Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Evaluation of lncRNAs role in the control of osteoclastogenesis in rheumatoid arthritis patients

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[1,2]. RA joint synovial cellular infiltrate consists of activated macrophages, B and T cells, which secrete proinflammatory cytokines and other mediators of inflammation[1,3,4] that not only perpetuate the inflammatory process but also increase bone resorption[5–8]. In addition, activated synovial fibroblasts, chondrocytes and osteoclasts contribute to the underlying cartilage and bone damage8. Long noncoding RNAs (lncRNAs) are a class of noncoding RNAs with size larger than 200 nucleotides, which expression is tissue-specific and alters across several stages of differentiation[9]. Many publications have explored lncRNAs expression profile and function in different cell types and diseases, but this remains a field with a vast and poorly explored research agenda[10–12]. Very recently, a group of researchers published a microarray analysis of the expression of several lncRNAs during osteoclastogenesis[13]. This work identified groups of thousands of lncRNAs that are upregulated or downregulated during osteoclasts differentiation. GAS5, NEAT1, MEG3 and DANCR are some of the lncRNAs, which expression levels changed during osteoclastogenesis. Our hypothesis is that the levels of expression of specific lncRNAs in the osteoclasts of RA patients are disturbed and that these lncRNAs influence bone damage.

The main goal of this project is to quantify the expression levels of GAS5, NEAT1, MEG3 and DANCR long noncoding RNAs in monocytes from RA patients and access their role in osteoclasts activity and bone degradation in a cell line.

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Webpage of the group: https://imm.medicina.ulisboa.pt/en/investigacao/labs/fonseca-lab/

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