PATHOPHYSIOLOGY OF OSTEOARTHRITIS AND SYNOVITIS

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LOSS OF FUNCTION

PAIN
### Pathophysiology of Osteoarthritis

#### Until late 20th century
- A passive consequence of tear and wear
- A degenerative disease
- A cartilage disease
- An inevitable fate

#### 21st century
- A cell-driven mechanism based on soluble mediators
- A pro-inflammatory disease
- A multiple-tissue disease
- A biological challenge open to therapeutic intervention
OSTEOARTHRITIS

BONE CELLS

CHONDROCYTES
SYNOVIOCYTES
MENISCUS

INFLAMMATION

- Cartilage defect +++
- Bony growth ++
- Abnormal subch. bone ++
- Synovial inflammation +

Hunter D & Felson D
BMJ 2006
PATHOPHYSIOLOGY OF OSTEOARTHRITIS

Anabolism
Cartilage matrix synthesis

Catabolism
Cartilage matrix degradation

Homeostasis
PATHOLOGY OF OSTEOARTHRITIS

**Anabolism**
Cartilage matrix synthesis

**Catabolism**
Soluble mediators: *IL-1, PGE2*

*Overexpression of Metalloproteinases 1, 3, 13 by chondrocytes*
Cytokines (including chemokines, adipokines) • Prostaglandins • Reactive oxygen species • RAGE ligands • Extracellular matrix components

Mechanical stress

Interaction
Ligands/specific receptors

MAPK
NF-kB
Others…

Transcriptional and post-transcriptional regulation

MMPs
ADAMTS
Cytokines
Reactive oxygen species
Prostaglandins

OSTEOARTHRITIS AND OBESITY: MECHANICAL ASPECTS

F. Berenbaum Primer in the Rheumatic Diseases, 13th Ed. (dec 07)
THE SYNOVIAL TISSUE IS INVOLVED IN THE OA PROCESS

Normal Synovial tissue

Fibrosis

Mild Inflammation

severe inflammation

X. Ayral
SEMIQUANTITATIVE GRADINGS OF SYNOVITIS IN THE OA KNEE JOINTS

GRADE 1
GRADE 2
GRADE 3

Rhodes et al. Rheumatology 2005
GRADING SCALE FOR OA SYNOVIAL INFLAMMATION

\[ \leq 1 \text{ perivascular lymphocytic infiltrate} \]

\[ >1 \text{ perivascular lymphocytic infiltrate} \]

Diffuse lymphocytic infiltrates

Pearle et al. Osteoarthritis Cart 2007
FOLLICULAR B-LYMPHOCYTE INFILTRATE IN OA SYNOVIAL TISSUE

anti-CD20 antibodies

Knorth et al. Osteoarthritis Cart 2004
MACROPHAGE INFILTRATION OF OSTEOARTHRITIC SYNOVIAL LINING LAYER

Control

CD68
(macrophage marker)

Young et al. Arthritis Rheum 2001
CRITICAL ROLE OF MACROPHAGES IN OA

Control

Clodronate
(deplete synovial macrophage)

VDIPEN neoepitope expression
(marker of cartilage degradation)

TGFβ injection
(promote osteophyte formation)

Van Lent Arthritis Rheum 2004
Blom et al. Arthritis Rheum. 2007
PATHOPHYSIOLOGY OF OSTEOARTHRITIS
TAKE-HOME MESSAGES

-Osteoarthritis is a chronic inflammatory arthritis
-Along with cartilage and bone, the synovial tissue is a key player involved in the degradative process of osteoarthritis
-Targeting OA synovitis is an « evidence-based » approach for treating not only pain but also structural damage in OA.