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

Klarmann GJ, Hurt EM, Mathews LA, Zhang X, Duhagon MA, Mistree T, Thomas SB, Farrar WL.

Cancer Stem Cell Section, Laboratory of Cancer Prevention, SAIC-Frederick Inc., National Cancer Institute at Frederick, Frederick, MD 21702, USA.

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.

PMID: 19221883 [PubMed - indexed for MEDLINE]