Aggregan Cartilage Synthesis Assay (CS846 ELISA)
Cat. # 60-1004

Brief literature review of some publications where IBEX CS846 ELISA assay was used.

- A common finding is that joint damage in knee OA is accompanied by increases in SF of biomarkers with even higher levels being seen in advanced OA. SF levels of CS846 reflect these changes (Lohmander *et al,* 1999) and in knee OA CS846 concentrations are on average 38 fold higher in OA than those observed in sera (Poole *et al,* 1994). This points to the damaged knee joint as the principal source of this biomarker.

- In patients with haemophilia both serum CS 846 and urine CTX-II increase by 5 days after joint bleeding (van Vulpen *et al,* 2015). Serum CS846, urine CTX-II and serum C1,2C correlate with joint damage and joint space narrowing (Jansen *et al,* 2009). A combination of cartilage biomarkers CS 846, urine CTX-II and serum COMP increased the degree of correlation with joint damage. Of a broad series of biomarkers examined only CS846 revealed a significant correlation with MRI score in patients but only in those receiving treatment with hyaluronan (Oldenburg *et al,* 2016).

- In patients with ankylosing spondylitis, those treated with etanercept for 16 weeks revealed a reduction in serum C2C and an increase in serum CS846 (Maksymowych *et al,* 2005). A subsequent study over 2 years revealed that etanercept treatment caused a decrease in C2C after 12 months and after 24 months CPII was increased (Briot *et al,* 2008). Both studies point to a reduction in cartilage damage by etanercept (reduced C2C) and suggest onset of reparative responses reflected by increases in CS846 and CPII.

- There is recent evidence that mechanically-induced changes in serum cartilage matrix biomarkers can predict regional changes in cartilage thickness 5 years later in human subjects with early knee OA (Chu *et al,* 2017). Subjects were exercised on a treadmill for 30 minutes and blood samples obtained 30 minutes and 5.5 hours after exercise. MRIs of the index knees were acquired at baseline and after 5-years. Serum biomarker concentrations of C1,2C and CS846 were measured. Changes in biomarker concentrations (0.5h vs 5.5h) were determined and correlations between changes in cartilage thickness and biomarker levels (as a percentage of 0.5 h post-activity levels) were assessed. For knees where the catabolic and anabolic marker concentrations increased, specific regions of articular cartilage were thinner. The study supports the hypothesis that a mechanical stimulus can produce a change in both markers of degeneration and synthesis that correlate with subsequent changes in cartilage thickness.

- In a study where patients treated for three weeks prior to arthroplasty with a metalloproteinase inhibitor compared to a placebo, the findings revealed significant increases in cartilage CS846 although there was no evidence of any changes in collagen cleavage or synthesis, yet collagen content was increased (Leff *et al,* 2003).

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1. Briot K, Roux C, Gossec L, Charni N, Kolta S et al. (2008). Effects of etanercept on serum biochemical marker of cartilage metabolism in patients with spondyloarthropathy. J Rheumatol 35:310-14.

2. Chu CR, Sheth S, Erhart-Hledik JC, Do B, Titchenal, MR, Andriacchi, TP. (2017). Mechanically stimulated biomarkers signal cartilage changes over 5 years consistent with disease progression in medial knee osteoarthritis patients. J Orthop Res. 2017 Sep 1. doi: 10.1002/jor.23720. [Epub ahead of print].

3. Jansen N.W., Roosendaal G., Lundin B., Heijnen L., Mauser-Bunschoten E., Bijlsma J.W., Theobald M. and Lafeber F.P. (2009). The combination of the biomarkers urinary C-terminal telopeptide of type II collagen, serum cartilage oligomeric matrix protein, and serum chondroitin sulfate 846 reflects cartilage damage in hemophilic arthropathy. Arthritis and Rheumatism 60: 290-298.

4. Leff RL, Elias I, Ionescu M, Reiner A, Poole AR. (2003). Molecular changes in human osteoarthritis cartilage after 3 weeks of oral administration of BAY12-9566, a matrix metalloproteinase inhibitor. J Rheumatol 30: 544-9.

5. Lohmander S.L., Ionescu M., Jugessor H. and Poole A.R. (1999). Changes in joint cartilage aggrecan after knee injury and in osteoarthritis. Arthritis and Rheumatism 42:534-544.

6. Maksymowych WP, Poole AR, Hiebert L, Webb A, Ionescu M et al. (2005). Etanercept exerts beneficial effects on articular cartilage biomarkers of degradation and turnover in patients with ankylosing spondylitis. J Rheumatol 32: 1911-7.

7. Oldenburg J, Zimmermann R, Katsarou O, Zanon E., Kellermann E., Lundin B. and Ellinghaus P. (2016). Potential biomarkers of haemophilic arthropathy: correlations with compatible additive magnetic resonance imaging scores. Haemophilia 22: 760-764.

8. Poole A.R., Ionescu M., Swan A. and Dieppe P.A. (1994). Changes in cartilage metabolism in arthritis reflected by altered serum and synovial fluid levels of the cartilage proteoglycan aggrecan: implications for pathogenesis. J Clin Invest. 94:25-33.

9. van Vulpen LF, van Meergeren ME, Roosendaal G, Jansen NW, van Laar JM et al. (2015). Biochemical markers of joint damage increase shortly after a joint bleed; an explorative human and canine in vivo study. Osteoarthritis Cart 23: 63-9.