MASTROPHAGE: GENERATING A FUSION BETWEEN MAST CELLS AND MACROPHAGES

Haleigh B. Eubanks¹, J. W. Ford², D. W. McVicar², A. A. Hurwitz² and S. K. Watkins²

¹Department of Biology, Jackson State University, Jackson, MS 39217, USA
²Cancer and Inflammation Program, National Cancer Institute, Frederick, MD, USA

Abstract: Chronic inflammation is affiliated with the development of malignancy in cancers. Research shows that persistent inflammation contributes to carcinogenesis by causing cellular damage, augmenting angiogenesis, and inducing a wound healing response. Specifically, in prostate cancer, inflammation is believed to play a role in both the initiation as well as in the advanced stages of the disease. Furthermore, this biological process establishes a milieu rich in cytokines, chemokines, and growth factors which enhance the recruitment, activation, and modulation of immune cells. Myeloid cells are a major component of the infiltrating immune cells, which are crucial for tumor progression. We hypothesize that in addition to the suppressive mediators which have been reported to be produced (e.g., IL-10, TGFβ, and Arginase), the infiltrating monocytes, macrophages, and neutrophils also produce and/or express inflammatory molecules that when chronically expressed, enhance tumor progression. Among these are the TREM molecules, Triggering Receptors Expressed on Myeloid cells. The TREMs are members of the immunoglobulin superfamily expressed on the surface of the myeloid lineage. TREM-1 has synergistic effects with toll-like receptor ligands that promote pro-inflammatory cytokine production, which activates inflammatory cells. TREM-2 has been shown to be up regulated in epithelial cells of the gut as well as on alternatively activated macrophages, where it is believed to play a crucial role in wound healing. Studies have also shown that TREM-2 participates in the promotion of fusing osteoclasts precursors into multinucleated cells. Interestingly we have identified a cell in advanced stages of prostate cancer which we believe to be a result of cell fusion. In physiology, cell-cell fusion is imperative for the development of multicellular organisms. Intracellular and virus induced membrane fusion have been studied in depth, however, the mechanism of spontaneous cell-cell fusion in macrophages remain elusive. Moreover, the function of multinucleated giant cells created from macrophage fusion, particularly in how the function relates to disease, is not completely understood. In the TRansgenic Adenocarcinoma of the Mouse Prostate (TRAMP) mouse model, we have observed a cell that has cellular characteristics of both macrophages and mast cells, thus termed —“Mastrophage”. We hypothesize that the “mastrophages” utilize TREM expression for cell fusion and may also play a role in the enhancement of tumor progression in prostate cancer.