Abstract

Introduction: Recent findings and better understanding to the pathogenesis of rheumatic diseases contributed to the development of biological therapies targeting cytokines and immune cells. Several S100 proteins exert cytokine-like effects and participate in the regulation of the inflammatory process. The aim of this work was to study the role of selected S100 proteins in the activity and in the pathogenesis of the rheumatic diseases.

Results: Our data show for the first time an association of S100A4 proteinwith RA disease activity and decrease of the bioactive form, but not the total amount of S100A4, after aplication of tumour necrosis factor (TNF) blocking biologic therapy in patients with RA. We demonstrated that in vitro S100A4 acts as a potent pro-inflammatory mediator inducing production of TNFα, interleukin (IL)-1β and IL-6 in PBMCs via Toll-like receptor 4 (TLR-4), transcription factor NFκB and tyrosine kinases erk1/2 and p38. Moreover, S100A4 can play an important role in the pathogenesis of inflammatory myopathies. S100A4 is present in the inflammatory infiltrate of the affected muscles and in the regenerating muscles and may act as a cytokine-like factor indirectly promoting muscle fiber damage by stimulating mononuclear cells to increase the synthesis of pro-inflammatory cytokines. We also show normalization of elevated S100A8/9 and S100A12 in patients with recent-onset RA after the initiation of conventional treatment. Both proteins were positively associated with the RA disease activity and the decrease of S100A8/9 may be an indicator of the improvement in the total number of swollen joints after succesful therapy of RA.

Conclusion: We provide further characterization of the role of S100 proteins in the activity and pathogenesis of rheumatic diseases and evaluation of the potential therapeutic implication in autoimmune diseases.

Key words: rheumatoid arthritis, inflammatory myopathies, S100 proteins