

James & Esther King Biomedical Research Program

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*Urology
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*2010 Program
New Investigator Research
(3-year project)*

Project Title: Tumor-infiltrated Myeloid Cells and Prostaglandin Catabolism in Human Bladder Cancer

Project Summary: Bladder cancer (BC) is common urologic cancer. Smoking causes about 50 percent of all BC. Existing therapies require a strong immune response. However, expressions of immunosuppressive factors by cancers lead to the formation of an immunosuppressive environment that protects cancer from immune system surveillance. A significant portion of tumor is represented by tumor-infiltrated inflammatory CD11b cells. These cells are recruited by the tumor from bone marrow and play a major supportive role in bladder cancer progression by inhibiting immune response. The most evident immunosuppressive factor in BC is prostaglandin E2 (PGE2). PGE2 is synthesized by cyclooxygenase-2 (COX-2), and biologically degraded by 15-PGDH. Our preliminary results show that CD11b cells isolated from tumor tissue produce large amounts of PGE2 but show reduced ability to inactivate it because of low expression of 15-PGDH. The major goal of this research is to establish whether correction of PGE2 imbalance in the BC microenvironment can reverse the immunosuppressive function of tumor-infiltrated CD11b cells and lead to the inhibition of tumor growth. We will explore the mechanisms underlying the association between imbalance of PGE2 and the immunosuppressive behavior of CD11b cells within the BC. Obtained results may directly lead to development of new therapeutic interventions for treatment of BC.