Cytokines Expression during OA Pathogenesis within an Experimental Rat Model".

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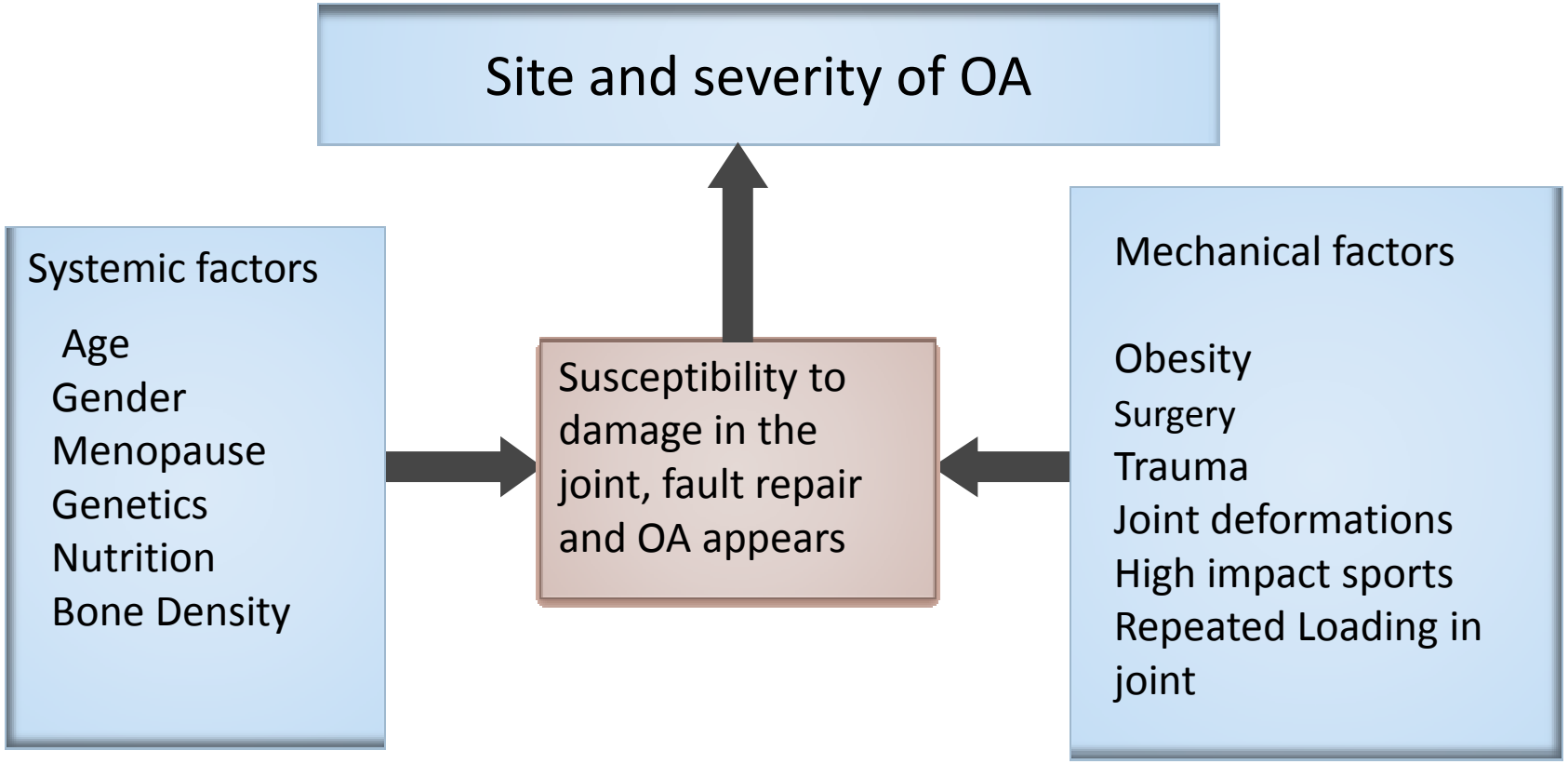
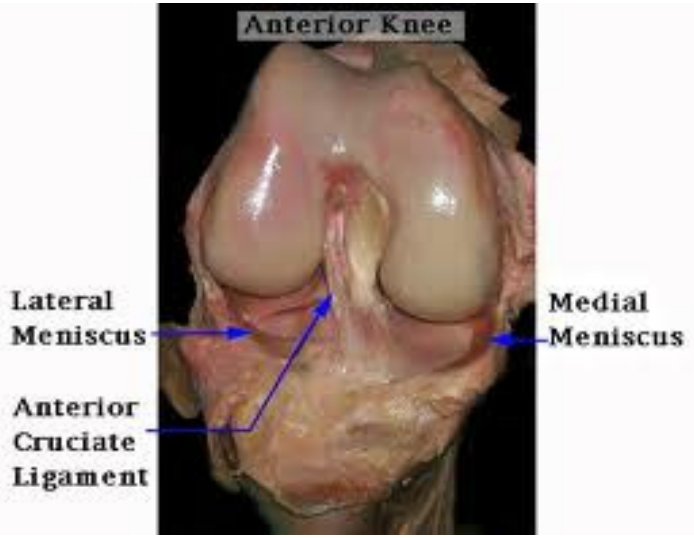
Osteoarthritis(OA) is a multifactorial disease and the most frequent of all musculoskeletal diseases including rheumatoid arthritis and osteoporosis

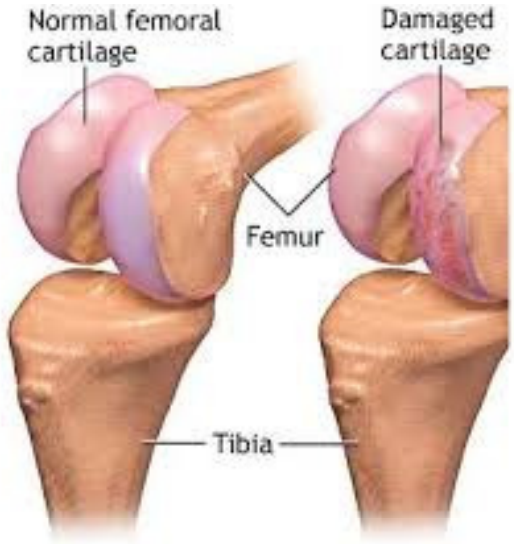


Arden N, Best Practice & Research Clinical Rheumatology 2006 Vol. 20, No. 1, pp. 3–25
Felson DT. Ann Intern Med. 2000 Oct 17;133(8):635-46,

