Abstract

Systemic scleroderma (SSc) is a systemic connective tissue disease affecting skin and internal organs. The pathogenesis of SSc is characterized by inflammation, vasculopathy and fibrosis. No agent has been proven effective in the treatment of SSc. There is a lack of suitable biomarkers for monitoring the disease activity or the response to the treatment of SSc. Therefore our aim was to analyse the extracellular levels of S100A4, Hsp90 (Heat shock protein 90) and IL-35 (interleukin-35) in SSc. S100A4 and Hsp90 have been initially studied in tumours; in some of them considered as suitable prognostic markers and candidates for future therapies. We have recently described the profibrotic role of S100A4 and Hsp90 in the pathogenesis of SSc. Our results showed that inactivation of S100A4 and Hsp90 effectively prevented the development of experimental skin fibrosis. This was consequently confirmed by the analysis of S100A4 and Hsp90 in the peripheral blood of patients with SSc, where significant associations with disease activity and organ involvement were detected. IL-35 may become another potential biomarker of SSc. We detected increased expression of IL-35 in the affected skin, dermal fibroblasts and in serum of patients with SSc. Moreover, the main profibrotic mediator transforming growth factor (TGF-β) induces the secretion of IL-35 which results in activation of fibroblasts and increased collagen secretion into the supernatant. Furthermore, serum IL-35 is associated with the early, inflammatory phase of SSc.

This project could contribute to the identification of potential new biomarkers suitable for monitoring the disease activity or the treatment efficacy in SSc.

Keywords: systemic sclerosis, S100A4, Hsp 90, interleukin-35