# INVESTIGATIONS OF GENE EXPRESSION IN OSTEOCLASTS FORMED FROM PERIPHERAL BLOOD MONOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS.

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Bone is a central element in the pathophysiology of inflammatory arthropathies, such as rheumatoid arthritis (RA). We hypothesized that the osteoclastogenic capacity of peripheral blood monocytes (PBMCs) in patients with RA correlates with the presence and/or severity of the disease. PBMCs were isolated from a transverse cohort of RA patients and a control population, and treated for 21 days with RANKL and M-CSF to induce osteoclast formation. RNA was isolated from mature osteoclast cultures and gene expression was assessed using quantitative real time RT-PCR. We first characterized the expression of the following five genes encoding proteins important for different aspects of osteoclast physiology; 1) RANK, a receptor for cytokine RANKL, critical in osteoclastogenesis; 2) c-fms, a receptor for M-CSF, critical for osteoclast differentiation and survival; 3) CCR1, a chemokine receptor potentially involved in osteoclast migration; 4) NFATc1, key osteoclastogenic transcription factor; and 5) cathepsin K, protease critical for osteoclast resorptive activity. As a reference control, we have used RNA isolated from human osteoclasts formed from commercially available precursors. We have found considerable differences in the expression of osteoclastic genes examined in 34 blind samples from both patient and control population. Of the five genes tested, the smallest variation was observed in the expression levels of c-fms, which varied from 0.1 to 2.3 fold of reference control. The highest variation was observed in the expression levels of cathepsin K, which varied from 0.2 to 2688 fold of reference control. In the next few months, we plan to expand the data set to include the total of 100 samples from patients with RA and 50 samples from control populations. The information for the expression of osteoclast-relevant genes will be incorporated within the comprehensive set of osteoclastic parameters obtained by different members of NET group. We will use a novel data mining approach, which allows determining potential correlations between any number and combination of osteoclastic parameters and clinical variables in large collections of data. We anticipate that our study will allow us to define the osteoclastic parameters that most strongly correlate with laboratory and radiologic measurements in RA patients.