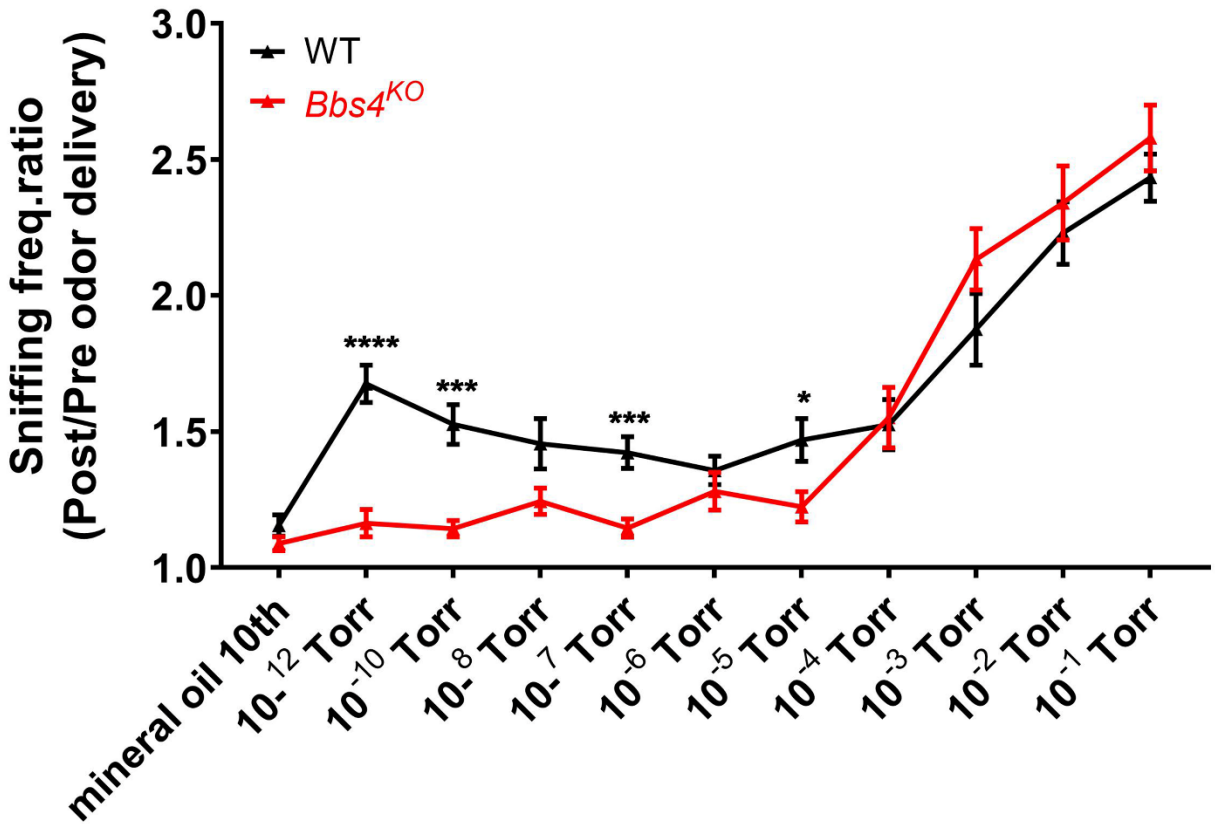
Supplemental Material.



