

Advances in Osteoarthritis Since the Founding of OARSI

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Disclosures

- Research support
 - National Institutes of Health.
- Member Advisory Board and/or Consultant
 - Bioiberica S.A., EMD Serono International S.A., Iroko Pharmaceuticals, Pfizer Inc., Samumed LLC, Strategic Science and Technology, and Theralogix LLC.
- Stock ownership
 - Theralogix LLC

OARSI: 25th Anniversary

- Initially registered under French law in 1990
- Charles Joel Menkes, 1st president
- Roy D. Altman, 1st Editor of OA&C
- Inaugural Congress held in Paris in 1992



Dr. and Mrs. Menkes dancing at the Inaugural OARSI Congress, 1992

Methods

- Email survey of current and past Presidents of OARSI requesting list of top 5 advances in OA since formation of OARSI (1990)
 - Thanks to Ms. Diann Stern
- Responses received from all but 2 persons
- Top 10 responses chosen for presentation

Top Ten List

- Feature of David Letterman's Late Night TV show since 18 Sept 1985
 - Started on NBC before switching to CBS in 1993
- Probably inspired by the "Top Ten" records of the week on "American Bandstand" hosted by Dick Clark (1956-89)



#10 Genetics of OA

- Candidate genes based on mutations in structural proteins of articular cartilage
 - Rodriguez-Fontela C, et al: Arthritis Rheumatol 2014;66:940-9.
- Genome-wide association studies
 - TREAT-OA Consortium, arcOGEN, others
 - OAI, JoCo OA Project, GOGO
 - Evangelou E, et al: Ann Rheum Dis 2014;73:2130-6.
 - Zeggini E, et al: Lancet 2012;380:815-23.
- Epigenetics
 - Loughlin J, Reynard LN: Nat Rev Rheumatol 2015;11:6-7.
 - Zufferey F, et al: Semin Arthritis Rheum 2014;43:692-700.

#9 OA Cohorts

- Osteoarthritis Initiative
 - “<http://www.oai-ucsf.edu>”
- Rotterdam Study
 - Schiphof D, et al: OA Cart 2014;22:440-6.
- Cohort Hip and Cohort Knee (CHECK)
 - Wesseling J, et al: Int J Epidemiol 2014 Aug 29.
- ROAD Study
 - Yoshimura N, et al: OA Cart 2012;20:1217-26.
- Chingford Study
 - Leyland KM, et al: Arthritis Rheum 2012;64:2243-51.

#8 Recommendations

- American College of Rheumatology (ACR)
- European League of Associations of Rheumatology (EULAR)
- National Institute for Clinical Excellence (NICE)
- Osteoarthritis Research Society International (OARSI)
- Chronic OA Management Initiative (COAMI) of U.S. Bone and Joint Initiative
 - Nelson AE, et al: Semin Arthritis Rheum 2014;43:701-12

#7 Clinical trials methodology

- OARSI Recommendations for conduct and reporting of clinical trials
 - Altman R, et al: OA Cart 1996;4:217-43.
 - Maheu E, et al: OA Cart 2006;14:303-22.
- Standardized imaging techniques
 - PA Semi-flexed knee radiographs
 - Brandt KD, et al: J Rheumatol 2002;29:1308-20.
 - AP Pelvis radiographs
 - Altman RD, et al: OA Cart 2004;12:515-24.
 - OARSI Atlas of Individual Radiographic Features
 - Altman RD, et al: OA Cart 1995;3(Suppl A):3-70.
 - Altman RD, Gold G: OA Cart 2007;15(Suppl A):A1-56.

