Orthopaedic Surgery
School of Medicine
University of Missouri Health

Thompson Laboratory for Regenerative Orthopaedics

Influences of Patient Medication Use on Osteoarthritic Chondrocyte Metabolism

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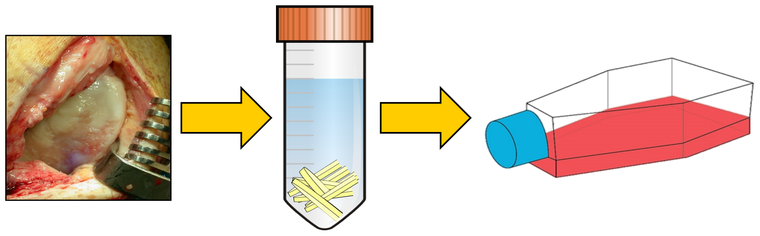
Introduction and Purpose

- The pathophysiology of OA is poorly understood, and there is significant patient to patient variability in the development and progression of OA
- OA Patients are often prescribed medications for the treatment of OA and other clinical conditions
- It is not known if medications commonly prescribed to patients impact the metabolism of the chondrocyte
- This study was designed to determine if patient medication use prior to surgery impacts the metabolic responses of OA chondrocytes during passage 0 culture

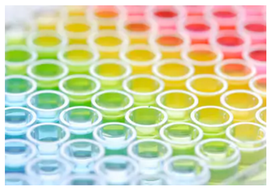
Hypothesis

There would be significant differences in OA chondrocyte metabolism based on patient medication use prior to surgery

Methods



1) With IRB approval (IRB#1208932) and patient consent, osteochondral tissue was recovered from OA patients (n=74) undergoing total knee arthroplasty (TKA)
2) Articular cartilage tissue was collected from joint surfaces, diced and digested in a collagenase solution to free chondrocytes from the extracellular matrix. Chondrocytes were cultured at passage 0 in 10% fetal bovine serum (FBS) media on a T25 culture flask until >90% confluent
3) Once confluent, media were changed, cells were cultured for 3 days, and then media were collected for biomarker analysis



4) Media were tested for IL-1RA, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, Fractalkine, GRO-α, ADAMTS4, MCP-1, MCP-3, MIP-1α, MIP-1β, TNF-α, RANTES, PDGF-AA, VEGF, MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-13, MMP activity, TIMP-1, TIMP-2, TIMP-3, TIMP-4, PGE2, and glycosaminoglycan (GAG) content using commercially available kits according to the manufacturer's protocol.

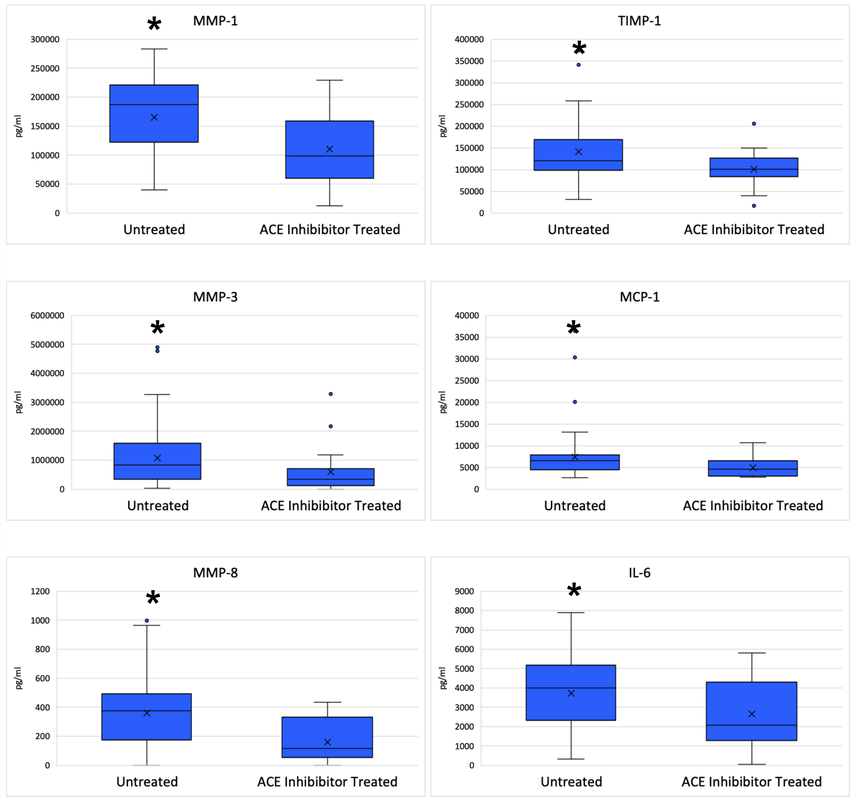
TKA Patient Medication Distribution		
Medication Group	Treated	Untreated
Thyroid Medication	21	53
Thiazide Diuretic	22	52
Proton-pump Inhibitor	27	47
ACE Inhibitor	20	54
COX-2 Inhibitor	16	58
NSAID	43	31
Corticosteroid	29	45
Opioid Analgesic	22	52
Statin	30	44

