Supplementary Materials

Supplementary Figures

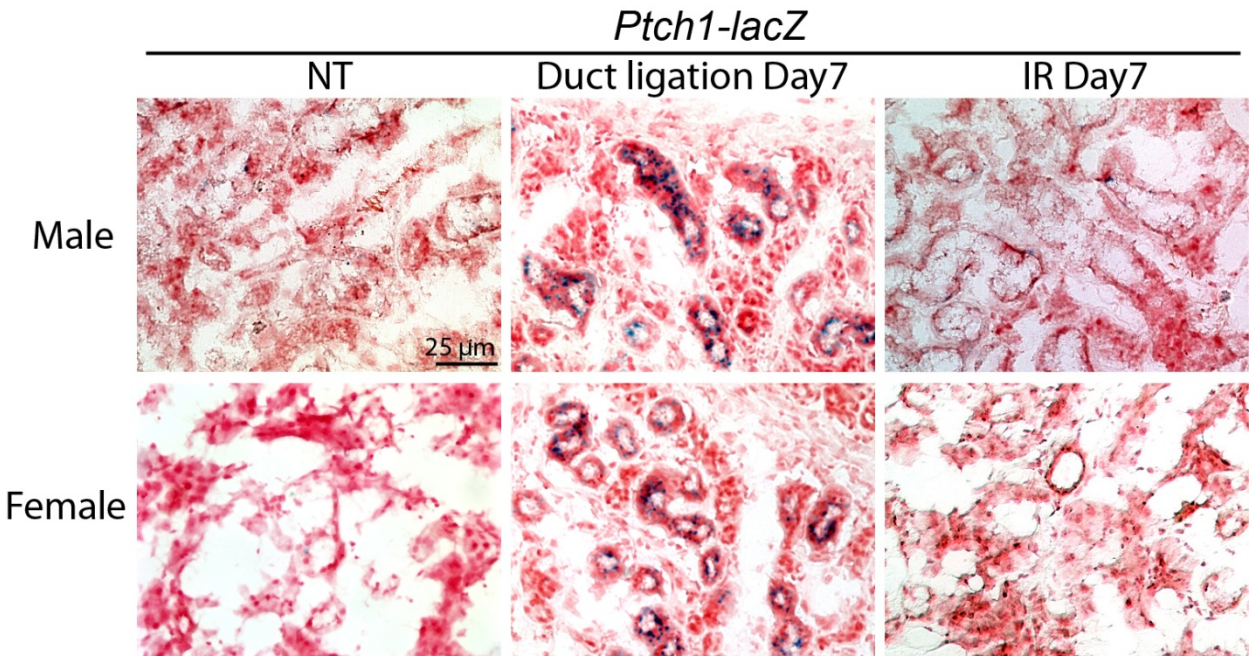

Fig. S1. X-gal staining of SMG sections from *Ptch1-lacZ* mice non-treated (NT), 7 days after ligation of main excretory ducts or IR.

