Advances in Understanding of Post-Traumatic Osteoarthritis: Implications for Treatment of Joint Injuries

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Excessive synovial joint loadings, acute single articular surface impacts and/or chronic repetitive aberrant contact stresses, cause joint degeneration leading to the clinical syndrome of osteoarthritis (OA). Common joint injuries that lead to post-traumatic osteoarthritis (PTOA) include joint impact injuries, joint dislocations and meniscal and ligament injuries. Intra-articular fractures (IAFs), joint injuries that fracture the articular surface and the underlying subchondral bone, are the injuries that most predictably lead to post-traumatic OA (PTOA). Both the acute injury and any residual joint incongruity and instability contribute to the risk of PTOA. Despite advances in treatment of joint injuries, this risk has not decreased in the last 50 years. However, recent work shows that the potential to prevent or mitigate PTOA exists. Quantitative methods of determining IAF energy and cumulative chronic joint overloading due to residual joint incongruity predict the risk of PTOA. They define joint loading thresholds that cause PTOA in human joints making it possible to assess the efficacy of treatments intended to reduce PTOA risk. In vitro and in vivo investigations of joint biologic responses to excessive loads show that reactive oxygen species (ROS) produced by chondrocytes cause mitochondrial damage and dysfunction, chondrocyte death, matrix degradation, and articular cartilage erosion. Excessive ROS after injury also accelerates chondrocyte aging and senescence, thereby increasing secretion of pro-inflammatory chemokines, cytokines, and matrix proteases that cause cartilage destruction. Small and large animal studies show that preventing ROS production or providing antioxidant support preserves chondrocytes and their matrix following IAFs and similar injuries. Repetitive lower energy mechanical insults associated with joint overloading result in a state of chondrocyte metabolic dysfunction comparable to that seen post-acute injurious impact suggesting that the osteoarthritis that occurs in clinical conditions such as joint dysplasia, joint instability and joint incongruity results from a similar mechanism, as summarized in the figure below.

In addition to ROS, injured chondrocytes release alarmins that activate chondrocyte progenitor cells that proliferate and migrate to damaged cartilage, contributing to inflammation as well as cartilage healing. These advances in understanding of how early pathologic responses after joint...
injury cause joint destruction provide the basis for new approaches to the prevention or mitigation of PTOA. Promising approaches include minimizing the deleterious effects of ROS, removal of senescent cells, and use of chondrocyte progenitor cells to restore articular cartilage.