# COLL2-1 AND COLL2-1NO$_2$, TWO ORIGINAL TYPE II COLLAGEN BIOMARKERS, ARE USEFUL IN ANIMALS MODELS AND IN HUMAN CLINICAL STUDIES

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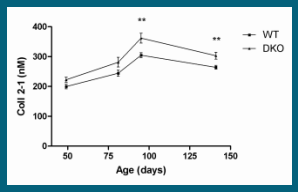
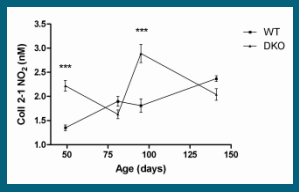
## PURPOSE

To summarize the results on two original biological markers of cartilage degradation, Coll2-1 and Coll2-1NO$_2$.

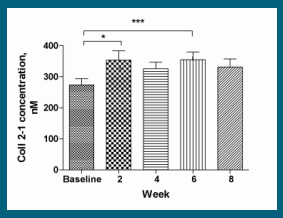
## RESULTS

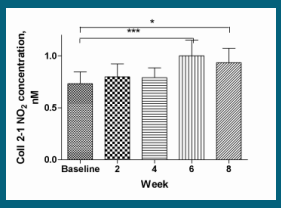
In double deficient mice for fibromodulin and biglycan, a strain that develops severe premature knee and temporomandibular osteoarthritis, Coll2-1 serum concentration was higher than in wild-type animals [1].



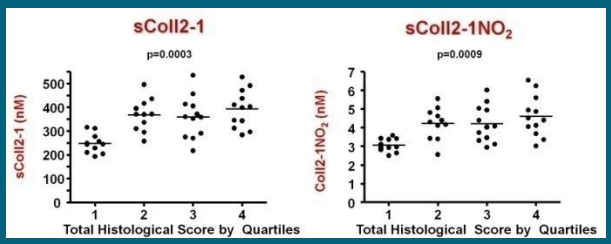




In dogs after an anterior cruciate ligament transection, Coll2-1 serum concentration increased by 23% after 2 weeks and by 18% after 6 weeks post-surgery [2].




In male Hartley guinea pig, a strain of guinea pig that spontaneously develop OA, Coll2-1 levels in serum increased with the appearance of the early disruption of the collagen fibril and was correlated with histological severity of the cartilage lesions [3].

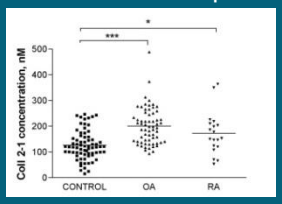


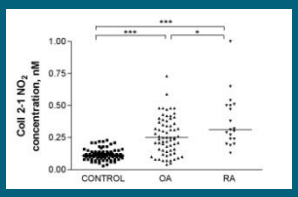

In horses developing a juvenile digital degenerative arthropathy (osteochondritis), an uncoupled variation of Coll2-1 and Coll2-1NO$_2$ levels in plasma was demonstrated [4]. Coll2-1NO$_2$ was increased whereas Coll2-1 levels trended toward a decrease.

**References:**

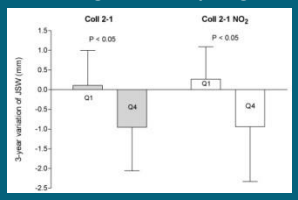
1. Ameye, L.G., et al. Arthritis Rheum, 2007. **56**(10): p. 3336-46.
2. Henrotin, Y., et al. Osteoarthritis Cartilage, 2008. **16**(4): p. S51.
3. Huebner, J.L., et al. Osteoarthritis Cartilage, 2007. **15**(Suppl C): p. C 70.
4. Lejeune, J.P., et al. Vet Res Commun, 2007. **31**(5): p. 591-601.
5. Deberg, M., et al. Osteoarthritis Cartilage, 2005. **13**(3): p. 258-65.
6. Deberg, M.A., et al. Osteoarthritis Cartilage, 2005. **13**(12): p. 1059-65.
7. Deberg, M., et al. Ann Rheum Dis, 2008. **67**(2): p. 168-74.

Serum Coll2-1 levels were 1.6 and 1.4 times higher in patients with osteoarthritis or with rheumatoid arthritis (RA), respectively, than in age-matched control. In contrast, the Coll2-1NO$_2$ concentration was higher in RA patients than in OA patients [5]

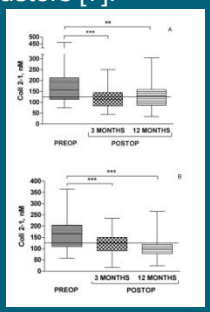


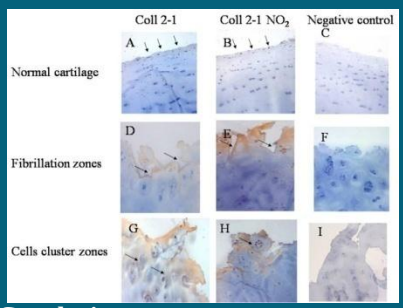




In the placebo group of a 3-year follow-up glucosamine sulfate study, the 1-year increase in urinary Coll2-1 and Coll2-1NO$_2$ was negatively correlated with the 3-year change in minimum joint space width, indicating that decreases in levels of these biomarkers in urine is predictive of the radiological OA progression [6].




Finally, the normalization of coll2-1 serum levels, 3 months after joint replacement in patients with isolated unilateral knee or hip osteoarthritis, indicates that Coll2-1 is a disease-specific marker that is sensitive to structural changes occurring in one single joint. Immunohistochemistry analysis revealed the extensive presence of Coll2-1 and Coll2-1NO$_2$ in the superficial layer of fibrillated cartilage and around some cells clusters [7].




## Conclusions

**Based on these experimental data, Coll2-1 and Coll2-1NO$_2$ are considered as pertinent diagnosis, prognosis and burden of disease biomarkers according the classification criteria of the newly proposed BIPED classification scheme by the Osteoarthritis Biomarkers Network, a consortium of five NIH designated sites.**