

## Coll2-1NO2

Coll2-1NO2 contains the same amino-acid sequence than Coll2-1 which is nitrated on its tyrosine residue [HRGY(NO2)PGLDG]. This degradation fragment, named Coll2-1-NO2, is derived from type II collagen and is released into the synovial fluid following the action of collagenases and gelatinase B. Subsequent tyrosine nitration results from the action of peroxynitrite (ONOO-), a strong oxidant generated during the inflammatory process.

As for Coll2-1, Coll2-1NO2 is able to discriminate patients with osteoarthritis (OA) or rheumatoid arthritis (RA) from asymptomatic control subjects. In addition, Coll2-1 NO2, but not Coll2-1, was correlated with C-reactive protein in the sera of OA and RA patients (Deberg, Labasse et al. 2005). Bringing information on the level of inflammation in the joint, Coll2-1NO2 allows to discriminate the form of erosive osteoarthritis of the hand (Ramonda, Lorenzin et al. 2013).

Beside inflammation processes, the predictive value of Coll2-1NO2 for radiographic knee osteoarthritis progression was evaluated using two distinct OA populations: population 1 was composed by 135 obese men and women aged 45 to 64 years with mild and moderate knee OA; population 2 included 182 obese women with unilateral radiographic knee OA (K&L II or III) aged 45 to 64 years from the placebo arm of the doxycycline study (Mazzuca, Brandt et al. 2004).

The creatinine-adjusted urinary Coll2-1NO2 concentration was measured on samples obtained at baseline, after 16 and 30 months for the patients from population 1 and at baseline and after 6, 12, 18, 24 and 30 months for the patients from population 2. Patients showing a decrease of JSW 0.5 mm over 30 months follow-up were designated radiographic progressors.

The results of the both studies agree well and show a consistent capability of urinary Coll2-1NO2 to predict knee OA progression. Specifically, the 16-month change in urinary Coll2-1NO2 is a useful predictor of radiographic progression of knee OA over 30 months in two independent populations totalling a sample size of 317 patients (Henrotin, Kraus et al. 2012).

Coll2-1NO2 is considered as a marker of burden of disease as for Coll2-1 according to the result of a prospective study wherein 75 patients with primary knee were followed. Mean joint space width (JSW) of the medial compartment of the femorotibial joint was measured with a computer assisted method on standardized radiographs taken at baseline and after a 3-year follow-up. Pain, stiffness, and physical function subscales of the Western Ontario and McMaster Universities (WOMAC) were assessed at the same time points. Type II collagen peptides Coll 2-1 and Coll 2-1NO2 were measured in urines at baseline, after 1 year and 3 years. At baseline, significant correlations were found between the urinary Coll 2-1 and Coll 2-1 NO2 levels and the global WOMAC score and its subscales for pain (Deberg, Labasse et al. 2005).

As for Coll2-1, Coll2-1NO2 was shown to be decrease in serum in patients who had received intra-articular injection of hyaluronic acid in OA knee. The serum concentrations of Coll2-1NO2 decreased between the day of the first HA injection (D1) and the two follow up visits at D30 and D90 (Henrotin, Chevalier et al. 2013).