II08. INNATE IMMUNE SENSING: TOLL LIKE RECEPTORS AND BEYOND

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RA is a chronic inflammatory condition that affects 1% of the population and is characterized by synovial inflammation and destruction of cartilage and bone, leading to progressive disability and reduced life expectancy. Cytokines play an important role in these processes, a fact highlighted by the clinical effectiveness of anti-cytokine therapeutic interventions. However it is still unclear what regulates cytokine production and what prolongs the inflammatory and tissue-destructive mediators in RA. Toll like receptors (TLRs), the inflammasome as well as complement have all been individually linked to RA. Several ligands linked with RA can activate all three of these receptors, but whether and how these three systems interact with each other in the context of RA has not been previously studied. In the current study we investigated whether interplay between these receptors is the key to the chronic inflammatory response observed in RA. We have demonstrated that these three classes of pattern recognition receptors co-operate leading to a chronic inflammatory response in synovial fibroblasts. By deciphering the molecular mechanisms involved, we will be able to identify novel therapeutic targets for RA in the future.

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