Trichomonas vaginalis homolog of macrophage migration inhibitory factor induces prostate cell growth, invasiveness, and inflammatory responses.

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Abstract

The human-infective parasite Trichomonas vaginalis causes the most prevalent nonviral sexually transmitted infection worldwide. Infections in men may result in colonization of the prostate and are correlated with increased risk of aggressive prostate cancer. We have found that T. vaginalis secretes a protein, T. vaginalis macrophage migration inhibitory factor (TvMIF), that is 47% similar to human macrophage migration inhibitory factor (HuMIF), a proinflammatory cytokine. Because HuMIF is reported to be elevated in prostate cancer and inflammation plays an important role in the initiation and progression of cancers, we have explored a role for TvMIF in prostate cancer. Here, we show that TvMIF has tautomerase activity, inhibits macrophage migration, and is proinflammatory. We also demonstrate that TvMIF binds the human CD74 MIF receptor with high affinity, comparable to that of HuMIF, which triggers activation of ERK, Akt, and Bcl-2-associated death promoter phosphorylation at a physiologically relevant concentration (1 ng/mL, 80 pM). TvMIF increases the in vitro growth and invasion through Matrigel of benign and prostate cancer cells. Sera from patients infected with T. vaginalis are reactive to TvMIF, especially in males. The presence of anti-TvMIF antibodies indicates that TvMIF is released by the parasite and elicits host immune responses during infection. Together, these data indicate that chronic T. vaginalis infections may result in TvMIF-driven inflammation and cell proliferation, thus triggering pathways that contribute to the promotion and progression of prostate cancer.

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