Relationships among Patient-Specific Variables and Osteoarthritic Chondrocyte Metabolism

DeLucia SE, Caisley AB, Stoker AM, Sullentrup AN, Greco NT, Stannard JP, Kenney JA, Cook JL
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Orthopaedic Surgery
School of Medicine
University of Missouri Health

Thompson Laboratory for Regenerative Orthopaedics

Introduction and Purpose

- The Pathophysiology of OA is poorly understood and there is considerable patients to patient variation in the development and progression of OA clinically
- Age, Sex, BMI, Tobacco Use, and Diabetes are consistent risk factors for OA
- The mechanistic effects of these factors on OA cartilage metabolism have not been fully characterized

Hypothesis

- As patient age, BMI, and pain at the time of total knee arthroplasty (TKA) increase, production of pro-inflammatory and degradative biomarkers by OA chondrocytes will significantly increase.
- Female sex, tobacco use, and diabetes mellitus will be associated with significant increases in the production of pro-inflammatory and degradative biomarkers by OA chondrocytes.

Methods

- With IRB approval (IRB #1208932) and informed patient consent

Pro-Inflammatory Biomarkers		Anti-Inflammatory Biomarkers		Pro-Degradative Biomarkers		Anti-Degradative Biomarkers		Matrix Molecule
GRO-α	MIP-1α	IL-1RA	IL-10	MMP-1	MMP-8	TIMP-1	TIMP-3	Media Glycosaminoglycan (GAG)
IL-6	MIP-1β	IL-2	PDGF-AA	MMP-2	MMP-9			
IL-8	PGE2			MMP-3	MMP-13	TIMP-2	TIMP-4	
MCP-1	RANTES	IL-4	VEGF	MMP-7	MMP Activity			
MCP-3	TNF-α			ADAMTS4				

Conclusions

- Patient BMI, sex, and tobacco use may directly or indirectly influence biomarker production by OA chondrocytes.
- Each patient factor assessed was associated with unique effects on osteoarthritic chondrocyte metabolism.
- Further characterization of the mechanistic effects that these key patient factors have on chondrocyte metabolism will provide insight into drivers of patient-to-patient variability in OA so that precision medicine strategies for diagnosis, prevention, and treatment can be developed and optimized

Results

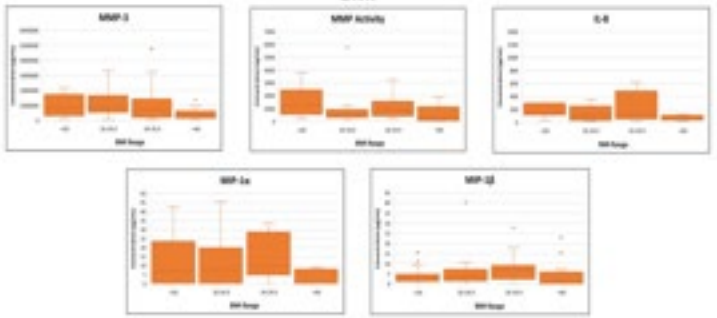
Correlations Between Patient Age, BMI, VAS Pain Score

	Gro-α	VEGF	MCP-3	IL-2	IL-6	IL-8	RANTES
Age	0.11	0.05	0.12	0.06	-0.01	0.22	-0.13
BMI	-0.13	0.02	-0.24	-0.28	-0.21	-0.29	-0.18
VAS Pain	-0.25	-0.23	-0.39	-0.19	-0.34	0.03	-0.27
	IL1-RA	MMP-3	MMP-7	MMP-8	MMP Activity	MGAG	
Age	0.01	-0.10	-0.18	-0.02	0.09	0.22	
BMI	0.16	-0.26	-0.26	-0.22	-0.23	0.29	
VAS Pain	0.24	0.16	0.23	0.20	-0.15	-0.26	

- There were only weak to negligible correlations observed between patient age, BMI, or VAS pain scores and the production of specific inflammation related and degradation related biomarkers by the OA chondrocytes.
- Surprisingly, the data indicates potential negative correlations between patient VAS Pain and the production of specific inflammation related biomarkers, as well as a negative correlation between patient BMI and the production of specific inflammatory and degradation related biomarkers.