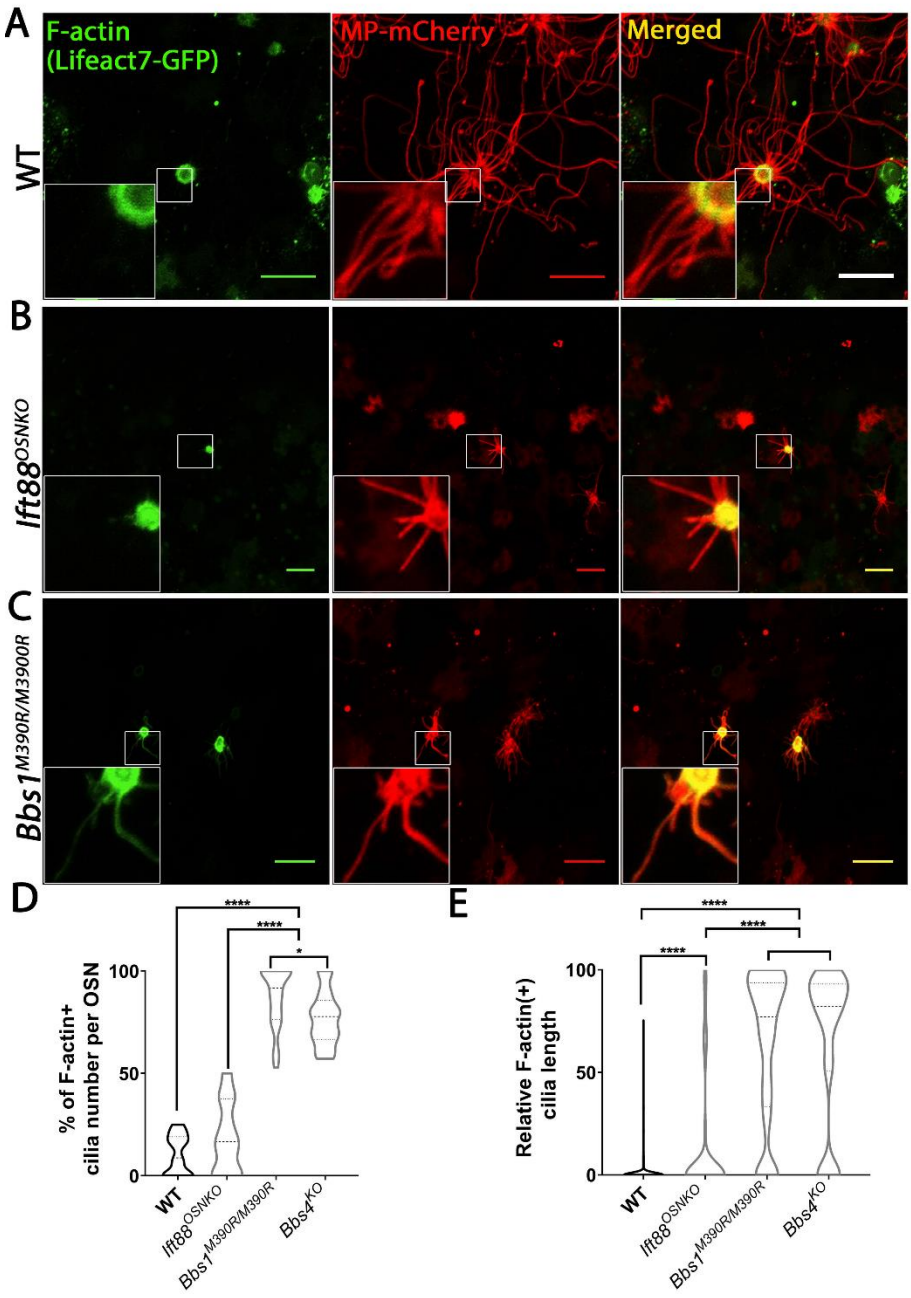
Supplementary Figure 1. PI(4,5)P_2 ciliary localization in other ciliopathy models. Representative *en face* images of PI(4,5)P_2 (PLCδ1-PH-GFP) in the WT **(A)**, *Ift88*^{OSNKO}**(B)**, and *Bbs1*$^{M390R/M390R}$ **(C)** olfactory cilia. The mice were infected with PLCδ1PH-GFP and MP-mCherry adenovirus and used for *en face* imaging. MP-mCherry was used to label the full length of the olfactory cilia. PLCδ1-PH-GFP was used to label the endogenous PI(4,5)P_2. Scale 10 μm. **(D)** Quantification data showing that the relative PI(4,5)P_2 positive cilia length (PI(4,5)P_2 positive cilia length/ full cilia length*100) was increased in the BBS group compared to the WT and *Ift88*^{OSNKO} group, One way ANOVA, ****p<0.0001. **(E)** The percentage of PI(4,5)P_2 positive cilia number (PI(4,5)P_2 positive cilia number/total cilia number*100) was increased in the BBS group compared to the WT and *Ift88*^{OSNKO} group. One way ANOVA, ****p<0.0001. Values represent means ± SEM.



