hypertension, and insulin resistance, suggesting that systemic factors could also play a role in the genesis of OA joint damage.

A number of defined metabolic diseases may also lead to non-inflammatory arthropathy with radiographic features predominantly of OA. The principal conditions that predispose to secondary OA are ochronosis, Wilson's disease, acromegaly, and hereditary hemochromatosis (HH). The most common form of HH is an autosomal recessive iron overload disorder associated with mutation of the HFE gene. Affected individuals may present with a severe arthropathy mimicking OA, typically involving the second and third metacarpophalangeal joints, which may seriously affect quality of life.

Other metabolic diseases, like chronic hypomagnesaemia or primary hyperparathyroidism may lead to deposition of calcium pyrophosphate crystals within cartilage. These deposits, named chondrocalcinosis when identified by X-Rays, are associated with OA, which may present with more inflammatory symptoms, an atypical distribution and prominent cyst and fissures on radiographs.

Despite all the advances in bone and cartilage biology, particularly in the recent bone and joint decade, there are still some deficiencies in our understanding of the pathogenesis of osteoarthritis (OA), as well as our ability to diagnose and treat OA. Nanomedicine is expected to improve the quality of life for the ADL of patients with OA through the advances in the technology for diagnosis and treatment.

(1) Oxidative DNA damage contributes to aging and degeneration of articular cartilage. During the development of OA, mechanical and chemical stresses on articular cartilage change the stable cellular activities of chondrocytes and produce excess amounts of reactive oxygen species (ROS) as well as proinflammatory cytokines and chemokines. Studies have provided ample confirmation of the accumulation of ROS and the chondrocyte aging in degenerated articular cartilage.

Our recent study revealed the potential involvement of accumulation of 8-Oxoguanine, an oxidized form of guanine, and impairment of mitochondrial DNA repair enzymes in the pathogenesis of OA. 8-Oxoguanine is produced by ROS in large amounts in both DNA and nucleotide pools and is a major causative lesion for mutagenesis by ROS in a variety of diseases.

We observed the increased level of 8-Oxoguanine and decreased level of Ogg1, a DNA repair enzyme, in osteoarthritic cartilage in comparison with chondrocytes of intact cartilage in animal models of OA and in patients with OA, suggesting the involvement of the accumulation of 8-Oxoguanine in articular cartilage and down-regulation of its repair enzyme Ogg1 in the degeneration of articular cartilage in OA. We found that over-expression of mitochondria-targeted human hOgg1 in human osteoarthritic chondrocytes prevents oxidant-induced mitochondrial dysfunction, OA-related catabolic stress-induced caspase-9 activation and apoptosis in vitro. Furthermore, hOgg1 silencing using siRNA reduced chondrocyte activity and augments apoptosis in human osteoarthritic chondrocytes.

(2) Application of nanotechnology to chondroprotection. In the previous studies, we have focused on nanocarbon particle, fullerene (C60), which acts as a strong free radical scavenger, as an anti-oxidative agent, to prevent the degeneration of articular cartilage in OA. We have demonstrated that water-soluble fullerene has a potential as a protective agent against the catabolic stress-induced degeneration of articular cartilage both in vitro and in vivo in OA models.

In this paper, we demonstrate that mitochondrial 8-Oxoguanine DNA glycosylase regulates the cellular function and survival of osteoarthritic chondrocytes in response to catabolic stresses in OA. In addition, we show that C60 fullerene may influence the expression of mitochondrial DNA repair enzymes and their functions in osteoarthritic chondrocytes, suggesting that C60 fullerene has a therapeutic potential, as a nanomedicine, to protect against the degeneration of articular cartilage in OA. We would like to conclude the pathomechanism of OA in terms of the chondrocyte ability and function in response to oxidative stress by augmenting DNA repair.

(3) Application of bone and cartilage imaging. Magnetic resonance imaging (MRI) is now thought an effective tool in the image diagnosis of OA. However, spatial resolution of MRI is limited to a span of one to several millimeters. While conventional X-ray imaging system has been used in the image diagnosis of various diseases, cartilage cannot be depicted with them. There has been a strong call for an X-ray imaging technology that can depict cartilage. More recently, Kido K. et al. demonstrated a novel X-ray imaging system which it would be easier to detect the onset of a disease, to diagnose the stage of the disease, and to monitor the effect of treatment for bone and cartilage diseases. We also show their excellent technology of image diagnosis, an X-ray Talbot-Lau interferometry, for degenerated bone and cartilage.