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Acquisition of tumorigenic potential and therapeutic resistance in CD133+ subpopulation of prostate cancer cells exhibiting stem-cell like characteristics

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Abstract

The role of CD133 (Prominin-1) as a cancer stem cell marker may be useful for therapeutic approaches and prognostication in prostate cancer patients. We investigated the stem-cell-related function and biological features of a subpopulation of CD133+ cells isolated from established primary human prostate cancer cell lines. The CD133+ cells sorted from human prostate cancer 22Rv1 exhibited high clonogenic and tumorigenic capabilities, sphere forming capacity and serially reinitiated transplantable tumors in NOD-SCID mice. Gene profiling analysis of CD133+ cells showed upregulation of markers of stem cell differentiation (CD44, Oct4, SOX9 and Nanog), epithelial-to-mesenchymal transition (c-myc and BMI1), osteoblastic differentiation (Runx2), and skeletal morphogenesis (BMP2), compared to side population of CD133- cells. These cells are highly malignant and resistant to γ-radiation and chemotherapeutic drug, docetaxel. Importantly, a docetaxel-resistant subclone was more enriched in CD133+ cells with significant increase in Runx2 expression, compared to CD133- cells. Furthermore, knockdown of Runx2 in these cells resulted in differential response to chemotherapy, sensitizing them to increased cell death. These results demonstrate therapy-resistant population with stem-like features are distinct subpopulation of malignant cells that resides within parental cell lines. The molecular signature of CD133+ cells may lead to identification of novel therapeutic targets and prognostic markers in the treatment of prostate cancer.