Table 1: Patient distribution based on medication use prior to TKA

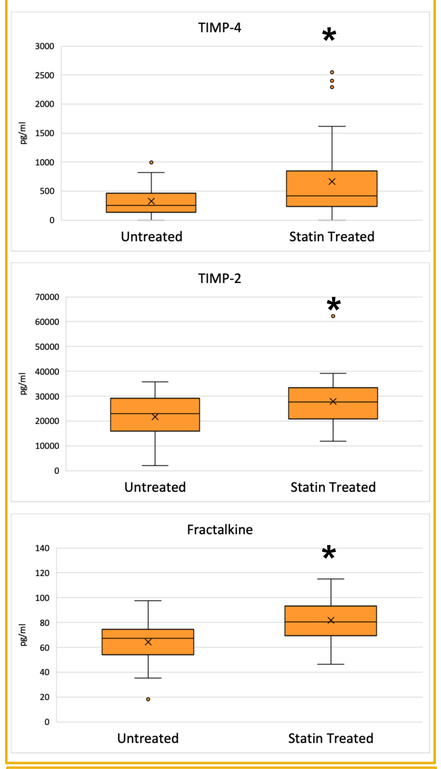
5) Patient medication use was determined based on medical records, and chondrocytes were grouped based on common medication classes taken by the patient at the time of surgery. (Table 1) A Mann-Whitney U test was used to determine significant differences between groups with $p<0.05$.

