Infiltrating Mesenchymal Stem Cells as Cell-based Vectors for Prostate Cancer

W. Nathaniel Brennen1, Baohui Zhang2, Ibrahim Kulac3, Michael T. Schweizer1, L. Nelleke Kisteman1, Lizamma Antony1, Hao Wang1, Alan K. Meeker1,3,4, Angelo M. De Marzo1,3,4, Isla P. Garraway2, Samuel R. Denmeade1,4, and John T. Isaacs1,4*

1Department of Oncology at the Sidney Kimmel Comprehensive Cancer Center (SKCCC) at Johns Hopkins, Baltimore, MD 21231. 2Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, California 90095. 3Department of Pathology at the SKCCC at Johns Hopkins, Baltimore, MD 21231. 4Department of Urology, James Buchanan Brady Urological Institute, Johns Hopkins University School of Medicine, Baltimore, MD 21231.

Abstract: Mesenchymal Stem Cells (MSCs) have been identified in prostate cancer, raising the critical question of their source. Therefore, MSCs were characterized in benign and malignant prostate tissue representing different disease states from fetal development through adult death using analytical and functional methodologies. In contrast to lineage-restricted Mesenchymal Progenitor Cells (MPCs) found in normal tissue, MSCs with tri-lineage differentiation potential (adipogenesis, osteogenesis, and chondrogenesis) are identified in prostate cancer patients, consistent with an influx of MSCs from the bone marrow. Tissue from a subset of primary prostate cancer patients is highly enriched in MSCs, suggesting potential prognostic value. Furthermore, this recruitment is an ongoing process as documented by the presence of MSCs in metastatic lesions from castration-resistant prostate cancer patients, which provides the rationale for a cell-based vector to deliver therapeutic agents. Critically, a Phase 0 clinical trial has demonstrated allogeneic MSCs can be safely given to men with prostate cancer.

Conflicts of Interest: The authors declare that no conflicts of interest exist.

Funding: We would also like to acknowledge the following sources of financial support: Prostate Cancer Foundation (PCF) Young Investigator Award (WNB), Allegheny Health Network-Hopkins Cancer Research Fund (WNB), Maryland Cigarette Restitution Fund (WNB), SKCCC CCSG developmental funds [P30 CA006973, (WNB)], PCF/Movember Challenge Award (SRD, JTI), NIH-Prostate SPORE Grant P50 CA058236 (SRD, JTI), the Department of Defense Postdoctoral Fellowship W81XWH-12-1-0049 (WNB) and Synergy Award W81XWH-13-1-0304 (SRD, JTI). NK was supported by the Master in Molecular Life Sciences training program at the Institute for Molecular Life Sciences, Radboud UMC (Jack Schalken, mentor). Additionally, we would like to acknowledge the Department of Defense Prostate Cancer Research Program, Award No W81XWH-10-2-0056 and W81XWH-10-2-0046 Prostate Cancer Biorepository Network (PCBN), the NIH-Prostate SPORE Grant Pathology Core and Biostatistics Core (P50 CA058236), the Flow Cytometry core, and the Tissue Services Core supported by the SKCCC CCSG (P30 CA006973) for their services and assistance, in addition to acknowledging the use of tissues procured by the National Disease Research Interchange (NDRI) with support from NIH grant 2 U42 OD011158.