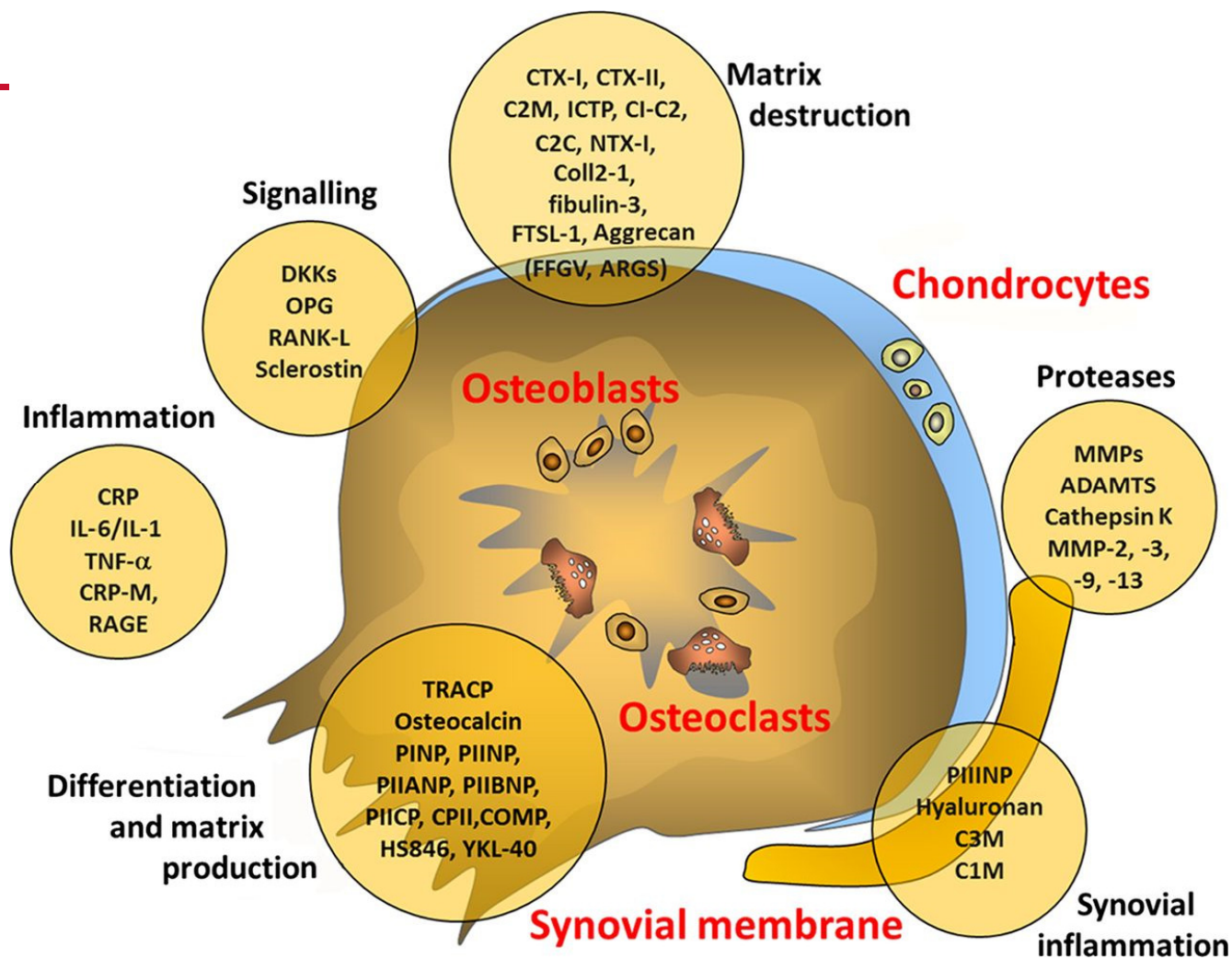
#7 Clinical trials methodology

- Standardized outcome measures
 - Knee and Hip
 - WOMAC (Bellamy N, et al: J Rheumatol 1988;15:1833-40.)
 - KOOS (Roos EM, et al: J Orthop Sports Phys Ther 1998;28:88-96.)
 - HOOS (Nilsson AK, et al: BMC Musculoskeletal Disord 2003;4:10.)
 - Hand
 - AUSCAN (Bellamy N, et al: OA Cart 2002;10:855-62.)
- Responder criteria
 - Pham T, et al: OA Cart 2004;12:389-99.

#6 Biomarkers

- **GREES Recommendations**
 - Vignon E, et al: OA Cart 2001;9:289-93.
- **NIH OA Biomarkers Network (BIPED Classification)**
 - Bauer DC, et al: OA Cart 2006;14:723-7.
- **OARSI Biomarker Panel**
 - Kraus VB, et al: OA Cart 2011;19:515-42.
- **ESCEO Biomarker Recommendations**
 - Lotz M, et al: Ann Rheum Dis 2013;72:1756-63.
- **FNIH Study**
 - Hunter DJ, et al: Best Pract Res Clin Rheumatol 2014;28:61-71.

