cartilage extracts. The dog ACLT model of acute injury showed higher levels of TN-C in surgery knees at 1-month post surgery (73-fold) and 3-months post surgery (48-fold) as compared to control knees. Higher levels of TN-C were maintained in surgery knees 6-months post surgery in this dog model. In the rat meniscal tear model, there was a significant increase (40-fold) in TN-C in surgery knees at 1wk as compared to no surgery contralateral controls, and this increase was maintained at 4 and 8 wks, albeit with a smaller absolute difference from control.

Conclusions: The potential of TN-C Large as a unique biomarker of joint disease/injury has been demonstrated using synovial fluids from humans with various joint diseases and from preclinical animal models of joint injury. Being elastic, TN-C might play an important role in degenerative/regenerative processes where the normal biomechanical environment of musculoskeletal tissue is compromised by disease/injury. As a binder of several ECM proteins, release of TN-C could have a larger impact on the integral structure/function of other ECM proteins, and has the potential to be a marker of joint pathobiology and healing. Our preliminary results indicate that TN-C levels may be applicable to determining pharmacodynamic activity of chondro-protecting drugs in humans. Work is ongoing to study the levels of TN-C during degeneration in other joint tissues such as tendon. Understanding the functions of TN-C would provide insights for pharmacologic intervention of musculoskeletal diseases/injuries.

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DEGRADATION TO SYNTHESIS RATIOS OF TYPE II COLLAGEN BIOMARKERS IN SYNOVIAL FLUID AND SERUM IN THOROUGHBRED RACEHORSES

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Purpose: Type II collagen biomarkers have shown promise in the study of osteoarthritis. CPII (cleaved C-propeptide of type II collagen) has been directly correlated with type II collagen synthesis. CTX II (crosslinked C-telopeptide fragments of type II collagen), C1,2C (neoepitope of types I and II collagen created after collagenase cleavage), and C2C (neoepitope of type II collagen created after collagenase cleavage) have been used to assess collagen degradation. The objective of the study was to compare type II collagen degradation to synthesis ratios in serum and synovial fluid (SF) from normal horses and those with osteochondral (OC) injury.

Methods: SF was taken from the carpal joints of 2 groups of Thoroughbred racehorses: (1) normal, adult horses $>$ 3 years of age (2) OC injured horses 2-7 years of age undergoing arthroscopic surgery for removal of OC fragments resulting from racing injury. From group 1 horses, serum was collected from 16 horses. SF was obtained from 10 middle carpal joints (MCJ), and 10 radiocarpal joints (RCJ). From group 2, serum was collected from 20 horses. SF was collected from 10 MCJ and 10 RCJ. SF was aseptically collected by needle arthrocentesis without lavage, centrifuged, and decanted. Commercially available ELISAs, were used to measure type II collagen markers (C1,2C, C2C, CPII, and CTX II). Differences between each group were evaluated using an unpaired t-test. $P<0.05$ was considered significant.

Results: Concentrations of C2C; C1,2C; and CTX II were all significantly higher in SF from OC injured joints compared to normal joints (Table 1). Concentrations of CPII were also significantly higher in SF from injured joints compared to normal joints. Degradation to synthesis ratios in SF were significantly higher in OC injured carpal joints compared to normal joints for C1,2C:CPII and CTX II:CPII, but not for C2C:CPII. In serum, concentrations of C1,2C were significantly higher from OC injured horses compared to normal horses. Serum concentrations of CTX II were significantly lower from OC injured horses compared to normal horses. Serum ratios were significantly higher in horses with OC injured carpal joints compared to normal horses for C1,2C:CPII only. The ratio was significantly lower in serum from horses with OC injured carpal joints compared to normal horses for CTX II:CPII only.

Conclusions: Joint injury affects concentrations of type II collagen degradation and synthesis biomarkers and their ratios when compared to normal horses. In SF, C1,2C:CPII and CTX II:CPII ratios demonstrate that degradation predominates over synthesis when the joint is injured because the ratios are higher than normal joints. The serum C1,2C:CPII ratio suggests that there is higher degradation after injury compared to normal horses with no difference in the amount of synthesis. The CTX II:CPII ratio suggests that the synthesis of type II collagen stays steady with less degradation. However, increasing or decreasing degradation to synthesis ratios must be interpreted in light of the known effect of injury on biomarker concentrations in both SF and serum. Injury may cause increase in SF concentrations, but may at the same time cause an increase or decrease in serum concentrations. Thus, SF biomarkers may be more indicative of degradation or synthesis in a single joint than serum biomarkers.

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SYNOVIAL FLUID URIC ACID AS A MARKER OF JOINT TISSUE DEGRADATION IN OSTEOARTHRITIS

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Purpose: Uric acid (UA) is constitutively present in normal cells, increased in concentration when cells are injured and released from dying cells. The products of cell stress and tissue damage may represent "danger signals" that function as endogenous adjuvants recognized by the immune system. UA has been identified as one of these principal endogenous "danger signals" released from injured cells. We sought to determine whether elevated synovial fluid (SF) UA might be a potentiating factor in osteoarthritis (OA).

Methods: *Patients:* A total of 159 participants were enrolled in the Strategies to Predict Osteoarthritis Progression (POP) study. Informed consent was obtained from all subjects and the entire study was approved by the Duke University IRB. Participants met

Abstract 115 – Table 1. Mean (± SD) concentrations of serum and SF type II collagen biomarkers and degradation to synthesis ratios for normal and osteochondral (OC) injured carpal joints

	Mean biomarker concentrations (± SD)				Degradation:Synthesis		
	C2C (pmol/mL)	C1,2C (pmol/mL)	CTX II (pg/mL)	CPII (ng/mL)	C2C:CP II	C1,2C:CP II	CTX II:CP II
Serum							
Normal	479±32.2	**452±16*** **	**70.3±9.0** **	1045±91	0.43±0.19	**0.47±0.14***	**0.07±0.03** **
OC injured	415±9.8	**580±21.6**	**39.6±3.4**	1019±90	0.43±0.12	**0.63±0.21**	**0.04±0.01**
Synovial Fluid							
Normal	**274±15.6** **	**278±31.6*** **	**160±45*** **	**1013±60*** **	0.26±0.06	**0.22±0.05*** **	**0.08±0.05*** **
OC injured	**409±32.6**	**1070±122**	**513±47.1**	**1637±110**	0.26±0.09	**0.65±0.37**	**0.37±0.28**

Bolded values indicate a significant difference between groups within serum or SF. *P≤0.05; **P≤0.01; ***P≤0.001.