Heat Shock Protein 60 Stabilizes Cartilage Integrity in Osteoarthritic Knees

Yi-Chih Sun, Feng-Sheng Wang, Jih-Yang Ko

Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

**Background:** Cartilage damage is a prominently deleterious feature in osteoarthritic (OA) knees. Deregulation of biological, genetic or biomechanical reactions reportedly accelerates cartilage injury in OA. Mechanistic events underlying extracellular stress impediment of cartilage homeostasis remains elusive. Heat shock proteins (HSPs) are conserved chaperone molecules that actively respond to biochemical, mechanical stimulations or deleterious stresses in arthritic joints [1]. We have previously demonstrated that HSP60 signaling is important to maintain bone mass and chondrocyte survival [2].

**Aims:** This study explores the biological significance of HSP60 in fate and metabolism of articular chondrocytes from OA patients and cartilage damage in mice with OA knees.

**Materials and Methods:** Primary chondrocyte and synovial fluid were harvested from patients with end-stage OA knee or non-OA injury underwent arthroplasty. Mice overexpressing human HSP60 driven by phosphoglycerate kinase promoter and wild-type mice were suprapatellarly injected with collagenase to induce OA knees. Joint structure, cartilage morphology and walking pattern of mice were evaluated by µCT imaging, safranin-O stain and Catwalk. Expression of chondrogenic gene and ubiquitination of SOX9 were analysed by qRT-PCR, immunoblotting and liquid chromatography-mass spectrometry.

**Results:** In clinical vignettes, OA patients had decrement HSP60 concentrations in defective cartilage and synovial fluid as compared to those in patients with non-OA joint injury. Low HSP60 levels correlated with Mankin and OARSI scores in injured sites. HSP60 reduced the deleterious actions of IL-1β on chondrogenic transcription factor SOX9 and aggregan expression in primary chondrocyte cultures. In collagenase-induced OA mouse model, HSP60 transgenic mice with injured knees displayed better gait profiles than wild-type mice. Injured joints in transgenic mice mildly exhibited articular cartilage destruction and synovial inflammation. Mechanistically, overexpression of HSP60 reduced the promoting effects of OA on SOX9 degradation by repressing proteasome ubiquitin action and restored IGF-1 signaling in injured joints.

**Conclusions and clinical implications:** HSP60 is potent protector against OA-mediated SOX9 degradation that accelerates cartilage deterioration. Restoration of HSP60 signalling is an alternative to maintain chondrocyte metabolism and articular cartilage function in OA knees.

**References:**


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