

P033 Tenascin-C regulates fibroblast migration within 3D fibrin–fibronectin matrices

Annette Trebaul¹, Emma Chan², Kim Midwood²

¹ Basel University, ² Kennedy Institute of Rheumatology, Imperial College London

Synthesis of new tissue by fibroblasts is required for tissue rebuilding in response to injury. Fibroblast migration from surrounding healthy tissue into the fibrin-fibronectin provisional matrix deposited upon injury is a key rate-limiting step of this stage of tissue repair. These events must be tightly regulated. Excessive deposition of scar tissue is the major hallmark of fibrotic disease.

Tenascin-C is an extracellular matrix glycoprotein that is transiently expressed upon tissue injury, where it is specifically localized to the wound edge, and persistently upregulated in fibrotic diseases such as pulmonary fibrosis, scleroderma and liver cirrhosis. We have shown that full-length tenascin-C promotes fibroblast migration within fibrin-fibronectin matrices and we have mapped the domains within the molecule critical for enhancing migration. We also demonstrated that specific fragments of tenascin-C inhibit fibroblast migration. These data suggest that transient expression of tenascin-C at the wound boundary is key to tissue repair: its induction recruits fibroblasts into the wound and fragments resulting from its breakdown prevent excessive fibroblast infiltration. Our results demonstrate for the first time how fibroblast migration in 3D provisional matrices may be differentially regulated by proteolysis of matrix molecules and could explain how persistent expression of tenascin-C contributes to the progression of fibrotic disease.