Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Studying the expression of lncRNAs in monocytes in rheumatoid arthritis

Synopsis:

Rheumatoid arthritis (RA) is a chronic immune mediated inflammatory disease that is mainly characterized by hyperproliferation of synovial cells, infiltration of mononuclear cells into the synovium and early destruction of articular cartilage and bone, causing progressive damage to the musculoskeletal system and leading to decreased physical function and quality of life. RA joint synovial cellular infiltrate consists of activated macrophages, B and T cells, which secrete proinflammatory cytokines and other mediators of inflammation that not only perpetuate the inflammatory process but also increase bone resorption. In addition, activated synovial fibroblasts, chondrocytes and osteoclasts contribute to cartilage and bone damage. Monocytes are also critical for these pathological processes, as for instance, they function as precursors for macrophages and osteoclasts. Long noncoding RNAs (lncRNAs) are a class of noncoding RNAs with a size larger than 200 nucleotides, which expression is tissue-specific and can be also modulated during differentiation. Many studies have explored the expression profile and function of distinct lncRNAs in different cell types and diseases. Recently, several lncRNAs have been shown to be differentially expressed during osteoclastogenesis. In addition, it has been observed that several lncRNAs present an altered expression in cellular types critical to RA pathogenesis, such as peripheral mononuclear cells and synoviocytes. However, our knowledge on the expression of lncRNAs in monocytes of RA patients is still scarce. Our hypothesis is that specific lncRNAs such as, GAS5, NEAT1 and DANCR, can be differentially expressed in monocytes of RA patients in comparison with those obtained from healthy donors, and that this differential expression may play a role in RA. To address this, we aim here to quantify the expression levels of specific lncRNAs in monocytes from both RA patients and healthy donors and correlate the observed expression variation with disease activity. The identification of differentially expressed lncRNAs in monocytes will hopefully provide us with insights on their putative function in the pathophysiology of RA.

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