

Evaluation of EC-SOD activity in human normal and sclerodermic fibroblasts

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Systemic sclerosis (SSc) is a multisystemic disease characterized by vascular injury, circulating autoantibodies and extensive fibrosis of skin, skeletal muscles, vessels and visceral organs. It is related to increased synthesis of ECM proteins by activated fibroblasts: this process is modulated by many cytokines such as TGF- α and - β , PLGF, EGF, interleukins and TNF - α and - β . Recent studies demonstrated a role of oxidative stress in SSc pathogenesis. In fact, reactive oxygen species (ROS) accumulation is involved in SSc through different mechanisms: autoantibodies production, changes in the protease – antiprotease balance leading to fibrosis, fibroblasts activation by TGF- β and PDGF. The antioxidant enzymes superoxide dismutases (SODs) constitute an ubiquitous metal enzymes family which catalyzes the dismutation of two superoxide radicals into hydrogen peroxide and oxygen. Extra cellular superoxide dismutase (SOD3) is copper and zinc superoxide dismutase, which is expressed in selected tissues and is secreted into the extracellular space. This enzyme is associated to inflammatory responses in several experimental models; furthermore, hydrogen peroxide produced by SOD3 during enzymatic activity, modulates the profile of cytokine secretion in some cell populations and induces increased proliferation and upregulation of collagen I gene in normal fibroblasts.

We investigated the expression and the intracellular localization of SOD3 in dermal fibroblasts from both SSc patients and healthy donors and evaluated SOD3 activity in fibroblasts culture medium.

RT-PCR analysis demonstrated increased levels of SOD3 mRNA in SSc fibroblasts when compared to control healthy fibroblasts. SOD3 staining by immunofluorescence displayed a characteristic "secretory" pattern in both healthy and SSc fibroblasts. SOD assay, performed with xanthine/xanthine oxidase method, demonstrated SOD3 enzymatic activity in SSc fibroblasts culture medium four times higher than in healthy fibroblasts.

Further studies will identify the factors regulating SOD3 expression in SSc fibroblasts and clarify the role of SOD3 enzymatic activity in SSc pathogenesis.

Key words

Systemic sclerosis (SSc), reactive oxygen species (ROS), superoxide dismutases (SODs), extra cellular superoxide dismutase (SOD3)