INTERLEUKIN–17A STIMULATES EXPRESSION OF CHEMOKINES AND CYTOKINE IN PROSTATIC EPITHELIAL CELL LINES.

Sen Liu, Dongxia Ge, and Zongbing You.

Department of Structural & Cellular Biology, Department of Orthopaedic Surgery, Tulane Cancer Center, Louisiana Cancer Research Consortium, and Tulane Center for Aging, Tulane University School of Medicine, New Orleans, LA.

Introduction and Objectives: T helper 17 (Th17) cells secret interleukin–17A (IL–17A) and interleukin–17F. Th17 cells and IL–17A are increased in prostate tumors. The role of IL–17A in prostate cancer is not clear. This in–vitro study was to investigate the effects of IL–17A on prostatic epithelial cells.

Methods: MTT assay, Western blot, and real–time quantitative RT–PCR analysis were used to measure the effects of IL–17A on immortalized normal human prostatic epithelial cell lines (RWPE–1 and pRNS–1–1), human high–grade prostatic intraepithelial neoplasia (PIN) cell line, human prostate cancer LNCaP cell line, and mouse prostate cancer TRAMP–C1 cell line.

Results: Recombinant human IL–17A (20 ng/ml) did not affect cell growth rate in any of the prostatic cell lines studied. IL–17A did not significantly activate NF–kappaB or ERK signaling pathway in RWPE–1, pRNS–1–1, or PIN cells. IL–17A activated NF–kappaB and/or ERK signaling pathways in LNCaP and TRAMP–C1 cells. When IL–17RC (receptor of IL–17A) was overexpressed in PIN and LNCaP cells, activation of NF–kappaB or ERK signaling pathway by IL–17A was significantly enhanced. IL–17A modestly induced mRNA expression of chemokines (CXCL1 and CXCL2) in RWPE–1, pRNS–1–1, and PIN cells. IL–17A induced mRNA expression of chemokines (CXCL1, CXCL2, CCL2, CCL5, CCL7, and CCL20) and cytokine IL–6 in LNCaP cells. In mouse TRAMP–C1 cells, IL–17A induced mRNA expression of chemokines (CXCL1, CXCL2, CXCL5, CCL2, and CCL5) and cytokine IL–6. When IL–17RC was overexpressed in PIN and LNCaP cells, chemokine expression was significantly enhanced.

Conclusions: IL–17A stimulates expression of chemokines and cytokine in prostatic epithelial cell lines, particularly in malignant epithelial cells. Although IL–17A has no effects on cell growth in–vitro, it is speculated that IL–17A–induced chemokines and cytokine may modulate the stroma–epithelial interaction in tumor microenvironment in–vivo.

Acknowledgement: NIH/NCRR 2P20 RR020152–06, DoD W81XWH–05–1–0567, NIH-Fogarty Center-Dr. Buekens Seed Grant/Tulane Framework for Global Health Seed Grant, Tulane Cancer Center Matching Fund, and LCRC Fund.