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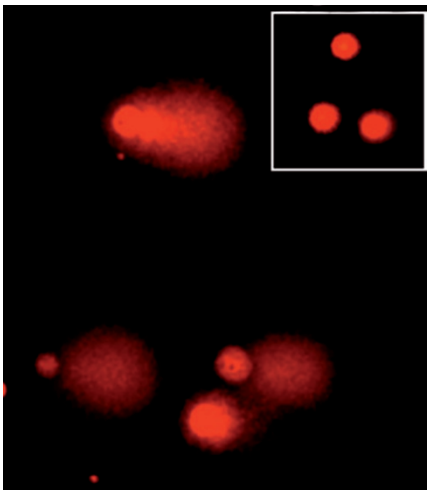
OA chondrocytes made senescent by genomic DNA damage

Articular chondrocytes in joints affected by osteoarthritis (OA) have a senescent phenotype that is induced by gradual accumulation of genomic DNA damage, according to new research published in *Osteoarthritis & Cartilage*. Thomas Aigner and colleagues report that stochastic DNA damage leads to diversification of gene expression, which then induces phenotypic variation and functional failure in aged chondrocytes.

The investigators first found that two genes constitutively expressed in normal articular chondrocytes, encoding vimentin and S-100 protein, have a more heterogeneous expression pattern in OA chondrocytes than in normal chondrocytes; notably, the discoordinated expression pattern of these genes was random and not related to any focal area or zone. They also identified significantly more cellular DNA damage in OA chondrocytes, independent of the age of patients from whom the cells were taken.

No evidence was found of replicative senescence: only minor telomere shortening was observed in the OA chondrocytes, and no critical shortening was detected. The expression of Ki67 antigen (which correlates with cell proliferation) was significantly increased in OA compared with normal chondrocytes, but remained at very low levels.



Genomic DNA damage in OA chondrocytes is revealed by the 'comet tail'; healthy chondrocytes (inset) lack tails. Image courtesy of T. Aigner.

In vitro experiments showed that chondrocytes from normal knee joints can be induced to show this senescent phenotype. Administration of genotoxic agents and oxidative stress were both able to increase DNA damage and dissociated gene expression.

Overall, says Aigner, "this study provides a biological explanation for the notoriously high heterogeneity of gene expression observed in most studies in OA tissues." Stochastic DNA damage can explain cellular malfunction and loss of tissue homeostasis. Furthermore, the data suggest that strategies to remedy genomic DNA damage might help to prevent joint damage in OA, which, notes Aigner, "links OA research to the increasingly exciting field of ageing research."

Sarah Onuora

Original article Rose, J. *et al.* DNA damage, discoordinated gene expression and cellular senescence in osteoarthritic chondrocytes. *Osteoarthritis Cartilage* doi:10.1016/j.joca.2012.05.009