

## Telocytes in normal and scleroderma skin

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Telocytes are a distinct population of interstitial (stromal) cells which were recently identified in a wide variety of tissues and organs, including the skin. Systemic sclerosis (SSc, scleroderma) is a complex connective tissue disease characterized by small-vessel vasculopathy and fibrosis of the skin and internal organs. In the present study, we investigated the distribution and ultrastructural features of telocytes in skin of SSc patients compared with healthy subjects. Forearm skin biopsies were obtained from 20 SSc patients (11 limited SSc [lSSc], 9 diffuse SSc [dSSc]) and 10 controls. Sections were subjected to double immunoenzymatic or immunofluorescence labeling for CD34, c-kit/CD117, CD31/endothelial cells, alpha-SMA, mast cell tryptase, CD11c/dendritic cells, and CD90/fibroblasts. Ultrathin sections were processed for transmission electron microscopy. In normal skin, numerous CD34+ cells were observed throughout the dermis. Many CD34+ cells were CD31-expressing endothelial cells, but there was also a large population of telocytes, which appeared as spindle-shaped cells with very long and thin prolongations forming an interstitial network in the papillary and reticular dermis. CD34+ telocytes were scattered between collagen bundles and retinacula cutis, and were concentrated around microvessels, nerves, and adnexal structures (hair follicles, arrector pili muscle bundles, sebaceous and sweat glands). Skin telocytes did not express c-kit, while many c-kit/tryptase double-positive mast cells were observed. CD34+ telocytes did not express alpha-SMA, CD11c and CD90. A striking reduction in CD34+ telocytes was found in SSc skin. In early-stage lSSc, telocytes were reduced throughout the papillary dermis and in some areas of reticular dermis. In late-stage lSSc, the loss of telocytes extended to affect more severely the reticular dermis. In dSSc skin, telocytes were severely reduced in both the papillary and reticular dermis starting from the early-stage. A few telocytes were still present around adnexal structures in early-stage, while they almost completely disappeared in late-stage dSSc. In SSc skin, telocytes exhibited ultrastructural features of degenerating cells (cytoplasmic vacuolization, loss of organelles). Abundant collagen and elastic fibres enveloped and separated telocyte prolongations from nerve fibres and microvessels. Because telocytes may be implicated in several processes, such as mechanical support, neurotransmission, intercellular signaling and connective tissue regeneration, the progressive loss of telocytes might have important pathogenetic implications in SSc.

Keywords: Telocytes, interstitial cells, skin, scleroderma.