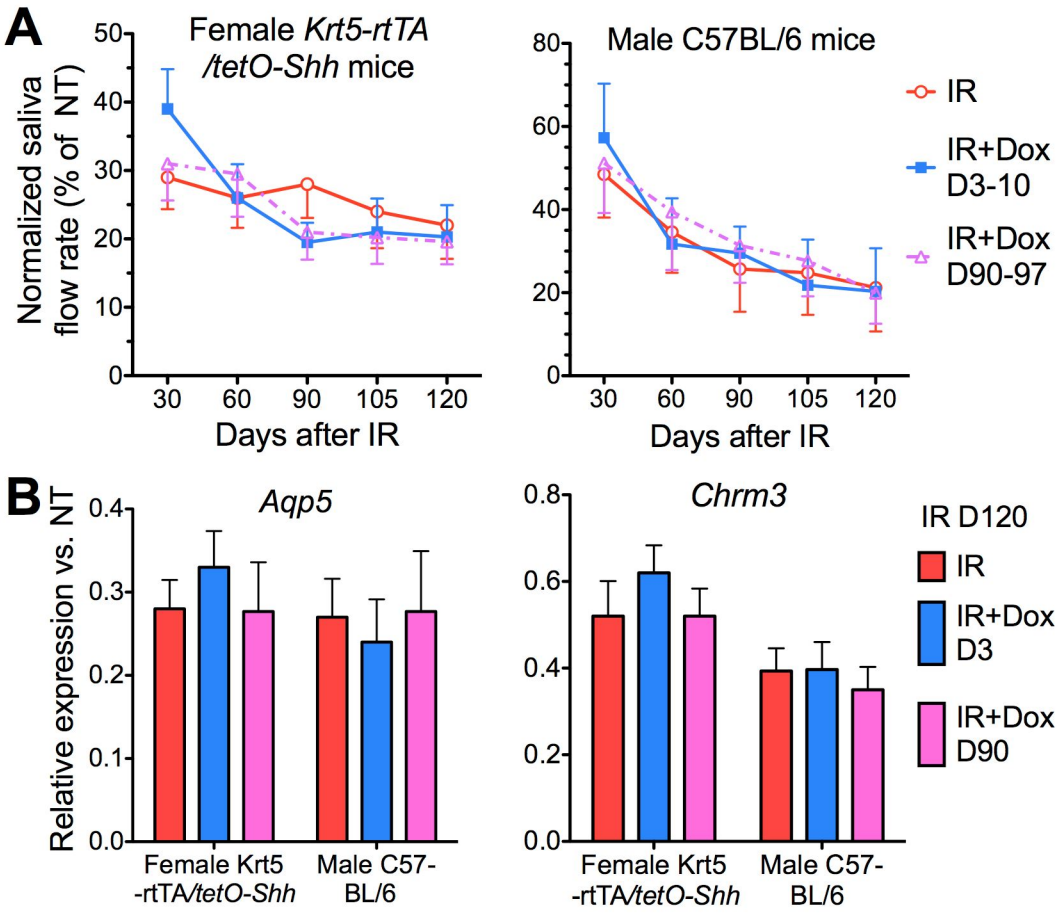

Fig. S2. 7 days of Dox treatment did not rescue IR-induced hyposalivation in female *Krt-rtTA/tetO-Shh* mice and male wild type mice. (**A**) Relative saliva flow rate. (**B**) Relative expression of acinar markers *Aqp5* and *Chrm3* determined by qRT-PCR.

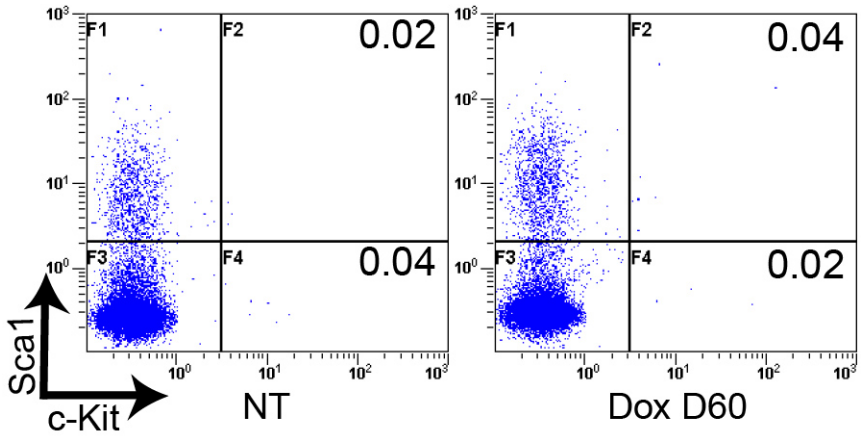

Fig. S3. Transient Hh activation has no long-term effect on percentage of putative salivary stem/progenitor cells. The percentages of c-Kit^{+}/Sca-1^{+} cells in SMGs of control mice (NT) and Krt5-rtTA/tetO-Shh mice on Day 60 after 7 days of Dox induction is 0.046±0.015% vs. 0.093±0.044%, n = 3, P = 0.199.

