A novel role for relaxin (RLX) and its receptor (LGR7) in Limited Systemic Sclerosis (ISSc)

Claudio Corallo
University of Siena, Italy

Relaxin (RLX) is a small dimeric hormone, with similar structure to insulin. It is involved in extracellular matrix remodeling and plays anti-fibrotic role in lung, liver, kidney and heart, promoting also wound healing. In humans, different RLX receptors (RXFPs) have been discovered. The isoform RLX-2 binds RXFP1/LGR7 receptor. In literature, it has been reported that increased serum levels of RLX were detected in patients affected by Systemic Sclerosis (SSc). Moreover, recombinant human relaxin (RH-RLX) has been used for improving skin disease and reducing functional disability in scleroderma patients; but the results remained controversial. In the present study, RXFP1/LGR7 receptor immunolocalization has been detected on skin biopsies and cultured fibroblasts from limited SSc (ISSc) patients (20 women; age in yrs 57 ± 7 yrs; disease duration in yrs 7 ± 2.4), undergoing unaffected and affected skin biopsies and compared to normal skin. RXFP1/LGR7 receptor showed cytoplasmic localization in skin cells (keratinocytes, gland epithelial cells, endothelium, smooth muscle cells and fibroblasts) from control subjects and non-lesional skin from ISSc patients. Immunogold electron microscopy confirmed a diffuse epithelial cytoplasmic localization of RXFP1/LGR7 receptor. A substantially lower expression has been observed in scleroderma skin, with a lack of staining in most cells, respect to normal skin and unaffected ISSc skin. Occasional weak reactivity has been found in cultured scleroderma fibroblasts, while control fibroblasts showed a diffuse cytoplasmic immunoreactivity of RXFP1/LGR7 receptor, as confirmed by Western blot findings. Finally, both desmin and alpha smooth muscle actin immunoreactivity on cultured fibroblasts confirmed the different phenotype among unaffected/control fibroblasts and affected fibroblasts (myofibroblasts). These data seem to demonstrate that the high serum levels of RLX-2 in SSc patients and the doubtful therapeutic efficacy of RH-RLX in the same patients could be related to RXFP1/LGR7 receptor alterations.

corallo.claudio@gmail.com