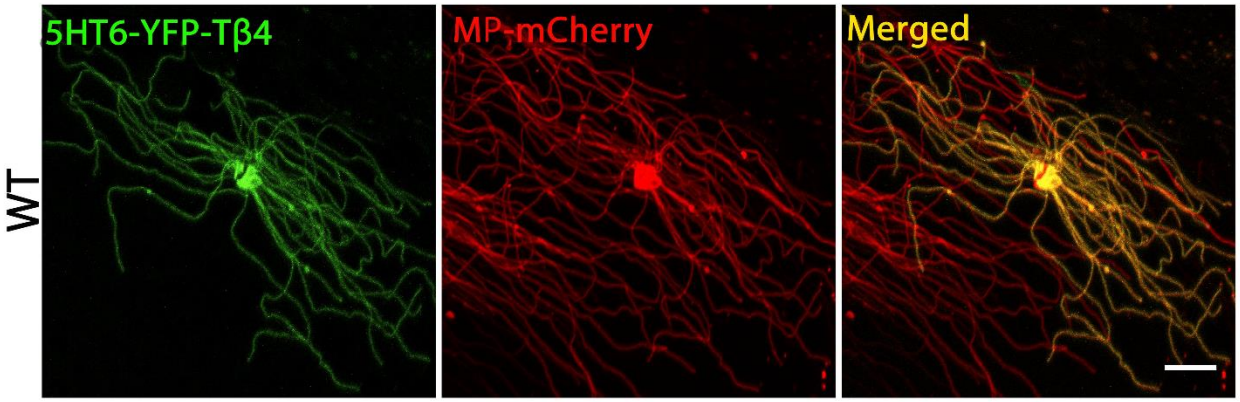
Supplementary Figure 2. Ectopic expression of INPP5E(D477N) does not rescue the impaired peripheral odor detection in *Bbs4^{KO}* mice. Quantified EOG data of 1month *Bbs4^{KO}* mice and AV-GFP-INPP5E(D477N) treated *Bbs4^{KO}* mice in response to different concentrations of amyl acetate (AA), and cineole. EOG response was not restored by ectopic expression of INPP5E(D477N). PV: vapor pressure. (*Bbs4^{KO}*: n=10 animals; *Bbs4^{KO}*+INPP5E(D477N): n=11 animals). Multiple *t-test*, ns: non-significant. Values represent means ± SEM.



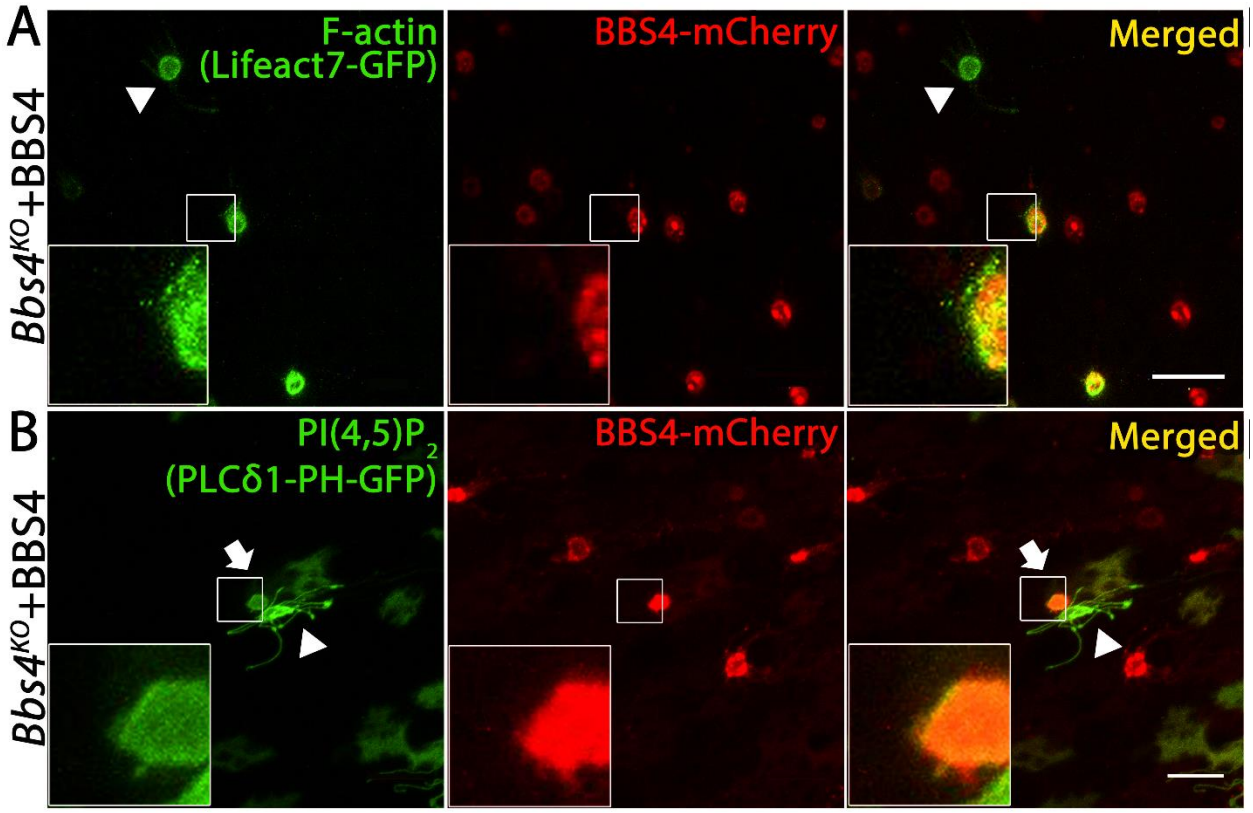
Supplementary Figure 3. *Bbs4^{KO}* mice exhibit a higher odor detection threshold. Odor detection thresholds of WT mice (n=13) and *Bbs4^{KO}* mice (n=12) (average of 4 odors / mouse) from an ascending staircase paradigm indicating that *Bbs4^{KO}* mice had reduced odorant sensitivity (increased detection thresholds). Each mouse was delivered 10 trials of vaporized mineral oil followed by presentations of an odorant at 10^{-12}, 10^{-10}, 10^{-8}, 10^{-7}, 10^{-6}, 10^{-5}, 10^{-4},10^{-3}, 10^{-2}, and 10^{-1}Torr. Sniffing frequency ratios (sniffing Hz pre vs during odor) were compared between groups. One way ANOVA, ****p < 0.0001. ***p < 0.001. **p < 0.01.*p < 0.05. Values represent means ± SEM.



Supplementary Figure 4. F-actin ciliary localization in other ciliopathy models. Representative en face images of F-actin (Lifeact7-GFP) in the WT **(A)**, *Ift88*^{OSNKO} **(B)**, and *Bbs1*$^{M390R/M390R}$ **(C)** olfactory cilia. The mice were infected with MP-mCherry and Lifeact7-GFP adenovirus and used for en face imaging. MP-mCherry was used to label