

Supplemental Figure S1. Determination of Smo Activation at 10 days of age. **A)** The PR^{cre} mouse model was mated to the *ROSA26-LacZ* reporter mouse [24] in order to determine the spatiotemporal activation of Cre activity in this model. Mice were sacrificed at 10 days of age and X-gal staining was performed on $PR^{+/+}R26R^{+}$ (left) and $PR^{cre/+}R26R^{+}$ (right) uteri. Cre activity is visualized as blue staining. **B)** X-gal staining of 10 day old control (left) and $PR^{cre/+}SmoM2^{+}$ (right) mice crossed to the *Ptch1-LacZ* reporter mouse which expresses LacZ under the control of the *Ptch1* promoter. Blue staining is indicative of *Ptch1* expression.

Supplemental Figure S2. Proliferation and apoptosis is unaffected by SMO activation in 3 month old uteri. **A)** Assessment of proliferation in control and $PR^{cre/+}SmoM2^{+}$ uteri at 3 months of age. Proliferation was assessed by determining the percentage of cells that were positive for BrdU in the epithelium and stroma. n=4 mice per genotype. **B)** Immunohistochemical analysis of cleaved caspase 3 in control (left) and $PR^{cre/+}SmoM2^{+}$ (right) uteri at 3 months of age. The inset is a positive control for the staining. Counterstained with hematoxylin.

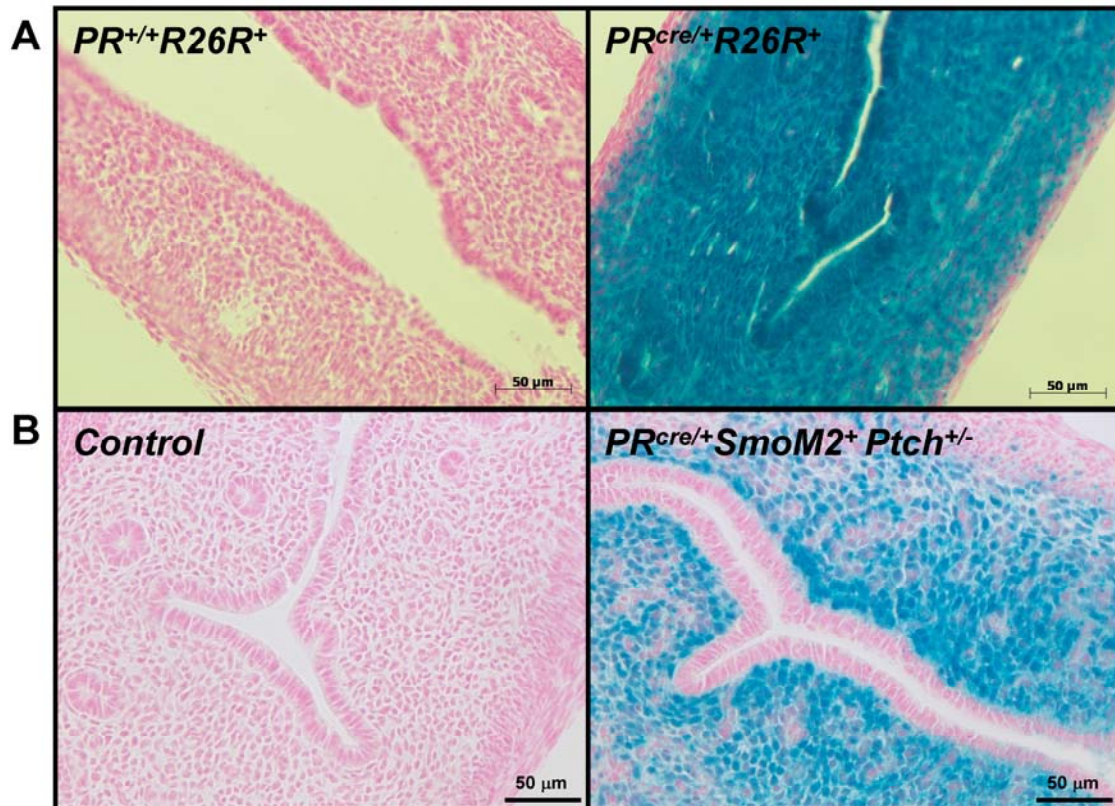
Supplemental Figure S3. Upper body tumors develop in $PR^{cre/+}SmoM2^{+}$ mice. **A)** Tumor in 5 month old $PR^{cre/+}SmoM2^{+}$ mice (right) compared to controls (left). **B)** Hematoxylin and eosin staining of control (top left) and $PR^{cre/+}SmoM2^{+}$ (top right) mammary glands and tumor in adjacent muscle of $PR^{cre/+}SmoM2^{+}$ (bottom right) mice.

Supplemental Figure S4. Steroid hormone receptor levels are normal in 3-mo-old $PR^{cre/+}SmoM2^{+}$ uteri. **A)** Immunohistochemical analysis of the progesterone receptor in control (left) and $PR^{cre/+}SmoM2^{+}$ (right) uteri at 3 mo of age. Counterstained with hematoxylin. **B)** Immunohistochemical analysis of estrogen receptor alpha in control (left) and $PR^{cre/+}SmoM2^{+}$ (right) uteri at 3 months of age. Counterstained with hematoxylin.

