

p63 regulates commitment to the prostate cell lineage

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Molecular mechanisms underlying prostate and urothelial development remain unclear. This situation presents major limitations in identifying the cell type(s) and molecular events involved in the development of prostate and bladder cancer. It has been shown that mice lacking the basal cell marker p63 present several epithelial defects, including epidermis and prostate buds agenesis and urothelial abnormalities. Here, we use the p63^{-/-} mouse as a tool to define cell lineages in the prostate epithelium and urothelium. By complementing p63^{-/-} blastocysts with p63^{+/+} β -galactosidase (β -gal)-positive ES cells, we show that secretory cells of the prostate originate from p63-positive basal progenitor cells. Importantly, our urogenital sinus transplantation studies demonstrate that p63 prevents intestinal differentiation of the urogenital sinus endoderm and is therefore required to maintain commitment to the prostate cell lineage. Finally, in contrast with the prostate findings, analysis of the urothelium from rescued p63^{-/-} chimeras shows that umbrella (superficial) cells can develop and be maintained independently from p63-positive basal and intermediate cells.

animal model | development | stem cell | urothelium | mouse model