CARTILAGE FROM HUMAN vs RATS

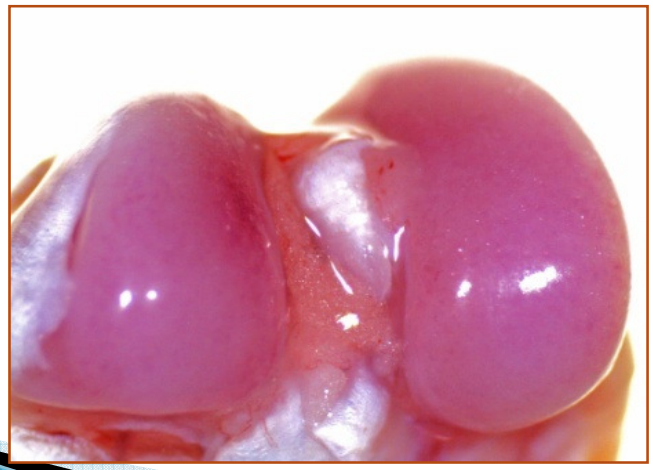
CARTILAGE FROM HUMAN

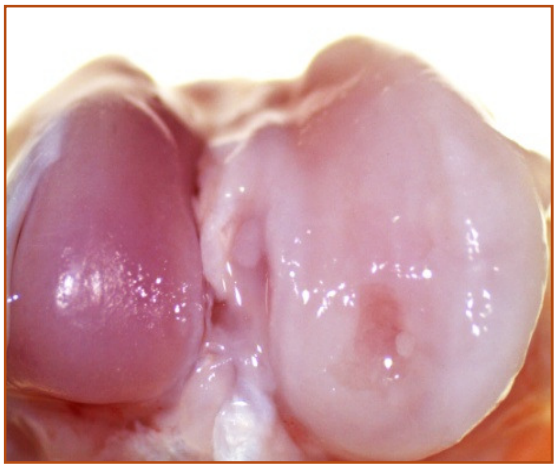




CARTILAGE FROM RAT

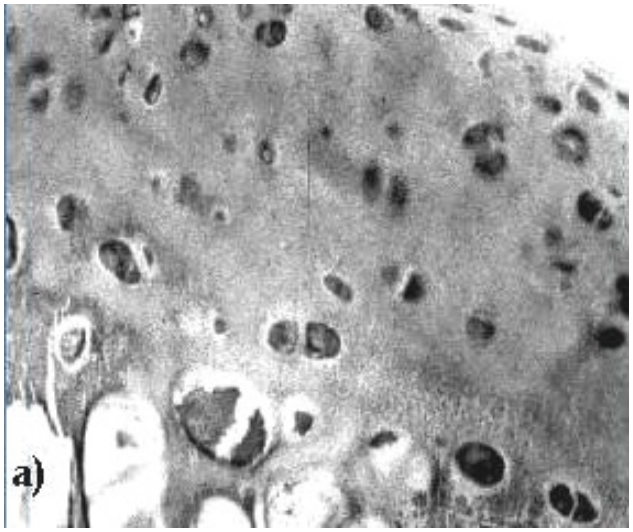
Normal

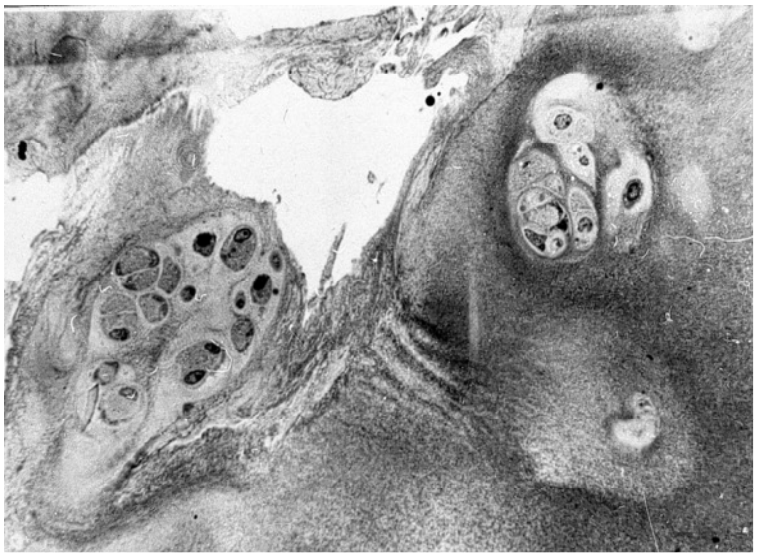




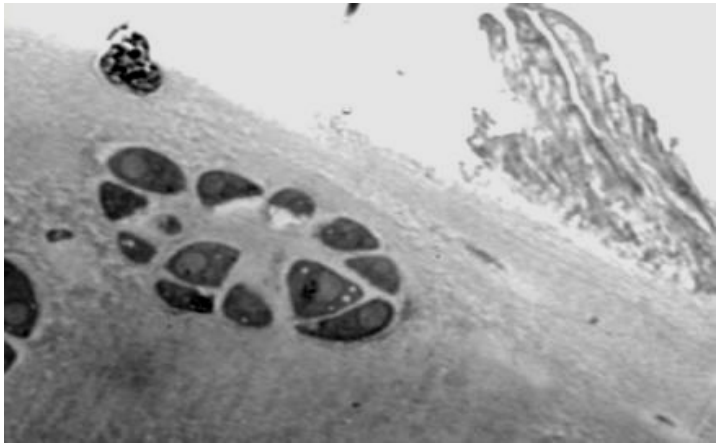
Microscopical Study

HUMAN





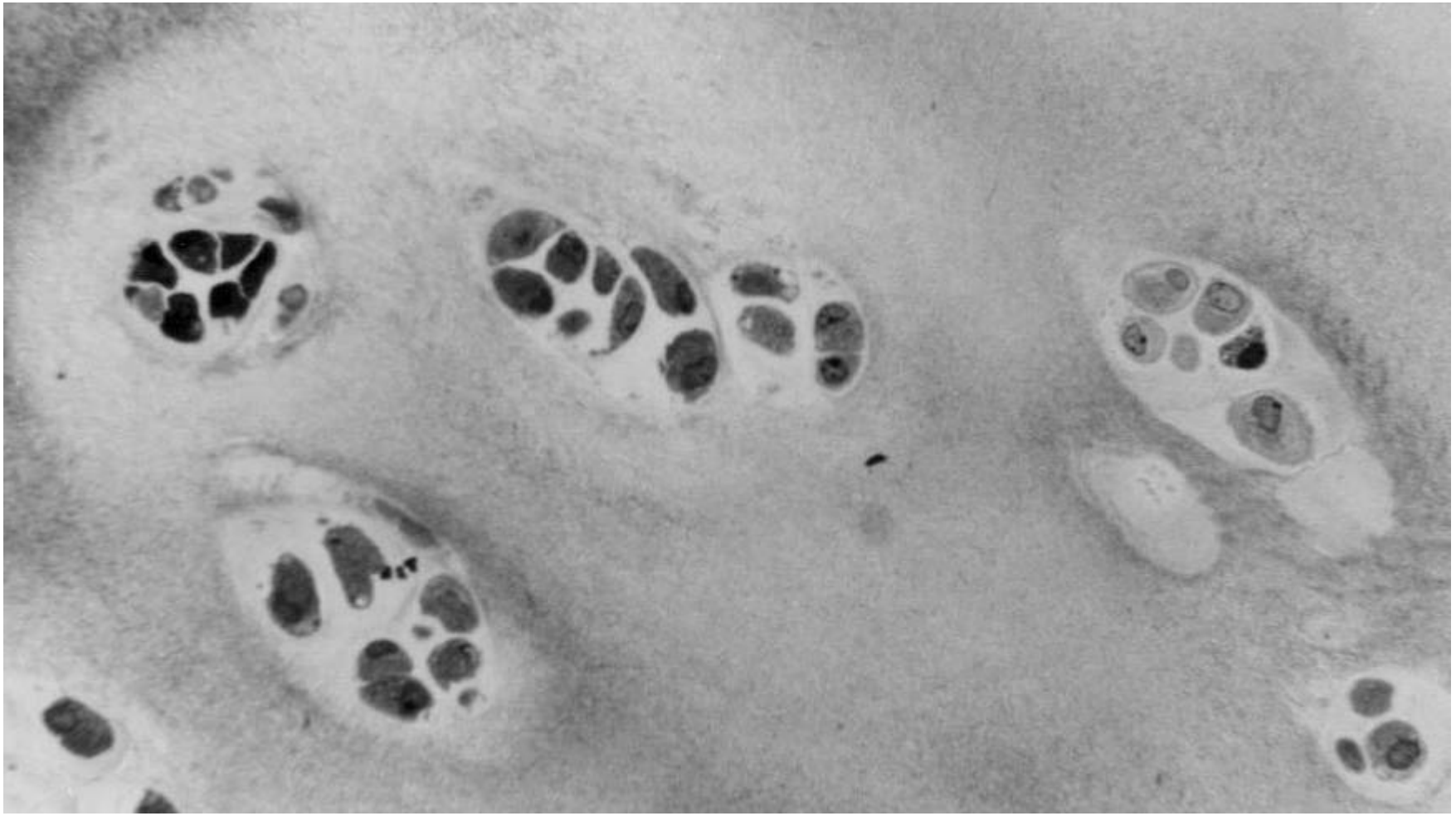
RAT



NORMAL

OA

Cellular Aggregates From Human OA Cartilage



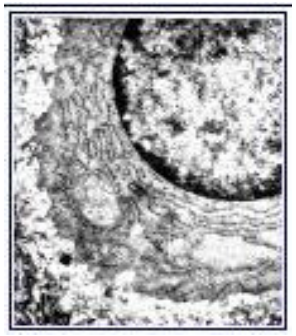
Phenotypic variability of OA chondrocyte

Kouri et al.1996

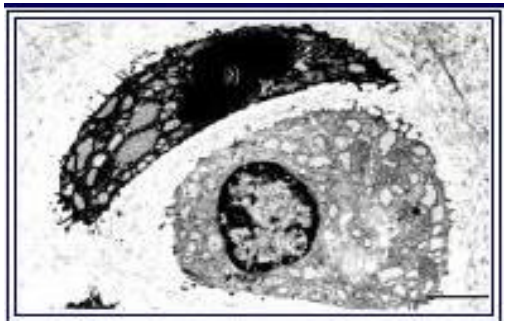
Phenotypic variability chondrocyte within an OA rat Modelo

