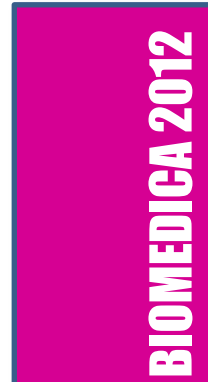


# G U I N E A P I G

## As a relevant spontaneous model to assess anti-rheumatic therapies

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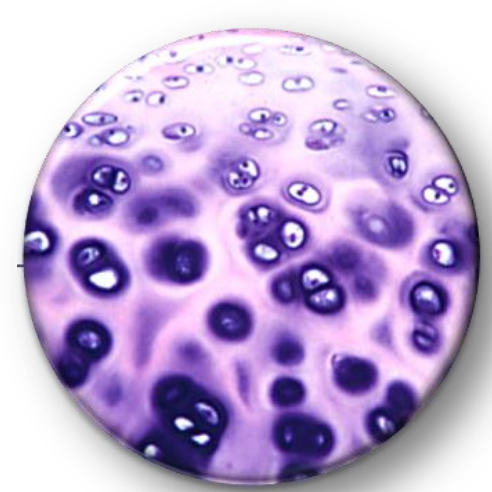
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**P U R P O S E.** On the contrary to osteoarthritis (OA) resistant strain 2 and 13, Dunkin-Hartley guinea pigs develop spontaneous knee OA. The attraction of the guinea pig as an OA model system is its histopathological similarity to human disease. The appearance of joint pathology in guinea pig and humans is both age-related and subject to a variety of well-recognized OA risk factors shared in common with humans including body weight, mechanical load, and high bone turnover. Spontaneous lesions in the knee are bilaterally symmetric, and appear first, and are more pronounced, in the medial knee compartment in the area not covered by the meniscus. This corresponds to the pattern of localization of idiopathic, non-traumatic knee OA in humans. This guinea pig OA model is characterized by an early collagen fibril disruption occurring in articular cartilage (2 months), bone cysts (2-3 months), subchondral bone thickening and osteophytes (3-12 months) are preceding histological proteoglycan loss (4-6 months) and fibrillations (8-12 months). Involvement of IL-1 $\beta$ , MMP-3, MMP-13 have been shown. ■

**M E T H O D S.** Male Dunkin-Hartley guinea pigs aged 3 weeks are obtained from Charles River Laboratories (Paris, France). Animals are housed 5 per cage, in solid bottom cages with environmental enrichments, and fed standard guinea pig chow containing Vitamin C and Vitamin D3, as well as water ad libitum. All animals will be allowed one week for acclimatization to housing conditions prior to any experimental procedure. Blood sampling can be obtained under ketamine/xylazine tranquilization at the superficial veins at the ears each 6 weeks. Individual metabolic cages are available for 24h urine sampling. Sacrifice could be performed between 8 and 12-month when OA lesions are well developed.



**V A L O R I Z A T I O N .** A variety of OA-related biomarkers, used to evaluate human OA, is detectable in guinea pig cartilage or body fluids. Imaging methods can be used and joints are also large enough to enable cartilage harvest for molecular analyses that can provide valuable quantitative outcomes to complement histological assessments. In particular, a marked increase in serum Coll2-1, a marker of type II collagen degradation, from 3 weeks to 4 months of age occurs concomitantly with collagen disruption, and levels remain elevated during the course of disease development. There was a statistically significant increase in both serum Coll2-1 and Coll2-1NO<sub>2</sub>, the nitrated form of Coll2-1 considered as a marker of oxidative stress related to cartilage degradation, with increasing severity of histological OA (Fig 1)

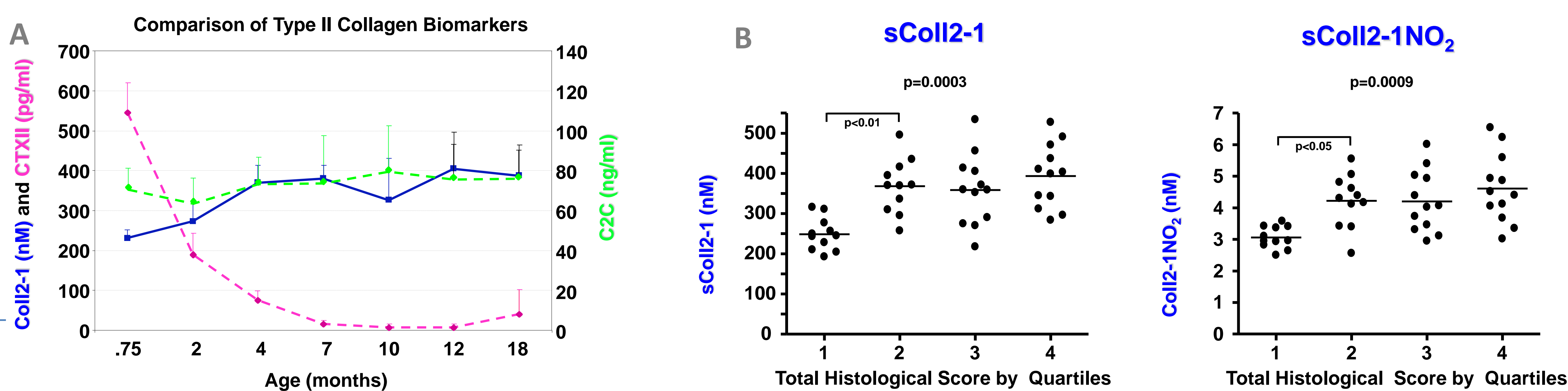


Fig. 1

**A:** Comparison of type II collagen biomarkers (Coll2-1, C2C, and CTXII) in a cross-sectional cohort of Hartley guinea pigs aged 3 weeks to 18 months of age (mean values  $\pm$  SD). **B:** Distribution of serum biomarker levels by quartiles of total histological score. Total histological scores were divided into quartiles (Q1: 0-9; Q2: 10-18; Q3: 19-32; Q4: 33-32) to examine the distribution of levels of serum biomarker by severity of histological OA. Reference: Huebner J et al Osteoarthritis Cart 2010

## C O N C L U S I O N

Spontaneous OA guinea pig model is an highly valuable animal model to evaluate anti-rheumatic therapies. Coll2-1 and Coll2-1NO<sub>2</sub> epitopes are likely generated from articular cartilage and may be useful as quantitative biomarker outcomes for early disease prevention and treatment in this model system.

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