Abstract

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Title of diploma thesis:

The role of miR-150 in the physiopathology of oligoarticular juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatoid disease affecting children, and its pathological mechanisms are still poorly understood. Innate and adaptive immunity including myeloid cells play a major role in these processes. Epigenetic deregulations along with non-coding microRNAs have been reported in many inflammatory diseases. Moreover, preliminary results obtained by the research group of Prof. Florence Apparailly showed accumulation of intermediate monocytes along with the high expression of miR-150 in the synovial fluid of children affected by oligoarticular JIA. Based on these findings a hypothesis has been postulated suggesting that miR-150 could have a role in the pathogenesis of this disease and in the regulation of monocyte differentiation and function. To study the impact of miR-150 on monocytes from the peripheral blood of healthy donors, transfection experiments were performed to neutralize miR-150. The phenotype of the cells was analysed by flow cytometry. In parallel, in silico analysis was carried out to find putative target genes using miRNA databases. RT-qPCR experiments were performed to analyse the expression of these genes in miR-150-modified monocytes. A decrease of intermediate monocytes was seen in 4 out of 6 transfection experiments with miR-150 inhibitor compared with the control. We also found 10 genes down-regulated and 27 up-regulated, 7 of them with statistical significance ($p<0.05$). Comparing both in silico and in vitro experimental data, the results suggest that CCR2 might be a direct target of miR-150-5p in human monocytes. Taken together, we suggest that miR-150 might play a significant role in the pathogenesis of oligoarticular JIA by influencing the egress of monocytes from the bone marrow and their homing to inflamed tissues.