Figure EV1. Phosphorylated-AKT expression correlates with genetic Pten loss.

A, B  Representative epi-fluorescent images from the young (A) and old (B) cohort at low magnification. Upper panels in green show pAKT Ser373 expression. Lower panels in blue show corresponding DAPI images (scale bar, 500 μm).
Figure EV2: Tumor and histological breakdown of all mice in the study by age and genotype.

In main figures, these mice were divided into two cohorts based on age. The young cohort is aged 10–12 weeks and the old cohort is aged 32–44 weeks. Note that the PtenKO mice in the old cohort tended to be younger, but still had more advanced cancer phenotype than double knockout mice.

A Tumor phenotype as seen on gross inspection for all mice in Fig 2B and C. Blue, no tumor; green, tumor.

B Histology phenotype as seen on H&E sections for all mice in Fig 3B and C. Blue, normal; green, hyperplasia; purple, dysplasia.
Figure EV3. Dgcr8 is required for Pten<sup>Δ/Δ</sup>-mediated basal cell expansion.
A, B Representative low-magnification epi-fluorescent images of basal (CK5; green) and luminal (CK8; red) cell populations in indicated genotypes from the young cohort (A) and the old cohort (B). Nuclei are stained with the DAPI (blue) (scale bars, 500 µm). Note expansion of basal cells in old Pten null mice, which is not seen in other genotypes. Quantification of old mice is shown in Fig 5B.
**Figure EV4.** Decreased proliferation in $\text{Pten}^{\Delta\Delta}$ $\text{Dgcr}8^{\Delta\Delta}$ relative to $\text{Pten}^{\Delta\Delta}$ prostates.

A, B Representative low-magnification epi-fluorescent images of Ki67 (green) staining in prostates from the young cohort (A) and from the old cohort (B). Nuclei are stained with the DAPI (blue) (scale bar, 500 μm). Note increased proliferation in both young and old Pten null mice relative to other genotypes. Quantification of old mice is shown in Fig 5D.
Figure EV5. DGCR8 is expressed preferentially in the basal cells of normal human prostates and aberrantly expressed in the luminal cells of tumors. Representative IHC images of DGCR8 staining in human prostate cancers. The normal gland in each panel is demarcated by the dotted line; L indicates lumen. DGCR8-positive basal cells lining the normal prostate gland are indicated by the arrowhead. Note that the overlying luminal cells are DGCR8 negative. Adjacent low grade (left panel) and high grade (right panel) showing increasing levels of DGCR8 protein in the tumor cells over normal cells.