

## **Fibrillin and MAGP-1 production by dermal blood and lymphatic microvascular endothelial cells challenged with systemic sclerosis sera**

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Systemic sclerosis (SSc) is a connective tissue disorder of unknown etiology with two different subsets: limited (lSSc) and diffuse cutaneous systemic sclerosis (dSSc) with different patterns of organ involvement, autoantibody profiles and survival (1). The disease is characterized by three major features: vascular endothelial injury, inflammation/autoimmunity and massive deposition of collagen. Many extracellular matrix proteins are altered in SSc, including fibrillin (2). Fibrillin microfibrils form anchoring filaments in lymphatic endothelium. In the wall of arteries they constitute a scaffold for elastin deposition and sequester in the matrix TGF $\beta$  and other molecules which regulate matrix formation and remodeling (3). The aim of this study was to evaluate the effect of SSc sera on fibrillin and microfibril associated glycoprotein-1 (MAGP-1) deposition by human adult dermal blood (BHMVEC) and lymphatic (LyHMVEC) microvascular endothelial cells.

Cells were cultured on gelatine-coated coverslips in EBM containing 15% of serum of lSSc or dSSc patients, naive or under pharmacological therapy, and of controls and fixed at days 2 and 4 of confluence. Double immunofluorescence was performed with a monoclonal antibody to fibrillin-1 and a polyclonal antibody to MFPA2. Fibrillin and MAGP-1 deposition were quantified on 30 random photographic fields/slide.

Fibrillin and MAGP-1 were produced by BHMVEC and LyHMVEC in all experimental conditions. They co-localized forming a honeycomb pattern in BHMVEC, as previously described (4), and a dense mesh of short segments in LyHMVEC. Comparative evaluation between LyHMVEC and BHMVEC indicated that, at day 4, LyHMVEC produced more fibrillin than BHMVEC in all experimental conditions. In BHMVEC, Fibrillin and MAGP-1 production significantly increased with time under challenge with naive lSSc sera, and with dSSc sera irrespective of therapy, as compared with control sera. In LyHMVEC, their production significantly increased with time after challenge with both SSc and control sera, without any significant difference.

Overall, LyHMVEC produced more but less organized fibrillin and MAGP-1 and were less influenced by SSc sera than BHMVEC.

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4) Rossi A et al. (2010) *J Anat* 217:705.

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