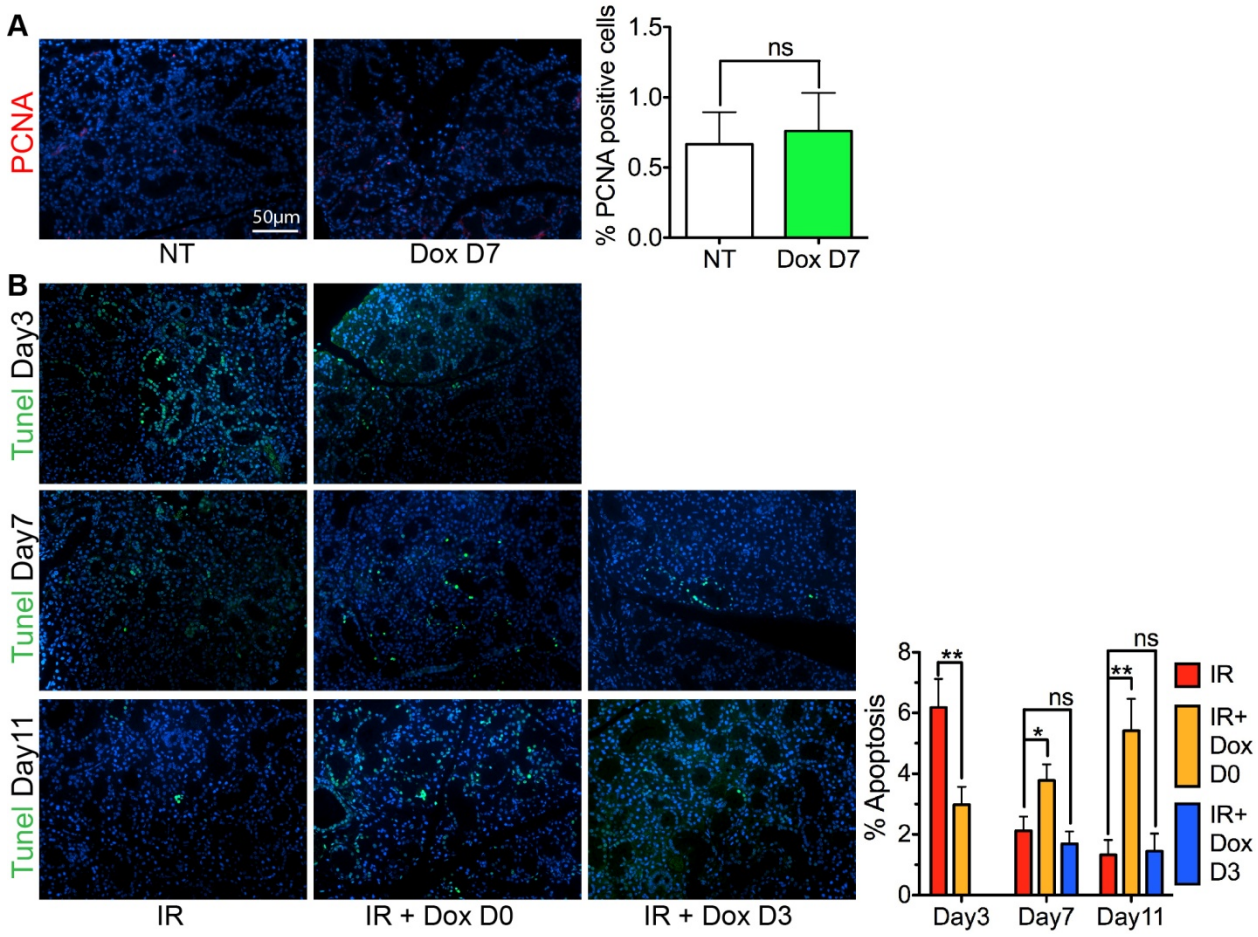

Fig. S4. Effects of transient Hh activation on proliferation and IR-induced apoptosis of SMG cells.

(A) PCNA staining of SMG sections from non-treated Krt5-rtTA/tetO-Shh mice (NT) or those induced with Dox for7 days (Dox D7). (B) Tunel staining of SMG sections from Krt5-rtTA/tetO-Shh mice treated with irradiation alone (IR) or with 7 days Dox induction starting on Day 0 or 3 after IR. Tunel- or PCNA-positive cells were quantified as the percentage of positive areas in DAPI-positive areas with NIS-Elements AR software (n=5, ns: not significant, *: $P< 0.05$. **: $P<0.01$).

