Abstract: Osteoarthritis is a painful and debilitating disease of the joints that is characterized by progressive degeneration of the articular cartilage that lines the joint surfaces. The etiology of osteoarthritis is poorly understood, although it is now well accepted that mechanical factors play an important role in the onset and progression of this disease. The goal of our studies has been to determine the physiological effects of mechanical loading on articular cartilage using a variety of in vivo and in vitro models, and to use these models to identify novel biomechanical and biochemical signaling pathways involved in cellular mechanotransduction - the conversion of mechanical signals into biological events. Coupled with physiological studies of early mechanical signaling events, we identified a class of ion channels on the cell membrane that appear to play a role in regulating cartilage physiology in response to biomechanical stimuli. These pathways may provide novel pharmacologic targets for the modification of inflammation or cartilage degeneration in osteoarthritis.