Predominant Ultrastructural Pattern

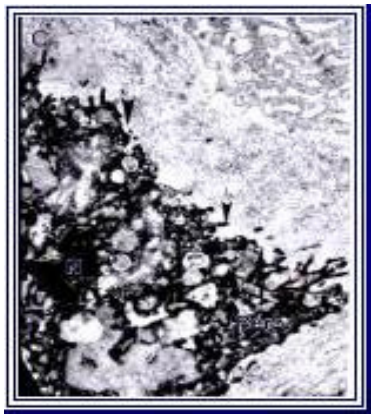
Normal



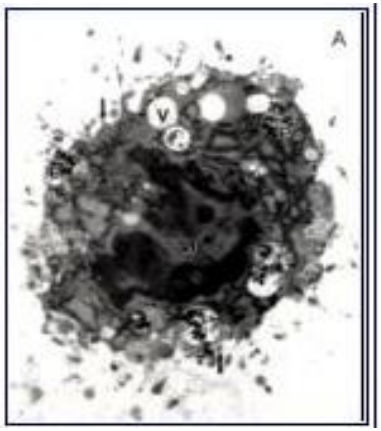
OA 5 days



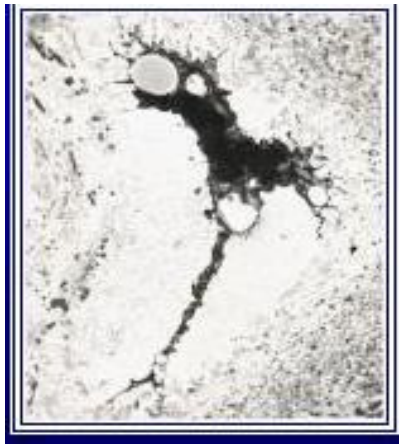
OA 10 days



OA 20 days



OA 45 days



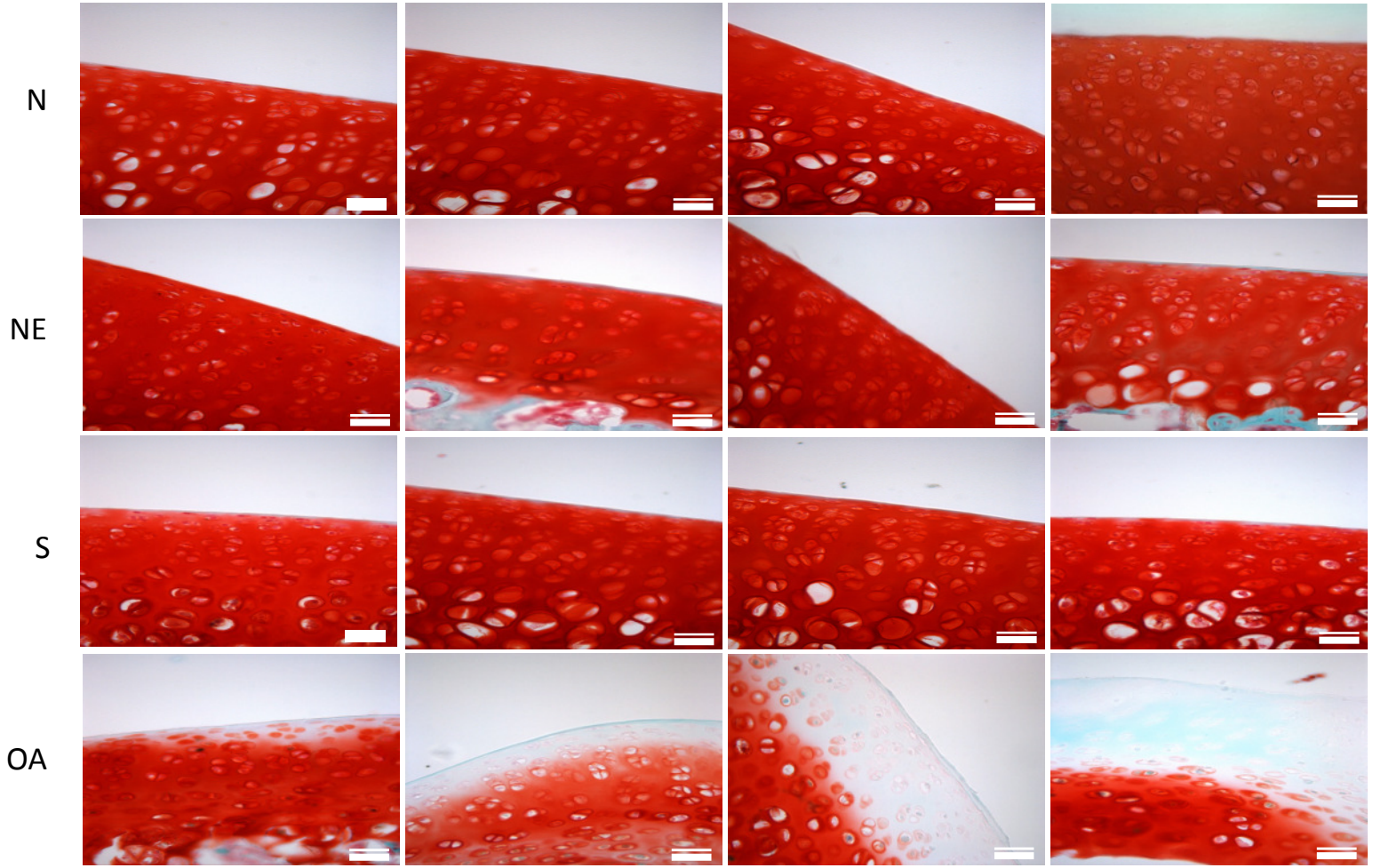
OA 60 days

Kourí, *et al.,* 2000

Extracelular Matrix

OA Rat Model

Safranin O Staining



HYPOTHESIS

"Activation" and "Transdifferentiation" of the chondrocyte phenotype

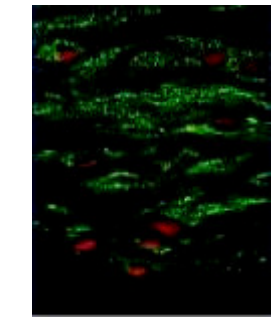
INJURY → REPARATIVE STAGE → DEGRADATIVE STAGE → CHONDROPTOSIS

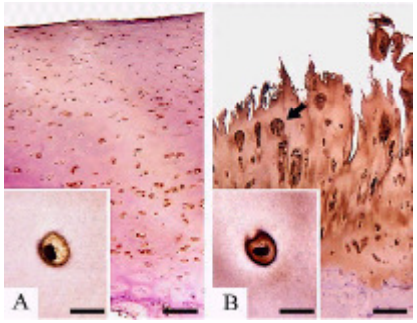
Normal

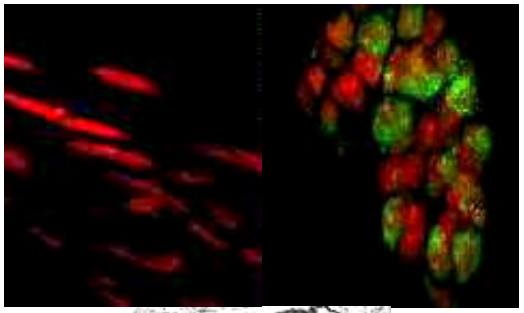
