INTRODUCTION: Peroxiredoxin 5 (PRDX5) is a novel antioxidant enzyme recently identified in a variety of human cells and tissues, which is considered to play an important role in oxidative stress protection mechanisms by eliminating hydrogen peroxide (H$_2$O$_2$) and other reactive oxygen species (ROS). However, little is known about its expression in tendon degeneration, a common and disabling condition that primarily affects older people, in which oxidative stress may be involved. The aim of this study was to investigate the expression of PRDX5 in normal and degenerative human tendon, therefore to gain insight into antioxidant protection mechanisms involved in tendon healing and tendon degeneration.

METHODS: Pairs of degenerating torn supraspinatus tendon (DT) and normal subscapularis tendon (NT) tissue were collected from patients with rotator cuff tears undergoing shoulder surgery. Polymerase chain reaction (PCR) and in situ hybridization were performed to assess PRDX5 mRNA expression. A rabbit antibody was raised against recombinant human PRDX5 and used in Western blotting and immunohistostaining for the detection of PRDX5 protein. The expression level of PRDX5 mRNA or protein was expressed by the ratio of the net intensity of the PRDX5 band to actin band of the same sample (semi-quantitative analysis) Comparison of PRDX5 expression in normal and degenerate tendon was made by Student’s $t$ test. The two-tailed $P$ values are reported.

RESULTS: PRDX5 mRNA and protein expression was significantly higher in degenerate tendon (DT) than in normal tendon (NT) ($p < 0.01$ for mRNA, Fig 1, lower panel; and $p = 0.024$ for protein, Fig 2, lower panel) assessed by PCR (Fig 1, upper panel) and Western blotting (Fig 2, upper panel) The PRDX5 protein expression was localized to fibroblasts in normal tendon (Fig 3A) and to both mature fibroblasts and endothelial cells in degenerate tendon (Fig 3B, circle F & arrow E). Fibroblast-like cells in hypercellular areas of degenerate tendon (Fig 3B, square G) expressed much less PRDX5 compared to that in non-hypercellular areas (Fig 3B, circle F) with a nearly normal tendon appearance. The differential expression of PRDX5 in degenerative tendon was further confirmed by in situ hybridization as shown in Fig 4, in which fibroblasts among normal collagen fibrils in degenerate tendon showed stronger PRDX5 mRNA staining (Fig 4A) compared with the fibroblast-like cells in the granulation tissue (Fig 4B, arrows).

DISCUSSION: The present study provides evidence for the first time that PRDX5 is expressed in human tendon, and its expression is upregulated at both mRNA and protein levels in degenerate tendon. In addition, we have localized the PRDX5 expression to tendon fibroblasts, especially to the mature fibroblasts and endothelial cells in degenerate tendon. The differential expression of PRDX5 in normal and degenerative tendon suggests that oxidative stress may be implicated in the pathogenesis of tendon degeneration. Increased PRDX5 production may be a counter-response to neutralize H$_2$O$_2$ and other ROS over-produced under certain pathological stimulation. PRDX5 may play a protective role against oxidative stress during tendon degeneration and/or tears.

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