Sources of Biomarkers in OA



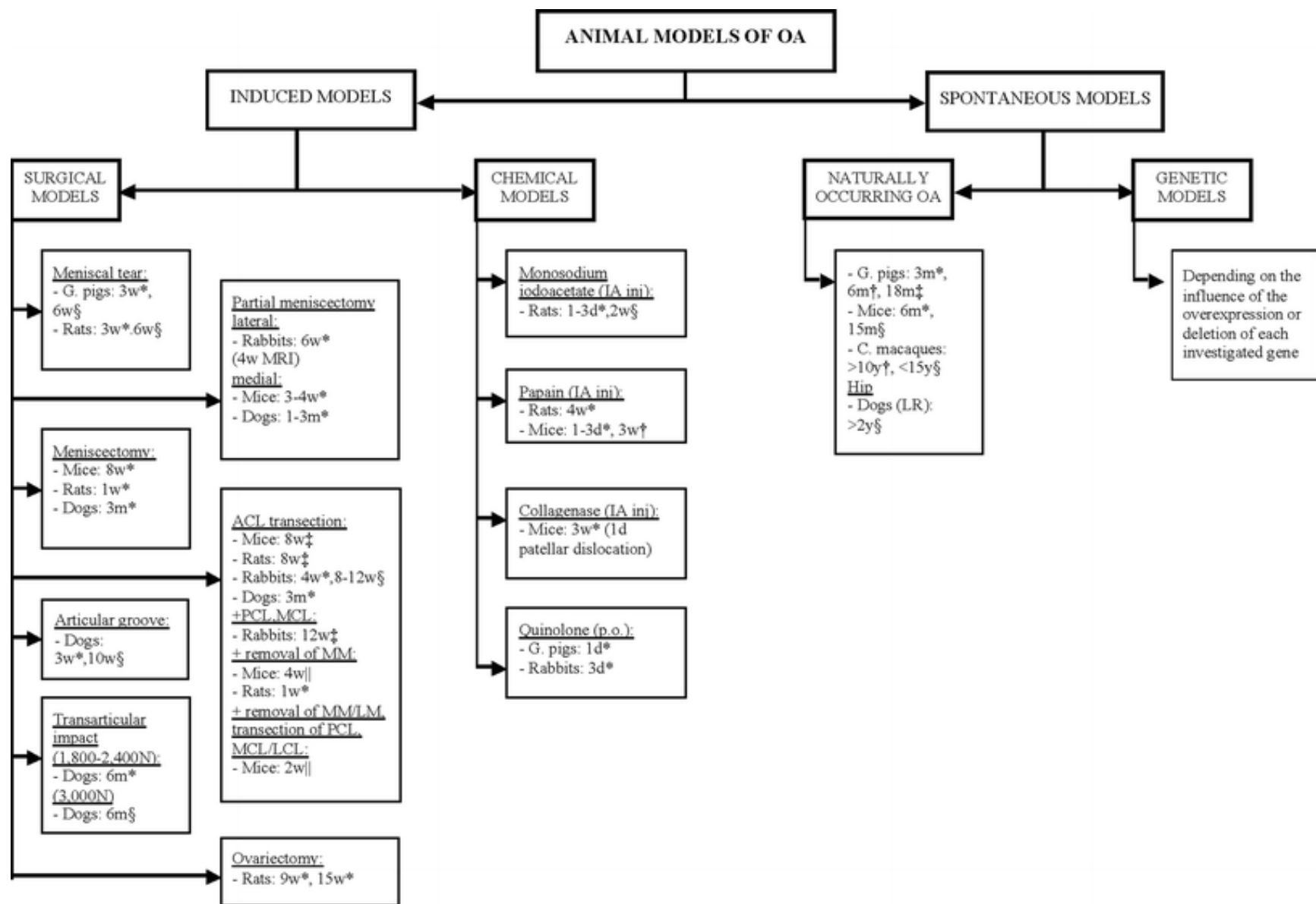
#5 Animal models of OA

Small and Medium animals

- Rabbits
 - Partial meniscectomy
 - Moskowitz RW, et al: 1973
- Guinea pigs
 - Hartley albino pigs
 - Bendele A, et al: 1988
- Rats and mice
 - Naturally occurring
 - Genetically modified
 - Post-surgical
 - Post-IA injections

