PROSTATE CANCER FROM BASAL CELLS

An enduring theory is that prostate cancer originates from luminal cells because the disease can be characterized by a lack of basal cells and by luminal cell expansion. This theory has recently been directly challenged by work performed in a novel human prostate cancer model.

A team led by Owen Witte at Howard Hughes Medical Institute isolated human basal and luminal prostate cells and inserted them into mice for observation. They then went on to use viral vectors to introduce genetic alterations known to be associated with prostate cancer into those cells. Witte comments “the major advantage of this approach is that each component is adaptable—we can test a range of oncogenes, target cells and supportive cell types.”

Witte and his colleagues were able to show that it is necessary for prostate cells to express oncogenes (*AR*, *AKT* and *ERG*) to initiate malignancy. Importantly, the expression of this combination of genes resulted in the development of adenocarcinoma from basal cells but not luminal cells.

In many glands of the basal-cell-derived prostate cancer, the basal layer had been lost, which is a histological feature used by pathologists in prostate cancer diagnosis. “It seems reasonable that long-lived basal cells with self-renewal capacity are targets for transformation”, Witte concludes.

Another interesting observation is that basal cells are androgen independent, a property they share with advanced-stage, castration-resistant prostate cancer cells, a disease that is inevitably fatal. This finding indicates that pathways involved in basal cell function may be implicated in tumor cell survival in the presence of androgen-deprivation therapy, which may help guide future treatments.

The importance of this research was summarized by Witte: “understanding where the malignant cell came from can give us unique hints into its biology.”

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