the full length of the olfactory cilia. Lifeact7-GFP was used to label the endogenous F-actin. Scale 10 μm. **(D)** Quantification data showing that the percentage of F-actin positive cilia number (F-actin positive cilia number/total cilia number*100) was increased in the BBS group compared to the WT and *Ift88*^{OSNKO} group. One way ANOVA, *p < 0.05, ****p<0.0001, Values represent means ± SEM. **(F)** The relative F-actin positive cilia length (F-actin positive cilia length/ full cilia length*100) was increased in the BBS group compared to the WT and *Ift88*^{OSNKO} group. One way ANOVA, ****p<0.0001, Values represent means ± SEM



Supplementary Figure 5. Ectopically expressed 5HT6-YFP-Thymosinβ4 distributes to the full length of the olfactory cilia. Representative *en face* confocal microscopy images of ectopically co-expressing 5HT6-YFP-Thymosinβ4 and MP-mCherry in the WT OSNs. MP-mCherry was used to label the full length of the olfactory cilia. Scale 10 μm.



Supplemental Figure 6. Normal F-actin and PI(4,5)P_2 ciliary distribution is restored by *Bbs4* single gene replacement in *Bbs4*^{KO}. (A) Representative *en face* images of F-actin (Lifeact7-GFP) in BBS4 rescued *Bbs4*^{KO} olfactory cilia. F-actin redistributed into the olfactory cilia in non-BBS4 expressed OSN (arrowheads). *Bbs4* single gene replacement excludes F-actin from olfactory cilia in *Bbs4*^{KO} mice. Scale 10 μm. **(B)** *En face* images of PI(4,5)P_2 (PLCδ1-PH-GFP) in *BBS4* rescued *Bbs4*^{KO} OSN cilia. The expression of BBS4-mCherry blocked PI(4,5)P_2 ciliary distribution (arrow). Arrowhead indicating the non-BBS4-mCherry infected OSN still had PI(4,5)P_2 ciliary redistribution. Scale 10 μm.