Inflammatory response of tumor associated lymphocytes promotes EMT in prostate cancer

Irtaza Khan[1], Samuel Bischoff[1], Victoria Hackert[1], Rumana Huq[1], Akanksha Verma[2], Olivier Elemento[2], Kamlesh K. Yadav[1], Ashutosh K. Tewari*[1], **Shalini S. Yadav*[1]**

[1]Department of Urology, Icahn School of Medicine at Mount Sinai, New York, NY 10029
[2]Institute for Computational Biomedicine, Weill Cornell Medical College, New York, NY 10065

Background: Prostate Cancer (PCa) is one of the leading malignancies for which immunotherapeutics are being evaluated. However, the variability in the outcomes of the clinical trials, coupled with poor understanding of the tumor associated immune microenvironment, suggests the existence of tumor-immune heterogeneity. Thus, there is an urgent need to understand this heterogeneity to enable the stratification of immunotherapeutic regimes for best clinical outcomes. *Methods:* We have utilized transcriptome sequencing of lymphocytic pockets near and away from the tumor of a human prostatectomy sample. To define the role of tumor-associated lymphocytes in PCa progression differentially expressed genes were then tested in their ability to promote invasion in co-culture studies using macrophages and PCa cell lines. *Results:* We observed marked differences in gene expression profiles of lymphocytes near the tumor (L-NT) versus lymphocytes away from the tumor (L-AT). The genes upregulated in L-NT were predominated by inflammatory response genes. One of the top hits, ISG-15, was also up-regulated in 43% of the publicly available NEPC tumor data set. Co-culture studies of IFN stimulated macrophage cell line THP-1 with VCaP cells shows upregulation of EMT markers Nanog and Vimentin. *Conclusions:* Tumor associated immune cells induce a local inflammatory response which can potentially lead to EMT transition in tumor cells. The long-term goal of our work is to define the role of tumor associated immune cells in PCa progression so we can determine best or novel personalized immunotherapy treatment options for patients with PCa.

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