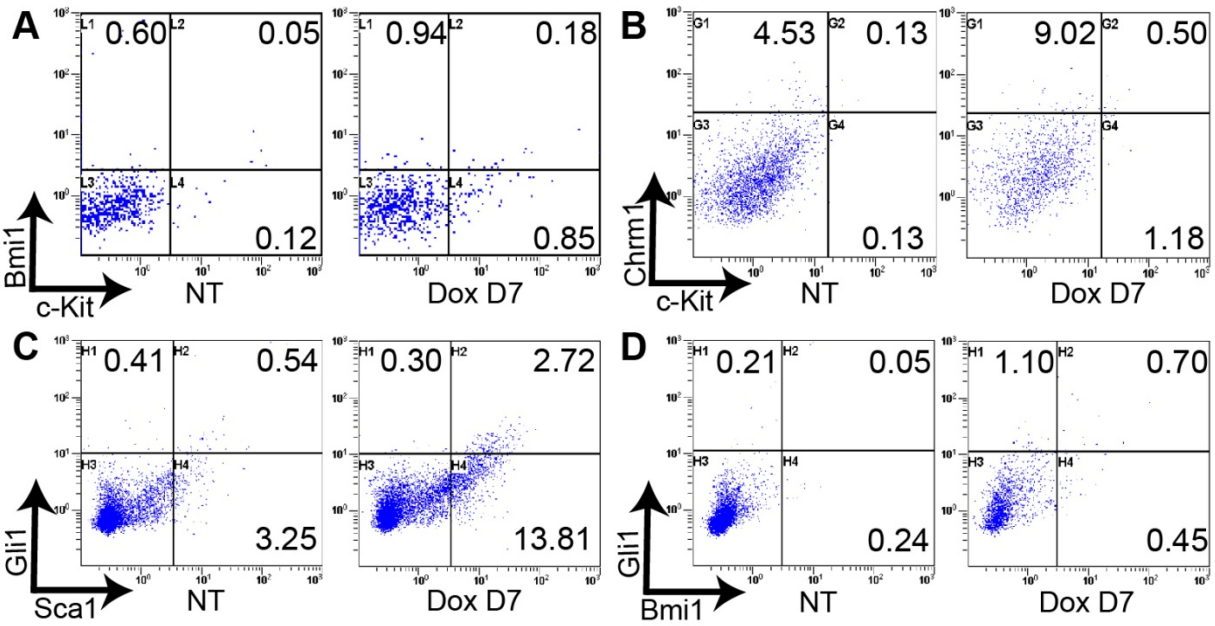

Fig. S5. Co-expression of makers for salivary stem/progenitor cells with Hh target genes. The percentages of c-Kit$^+$/Bmi1$^+$, c-Kit$^+$/Chrm$^+$, Gli1$^+$/Sca1$^+$ or Gli1$^+$/Bmi1$^+$ cells in SMGs of *Krt5-rtTA/tetO-Shh* mice induced with Dox for 7 days (Dox D7) were significantly higher than that in non-treated mice (NT) ($n = 3$, $P < 0.05$).

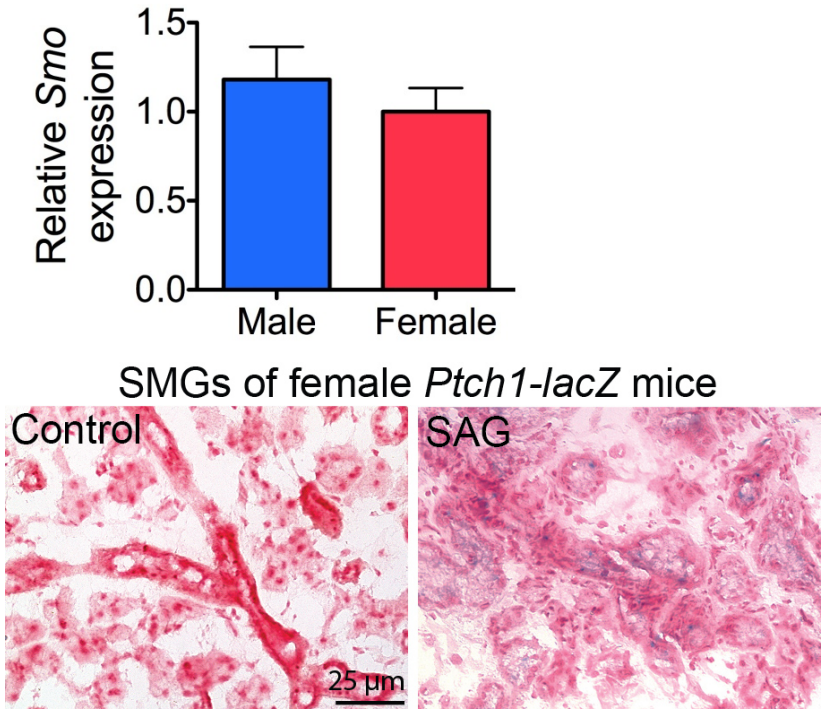

Fig. S6. Activation of Hh pathway in female mouse SMGs by SAG. Upper panel: the expression of *Smo* mRNA in SMGs is comparable between male and female mice. Lower panel: the expression of Hh reporter Ptch1-lacZ in SMGs was activated by retrograde delivery of the small molecule Smo agonist SAG.

