MACROPHAGE MIGRATION INHIBITORY FACTOR AND ITS RECEPTOR CD74 ARE UPREGULATED IN THE UROTHELIUM OF INTERSTITIAL CYSTITIS PATIENTS

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Introduction and Objective: Macrophage Migration Inhibitory Factor (MIF) is a pro-inflammatory cytokine constitutively expressed in the urothelium. We previously demonstrated MIF upregulation and release into the bladder lumen during inflammation. CD74, the cell surface MIF receptor, is also upregulated in the urothelium by inflammation. Binding of MIF and CD74 activates ERK1/2-mediated signal transduction pathways. Therefore, we proposed that MIF and CD74 immunostaining would be increased in chronic bladder inflammation.

Methods: We examined bladder sections from patients with interstitial cystitis (IC) and compared them to those of patients with pathologic diagnoses of nonspecific inflammation (non-IC) and to those of patients with histologically normal bladders. Bladder sections from IC patients (N=20), non-IC (N=14) and normal bladder (N=17) were immunostained for MIF and CD74 using standard immunohistochemical protocols. The sections were evaluated for staining intensity and analysis was performed using Kruskal-Wallis ANOVA followed by post-hoc tests.

Results: MIF immunostaining was slight to moderate in normal bladder and predominantly in superficial cells. MIF was not increased in non-IC (p>0.05). In IC bladders, however, the staining intensity was increased (p<0.001) and the staining included the full-thickness of the urothelium. CD74 immunostaining was slight in the normal bladder and was increased in non-IC (p<0.05) and IC (p<0.01) bladders and was particularly intense in superficial cells. Conclusions: MIF and CD74 are both upregulated in the urothelium of IC patients. MIF stands upstream of other inflammatory mediators and is thus a key regulator of the inflammatory cascade. Therefore, increased production of MIF and CD74 (binds to MIF and mediates signal transduction) in the urothelium of IC patients suggests that MIF may be involved in IC by maintaining inflammatory cytokine production. MIF and CD74 may provide novel therapeutic targets in IC and other forms of cystitis.

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