Supplementary Data

Conditional ablation of fgfr1 in embryonic prostate progenitor cells does not affect prostate development and function.

Nkx3.1-Cre transgenic mouse has been used to conditionally knock out fgfr2 alleles in the epithelial cells of the urogenital sinus that later differentiate to prostate epithelium of mice (1). To determine whether fgfr1 ablation in urogenital sinus/prostate epithelium affects prostate development and function, Nkx3.1-Cre mice were similarly crossed with fgfr1loxP/loxP mice (2-4) to conditionally knock out fgfr1 from prostate epithelium at late embryonic stages (E17.5). No differences in prostate gland size, morphology, lobe structure, or histology were observed in adult prostate tissues from control fgfr1loxP/loxP mice and the Nkx3.1-Cre/fgfr1loxP/loxP mice (Supplementary Fig. S1 A-B). To test whether fgfr1 ablation affects AR signaling, an androgen ablation / recovery experiment was conducted. Prostate glands from both control fgfr1loxP/loxP mice and NKx3.1-Cre/fgfr1loxP/loxP mice regressed two weeks after castration, and both regenerated to normal gland size and histology two weeks after androgen administration (Supplementary Fig. S1 A-B), suggesting intact AR signaling and induced biology within the fgfr1KO prostate epithelial cells. No differences were observed in AR expression pattern between the fgfr1KO prostates and the control prostates from intact mice, castrated mice and mice after androgen administration (Supplementary Fig. S1 C-D).

Development of the ARRzPBi-Cre/TRAMP/fgfr1loxP/loxP transgenic mouse model of prostate cancer.

Figure S2 shows the step-wise protocol for generation of the ARRzPBi-Cre/TRAMP/fgfr1loxP/loxP transgenic mice.

In situ hybridization controls.

Fig. S3A shows serial sections of a carcinoma foci stained with anti-sense riboprobes for fgfr1 mRNA and with control sense riboprobes (Fig. S3B) showing specificity of the in situ hybridization staining protocol.

TUNEL staining.

Tissues were evaluated using TUNEL staining as an indicator of apoptosis and/or necrosis. Foci of carcinoma in TRAMP control tumors exhibited very few positive cells (Fig. S4B). Tumors with KO+ (positive for the fgfr1 knockout allele) also exhibited a similar pattern (Fig. S4C). Tumors classified as KO- (non-detectable knockout allele) exhibited a poorly differentiated phenotype and some focal areas of apparent apoptosis / necrosis (Fig. S4D).
Literature Cited.