

**Invasive prostate cancer cells are tumor initiating cells  
that have a stem cell-like genomic signature.**

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Development of metastasis is a leading cause of cancer-induced death. Acquisition of an invasive tumor cell phenotype suggests loss of cell adhesion and basement membrane breakdown during a process termed epithelial-to-mesenchymal transition (EMT). Recently, cancer stem cells (CSC) were discovered to mediate solid tumor initiation and progression. Prostate CSCs are a subpopulation of CD44(+) cells within the tumor that give rise to differentiated tumor cells and also self-renew. Using both primary and established prostate cancer cell lines, we tested the assumption that CSCs are more invasive. The ability of unsorted cells and CD44-positive and -negative subpopulations to undergo Matrigel invasion and EMT was evaluated, and the gene expression profiles of these cells were analyzed by microarray and a subset confirmed using QRT-PCR. Our data reveal that a subpopulation of CD44(+) CSC-like cells invade Matrigel through an EMT, while in contrast, CD44(-) cells are non-invasive. Furthermore, the genomic profile of the invasive cells closely resembles that of CD44(+)CD24(-) prostate CSCs and shows evidence for increased Hedgehog signaling. Finally, invasive cells from DU145 and primary prostate cancer cells are more tumorigenic in NOD/SCID mice compared with non-invasive cells. Our data strongly suggest that basement membrane invasion, an early and necessary step in metastasis development, is mediated by these potential cancer stem cells.

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