Perlecan

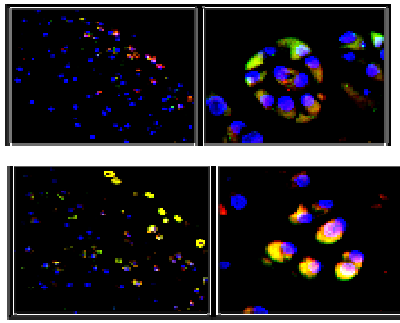
MMP-3

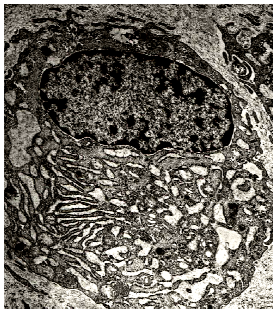
Caspase 3-LC3

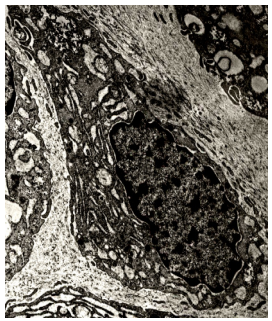


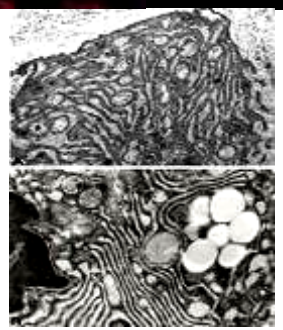


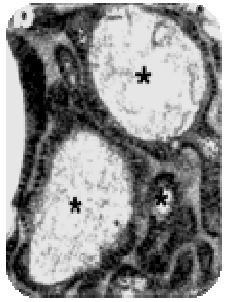


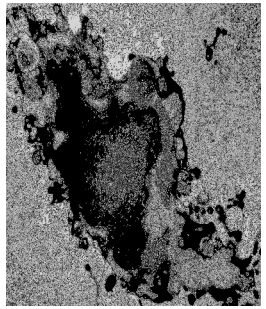










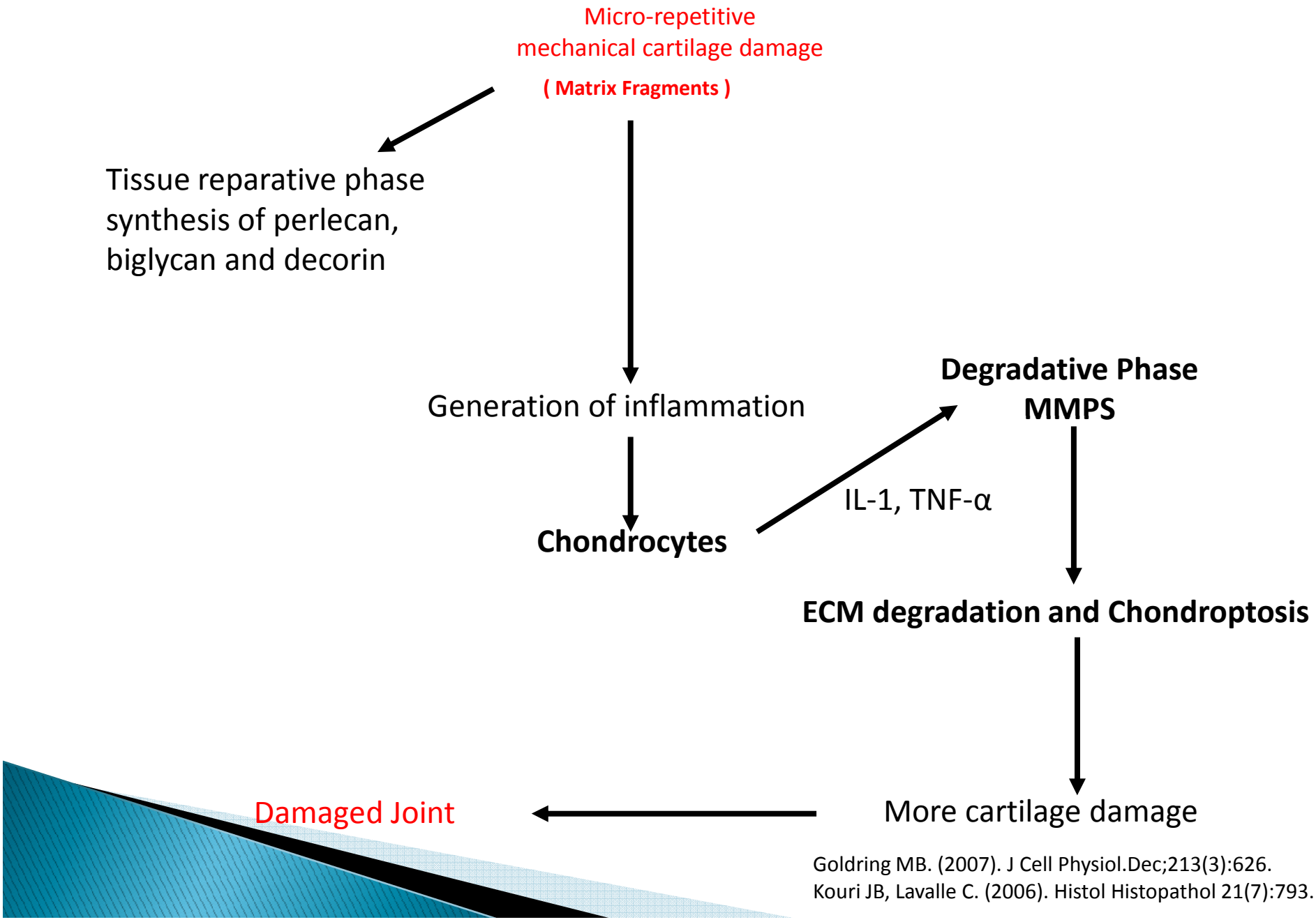


Kouri JB, Lavalle C. 2006

Roach T. Aigner T Kouri J.B. 2004

Almonte et al. 2010

Osteoarthritis Pathogenesis

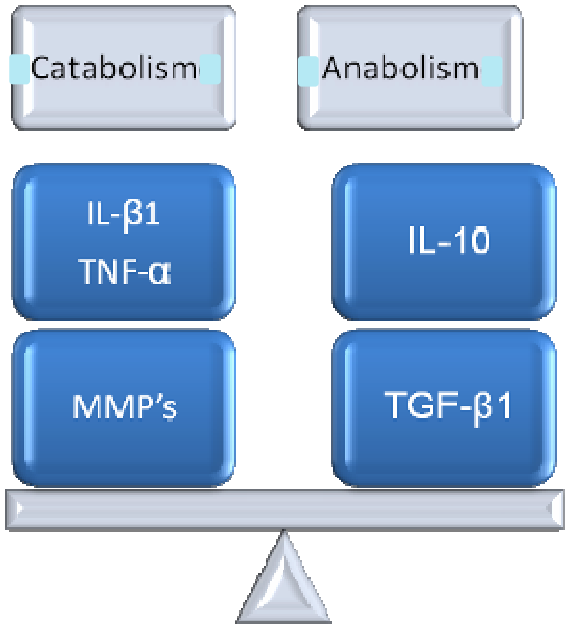


Goldring MB. (2007). J Cell Physiol.Dec;213(3):626.
Kouri JB, Lavalle C. (2006). Histol Histopathol 21(7):793.

