

Mannose Receptor positive macrophage infiltrate correlates with prostate cancer onset and metastatic castration-resistant disease

Jelani C. Zarif^{1,4}, Javier A. Baena-Del Valle^{2,3}, Jessica L. Hicks², Christopher M. Heaphy^{2,4}, Igor Vidal², Jacob Luo², Tamara L. Lotan², Jody E. Hooper², William B. Isaacs^{1,4}, Kenneth J. Pienta^{1,4,5}, Angelo M. De Marzo^{2,4}

¹The James Buchanan Brady Urological Institute at the Johns Hopkins University School of Medicine Baltimore, MD 21287 USA

²Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD 21287 USA

³Department of Pathology and Laboratory Medicine, Fundacion Santa Fe de Bogota University Hospital, Bogota DC, Colombia.

⁴Department of Oncology, Johns Hopkins School of Medicine and The Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD 21231 USA

⁵Department of Pharmacology and Molecular Sciences, Johns Hopkins School of Medicine, Baltimore, MD 21287 USA

M2-Tumor Associated macrophages (M2-TAMs) can suppress inflammation within the tumor microenvironment and have been reported to modulate cancer progression. We and others have previously reported infiltration of M2 macrophages in metastatic castrate-resistant prostate cancers (mCRPC). The objective of this study was to determine whether the extent of M2 macrophage infiltration correlates with prostate cancer aggressiveness, we applied immunohistochemistry to normal prostatic tissue, localized prostate cancer and metastatic castrate-resistant prostate cancer (mCRPC) from 192 patients. To assess M2 macrophage involvement, we analytically validated an IHC assay to detect the human mannose receptor (CD206). Also, we used multiplex immunofluorescent staining to show that a small fraction of CD206 staining co-localizes with endothelial cells of lymphatic vessels, while the vast majority of staining occurs in CD68-positive macrophages. The area fraction of staining for CD206-positive macrophages increased in a stepwise fashion going from normal (i.e. non-inflammation) prostatic tissue, to primary untreated carcinomas, to hormone na.ve regional lymph node metastases to castration resistant prostate cancer. Complimentary studies using flow cytometry confirmed CD206-positive M2-TAM infiltration. Altogether, this study revealed a progressive increase in CD206-positive macrophages from normal prostate to metastatic CRPC. Given the immunosuppressive nature of these cells and lack of clinical success of immunotherapy for prostate cancer patients, our results provide a rationale for therapeutic development to deplete these cells in the prostate cancer microenvironment as a potential method to augment immunotherapeutic approaches in prostate cancer.

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