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Rheumatoid arthritis (RA) specific therapy with disease-specific monoclonal antibodies

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CD44 and RHAMM (CD168) are migration-supporting molecules in cancer and inflammatory cells ,including synovial fluid cells from RA patients.. In addition, CD44 is a transmitter of apoptotic signals. Exploring the human rheumatoid arthritis disease, we have discovered a CD44 variant (designated CD44vRA), that is generated by alternative splicing, and exclusively expressed on joint inflammatory cells of the RA patients (Nedvetzki et al., J Clin Invest 111:1211-1220,2003). Monoclonal antibodies (mAbs) directed against human CD44vRA (anti-CD44vRA mAbs) bind exclusively to joint inflammatory cells of RA patients and kill them by apoptosis ,whereas peripheral blood leukocytes derived from the same patient remained undamaged when treated with the same antibodies. Anti-CD44vRA mAb injected at the onset of collagen–induced arthritis of DBA/1 mice markedly reduces the joint inflammation, indicating cross-reactivity between the mouse arthritic CD44 and human CD44vRA. We have shown earlier (Nedvetzki et al, PNAS, 101:18081-18086, 2004) that RHAMM can compensate for CD44 in supporting in vitro cell migration and in vivo joint inflammation, when CD44 is genetically deleted (e.g.,by CD44 Knock out). Hence, Injection of anti-RHAMM antibodies at the onset of CIA can also reduce the joint inflammation, but only when CD44 is genetically deleted. The clinical feasibility of anti-CD44vRA and anti-RHAMM mAbs is now under investigations in preclinical studies and part of available conclusions will be discussed.

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Proteomic analysis of the secretome in explant models of articular cartilage

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The aim of this presentation is to review data from our laboratory relating to the use high throughput proteomics for identifying the major proteins present in the secretome of articular cartilage. Proteomic studies of the cartilage secretome have confirmed the presence of a similar set of extracellular matrix (ECM) proteins in the secretomes of canine and equine cartilage explant models. Many of the ECM proteins we have identified possess well-established matrix-related functions and are associated with matrix organization and cell-matrix interactions. The expression of some of the proteins identified using this approach has been validated in equine explant supernatants by quantitative western blotting. High-throughput proteomic analysis has enabled detection of protein profiles within the secretomes of canine and equine cartilage explant models. The data presented supports the view that using high throughput proteomics may be a useful strategy for studying dynamic changes in the secretome of cartilage explants in response to pro-inflammatory cytokines, anti-inflammatory compounds and nutraceutical compounds.

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