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Attenuation of inflammatory events in human intervertebral disc cells with a tumor necrosis factor antagonist

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Abstract

Study design: The inflammatory responses of primary human intervertebral disc (IVD) cells to tumor necrosis factor α (TNF-α) and an antagonist were evaluated in vitro.

Objective: To investigate an ability for soluble TNF receptor type II (sTNFRII) to antagonize TNF-α-induced inflammatory events in primary human IVD cells in vitro.

Summary of background data: TNF-α is a known mediator of inflammation and pain associated with radiculopathy and IVD degeneration. sTNFRs and their analogues are of interest for the clinical treatment of these IVD pathologies, although information on the effects of sTNFR on human IVD cells remains unknown.

Methods: IVD cells were isolated from surgical tissues procured from 15 patients and cultured with or without 1.4 nmol/L TNF-α (25 ng/mL). Treatment groups were coincubated with varying doses of sTNFRII (12.5-100 nmol/L). Nitric oxide (NO), prostaglandin E_2 (PGE_2), and interleukin-6 (IL6) levels in media were quantified to characterize the inflammatory phenotype of the IVD cells.

Results: Across all patients, TNF-α induced large, statistically significant increases in NO, PGE_2, and IL6 secretion from IVD cells compared with controls (60-, 112-, and 4-fold increases, respectively; $P < 0.0001$). Coincubation of TNF-α with nanomolar doses of sTNFRII significantly attenuated the secretion of NO and PGE_2 in a dose-dependent manner, whereas IL6 levels were unchanged. Mean IC_{50} values for NO and PGE_2 were found to be 35.1 and 20.5 nmol/L, respectively.

Conclusion: Nanomolar concentrations of sTNFRII were able to significantly attenuate the effects of TNF-α on primary human IVD cells in vitro. These results suggest this sTNFR to be a potent TNF antagonist with potential to attenuate inflammation in IVD pathology.

Figures

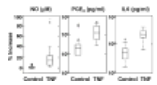

Figure 1 Box plots of NO, PGE...

Figure 2 Dose-dependent attenuation of TNFα-induced release...

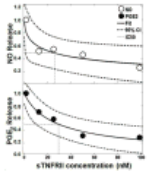

Figure 3 Logistic regression modeling of dose-dependent...

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