Tissue protective properties of neutrophil microvesicles in inflammatory diseases

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Microvesicles (MVs) mediate inter-cellular communication by transferring cellular components to target cells, endowing them with an enhanced lipid, nucleic acid and protein repertoire. Whilst most studies (>400 per year in the last 5 years) monitored the biology of cell-derived MVs as a homogenous pool, we proposed that there is heterogeneity in MV generation from a given cell to reflect its status (resting, activated, inflamed, resolving), a feature certainly demonstrated for human neutrophil derived MVs.

With a focus on neutrophil-derived MVs, recent work indicated heterogeneity in content and function with a subset enriched in alpha-2-macroglobulin (A2MG) being typical for invtravascularly-activated neutrophils, whereas an annexin A1 (AnxA1) positive vesicles being typical of exudate neutrophils. The latter type was tested in experimental settings of inflammatory arthritis. In vitro, exogenous neutrophil MVs activated anabolic gene expression in chondrocytes leading to extracellular matrix accumulation and cartilage protection. In vivo, intra-articular injection of MV lessened cartilage degradation caused by inflammatory arthritis. Arthritic mice receiving adoptive transfer of whole labeled neutrophils had abundant MVs within cartilage matrix; the first evidence that MVs can penetrate cartilage. Mechanistic studies support a model whereby MV-associated Annexin A1 interacts with its receptor FPR2/ALX, increasing TGF-β production by chondrocytes, ultimately leading to cartilage protection.

This line of research endorses innovative approaches whereby MVs – either directly or cargoed with specific molecules - can be harnessed as a novel unique therapeutic strategy for tissue protective actions protection of cartilage and treatment of cartilage-erosive diseases.