Results

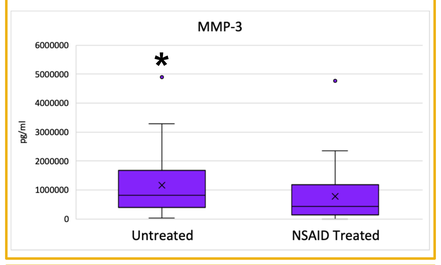
ACE Inhibitor



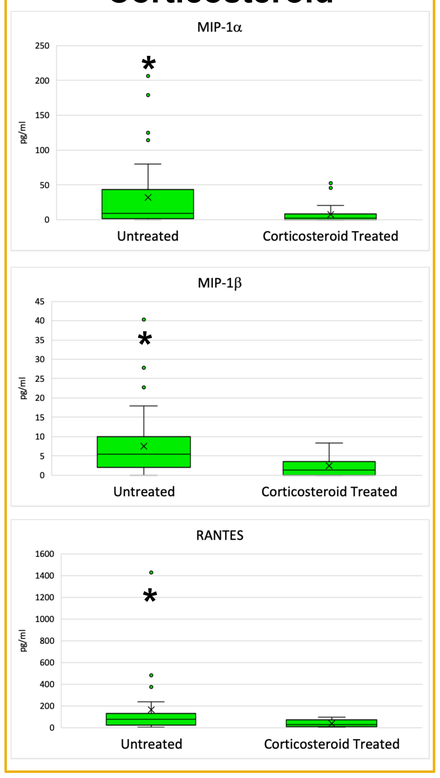
Statin



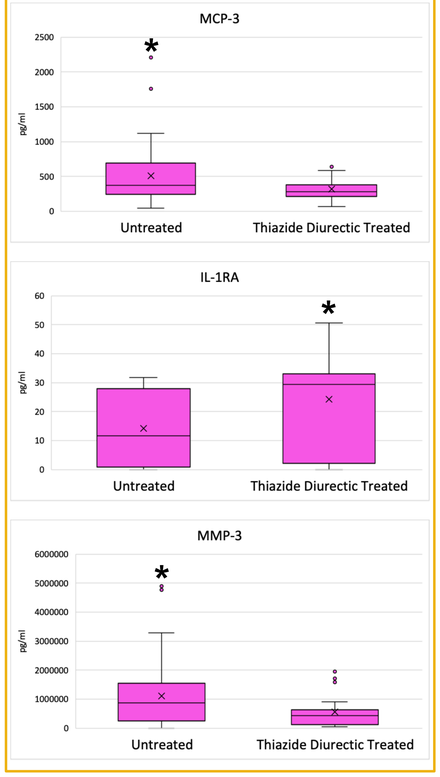
NSAID



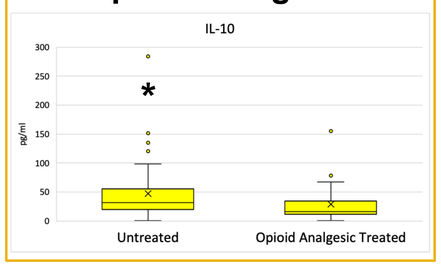
Corticosteroid



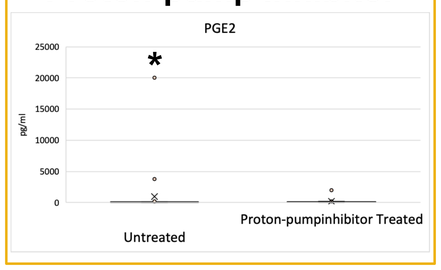
Thiazide Diuretic



Opioid Analgesic



Proton-pump Inhibitor



- Of the drugs assessed, ACE inhibitor use by the patient affected the production of the highest number of biomarkers analyzed, and significantly affected both degradative and pro-inflammatory metabolic responses of the OA chondrocyte during culture
- Statin use appears to stimulate an anti-degradative response by the chondrocytes during culture through increased TIMP production
- Corticosteroid use appears to decrease specific pathways in the inflammatory cascade by the chondrocytes during culture
- Thiazide Diuretic use appears to have anti-inflammatory and anti-degradative effects on OA chondrocyte metabolic responses during culture
- NSAID use reduced the production of MMP-3 by OA chondrocytes during culture
- Opioid Analgesic use decreased the production of IL-10 by OA chondrocytes during culture
- Proton-pump Inhibitor use reduced the production of PGE2 by OA chondrocytes during culture.

Conclusions

- **Based on the data from this study, the metabolism of OA chondrocytes during initial *in vitro* culture may be significantly altered by patient treatment with commonly prescribed medications prior to surgery**
- **This indicates that use of medications from each of these commonly prescribed drug classes may affect the metabolic responses of articular cartilage in the healthy and osteoarthritic joint**
- **Further study is required to relate the differences in chondrocyte metabolism based on medication use by the patient to the metabolism of articular cartilage *in vivo* during OA development and progression to determine potential roles for these medications in pathobiology and production of biomarkers during OA**