Large animals

- Nonhuman primates
- Sheep and goats
 - Medial meniscectomy
 - Ghosh P, et al: 1993
- Dogs
 - ACL Transection Model
 - Pond MJ, Nuki G: 1973
 - ACL Transection with dorsal root ganglionectomy
 - Brandt KD, et al: 1985



#4 Magnetic resonance imaging

- Visualizes all the tissues of the joint in 3 dimensions and detects pathologic changes earlier than conventional X-ray
- Semi-quantitative scoring systems for knee OA
 - WORMS, BLOKS, KOSS, MOAKS, ...
- Quantitative measurement of cartilage thickness and volume
- Various features predict total knee arthroplasty
- Proposed as an outcome measure in trials of DMOADs

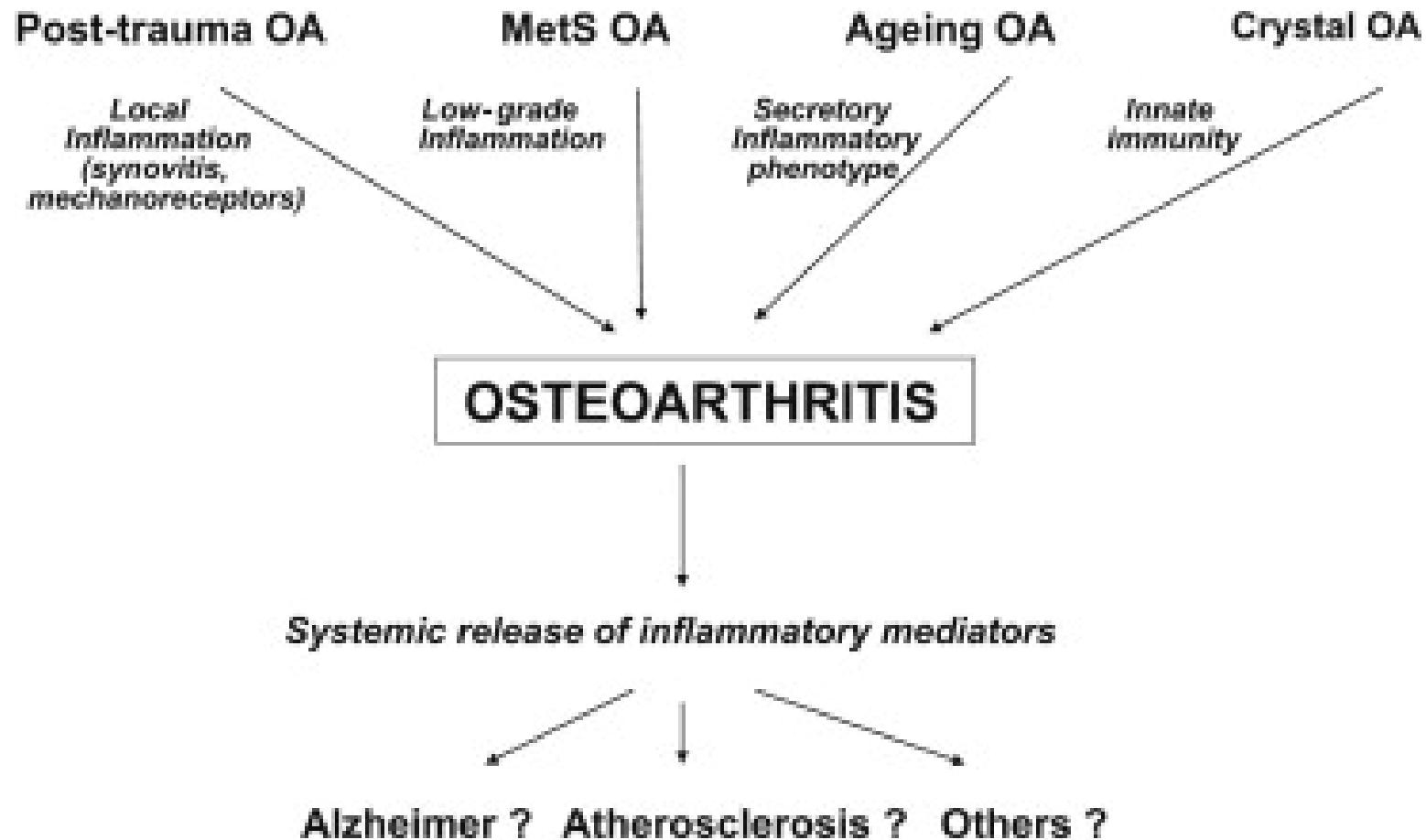
MRI Definition of Knee OA

- Systematic review
