

Infections/Inflammation of the GU Tract: Interstitial Cystitis
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EFFECTS OF INTERLEUKIN 8 EXPRESSION ON UROTHELIAL HOMEOSTASIS

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Introduction and Objective: Interleukin 8 (IL8) is a cytokine known to participate in tissue defenses against infections by its chemotactic effect on white cells, especially polymorphonuclear blood leukocytes. IL8 is released by urothelial cells in response to urinary tract infections. We have previously established an *in vitro* system, culturing human urothelial cells under undifferentiated and/or differentiated conditions, to study urothelial differentiation. IL8 was found to be up-regulated in both differential display RT-PCR and cDNA micro-array during urothelial differentiation *in vitro*. Increased IL8 expression in differentiated urothelial cells is consistent with this function in protecting the body from potential urinary bacterial pathogens. However, in other epithelial cells, IL8 has been shown to have additional homeostatic effects. Furthermore, our previous data showed that IL8 mRNA was down-regulated in bladder biopsies from patients with interstitial cystitis compared to normal controls. Therefore, we explored the function of IL8 in cultured normal human urothelial cells. **Methods:** Cultured normal urothelial cells were transfected with small inhibitory RNA (si RNA, Ambion) for IL8, or control siRNA in low calcium, serum free medium (SF-KGM) to maintain an undifferentiated state. The cells were then switched to culture in high calcium, serum containing medium (MEM+ 10% fetal calf serum) to induce differentiation. Levels of IL8 were determined using IL8 specific enzyme-linked immunosorbent assays (ELISA). Morphology and adherence were monitored via phase contrast microscopy. **Results:** Using IL8 specific siRNA, we were able to significantly inhibit the level of IL8 protein in differentiated normal human urothelial cells. These cells had markedly reduced adherence to culture substrate, showed significantly altered morphology, and failed to survive in culture. No differences were noted in cells transfected with the control siRNA. **Conclusions:** These data suggest that IL8 plays a role in the cellular maintenance of normal urothelial cells beyond the role of IL8 in the immune defense. Loss of IL8 expression in interstitial cystitis not only reflects altered urothelial differentiation but may contribute to poor urothelial survival in this disorder. Future studies will continue to elucidate the role of IL8 in urothelial biology.

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