Characterization of Tendon Stem/Progenitor Cells in Tendon Tissue in vivo

INTRODUCTION:

Tendon-derived stem cells (TDSCs) have been isolated from tendon tissues and characterized in vitro in recent studies [1]. However, the distribution of tendon stem / progenitor cells in tendon tissues in vivo has not be described in details and have never been characterized. Tendon heals poorly and inefficiently after acute injury and tendon non-healing was reported in tendinopathy. As stem cells residing in tendons, tendon stem / progenitor cells are expected to play roles in maintaining tissue homeostasis and participate in tendon repair upon injury. Therefore, better understanding of the in vivo niche of tendon stem / progenitor cells can provide hints about the possible cause of poor tendon healing and non-healing. This study thus aimed to investigate the in vivo distribution of tendon stem / progenitor cells in tendon tissue and characterized the expression of pluripotent markers, pericyte markers and tendon-lineage markers in these cells.

METHODS:

This study was approved by the animal research ethics committee of the authors’ institution. IdU label-retaining method was used for the labeling of tendon stem/progenitor cells. Briefly, iodo-deoxyuridine (IdU) (Sigma) was injected into 3-day-old rats for one week. At week four, the rat patellar tendons were harvested for frozen and paraffin sectioning. The expression of pluripotent makers (Nanog, Oct4, Sox2, nucleostemin), pericyte markers (CD146, α-Sma) and tendon-lineage markers (Tnmd, Mkx) in the IdU+cells was then investigated by immunofluorescent staining. (DAPI, IdU+, Markers+ and Merge images were shown in the pictures)

RESULTS:

Single IdU+ cells were observed throughout the tendon tissue including paratendon, tendon mid-substance and blood vessels (Figure 1). More IdU+ cells were observed in paratendon compared to tendon mid-substance (Figure 1). Few IdU+ cells expressed nucleostemin (Figure 2) and Nanog (Figure 3). However, all IdU+ cells were negative for the expression of Sox2 and Oct4 (results not shown). CD146+ (Figure 4) and α-Sma+ (result not shown) cells were found throughout the tendon tissue in addition to the blood vessels inside tendon. Most of the IdU+ cells expressed CD146 (Figure 4), α-Sma (Figure 5) and Tnmd (results not shown) but not vice versa. No Mkx expression could be observed in tendon tissue.

DISCUSSION:

We have identified tendon stem/progenitor cells in para-tendon, mid-substance and blood vessels in vivo. Some IdU+ positive cells were positive for nucleostemin and Nanog, but they did not expressed Sox2 and Oct4, consistent with the previous study that Oct4 was not essential for the self-renewal of somatic stem cells [2]. Most of the IdU+ positive tendon stem/progenitor cells were positive for CD146 and α-Sma, suggesting that they might be derived from the pericytes [3].

SIGNIFICANCE:

This present study provides evidence for the existence of tendon stem/progenitor cells in tendon tissue in vivo. Characterization of the in vivo niche of tendon stem/progenitor cells will aid our understanding of the mechanisms of poor tendon healing and non-healing. This might provide hints for the mobilization of these endogenous stem / progenitor cells for the management of these tendon injuries in the future.

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REFERENCES: