Human and rat tendons harbour a population of insulin producing cells expressing stem- and pancreatic β-cell associated markers

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Abstract

Diabetes and obesity are risk factors for tendinopathy, tendon injury and impaired tendon healing. So far, the mechanisms of tendon impairment in diabetic patients remain a matter of debate. Altered metabolic parameters as well as changes in the vasculature may play a role. Along our search for stem cells suitable for tendon repair, we discovered a tendon-derived cell type readily differentiating towards insulin producing cells in vitro. Here we describe a population of tendon cells expressing the pancreatic β-cell associated proteins Insulin and Glucagon in vivo.

Tissue samples from intact human biceps-, supraspinatus, and semitendinosus tendons were obtained with patients’ informed consents, tissue donors were aged from 23-63 (n=5) years.

By immunocytochemistry, Laser Capture Microdissection and quantitative PCR we show that these cells are mainly located in the perivascular area, but also in the dense, collagenous parts of tendon tissue. Single cell PCR analysis of isolated tendon perivascular cells reveals a coexpression of Insulin with the stem cell-associated markers Oct4 and Nanog. Both Insulin and Insulin-related mRNA are significantly reduced in Achilles tendons of rats treated with 60µg/kg of the β-cell specific cytostatic agent Streptozotocin 5 days after the treatment. Biomechanical testing revealed that this treatment also results in a significant (p=0.018) reduction in tendon tensile strength of 39.9% (n=12) after 5 days.

In our hands, enzymatically released tendon cells neither show glucose-dependent insulin secretion nor staining with Dithizone, a zinc-chelating agent commonly used for the detection of pancreatic β-cells. These findings indicate that, despite several similarities with pancreatic β-cells, these tendon-derived cells have different properties and functions. Whether these cells are affected by changing metabolic parameters or diabetes, or whether these cells may be a potential source for tissue engineering or cell therapy in diabetes treatment will have to be elucidated by further experiments.