Results

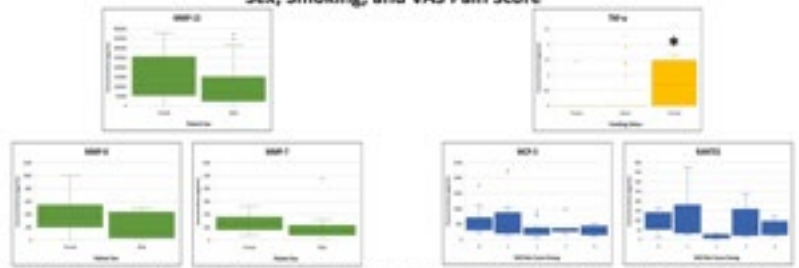
BMI



- In all cases the patients in the highest BMI group had the lowest production of the biomarkers

Results

Sex, Smoking, and VAS Pain Score



- When patient chondrocytes were groups based on sex (green), female OA chondrocytes produced significantly higher levels of the degradative enzymes MMP-7, MMP-8, and MMP-13
- Chondrocytes from current smokers (yellow) produced significantly higher levels of TNF-α compared to former and non-smokers
- When chondrocytes were groups based on Patient VAS pain scores at the time of surgery (blue), the only significant difference was observed between the 0 group (score of 0) and the 2 group (score of 4-5) for MCP-3 and RANTES

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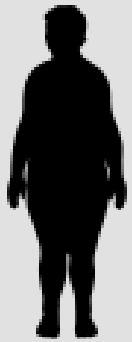
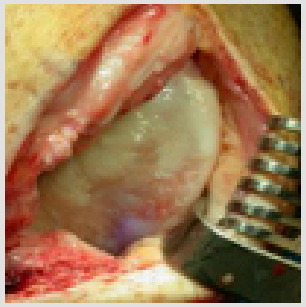
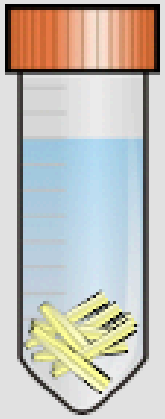
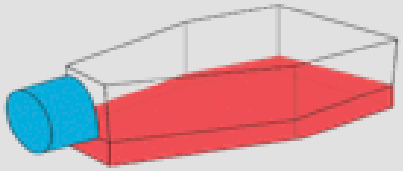


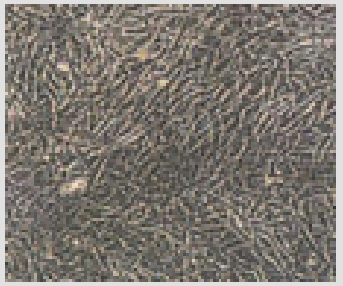


TKA for Knee OA (n=74)
Mean age 62y (28-87)
Mean BMI 35 (23-49)
49 Female, 25 Male

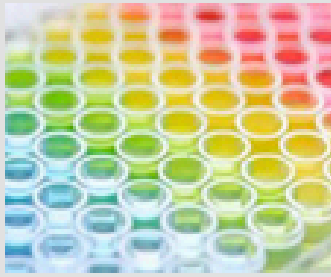




DMEM 10%
FBS
5% CO_2
90% Humidity



90% Confluence
Δ media
Culture 3 days
Collect media



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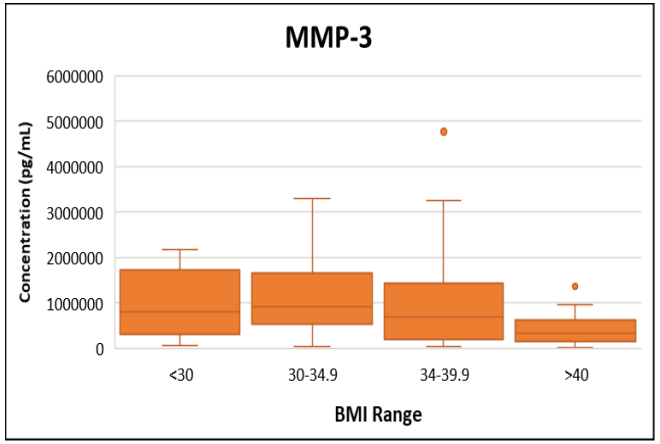

