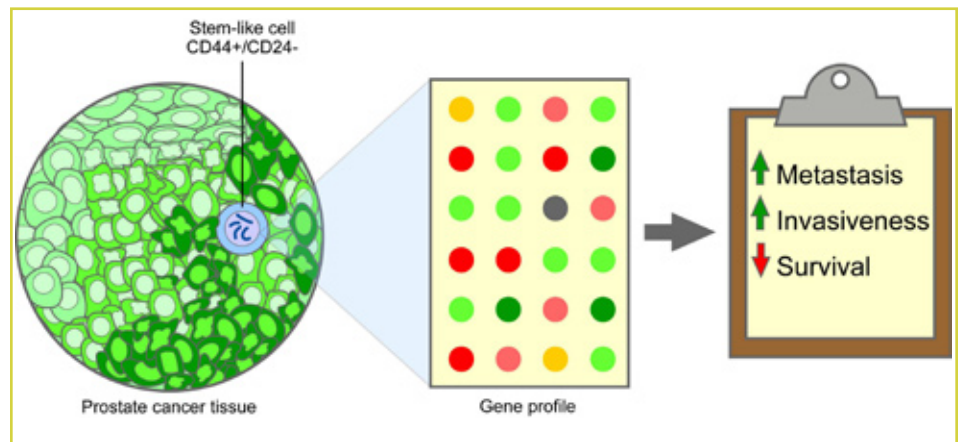


Prostate Cancer Stem-Like Cells

Prostate cancer is the third leading cause of cancer-related death among men, killing an estimated 27,000 men each year in the United States. Men with advanced prostate cancer often become resistant to conventional therapies. Many researchers speculate that the emergence of resistance is due to the presence of cancer stem cells, which are believed to be a small subpopulation of tumor cells that can self-renew and give rise to more differentiated tumor cells. It is thought that these stem cells survive initial therapies (such as chemotherapy and hormone therapy) and then generate new tumor cells that are resistant to these standard treatments. If prostate cancer stem cells could be identified and characterized, it might be possible to design treatments that prevent resistance.

A group of CCR scientists led by William Farrar, Ph.D., Head of the Stem Cell Section of the Laboratory of Cancer Prevention, recently published a paper in the *British Journal of Cancer* describing a population of prostate cells with stem-like properties. The study built on previous research showing that breast cancer stem-like cells express the cell surface protein CD44 and lack expression of CD24 (i.e., CD44⁺CD24⁻). Using a well-known prostate cancer cell line, Farrar and his colleagues set out to determine



Men with advanced prostate cancer often become resistant to standard treatments, such as chemotherapy. Researchers speculate that resistance may be caused by cancer stem cells, a small subpopulation of tumor cells. William Farrar, Ph.D., and colleagues performed gene expression profiling of CD44⁺CD24⁻ prostate cancer cells, which exhibit stem-like properties. The group found that the CD44⁺CD24⁻ gene signature was associated with invasiveness, increased risk of metastasis, and decreased overall survival. Future studies on these cells should provide insight into the mechanisms that support survival and self-renewal of cancer stem-like cells.

whether CD44⁺CD24⁻ prostate cancer cells also exhibit stem-like properties.

The researchers discovered that CD44⁺CD24⁻ cells were relatively rare in the prostate cancer cell line, making up only 0.04% of the cells. Purified CD44⁺CD24⁻ cells exhibited strong tumorigenic properties in cell culture and also were able to form tumors when injected into mice. In contrast, prostate cancer cells from which CD44⁺CD24⁻ cells had been removed were unable to form tumors in mice, indicating that CD44⁺CD24⁻ cells play a critical role in tumor formation. Importantly, the tumors formed by

these cells were very heterogeneous, illustrating that like all stem cells, CD44⁺CD24⁻ prostate cancer cells are able to give rise to a number of different cell types.

The Farrar laboratory also performed gene expression profiling of the CD44⁺CD24⁻ prostate cancer cells. The researchers found that the cells exhibit a gene signature previously identified in breast cancer and associated with invasiveness, increased risk of metastasis, and decreased overall survival. These data suggest that there may be considerable similarity between breast and prostate tumor-initiating cells.

This research supports the notion that cancer stem-like cells may play a role in the development of prostate cancer. Future studies on CD44⁺CD24⁻ prostate cancer cells should provide insight into the mechanisms that

support survival and self-renewal of these stem-like cells. These cells may provide a valuable tool for developing and testing therapeutics to target prostate cancer cells with stem-like qualities.

Reference

Hurt EM, Kawasaki BT, Klarmann GJ, Thomas SB, Farrar WL. CD44⁺ CD24⁽⁻⁾ prostate cells are early cancer progenitor/stem cells that provide a model for patients with poor prognosis. *Br J Cancer* 98:756–765, 2008.