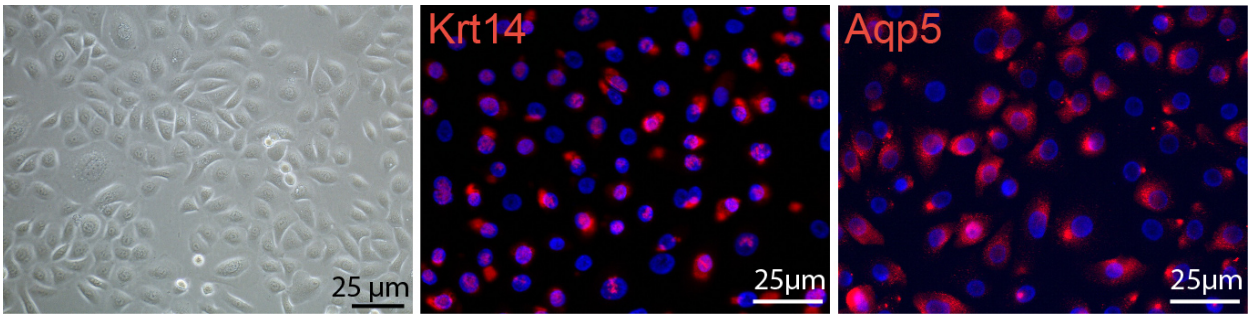

Fig. S7. Morphology of cultured human salivary epithelial cells.

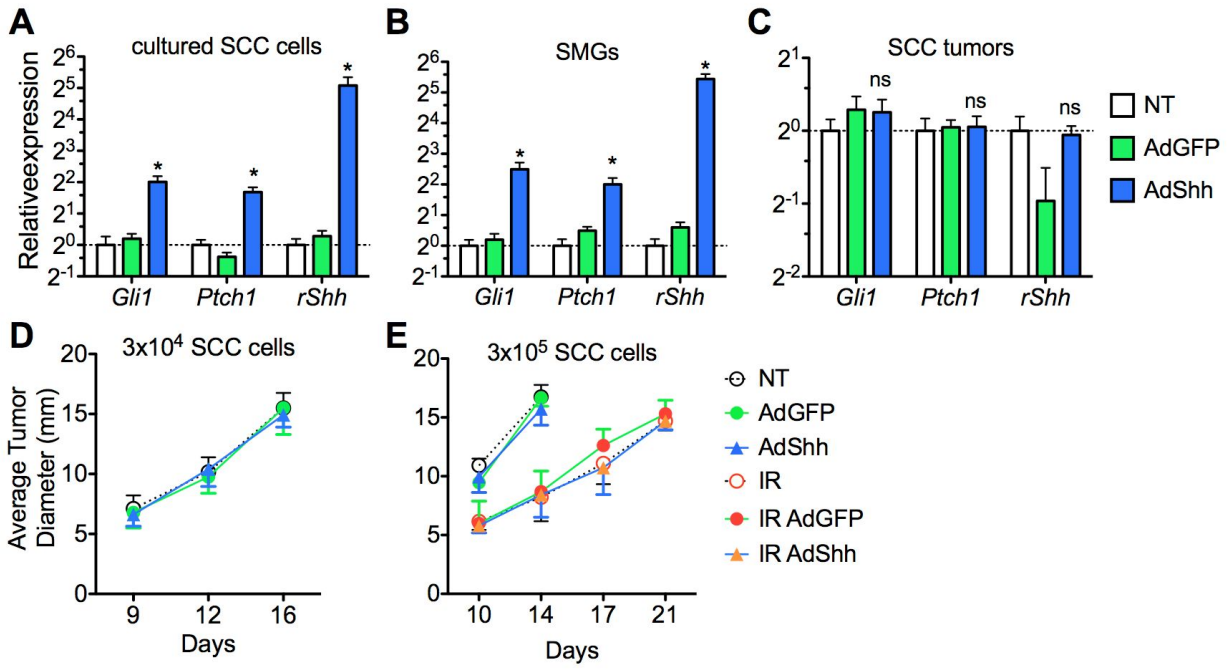

Fig. S8. Effects of retrograde Shh gene transfer into SMGs on expression of Hh target genes and SCC VII tumor growth. Expression of Hh target genes *Gli1* and *Ptch1* and the rat *Shh* transgenes were examined by qRT-PCR in cultured SCC VII cells 7 days after infection (A) or in SMGs (B) and SCC VII tumors (C) 7 days after retrograde delivery of AdShh into SMGs of mice carrying tumors. rShh and Hh target genes was significantly upregulated in cultured SCC cells after AdShh infection and in SMGs but not in tumors after AdShh delivery (n=4; *: $P < 0.05$ vs. NT; ns: not significant vs. NT). (D) AdShh delivery into SMGs has no significant effects on growth or IR-induced regrowth delay of established SCC tumors (n=4, $P>0.05$). (E) AdShh delivery into SMGs has no significant effects on growth of tumors from much less tumor cells inoculated concurrently (n=4, $P>0.05$).