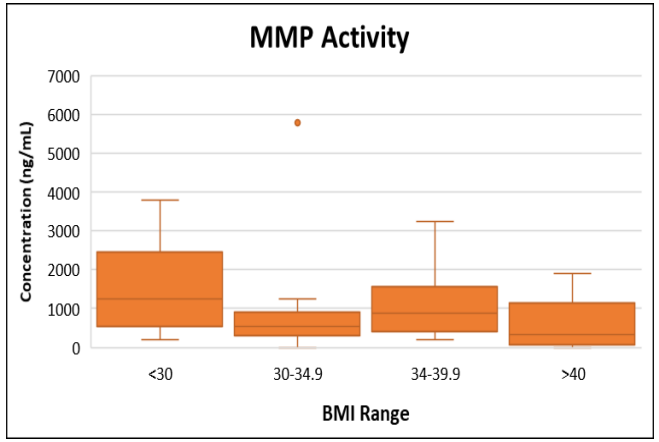

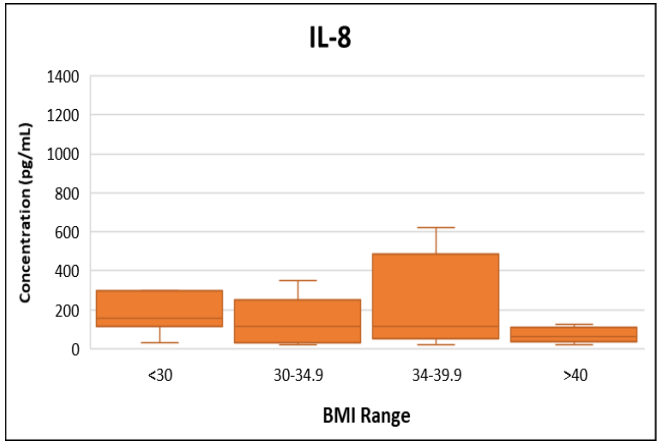

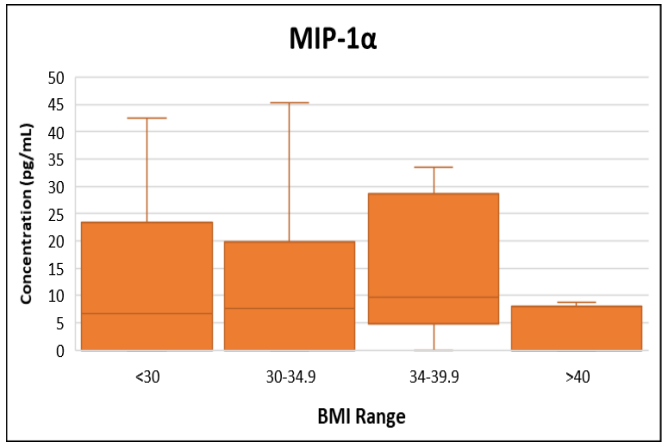

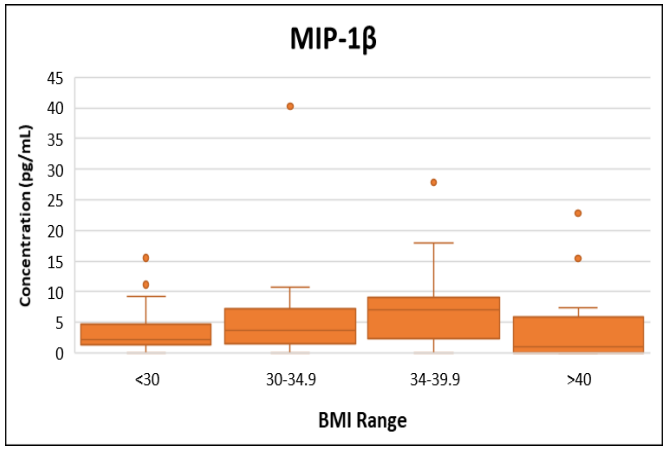

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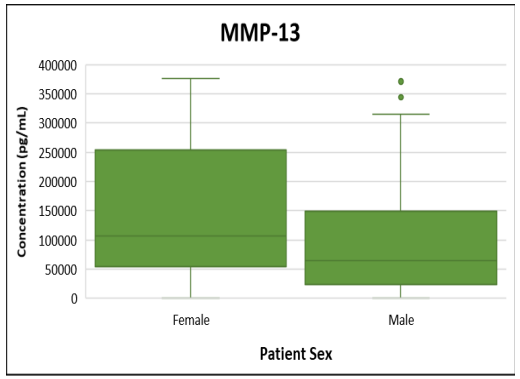