 - Clinimetric properties of MRI in knee OA
- Delphi exercise
 - OARSI Knee OA Imaging Workgroup
- Validation in subset of 160 OAI participants
- Group A
 - Definite osteophyte
 - Full thickness cartilage loss
- Group B
 - Subchondral BML
 - Meniscal subluxation, maceration or tear
 - Partial thickness cartilage loss
 - Bone attrition

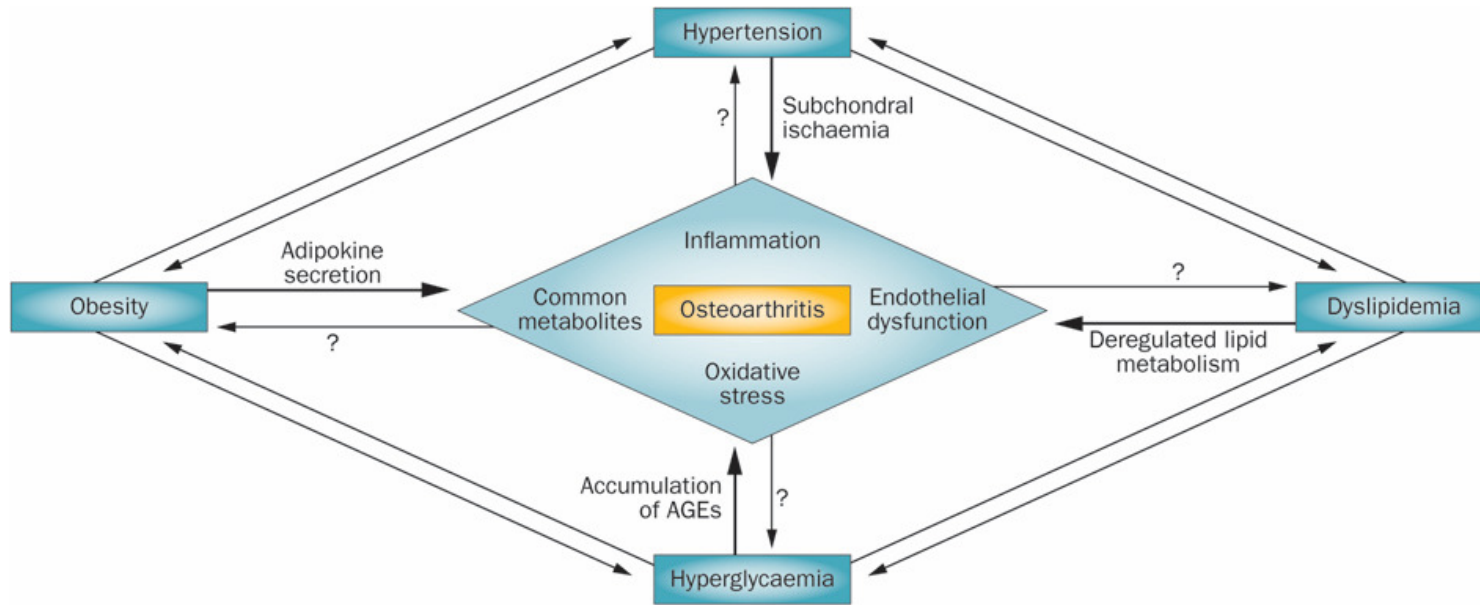
#3 Role of inflammation in OA

- Prostaglandins and eicosanoids
 - Rationale for use of NSAIDs
- Synovitis
- Cytokines, especially IL-1, and NF-KB signalling
- Relationship to obesity, metabolic syndrome and adipokines
- Role of innate immune system
 - Toll-like receptors (TLRs) and complement
 - Damage-associated and pathogen-associated molecular patterns

