Single cell transcriptome profiling of prostate epithelial cell types: monitoring androgen responsiveness

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The prostate gland is a glandular organ that facilitates reproduction and is highly susceptible to diseases such as benign prostatic hyperplasia and prostate cancer upon aging. The prostatic epithelial hierarchy has been intensely studied to determine the cellular origins of disease. There are two major epithelial cell types, basal and luminal cells, both with proven stem cell and tumourigenic potential. As the prostate is a highly androgen-dependent organ, the cells that survive in the absence of androgens are of great therapeutic interest. In this study, we used patient-derived xenografts (PDXs) of human prostate tissues to study the transcriptome of prostatic basal and luminal cells and investigate their response to androgen withdrawal. Classic castration studies in rodents showed that luminal cells undergo apoptosis in response to androgen deprivation, but basal cells remain intact. We aimed to test the hypothesis that androgen withdrawal induces a growth quiescent, stem-like phenotype in basal, but not luminal cells. To do this, we enriched for prostate epithelial cells from PDXs pre and post-castration using a panel of 16 fluorescent surface-markers to segregate and enrich for basal and luminal prostate cells by FACS. We performed RNA sequencing using the Illumina HiSeq in rapid mode with 50 bp fragment sequencing chemistry (3 million reads/cell). This approach, combining PDX technology and genomics provided us a unique opportunity to interrogate the transcriptome of human basal and luminal cells and determine their response to androgen deprivation. Our preliminary data showed cytoskeleton rearrangement, apoptosis and the MAP kinase signaling pathway were significantly altered upon androgen withdrawal in luminal, but not basal cells. These data indicate that the transcriptional networks are different between these epithelial cell types. In summary, this unique dataset will allow us to interrogate the common and differential signaling pathways in basal and luminal cells and determine how they respond to castration. This new information will provide important information about the cellular origins of prostate disease.