Tendon progenitor cells - their appearance and distribution in degenerated and ageing tendon

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Tendons are specialized tissues that connect muscle to bone and transmit the forces generated by muscle to bone, resulting in joint movements. They are characterized by a sparse vascular bed, low cell density and a decreased healing capacity. Only little is known about the molecular composition of tendon cells, their extracellular matrix and their progenitor cells. We analysed biopsies of human supraspinatus tendon (ST) from patients of various ages for the existence and the distribution of progenitor cells using immunohistochemistry. The expression of various cellular markers: for tendon cells (Scleraxis, Tenomodulin), extracellular matrix (ECM) proteins (Col1A1 and 3A1, MMP-2, -9, Lox), progenitor cells (Nestin, CD 133, CD11b, VCAM-1) and for cell differentiation (Aggrecan, Sox-9, Osterix, REST, CoREST) was studied with RT-PCR and qRT-PCR. In tendon biopsies of patients >50 years the yield of total RNA was significantly lower than in biopsies of younger patients (<50 years) and the expression frequencies of progenitor cell markers was decreasing with age. To further study tendon ageing we isolated RNA from Achilles tendons of young adult (6 weeks) and old NMRI mice (>24 months) and performed expression analysis of Nestin, Aggrecan, Scleraxis, Col1A1, Col3A1, MMP-2, MMP-9 and Lox. The expression of Scleraxis and Aggrecan was significantly down-regulated and Nestin mRNA was not detectable in tendons of old mice. The ECM proteins MMP-2, Col1A1, Col3A1 and Lox showed significant down-regulation in old mouse tendons, whereas MMP-9 was up-regulated in old mice. We also analysed biopsies of ruptured human ST for the expression of the above mentioned markers, interestingly the age dependency was not detectable anymore. Regarding to tissue degenerations, like fatty infiltrations, hypervascularization or cartilagenous modifications as well as the increase of the dense connective tissue in the ST, the expression of cellular markers revealed significant differences. Between males and females we found the most striking and highly significant differences in the expression of ECM markers. In conclusion progenitor cells are still detectable in older individuals although to a lesser extent, depending on individual susceptibility and pathological status of the patients.