

## WHY STUDY BIOMARKERS OF OSTEOARTHRITIS?

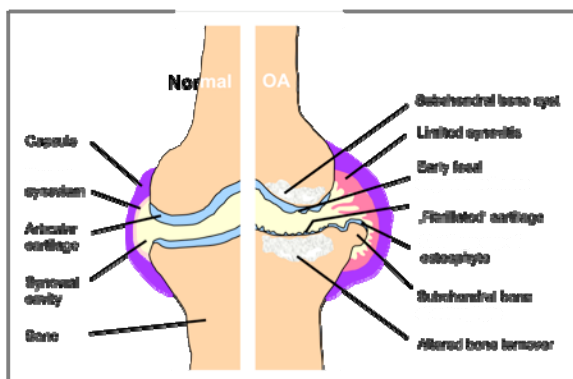
Cartilage and other tissues of the synovial joint are made up of a relatively small number of cells and a large amount of functional “extracellular matrix” in cartilage, synovium, tendon, ligaments and meniscus. The majority of degeneration of tissue is observed in the cartilage and meniscus. In osteoarthritis, two major events occur: (1) the cells become unusually active, and (2) the extracellular matrix is fragmented and rendered nonfunctional. Biomarkers can be indicative of the high activity of the cells (anabolic biomarkers) or the degeneration of the matrix (catabolic biomarkers) or other events associated with osteoarthritis such as inflammation.

Until now, only a few “OA biomarkers” have been developed to the point that they can be used in a large number of patient groups (called cohorts). In order to move the field of research and treatment for OA, there is a critical need for the development of additional biomarkers, commercialization so there is wide access to biomarkers, and use of biomarkers in patient cohorts and animal models. By this development and deployment of biomarkers, we will find out the:

- (1) natural history of the development of OA
- (2) progression timeline of OA
- (3) efficacy of treatments for OA.

## BACKGROUND and NEED for OA BIOMARKERS

- To fully understand the progression and treatment of OA, we need a range of markers for different events that are occurring, i.e. synthesis, degradation, inflammation, remodeling, repair in the different tissues of the joint, cartilage, tendon, meniscus, synovial lining, ligaments, etc. Each tissue has a molecular “signature” therefore specific markers can be developed to identify what is happening where.
- OA Biomarkers must be validated in animal models and in human cohorts.



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- Need to know the normal course of persistence of biomarkers in sera, urine and synovial fluid over age, sex, and prevalent diseases such as atherosclerosis, spine disease, and diabetes. The presence and source of OA biomarkers in “normal” individuals is critical.
- Within cartilage, there are different “zones” with different molecular signatures and different responses to OA.
- Both degradation and synthesis will reflect the metabolic state of the tissue. For example, antibodies can recognize newly created fragments of collagen and aggrecan that appear only after they have been broken down by enzymes. On the synthetic side, increased collagen can be measured by identifying a portion of the protein that is made only upon synthesis and doesn't stay on the mature molecule.
- Need to establish the rate of normal turnover – not all molecules have the same turnover characteristics, i.e. collagen has a much longer half life than aggrecan.
- Need markers for post-translational modifications that occur due to inflammation (tyrosine nitration), age (isomerization), biosynthesis (sulfation).
- Investigate biomarkers from new genetic screens, new sources such as blood white cells, and a combination of imaging and molecular biomarkers such as the dGEMRIC technique for identifying charge molecules such as proteoglycans, in tissues.
- Need translation of OA Biomarkers to the clinic understanding the special considerations of the clinical setting for patients and health professionals.
- Need a forum for discussion of OA Biomarkers where negative as well as positive results can be discussed, validation can be established, and standards for reporting studies can be evaluated.

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