Researchers find cancer aggression differences in different types of prostate cells

25 February 2013, by Bob Yirka

(Medical Xpress)—A research team made up of representatives from several cancer research centers in the United States has found that cancers that develop in the prostate of mice may be either aggressive or sluggish depending on the origin of their stem cell type. In their paper describing their findings, published in the journal *Nature Cell Biology*, the team describes how they found that tumors that develop in parts of the prostate that have luminal stem cells showed more aggressive tendencies than did those that developed in areas with basal type stem cells.

Prior research has found that there are three different types of epithelial cells in the prostate, and that two types of stem cells exist in two of those: basal and luminal cells. This is relevant because other prior research has found that solid tumors, of the kind that develop in the prostate, tend to arise from areas where there are stem cells. In this new effort, the researchers investigated the aggression tendencies of cancerous tumors that originated in both kinds of stem cells in mice. The thinking was if there are different aggression tendencies, then it would make sense to use different types of therapies to treat them.

To find out, the researchers modulated androgen levels in mice test subjects, which is known to cause prostate cancer over time and compared the aggressiveness of those tumors that originated in areas where basal stem cells were present with those that originated in areas with luminal stem cells. They found that those that originated in areas with luminal stem cells tended to be more aggressive and difficult to treat than were those that originated in basal areas.

The researchers also found as part of their research that stressing stem cells via modulating androgen levels caused some of the basal cells to actually change over to luminal cells—and when tumors arose in them later, they too were more aggressive, indicating that there is still an as yet unknown property associated with luminal stem cells that leads to more aggressive tumors and deadly outcomes for those who get them.

The next stage of the research will involve looking into whether the same differences exist in stem cells in people, and if so, whether a simple biopsy might be used in the future to offer doctors and patients valuable information about the nature of a particular prostate tumor and some insight into which therapies might work best to treat it.

More information: Lineage analysis of basal epithelial cells reveals their unexpected plasticity and supports a cell-of-origin model for prostate cancer heterogeneity, *Nature Cell Biology* (2013) doi:10.1038/ncb2697

Abstract

A key issue in cancer biology is whether oncogenic transformation of different cell types of origin within an adult tissue gives rise to distinct tumour subtypes that differ in their prognosis and/or treatment response. We now show that initiation of prostate tumours in basal or luminal epithelial cells in mouse models results in tumours with distinct molecular signatures that are predictive of human patient outcomes. Furthermore, our analysis of untransformed basal cells reveals an unexpected assay dependence of their stem cell properties in sphere formation and transplantation assays versus genetic lineage tracing during prostate regeneration and adult tissue homeostasis. Although oncogenic transformation of basal cells gives rise to tumours with luminal phenotypes, cross-species bioinformatic analyses indicate that tumours of luminal origin are more aggressive than tumours of

basal origin, and identify a molecular signature associated with patient outcome. Our results reveal the inherent plasticity of basal cells, and support a model in which different cells of origin generate distinct molecular subtypes of prostate cancer.

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