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).


