LINK BETWEEN CYTOKINE EXPRESSION AND AUGMENTED PURINERGIC SIGNALING IN INTERSTITIAL CYSTITIS (IC) BLADDER UROTHELIAL CELLS (BUC)

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Introduction and Objective: Cultured IC BUC, compared to normal BUC, have altered cytokine expression, including increased epidermal growth factor (EGF) and decreased heparin-binding epidermal growth factor-like growth factor (HB-EGF) secretion. Furthermore, IC BUC manifest increased purinergic signaling by releasing high amounts of adenosine triphosphate (ATP) when stimulated with exogenous ATP. We determined if cytokine alterations are linked to altered ATP release. This was accomplished by experimentally changing the cytokine environment and measuring how much ATP was released when BUC were challenged with an ATP stimulus. Because cytokines work via protein phosphorylation, genistein, a non-specific blocker of phosphorylation, was also used to determine its effect on ATP release.

Methods: Cultured IC BUC were treated with genistein (100 uM) and HB-EGF (20ng/mL) while normal BUC were exposed to EGF (10ng/mL and 20ng/mL.) After 24-48 hours of treatment, 30uM of exogenous ATP was added to BUC. Cell supernatants collected over 3 hours for ATP measurements using the luciferin-luciferase assay. Results: Genistein (figure 1) and HB-EGF (not shown) treatments significantly reduced ATP release by IC cells whereas EGF treatment significantly increased ATP release by normal cells in response to the exogenous ATP (figure 2.) Conclusions: EGF, HB-EGF, and genistein treatments reversed the purinergic signaling phenotype (measured by response to ATP stimulus) of these BUC. This suggests that there is a link between the EGF / HB-EGF / protein phosphorylation and purinergic signaling pathways in human BUC.
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