if TLR-2 induced cell migration and invasion is mediated through $\beta 1$ -integrin signalling pathways and cytoskeletal dynamics.

Materials and methods IA patients (n=20) underwent clinical assessment, video-arthroscopy and synovial biopsy pre/postbiologic therapy. Macroscopic synovitis/vascularity was measured by visual analogue scale. Immunohistology/immunofluorescence examined $\beta 1$ integrin and filamentous actin (F-actin) expression in synovial tissue (ST), primary RA synovial fibroblasts (RASFC) and microvascular endothelial cells (MVEC). Cytoskeletal rearrangement following Pam₃CSK₄ (1 μ g/ml) (TLR-2-ligand) stimulation was examined by F-actin immunofluorescent staining. Pam₃CSK₄ induced adhesion, cell migration and invasion was assessed by FACS analysis, wound repair assays and transwell matrigel invasion chambers in the presence or absence of anti- $\beta 1$ integrin (10 μ g/ml) or IgG control antibody (10 μ g/ml). Rac1 was assessed by immunoprecipitation and western blotting.

Results $\beta 1$ integrin was highly expressed in IA ST compared to osteoarthritis and control tissue. $\beta 1$ integrin lining and sublining layer expression significantly correlated with macroscopic synovitis (p<0.05), vascularity (p<0.05), and was significantly reduced in biologic responders. $\beta 1$ -integrin and F-actin expression predominantly co-localised to synovial blood vessels and lining layer. Pam₃CSK₄ induced cell surface expression of ICAM (p<0.05). Using RASFC and HDEC, Pam₃CSK₄ induced cell migration and cytoskeletal disassembly, resulting in filopodia and microspike formation and significantly induced Rac1 activation and cell invasion through a matrigel (p<0.05). Finally, the authors demonstrated that Pam₃CSK₄ induced cell migration was inhibited in the presence of anti- $\beta 1$ integrin, an effect that was also observed for Pam₃CSK₄ induced cellular invasion and Rac1 activation (p<0.05). No effect was observed for IgG matched control antibody.

Conclusion $\beta 1$ -integrin is highly expressed in the inflamed joint and mediates cell TLR-2 induced migrational and invasive mechanisms, critical to the pathogenesis of IA.

12 $\beta 1$ INTEGRIN MEDIATES TOLL-LIKE RECEPTOR 2 INDUCED MIGRATION AND INVASION VIA RAC1 ACTIVATION

McGarry T, Connolly M, McCormick J, Gao W, Veale D J, Fearon U *Dublin Academic Medical Centre, University College Dublin, Dublin, Ireland*

10.1136/annrheumdis-2011-201238.12

Background and objectives Rheumatoid arthritis (RA) is a chronic inflammatory disease characterised by synovial inflammation and destruction of cartilage and bone. TLR-2 is implicated in the pathogenesis of RA. This study investigates