ARTICULAR CARTILAGE

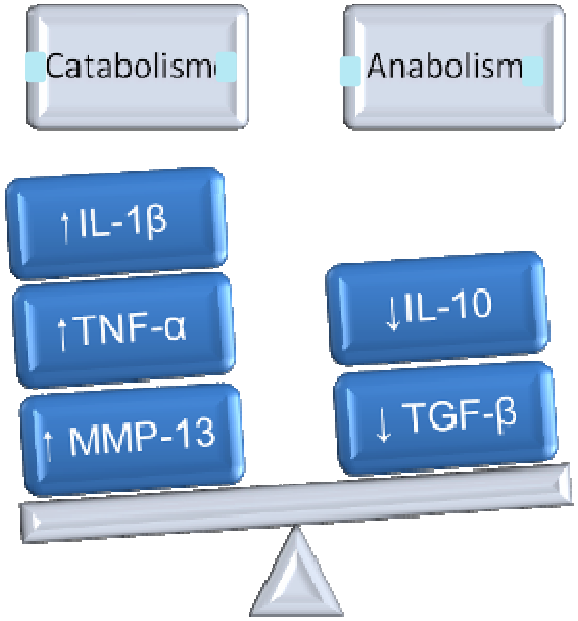
Cytokines balance

NORMAL



KEEPING EQUILIBRIUM

OA



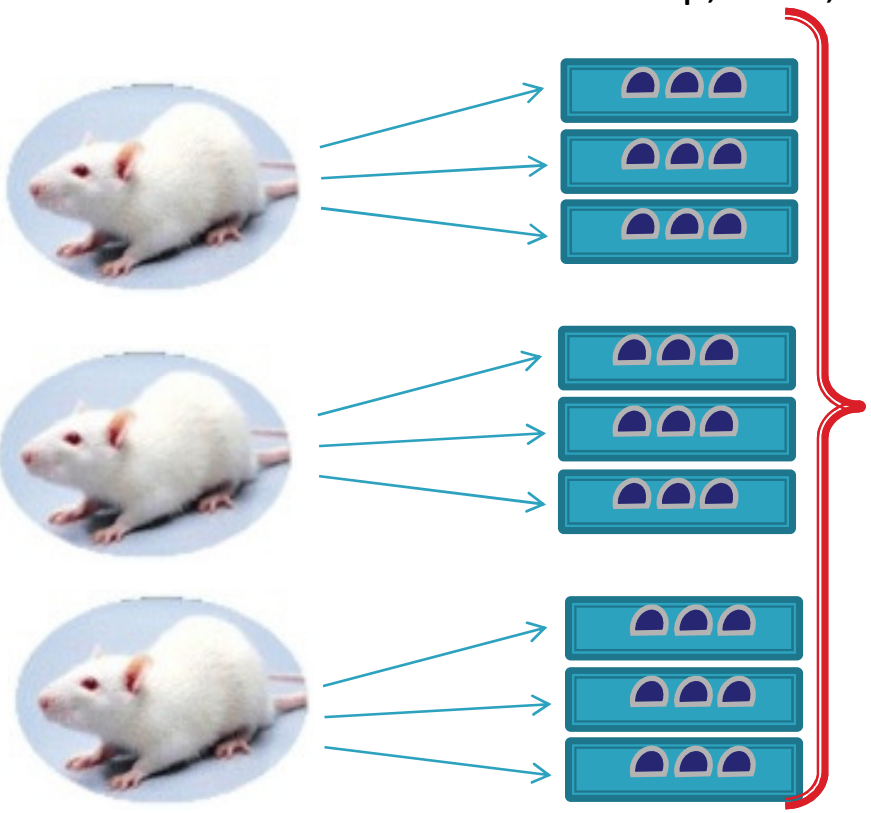
EQUILIBRIUM IS LOST

EXTRACELLULAR MATRIX IS LOST,THE NUMBER OF CHONDROCYTES ARE REDUCED AND THEIR FUNCTIONS ARE MODIFIED

Statistical Microscopical Analysis

Experimental Groups : Normal, Normal with excercise, OA and Sham

IL 1-β, IL-10, TGF-β1,



Each sections
3 RANDOM FIELDS

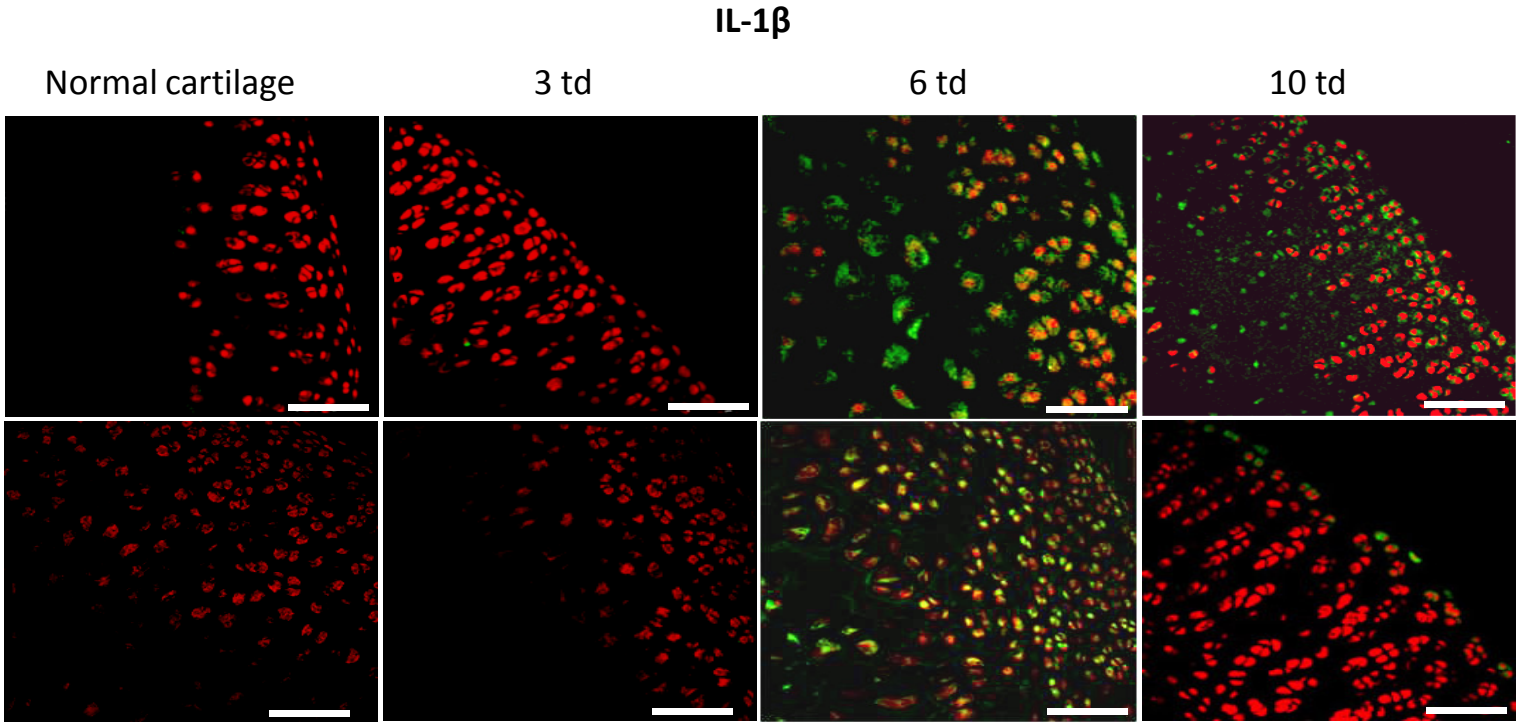
CONFOCAL ANALYSIS
(% of positives cells)

