A NOVEL ANTIOXIDANT ENZYME PEROXIREDOXIN 5 IN HUMAN OSTEOARTHRITIS: ITS EXPRESSION AND REGULATION

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Introduction: Peroxiredoxin 5 (PRDX5) is a novel antioxidant enzyme recently identified in a variety of human cells and tissues. It plays an important role in oxidative stress protection mechanisms by eliminating hydrogen peroxide (H₂O₂) and other reactive oxygen species (ROS). However, the expression of this enzyme in human cartilage, particularly in osteoarthritic cartilage, has not been investigated. The aim of this study was to investigate the expression and regulation of PRDX5 in human normal and osteoarthritic cartilage, therefore to gain insight into antioxidant protection mechanisms involved in osteoarthritis.

Methods: Human osteoarthritic cartilage was removed from knee joints of patients undergoing total knee-replacement surgery. Normal human cartilage was removed immediately adjacent to the insertion site of supraspinatus tendon as part of the surgical procedure to repair the tendon to bone. Human chondrocytes were isolated from cartilage by collagenase digestion. Cartilage explant and chondrocytes were maintained in primary culture to investigate the expression and regulation of PRDX5. A rabbit antibody was raised against recombinant human PRDX5 and used for immunodetection of PRDX5. Northern blot and Western blot analysis was performed to evaluate PRDX5 mRNA and protein levels in cartilage and chondrocytes. Fluorescence-activated cell sorting (FACS) analysis was carried out to assess chondrocyte intracellular production of reactive oxygen species (ROS) under the stimulation of inflammatory cytokines.

Results: Higher PRDX5 protein expression was detected in osteoarthritic cartilage than that in normal cartilage (Fig 1). TNFα or IL-1 may contribute to this higher expression, as increased PRDX5 was observed 24 hours after the addition of TNFα or IL-1 in cartilage explant culture (Fig 2). In primary human chondrocyte culture, TNFα markedly increased intracellular ROS production (peak levels at 1-12 hours, Fig 3). In parallel to ROS levels, PRDX5 mRNA and protein expression was also increased but the up-expression started from 3 hours following TNFα stimulation and peaked at 24 hours (Fig 4) when intracellular ROS started declining (Fig 3).

Discussion: This study demonstrates, for the first time, that PRDX5 is expressed in human cartilage and the expression is up-regulated in osteoarthritis. Inflammatory cytokines (TNFα and IL-1) contribute to this up-regulation by a rapid increase of intracellular ROS production, followed by an increase of PRDX5 expression in chondrocytes. One of the important factors implicating age-related tissue degeneration, such as osteoarthritis, is oxidative stress caused by over-production of ROS. The highly reactive ROS molecules are potentially destructive, as they attack DNA, lipids and proteins leading to cell death and tissue damage. Understanding the antioxidant defence mechanisms may lead to improved treatment for oxidative stress-related diseases. Our data suggest that oxidative stress may be involved in the pathogenesis of osteoarthritis. PRDX5 may play a protective role against oxidative stress in human cartilage.

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