A

B

C2C/CPII were demonstrated to discriminate OA-prone Hartley and strain 13 animals. Moreover, in mice, serum levels of MDA, CTX-II and CPII were elevated in obese and hyperlipidemic STR/ORT (STR) mice compared to control CBA mice. Finally, to our knowledge there is no biomarker that can be classified as prognostic biomarkers.

Conclusions: In conclusion, this systematic review indicates that some markers could be valuable to evaluate the burden of OA disease and to assess the therapeutic response in animal models. The most investigated biomarker in terms of burden of disease assessment are those derived from type II collagen metabolism. Since OA represents a process of matrix damage, turnover, and attempted repair, the use of multiple biomarkers, both anabolic and catabolic, could likely be most accurate in characterizing OA disease. Finally, soluble biomarkers can be as useful "drug development tools" that should be early integrated in the research program of new drugs.

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ANALYSIS OF THE EXPRESSION OF CONNEXIN 43 IN SYNOVIAL TISSUE OF PATIENTS WITH ARTHRITIS

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Purpose: Connexins, the major proteins of gap junctions, are expressed in various cell types and are important in the key process of intercellular communication. Connexins 26, 32 and 43 are expressed in synoviocytes, and connexin 43 (Cx43) is the most highly expressed connexin in normal human synovial membranes. Cx43 regulates immunological response in several tissues such as kidneys and lungs. Although, the role of Cx43 in synovium of arthritis is almost unclear. The aim of this study is to examine the expression level of Cx43 gene in synovial tissue in patients with rheumatoid arthritis (RA) compared with osteoarthritis.

Methods: The expression of Cx43 in synovial tissue from eight patients with RA (2 males, 6 females; mean age 59.5 ± 2.7 years; range 52 to 71 years), five patients with osteoarthritis (2 males, 3 females; mean age 68.4 ± 2.7 years; range 61 to 81 years), and one normal female subject (mean age 61 year) was analyzed by quantitative reverse transcriptase polymerase chain reaction (RT-PCR) and immunohistochemistry of tissue sections. All patients was analyzed with their demographic and clinical features about disease duration, Larsen scores for RA, CRP levels on presurgery, the disease activity scores including a 28-joint count (DAS 28ESR), and their medication.

Results: Cx 43 was highly expressed in RA synovial tissue, which TNF-a was also highly expressed, but was expressed lower in osteoarthritis and normal synovial tissue than in RA. The expression of Cx43 protein was highly in the superficial and sublining layers of RA synovium. But one of all patients with RA was not highly expressed. The expression of Cx43 and TNF-a mRNA were hardly detected in OA and normal synovial tissue. All of the RA patients were being treated with disease-modifying anti-rheumatic drugs (methotrexate or bucillamine or sulfasalazine), four patients were also receiving corticosteroids and two patients were also receiving an anti-IL-6 monoclonal antibody therapy (tocilizumab). Disease duration of RA patients were ranged 7 to 29 years(mean duration 15.4 years). All of their Larsen score for RA are stage IV. Their CRP levels on presurgery are ranged 0.03 to 2.31(mean level 0.70). Their DAS 28ESR patients were similar score (mean score 3.81 ± 1.22 range 3.64 to 5.03).

Conclusions: This study showed that Cx43 was strongly expressed in RA patients and TNF-a expression was also highly expressed. In our previous study, we demonstrated that siRNA targeting rat Cx43 inhibited TNF-a, IL-6, and IL-1b induced by lipopolysaccharide in rat fibroblast-like synoviocytes, and that transfection of siRNA targeting rat Cx43 in the joint significantly reduced synovitis in CIA rats. These observations suggest that the high expression level of Cx43 may be accompanied by TNF-a expression in synovial tissue of RA patient. On the other hand, Cx43 was not highly expressed in synovium of one of all RA patients. In this RA patient, the demographic and clinical features, such as disease duration, Larsen scores for RA, CRP levels, DAS 28ESR, and their medication, were not so different from other RA patients. This suggest that the expression of Cx43 may be involved in a mechanism of synovitis which is unregulated by the existing factors of disease activity of RA, such as pro-inflammatory cytokines. Thus, Cx43 might be a novel marker of inflammation in RA synovial tissue.

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REVIEW OF SOLUBLE BIOMARKERS OF OSTEOARTHRITIS: LESSONS FROM ANIMAL MODEL

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Purpose: Osteoarthritis (OA) is one of the leading causes of disability within the adult population. Currently, its diagnosis is mainly based on clinical examination and standard radiography. To date, there is no way to detect the disease at a molecular level, before the appearance of structural changes and symptoms. So an attractive alternative for monitoring OA is the measurement of biochemical markers in blood, urine or synovial fluid, which could reflect metabolic changes in joint tissue and therefore disease onset and progression. Animal models are relevant to investigate the early stage of OA and metabolic changes occurring in joint tissues. The goal of this review is to summarize the scientific data available in the literature on soluble biomarkers in animal models of OA.

Methods: A literature search was conducted using the Pubmed/Medline and Scopus databases between February 1995 and December 2014. All original papers, systematic and narrative reviews published in French or in English were considered.

Results: We summarized the data of 59 studies and proposed a classification scheme for OA biomarkers in animal studies, largely inspired of the BIPED classification. The most investigated biomarkers in terms of burden of disease assessment are those derived from type II collagen metabolism. Most particularly, Coll2-1 is particularly precocious. In serum of guinea pig, Coll2-1 increase is coincident with the early disruption of the collagen fibril visible by birefringence before the appearance of structural changes observable by conventional microscopy. Many interventions have been tested in rat, dog, horse and guinea pig models using biomarkers derived from type II collagen and aggrecan. Among diagnostic biomarkers, in guinea-pigs, only the ratio