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**Decreased expression of PTEN enhances CXCR4-mediated proliferation and tumorigenesis in prostate cancer cells**

**Short Title:**
PTEN hinders prostate tumorigenesis

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*Abstract:* The progression of human prostate cancer is a result of metastasis from the primary tumor to vital organs. Metastasis is a complex process that involves invasion, intravasation, extravasation, and metastatic colonization. To date, the biology underlying the various mechanisms of metastasis has not been fully elucidated. Chemokines are pro-inflammatory molecules that bind to chemokine receptors, which are members of the G-protein coupled receptor (GPCR) family. The interaction between chemokines and their receptors results in a diverse array of biological and biochemical functions, such as chemotaxis, hematopoiesis and angiogenesis. Likewise, neoplastic cells employ chemokines and their receptors to promote metastasis, and encourage cell survival. It has been observed that the CXCR4 chemokine receptor is overexpressed on the cell surface of prostate cancer cells, which directed metastatic cells to tissues where its CXCL12 ligand is overexpressed, such as the bones and lungs. The Phosphate and Tensin homolog deleted on chromosome 10 (PTEN) is the second most mutated tumor suppressor in human cancer, and has been shown to be mutated in metastatic prostate cancer cells. Gao *et al* demonstrated that reconstituted PTEN in lymphocytes down-regulated CXCR4-mediated chemotaxis towards its ligand, CXCL12. Additionally, progenitor PTEN-deficient smooth muscle cells (SMC) increased migration towards CXCL12-producing SMC, suggesting that an alteration in PTEN expression negatively regulated CXCR4-mediated events. We analyzed prostate cancer cells for the expression of CXCR4 by flow cytometry, and observed that CXCR4 was expressed in human metastatic prostate cancer cell lines, PC3 and LnCaP. We analyzed for the expression of PTEN, and observed no expression of PTEN in PC3 and LnCaP cells at the protein level by western blot, nor at the mRNA level in PC3 cells by PCR. Furthermore, when reconstituted with PTEN, PC3 cells demonstrated a mesenchymal to epithelial-like phenotypic change in morphology. Additionally, we observed that reconstituted PTEN inhibited CXCR4-meditated proliferation via an MTT assay. Therefore, we hypothesize that the absence of PTEN expression correlates with an up-regulation of CXCR4-mediated proliferation and tumorigenesis in prostate cancer cells. In summary, our results showed that PTEN induced an epithelial-like morphological change, and inhibited CXCR4-mediated proliferation in metastatic prostate cancer cell lines. In future studies, we will investigate if the reconstituted expression of functional PTEN regulates CXCR4-mediated metastatic events in prostate cancer cells.
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**Author Disclosure Information: M.A. Chetram**, None; **C.V. Hinton**, None.
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