Table 1

Cartilage measure variable	Meniscus volume measure (mm^3)		
	AH	PH	Total
CLTPD	–	<0.0001	–
ILTPD	–	0.0005	–
IMTMTH	–	–	<0.0001
WLTACS	<0.0001	<0.0001	<0.0001
WLTCAAB	<0.0001	<0.0001	<0.0001
WLTFVCL	–	–	<0.0001
WLTPD	–	0.0003	–
WLTSBA	0.0003	–	–
WLTVCL	–	–	<0.0001
WMTACS	–	–	<0.0001
WMTCAAB	–	–	<0.0001
WMTSBA	–	–	<0.0001
WMTVCL	–	–	0.0002

Cartilage measure variable	Cartilage measure description
CLTPD	% area of subchondral bone denuded of cartilage – lateral tibia (center) (cLT.dAB%) [%]
ILTPD	% area of subchondral bone denuded of cartilage – lateral tibia (internal) (iLT.dAB%) [%]
IMTMTH	mean cartilage thickness – medial tibia (internal) (iMT.ThCtAB) [mm]
WLTACS	area of cartilage surface – lateral tibia (LT.AC [cm^2]
WLTCAAB	area of subchondral bone covered by cartilage – lateral tibia (LT.cAB) [cm^2]
WLTFVCL	cartilage volume – lateral tib-fem compartment (LFTC.VC) [m^3]
WLTPD	% area of subchondral bone denuded of cartilage – lateral tibia (LT.dAB%) [%]
WLTSBA	total area of subchondral bone – lateral tibia (LT.tAB) [cm^2]
WLTVCL	volume of cartilage – lateral tibia (LT.VC) [mm^3]
WMTACS	area of cartilage surface – medial tibia (MT.AC) [cm^2]
WMTCAAB	area of subchondral bone covered by cartilage – medial tibia (MT.cAB) [cm^2]
WMTSBA	total area of subchondral bone – medial tibia (MT.tAB) [cm^2]
WMTVCL	volume of cartilage – medial tibia (MT.VC) [mm^3]

respond similarly, perhaps even in unison, to changes due to OA. The current study analyzed meniscus and cartilage relationships for subjects with a wide range of radiographic and symptomatic features of OA. Further work will focus on characterization of the interactions between meniscus and articular cartilage and stratification of associations with respect to clinical measures of OA severity such as KL grade.

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A REDUCTION IN SIRT1 LEVELS IN OA ARTICULAR CARTILAGE IS ASSOCIATED WITH AN INCREASE IN PTP1B, MMP13 AND CHONDROCYTE APOPTOSIS

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Purpose: Osteoarthritis is a multi-factorial disease that results from an imbalance between cartilage anabolism and catabolism. This imbalance results from the over-expression of pro-inflammatory mediators, which induce the expression of matrix-degrading enzymes. Elevation in chondrocyte apoptosis is also evident in OA cartilage, contributing to matrix damage. Since OA is a disease associated with aging, the role of the SirT1 protein in chondrocyte biology was examined since SirT1 is recognized to be a longevity factor. SirT1 is a lysine deacetylase that can prolong lifespan in a variety of organisms by inhibiting the onset of diseases of aging. Here we examine the role of SirT1, and its regulatory factors, in a number of critical features of OA. We find that SirT1 displays aspects of an anti-OA protein, consistent with its function in prolonging lifespan.
Methods: Human articular cartilage samples were obtained from OA patients undergoing total knee arthroplasty while normal samples were obtained from cadeavers (NDRI). Cartilage was embedded sectioned and processed for immunohistochemistry using antibodies for SirT1, AROS, DBC1, PTP1B and MMP13. Additionally, chondrocytes isolated from cartilage samples were cultured in vitro and used for the generation of RNA for analysis of gene expression and for generation of protein extracts for immunoblotting, using the antibodies just mentioned. Human chondrocytes were Amaxa transfected with a SirT1 expression plasmid.
Results: In human chondrocyte cell culture we find that overexpression of SirT1 enhances expression of cartilage specific matrix genes (collagen 2, aggrecan) while repressing expression of matrix degrading metalloproteinases (MMP3, 8, 13, Lee et al., 2009 submitted). Further, Sirt1 was found to be a potent inhibitor of apoptosis in human chondrocytes through repression of the protein tyrosine phosphatase 1B (PTP1B, Gagarina et al, 2009 submitted), an extremely potent pro-apoptotic protein in chondrocytes. Examination of tissue sections revealed that SirT1 levels were significantly downregulated in OA cartilage compared to normal cartilage, while PTP1B and MMP13 levels were elevated in OA tissue. Proteins known to associate with Sirt1 and regulate its enzymatic activity (Aros and DBC1) were also examined in chondrocytes and cartilage sections. Aros (a Sirt1 activator) was down regulated in OA samples while DBC1 (a SirT1 repressor) was upregulated in OA. These data are consistent with the finding that SirT1 enzyme activity is significantly decreased in OA chondrocytes
Conclusions: We show that longevity protein SirT1 is a powerful regulator of cartilage matrix and MMP gene expression and chondrocyte apoptosis in human chondrocytes. Further we show that SirT1 is down regulated in OA cartilage, which correlates well with an elevation in MMP and PTP1B levels and an increase in apoptosis. These data suggest that SirT1 has features of an anti-osteoarthritic protein, consistent with its positive effects on aging.

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OXIDIZED LDL INDUCES STRESS-INDUCED PREMATURE SENESCENCE IN CULTURED BOVINE ARTICULAR CHONDROCYTES

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Purpose: In addition to replicative senescence with critical telomere shortening, stress-induced premature cell senescence (SIPS) occurs by which cells without discernible attrition of telomeres show a growth arrest. There are some stressors already identified include DNA damage, oxidative stress, suboptimal culture conditions, and oxidized LDL (ox-LDL). Both modes of senescence are associated with suppressed cell proliferation, impaired physiological cell function and a distinct pattern of gene expressions and may contribute jointly to the pathogenic process of chronic diseases in vivo. The purpose of this study was to investigate whether ox-LDL induces SIPS of cultured bovine articular chondrocytes (BACs) through the lectin-like ox-LDL receptor-1 (LOX-1) expressed on the chondrocyte.
Methods: Chondrocytes were isolated from articular cartilage of 10-month-old cows by enzymatic digestion and cultured in DMEM supplemented with 10 % FBS at 37 °C in a humidified and hypoxic atmosphere (5% O2 and CO2) to avoid cell senescence caused by oxidative stress. Senescence-associated β-galactosidase (SA β-gal) activity was detected by cytochemical staining of chon-