Supporting Information

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Fig. S1. CRE-mediated recombination in OSNs of transgenic OMP-CRE mice. OMP-CRE mice were crossed to a reporter mouse line (R26-mCherry-Rpl10a) that carry a mCherry reporter gene under the transcriptional control of a floxed (ROSA)265or locus (38). (A–C) A double mCherry and OMP immunohistochemical analysis showing that mCherry expression, activated by CRE-mediated recombination, is specific to OMP-positive OSNs.



Fig. S2. Genetic and pharmacological inhibition of Smo does not affect body weight. (A) Body weight change of PD0–PD15 Smo^{+/+} and Smo^{+/-} mice. Values represent mean \pm SEM, n = 7, n.s., not significant. (B) Body weight of vismodegib-treated and vehicle (DMSO)-treated control mice during the treatment period (PD12–PD15). Values represent mean \pm SEM, n = 12. n.s., not significant.



Fig. S3. OSN differentiation, survival, and ciliary expression of Ac-Tubulin, AC3, $G\alpha$ olf, and CNGA2 are not affected by vismodegib. Double immunohistochemical analyses showing similar expression in DMSO (vehicle)-treated control mice and vismodegib-treated mice of (A) STMN2 and OMP in immature and mature OSNs, respectively. (B) Ac-Tubulin in cilia, (C) AC3, (D) $G\alpha$ olf, (E) CNGA2, and (F) activated caspase-3. (G and H) Quantification of OSNs immunopositive for activated caspase-3, M71/M72, and MOR28. All values represent mean \pm SEM, n = 3. n.s., not significant.

A Z d



Fig. S4. OR-positive puncta do not colocalize with Rab11A, Golgi markers, and Caveolin. Double immunohistochemical analyses of OSNs, in vismodegibtreated mice, with anti-M71/M72 antibody and antibodies for (*A*) Rab11A, (*B*) GM130 (*cis*-Golgi marker), (*C*) TGN46 (*trans*-Golgi marker), and (*D*) Caveolin. In each panel, the three images to the *Right* are a close-up of the area that is boxed in the image to the *Left*.

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Fig. S5. Olfr412-positive puncta that colocalize with CNGA2 do not increase in number. (*A*) Identification of Olfr412-positive puncta in vismodegib-treated mice that colocalize with CNGA2 (arrow in *A1*) as well as Olfr412-positive puncta that do not colocalize with CNGA2 (arrowheads in *A2*). In each panel, the three images to the *Right* are a close-up of the area that is boxed in the image to the *Left*. (*B* and C) Quantification of Olfr412-positive puncta that are negative and double-positive CNGA2 in vehicle (DMSO)-treated, visomdegib-treated, Smo^{+/+}, and Smo^{fl/+} mice. All values represent mean \pm SEM. The *n* values in *B* and C are 43 (DMSO treated), 46 (vismodegib treated), 52 (Smo^{+/+}), and 63 (Smo^{fl/+}). Three pairs of mice for both the DMSO/vismodegib comparison and the Smo^{+/+}/Smo^{fl/+} comparison were analyzed. ***P* < 0.01. n.s., not significant.

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