NO-PARAMETRIC ANOVA STATISTICAL TEST

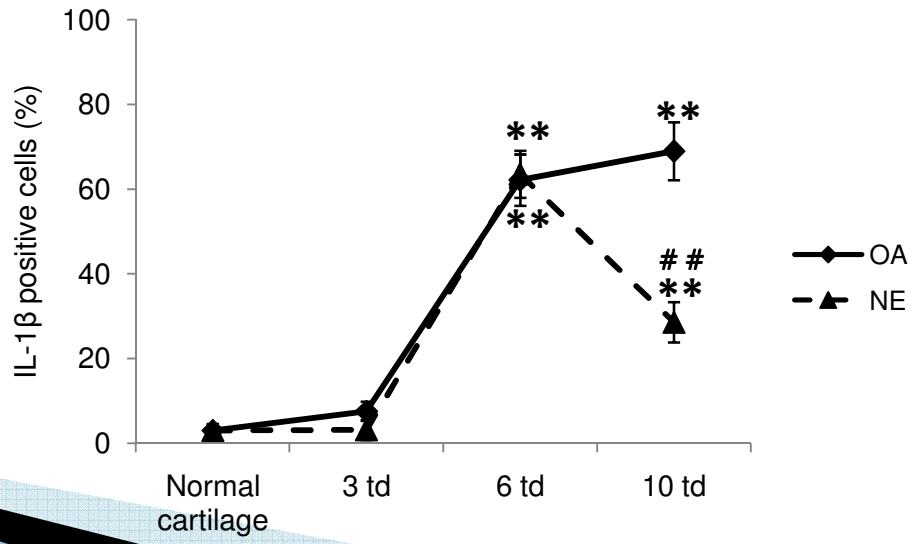
Wistar Rats ♂
130 – 150 g

EACH EXPERIMENT WAS FROM 9 SLIDES, 27 SECTIONS, 81 FIELDS

A



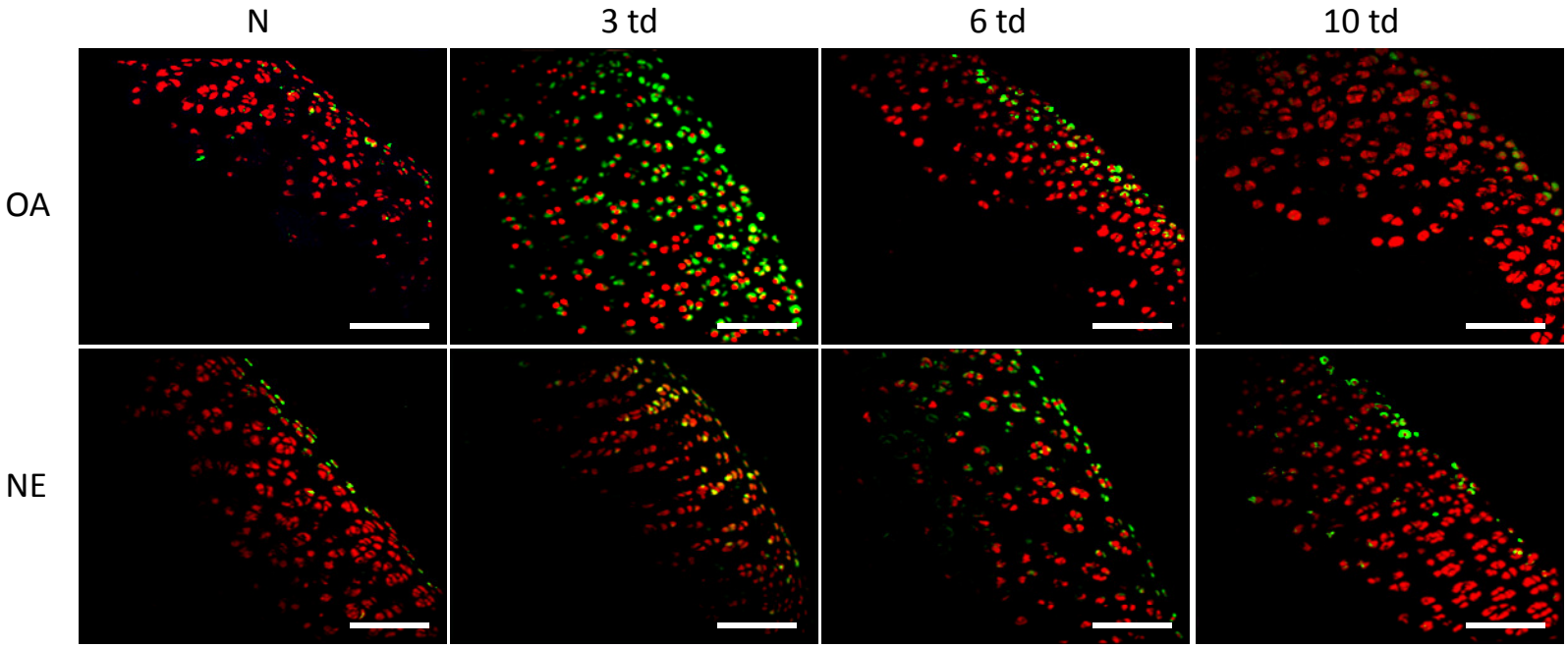
B



*vs Normal

vs OA

A



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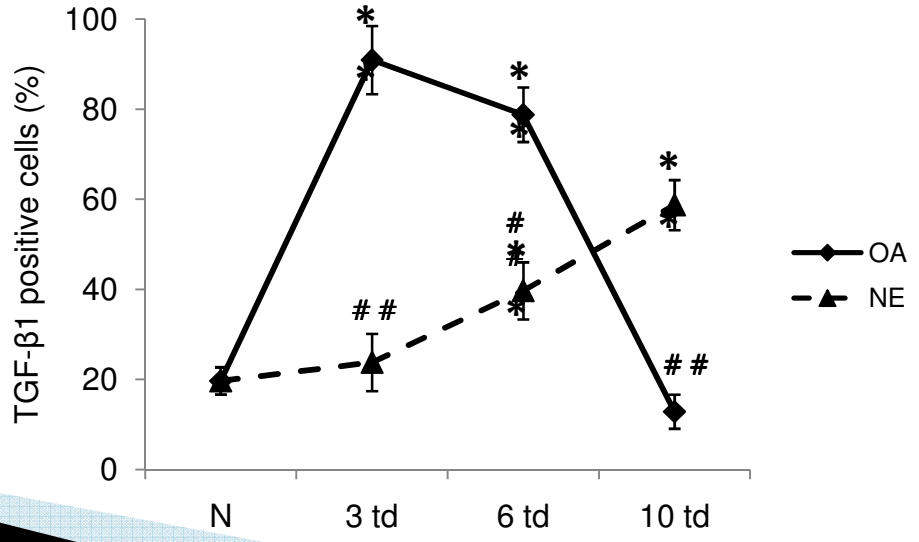
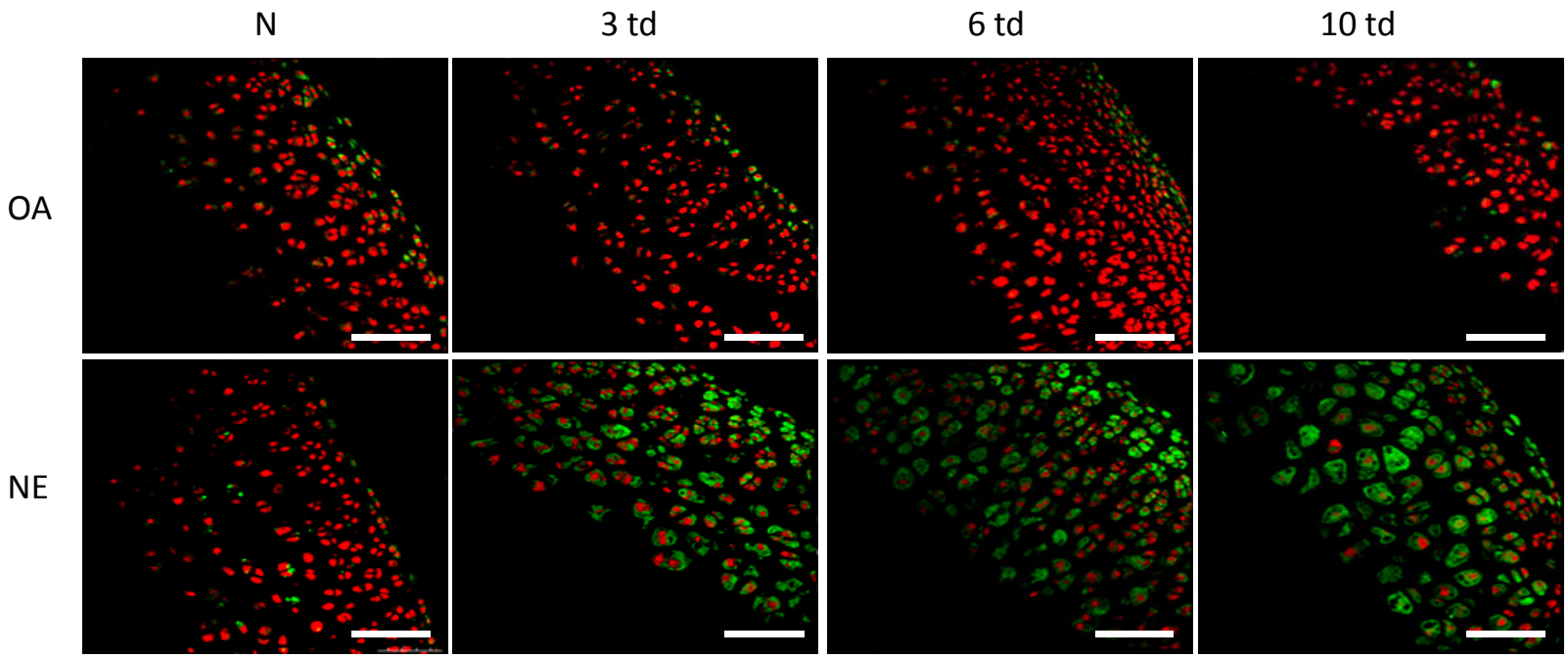


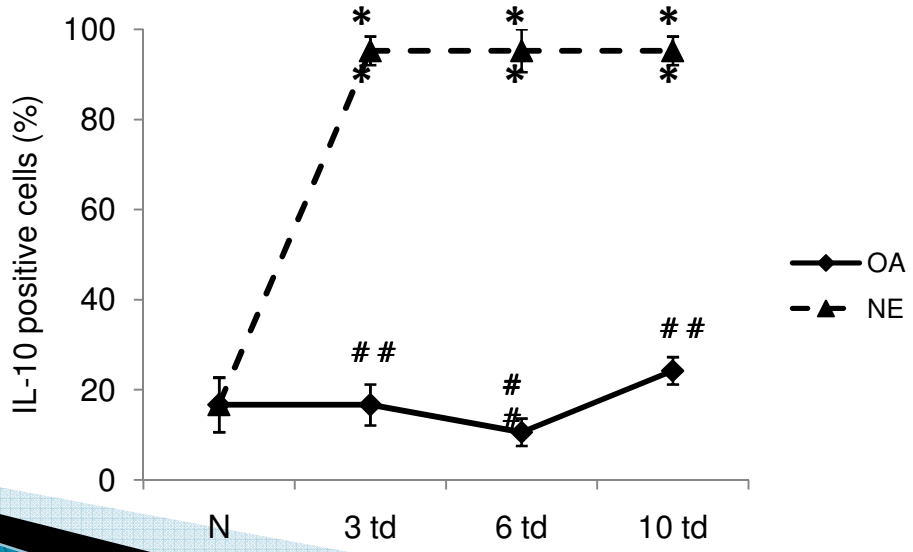
*vs Normal

vs OA

A



B



*vs Normal

vs OA

Statistical Western Blott Analysis

Pool of cartilage

X 10 ⟶ n=1

X 10 ⟶ n=1

X 10 ⟶ n=1

n=3

Wistar rats ♂
130 – 150 g

Protein extraction for each experimental group.

↓

Western blot for IL-1β, TNF-α, TGF-β and IL-10.

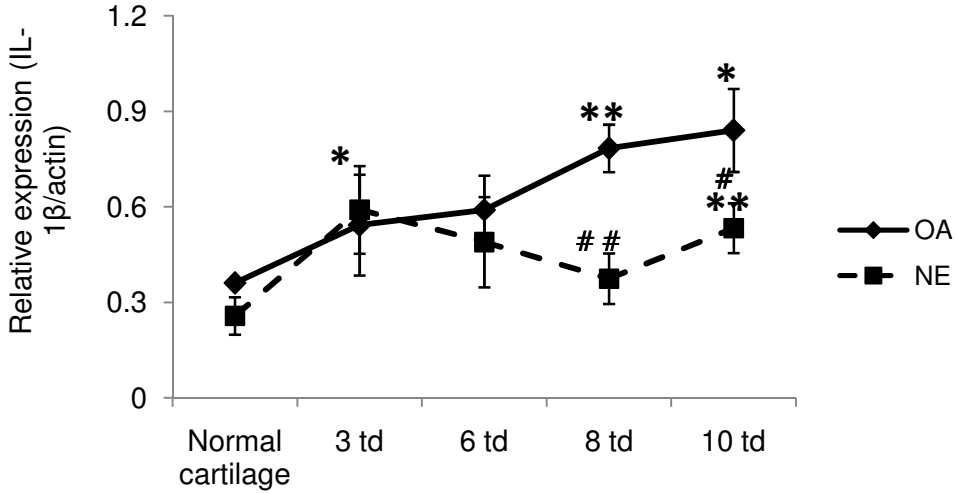
↓

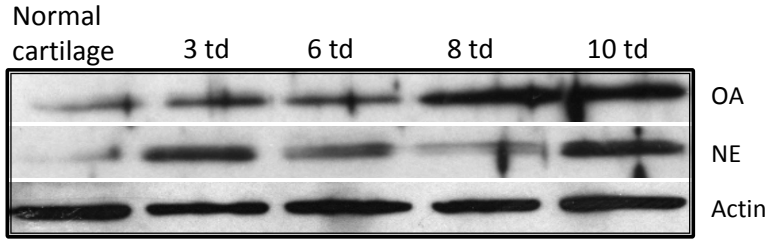
Quantification by densitometry with the Image J software