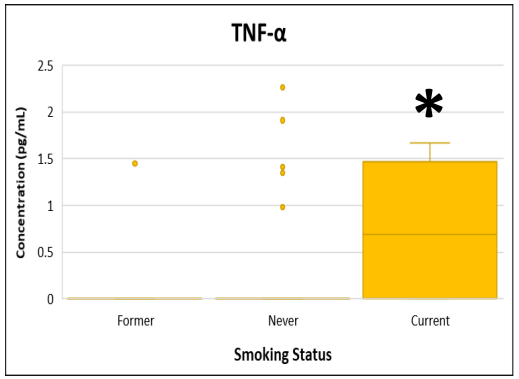

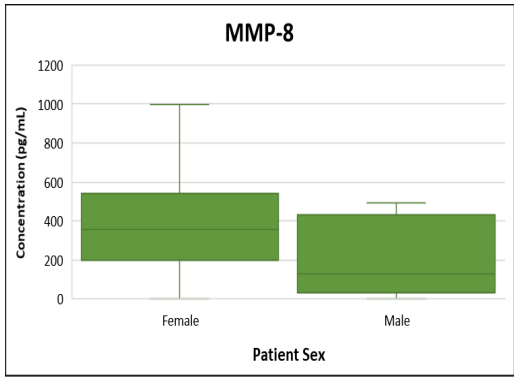

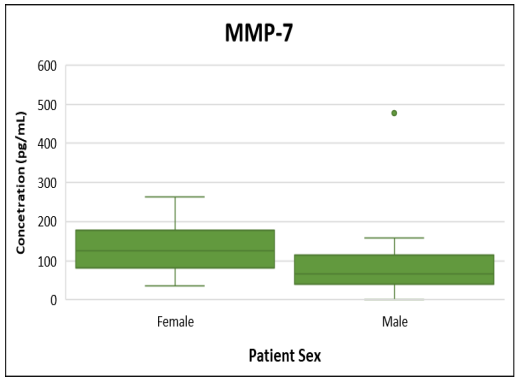

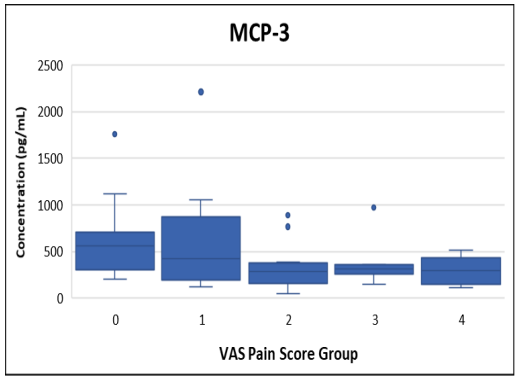

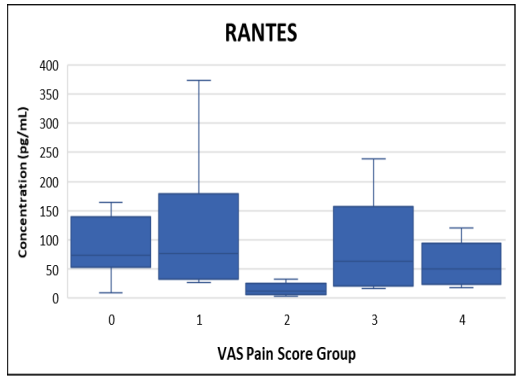

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