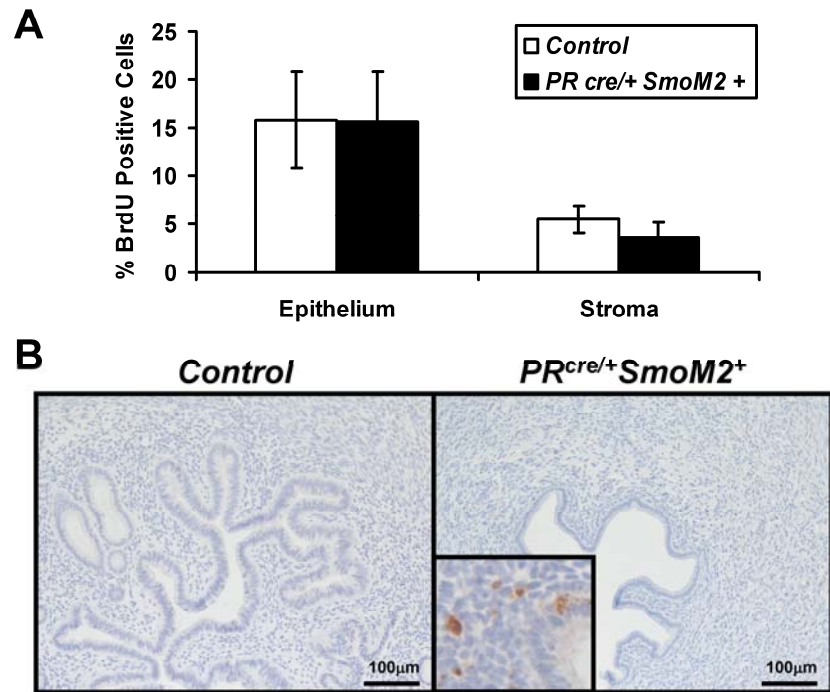
REFERENCES USED IN SUPPLEMENTAL DATA (Numbered as presented in manuscript text)

24. Soriano P. Generalized lacZ expression with the ROSA26 Cre reporter strain. *Nat Genet* 1999; 21: 70-71.

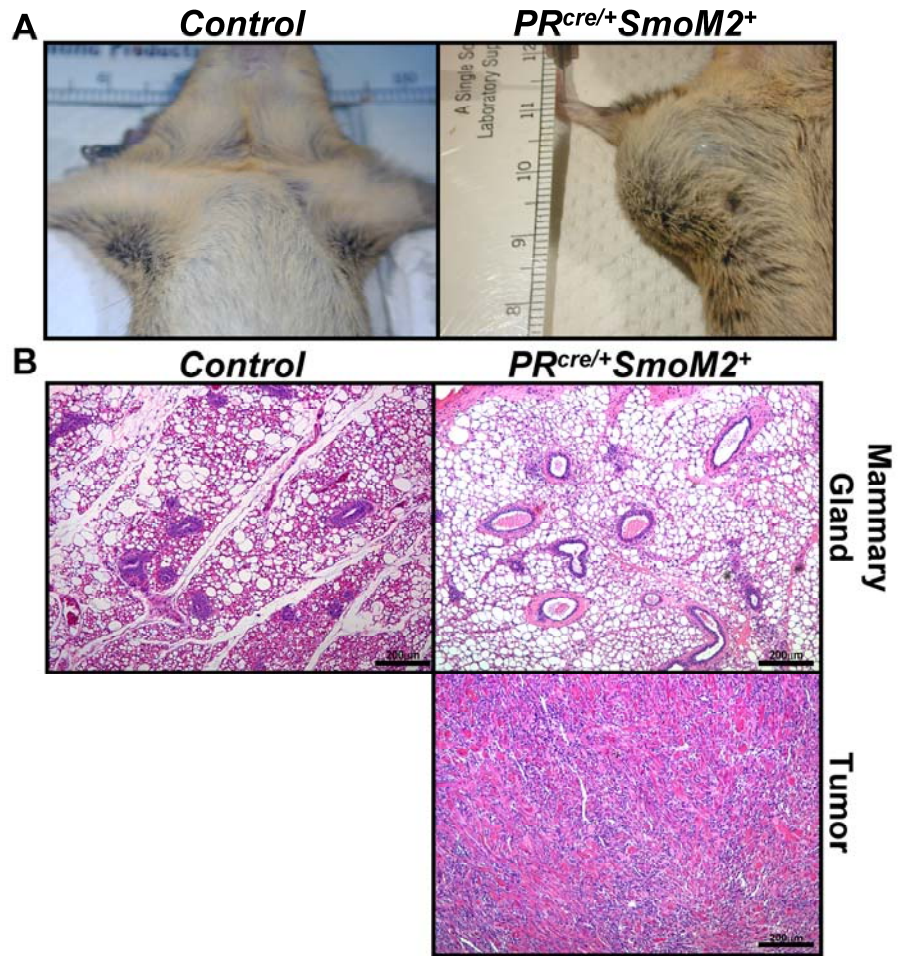
Supplemental
Figure 1



Supplemental Figure 2



Supplemental
Figure 4



Supplemental
Figure 3