↓

Statistical analysis (ANOVA)

A





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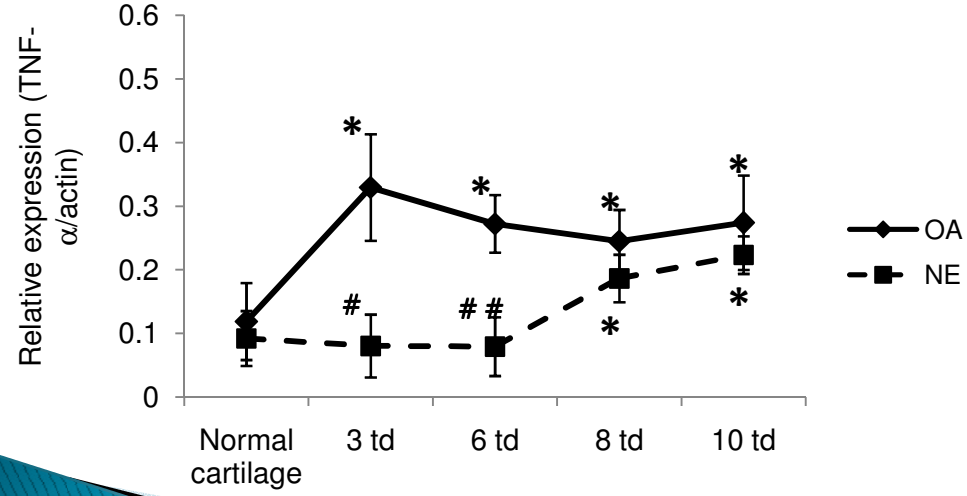
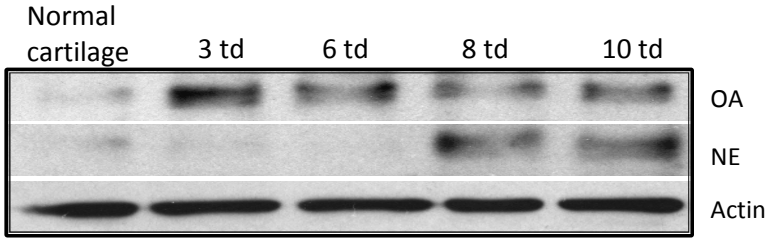
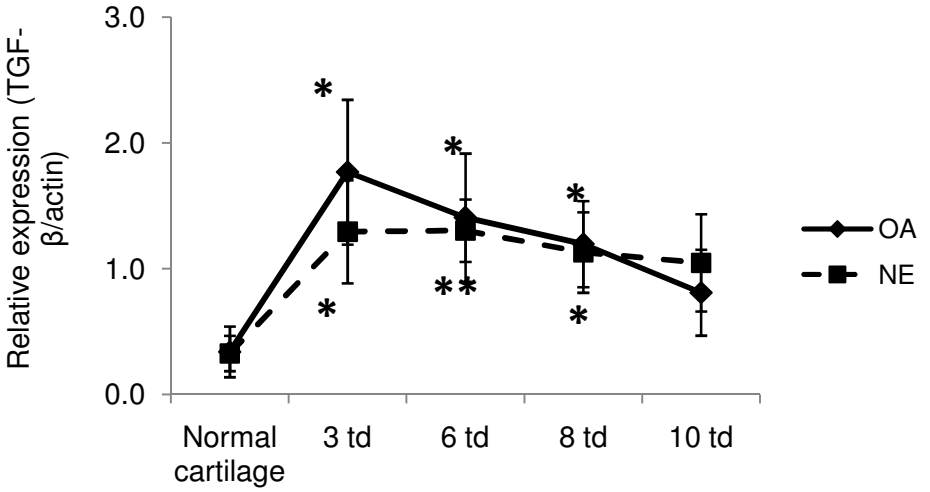