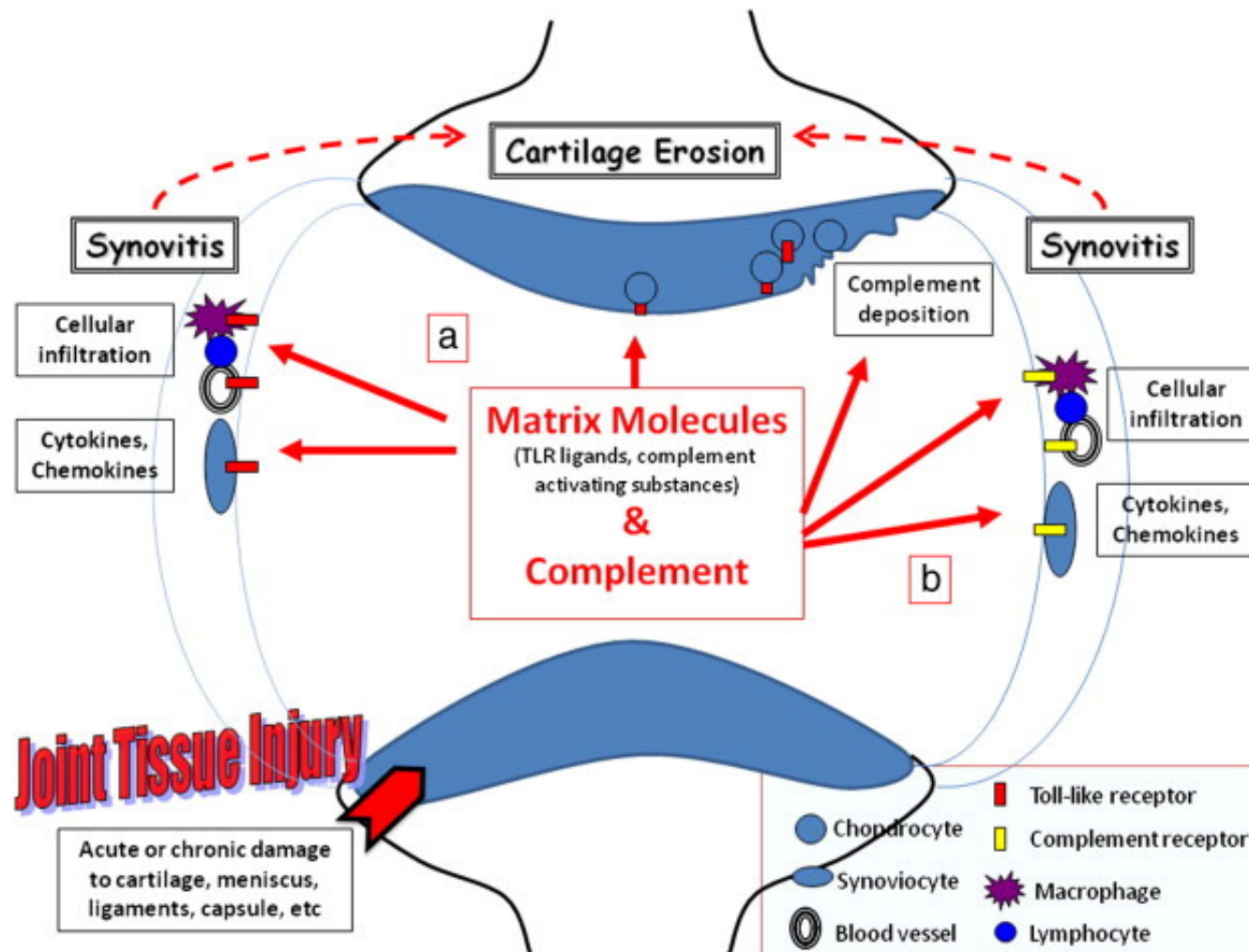
An hypothesis for the role of inflammation in the pathogenesis of OA according to the phenotype.



