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Insights: Publications

Differential Regulation Of Macrophage Inflammatory Activation By Fibrin And Fibrinogen

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Fibrin is a major component of the provisional extracellular matrix formed during tissue repair following injury, and enables cell infiltration and anchoring at the wound site. Macrophages are dynamic regulators of this process, advancing and resolving inflammation in response to cues in their microenvironment. Although much is known about how soluble factors such as cytokines and chemokines regulate macrophage polarization, less is understood about how insoluble and adhesive cues, specifically the blood coagulation matrix fibrin, influence macrophage behavior. In this study, we observed that fibrin and its precursor fibrinogen elicit distinct macrophage functions. Culturing macrophages on fibrin gels fabricated by combining fibrinogen with thrombin stimulated secretion of the anti-inflammatory cytokine, interleukin-10 (IL-10). In contrast, exposure of macrophages to soluble fibrinogen stimulated high levels of inflammatory cytokine tumor necrosis factor alpha (TNF-a). Macrophages maintained their anti-inflammatory behavior when cultured on fibrin gels in the presence of soluble fibrinogen. In addition, adhesion to fibrin matrices inhibited TNF-a production in response to stimulation with LPS and IFN-c, cytokines known to promote inflammatory macrophage polarization. Our data demonstrate that fibrin exerts a protective effect on macrophages, preventing inflammatory activation by stimuli including fibrinogen, LPS, and IFN-c. Together, our study suggests that the presentation of fibrin(ogen) may be a key switch in regulating macrophage phenotype behavior, and this feature may provide a valuable immunomodulatory strategy for tissue healing and regeneration.