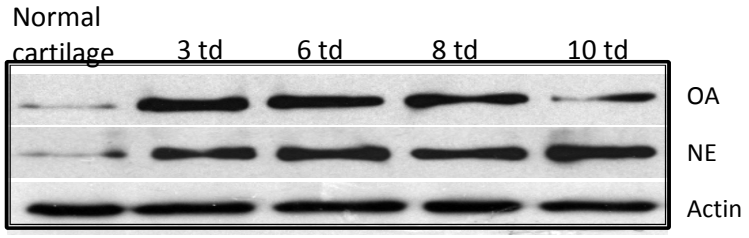


*vs Normal
vs OA

A

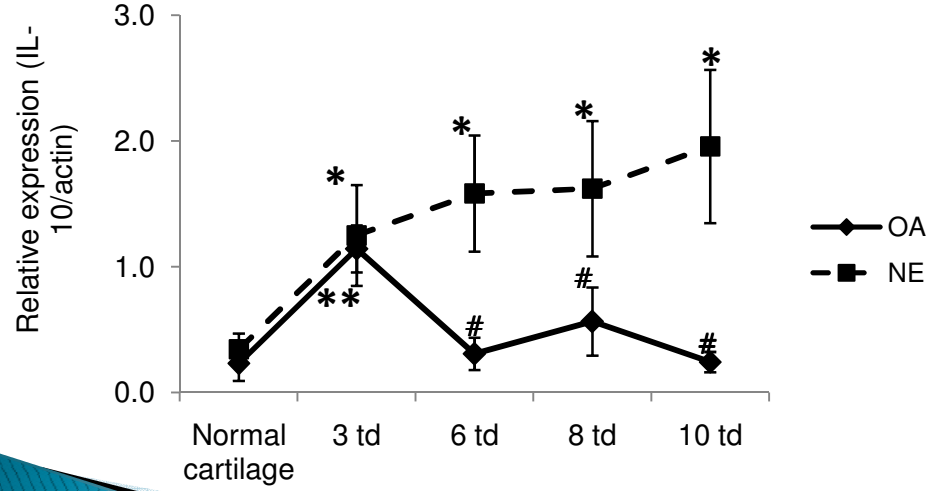
TGF-β1

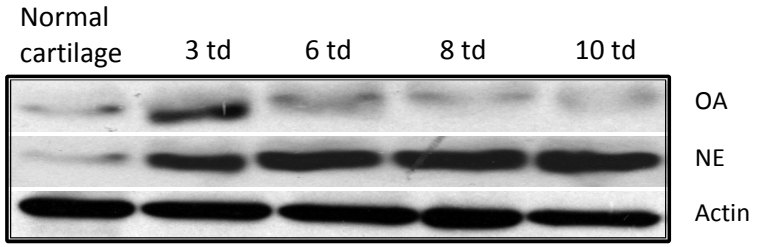




B

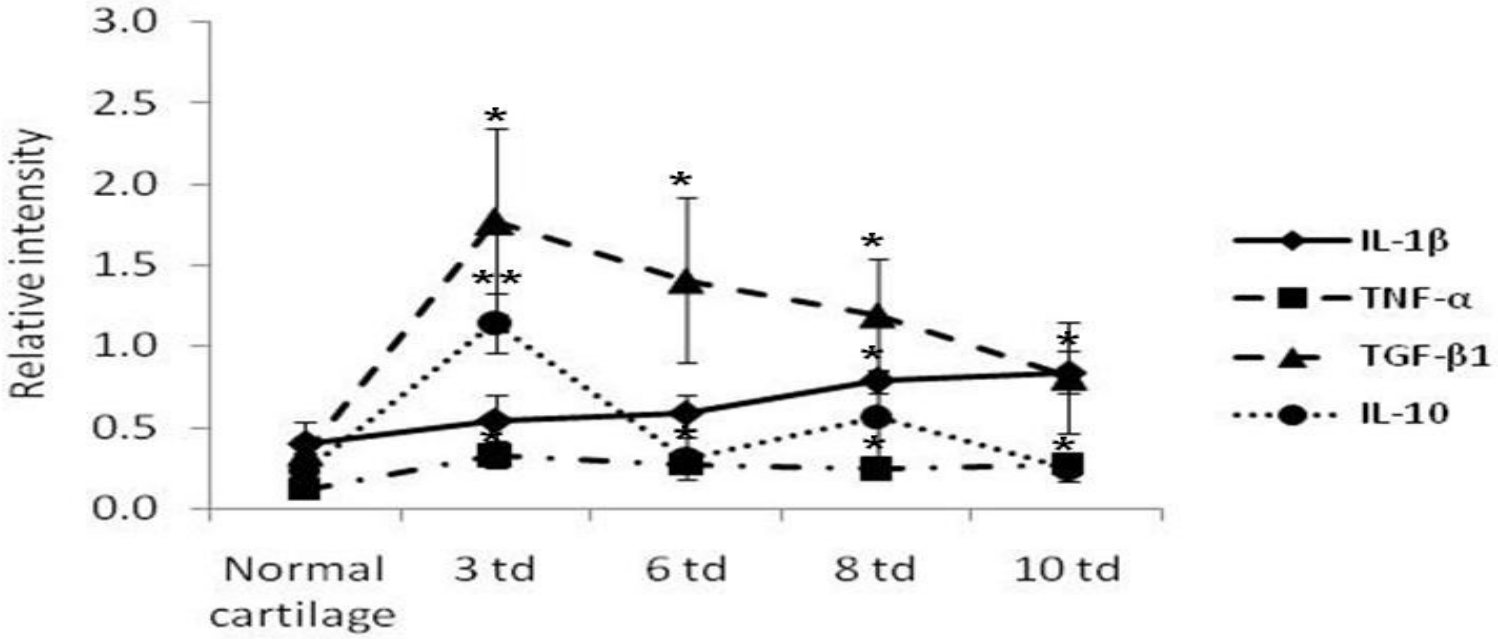
IL-10

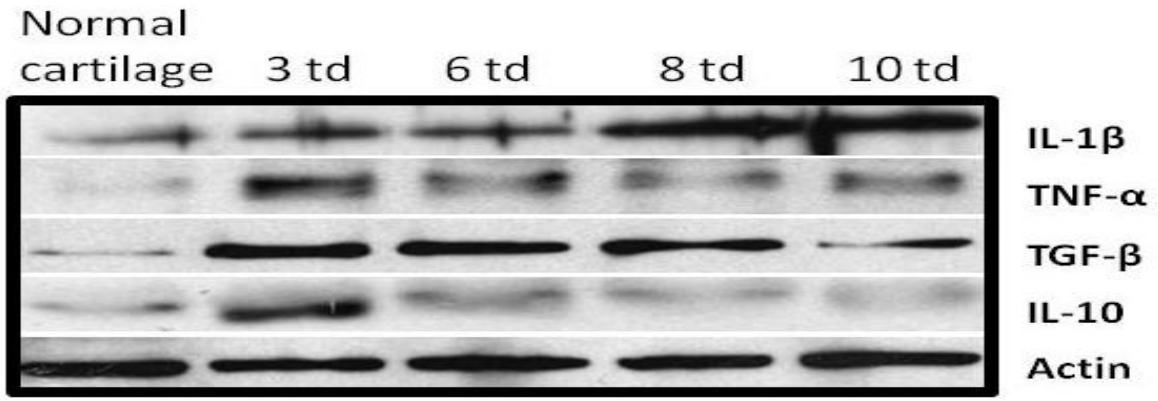




*vs Normal

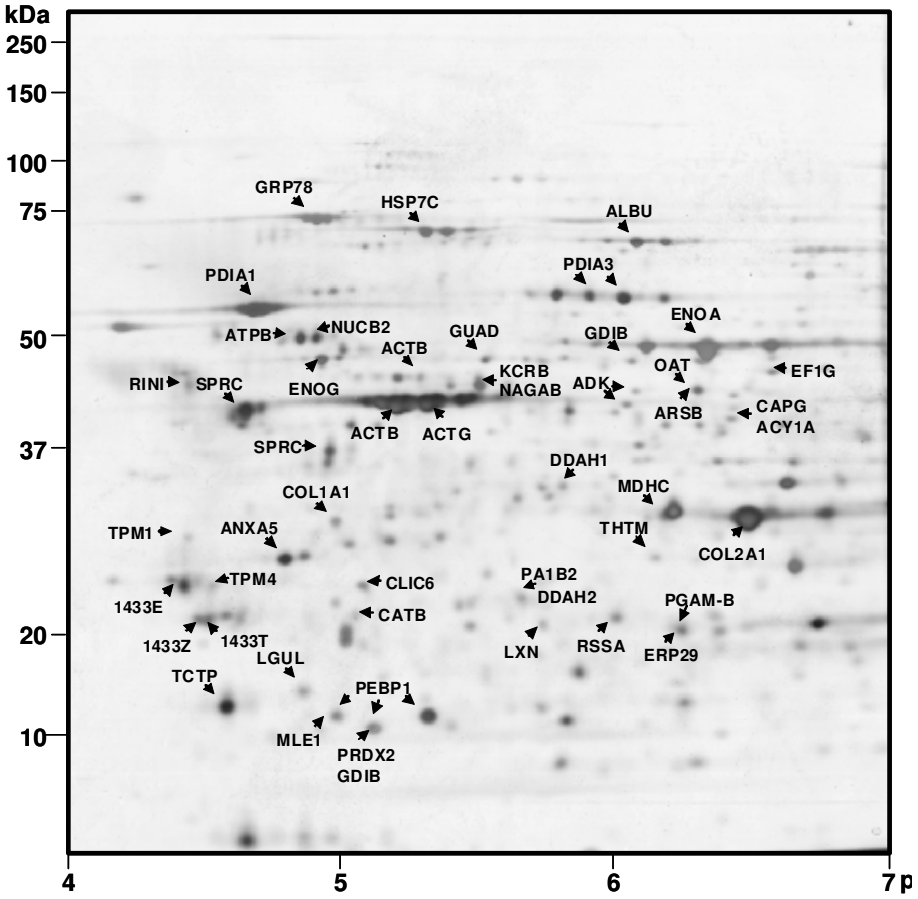
vs OA


3.0
2.5
2.0
1.5
1.0
0.5
0.0
Relative intensity
Normal cartilage
3 td
6 td
8 td
10 td
IL-1β
TNF-α
TGF-β1
IL-10


Normal cartilage
3 td
6 td
8 td
10 td
IL-1β
TNF-α
TGF-β
IL-10
Actin

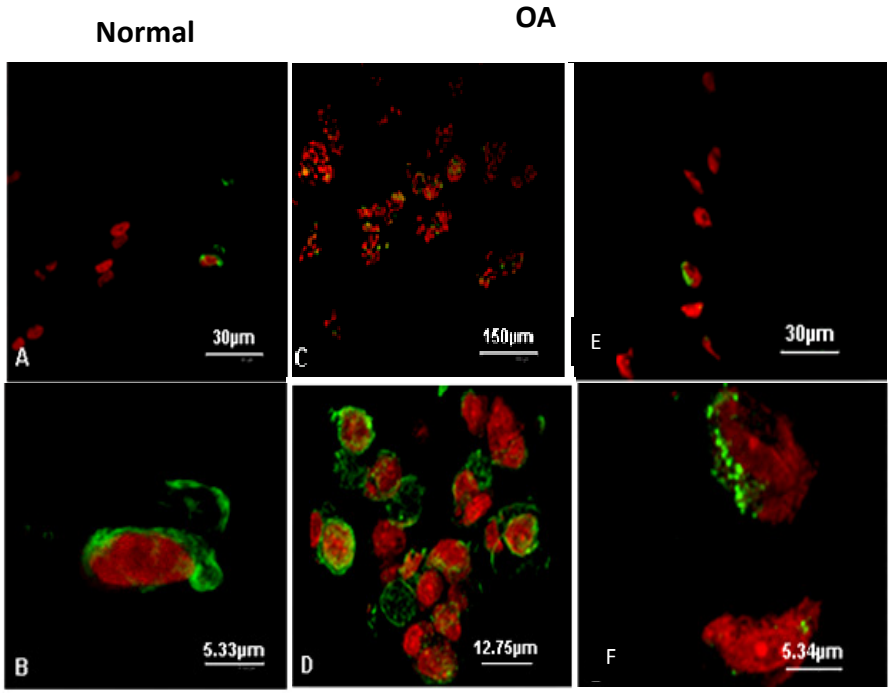
Expression of Latexin in the articular cartilage

RAT



Proteins bidimensional map normal rat AC (SDS-10% acrylamide, pH 4-7 nonlinear, silver staining). Protein names are indicated according to the Pilot Protein database

HUMAN



Anti-latexin/FITC: A, B-chondrocytes SZ(N); C, D (OA cartilage "clones" cell SZ); E, F (OA cartilage, MZ. . Confocal.Microscopy

Pérez et al, 2010. *Proteome Science*

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THANK YOU

CONCLUSION

Our results suggest that during OA progression chondrocytes undergo dramatic phenotypic changes and display signaling transduction machinery capable of inducing its own morpho-functional changes. In early OA, chondrocytes increase ER and Golgi in order to synthesize proteins required for ECM reparation. However, when the repair capacity is overwhelmed, chondrocytes begin the synthesis of catabolic molecules like IL-1β, IL-6, TNF-α that stimulate an inflammatory process and degradation of ECM by metalloproteases like MMP3 and MMP-13. Furthermore, the decrease of anti-inflammatory molecules in OA could be involved at the beginning of the disease. Finally, when chondrocytes loose their reparative capacity, execute its own cell death program that includes both autophagy and apoptosis, which called chondroptosis.