Relationship of OA to Metabolic Syndrome



Immune-mediated inflammation in OA



#2 Improved understanding of cartilage metabolism

- Mechanisms of cartilage homeostasis
 - Degradation (catabolism) of matrix
 - Matrix metalloproteinases (collagenases and gelatinases), including MMP-1, -2 and -13
 - Aggrecanases, including ADAMTS-4 and -5
 - Synthesis (anabolism) of matrix
 - Aggrecans
 - Collagens and non-collagenous proteins
 - Role of growth factors, including BMPs
- Role of chondrocyte activation, proliferation, senescence and apoptosis

#1 All of the tissues are involved in the OA process

- “ ... the name osteoarthritis is a misnomer insofar as it implies an inherently inflammatory process, ... the more accurate term [is] *degenerative joint disease*.”
 - Sokoloff L: Chapter 73 in McCarty DJ, ed: Arthritis and Allied Conditions, 9th ed., 1979, 1135-53.
- “ ...wear and tear processes play a central role in initiating the degenerative process in cartilage.”
 - Mannik M, Gilliland BC: Degenerative Joint Disease. Chapter 351 in Petersdorf RG, et al: Harrison’s Principles of Internal Medicine, 10th ed., 1983, 1999-2002.

**Degenerative Joint Disease is a misnomer
and should be discarded from the lexicon**

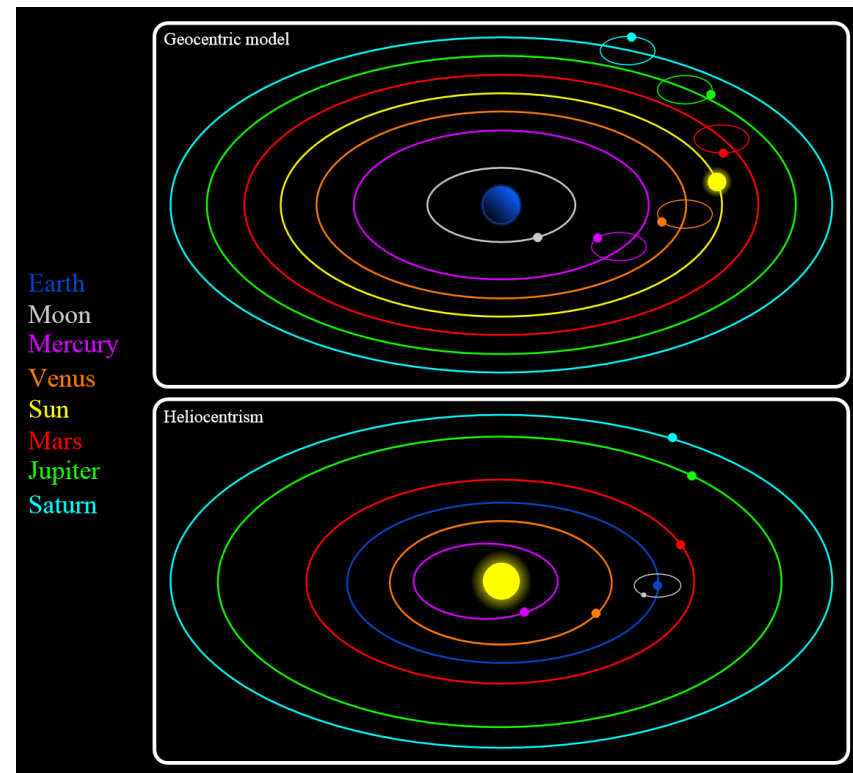


#1 All of the tissues are involved in the OA process

- OA is not a cartilage centric disease

Heliocentrism vs. geocentrism

- Geocentric model proposed by Aristotle and standardized by Ptolemy (2nd c.)
- Copernicus (16th c.) presented model of heliocentric system that was expanded upon by Galileo and Kepler.



OA: OARSI Definition

- OA is a progressive disease representing the failed repair of joint damage that, in the preponderance of cases, has been triggered by abnormal intra-articular stress.
- All of the tissues of the joint are involved, including the articular cartilage, subchondral bone, ligaments, menisci (when present), periarticular muscles and peripheral nerves.
- OA may be initiated by an abnormality in any of these tissues. Thus, OA is not a disease merely of cartilage but is a failure of the synovial joint.

Thank you for your attention



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