ABSTRACT

Rheumatic diseases are common, usually chronic, painful and to some extent invalidating medical conditions. Understanding of the disease pathogenesis is still very fragmentary. Hyperreactivity of the immune system and defect of autotolerance are probably contributed by local factors, which helps to explain, why some joints/muscles are more affected than others. All this results from a complex net of interactions between immune cells, synovial fibroblasts, chondrocytes, osteocytes, myocytes and other cells.

In the submitted PhD thesis I have focused on three groups of molecules: regulatory RNAs, S100 proteins and autoantibodies. In the theoretical part, I sum up the current knowledge on their biogenesis, function and the role in rheumatology. In the investigative part, I present six original publications and one review on the role of those molecules in development of rheumatoid arthritis (RA) and idiopathic inflammatory myositis (IIM).

One of the main studies was focused on expression of PIWI-interacting RNAs (piRNAs) in RA synovial fibroblasts (SF). piRNAs are small regulatory RNAs which in complex with PIWIL proteins regulate gene expression and silence transpozoms. piRNA expression was considered to be limited to germline and cancer cells. We have found 267 PIWI-interacting RNAs to be expressed in RA synovial fibroblasts and described their deregulation when compared to osteoarthritis SF. We have also described the presence of PIWIL4 protein in the nuclei of synovial fibroblasts and its regulation by proinflammatory cytokines and TLT-ligands. We have also studied a possible use of miRNAs as biomarkers in IIM and use of S100A8/9 as biomarker in early RA. When investigating the function of S100A4, a protein also known as metastasin, a possible link with malignity in cancer associated myositis was considered. We were not able to confirm this association, but somewhat surprisingly, we observed a correlation of the S100A4 serum levels with clinical activity in myositis. Autoantibody results detected by the radioimmunoprecipitation method were used for a descriptive study on autoantibodies associations and clinical form of arthritis in IIM and for a report on the increasing incidence of the immune mediated necrotizing myopathy.

Results of this PhD. thesis aim to improve our understanding of pathogenesis of musculosceletal diseases and their treatment.

Key words:
Rheumatoid arthritis, myositis, miRNA, piRNA, S100 proteins, autoantibodies