Abstract

The biological half-life of several pro-inflammatory mediators involved in the pathogenesis of rheumatoid arthritis (RA) is controlled by molecules exhibiting dipeptidyl peptidase-IV (DPP-IV)-like enzymatic activity (Dipeptidyl peptidase-IV activity and/or structure homologues- DASH).

The aim of this thesis was to identify the molecular source of the DPP-IV-like enzymatic activity in the peripheral blood and synovial fluid in patients with rheumatoid arthritis as compared to control patients with osteoarthritis (OA), and to evaluate the association of DPP-IV with the disease activity.

We found that the main source of the DPP-IV-like enzyme activity in the plasma and in the synovial fluid in patients with RA is the canonical DPP-IV. DPP-IV-like enzymatic activity and canonical DPP-IV were also detected on the cell surface of blood and synovial fluid mononuclear cells.

Significantly lower DPP-IV-like enzymatic activity and DPP-IV expression in the synovial fluid mononuclear cells was found in RA as opposed to OA patients. In the synovial fluid of RA patients there was also a negative correlation between the concentration of the pro-inflammatory DPP-IV substrate SDF (stromal cell-derived factor-1α) and the proportion of the DPP-IV+ T cells. The blood plasma DPP-IV-like enzymatic activity and concentration were lower in patients with active RA as compared to OA, while there were no differences in DPP-IV expression on the blood mononuclear cells (BMNC). In a follow-up study, intraindividual comparison in patients with disease remission revealed that there was an increase of the blood plasma DPP-IV and a decrease of DPP-IV on BMNC in RA patients during the less active phase of their disease.

The association between RA activity and the changes in the blood plasma and the blood mononuclear cell DPP-IV in individual patients supports the possible role of DPP-IV as a disease activity marker. The lower local availability of DPP-IV in the synovial fluid in RA may in addition participate on the disease progression by the reduced degradation of the pro-inflammatory chemokine SDF.