

August 2022

Did you know?

The ORS Preclinical Models Research Section has an online community group which you can access upon logging into the ORS Member Center. <u>Learn more</u> and connect with the section community!



Busy First Half of 2022!

It has been a busy first half of 2022 for the ORS Preclinical Models Research Section! This e-newsletter includes highlights from the Section 2022 Scientific Meeting, ORS 2022 Annual Meeting, virtual sessions and more to look forward to over the next several months.

2022 ORS Preclinical Models Research Section Officers

<u>Section Chair</u> Uma Sankar, PhD, Indiana University School of Medicine

<u>Section Chair Elect</u> Aimee Colbath, DVM, MS, DACVS, Michigan State University <u>Section Past Chair</u> D. Joshua Cohen, MD, Virginia Commonwealth University

<u>Section Secretary</u> Sara Hassouna Elsayed, PhD, University of Cambridge

<u>Section Treasurer</u> Drew Koch, DVM, MS, North Carolina State University

<u>Section Research & Education Chairs</u> Annette McCoy, DVM, MS, PhD, DACVS, University of Illinois

<u>Section Membership Chair</u> Kirk McGilvray, PhD, Colorado State University

<u>Section Communications Chair</u> Catherine Ambrose, PhD, UTHSC-Houston



Abstract Submission Deadline: August 29, 2022

Whether 2023 will be your first meeting, or you're looking forward to coming back again – the annual meeting has something for every career stage and research interest.

ORS provides awards and grants for all career stages based on high-quality abstracts including **ORS Preclinical Models Research Section 3Rs, Podium, and Poster Awards for Section members**.

- Section Podium and Poster Awards follow the <u>ARRIVE Guidelines</u>.
- 3Rs Award follows the 3R's (replacement, reduction, refinement).

Submit Your Abstracts



Looking Back: ORS 2022 Annual Meeting Highlights

Bench to Bedside: How Appropriate Preclinical Models Are Imperative to Translation Workshop

and Networking Event

We kicked off the ORS 2022 Annual Meeting in Tampa by hosting our Bench to Bedside <u>workshop</u> and networking event. During the <u>workshop</u>, three teams presented the role preclinical models played in developing new treatments for orthopaedic conditions:

Braden Fleming, PhD, Rhode Island Hospital/Warren Alpert Medical School, and Martha Murray, MD, Children's Hospital Boston, discussed the progression of their work on the bridge-enhanced ACL restoration (BEAR) technique for treating ACL injuries highlighting the journey from concept to commercialization for this implant, including the preclinical trials, clinical trials, and FDA marketing approval process.

Todd McKinley, MD, IU Health Methodist and **Uma Sankar, PhD**, Indiana University School of Medicine discussed the lessons learned during the development of adjuvant therapy to mitigate or prevent posttraumatic osteoarthritis, including the progression from initial molecular level and tissue-level experiments through preclinical small and large animal modeling that has led to obtaining an IND to begin in-human testing.

Jeremiah Easley, DVM, Preclinical Surgical Research Laboratory, Colorado State University; Brian Margulies, MS, PhD, Zetagen Therapeutics, Inc.; and Kirk McGilvray, PhD, Colorado State University discussed their work in bone regeneration technologies including the regulatory pre-submission process, designing and carrying-out numerous translational preclinical studies utilizing the three R's, and putting the pieces of the puzzle together to present an accurate, concise, and thorough data package to a regulatory agency for review.

Section 2022 Scientific Meeting

We also hosted our annual <u>scientific</u> meeting that included poster pitch sessions and video introductions to some of our researchers from around the globe:

Preclinical Models Around the World Video Presentations

- Dr. Francis Wong
- Dr. Nam Hui Yin
- Dr. Raquel Baccarin
- Dr. Bruno Carvalho Menarim

Pain: An Outcome or A Confounder?

Introduction Annette McCoy, DVM, MS, PhD, DACVSv, University of Illinois

Pain in Mouse Models Rachel Miller, PhD, Rush University Medical Center

Pain in Small Animals

Duncan Lascelles, BSc, BVSc, PhD, FRCVS, DSAS(ST), DECVS, DACVS, NC State University, College of Veterinary Medicine

Pain in Large Animals Nicole Trenholme, DVM, MS, DACVECC, DACVAA, University of Illinois at Urbana-Champaign, College of Veterinary Medicine

These talks led to the topics for our first 3 Virtual Scientific Sessions of 2022.





Virtual Scientific Session: Highlights and Upcoming

The Section hosted 3 virtual scientific sessions in 2021 and have already hosted 3 for 2022.

Upcoming virtual sessions are planned for September 7, October 5, and November 2 at 12:00 PM Central Time. The September session will be in collaboration with the ORS Tendon Research Section.

View the Session Recordings



Pictured: Jason Horton, PhD

Dr. Horton is an assistant professor of Orthopaedic Surgery, with Joint appointments in the Departments of Cell & Developmental Biology and Radiation Oncology at Upstate Medical University, in Syracuse, NY.

ORS Research Section Member Spotlight

This issue features **Jason Horton**, **PhD**, Upstate Medical University.

What is your background and have been your mentors?

After my undergraduate studies in Biology and Anthropology at Oswego State University, I worked as a technician in clinical-diagnostic and research labs for a few years, which lead me to enroll in the College of Graduate Studies at Upstate, first as a master's student then transitioning to the doctoral program in Physiology. My dissertation research focused on the response of the skeletal growth plate to ionizing radiation. Tim Damron, MD, was my PhD advisor, and **Matthew Allen, VetMB, PhD**, and Joe Spadaro, PhD, each having major mentoring roles while I was a grad student. After grad school, I was a post-doc at the NIH in Bethesda Maryland.

My first fellowship was in the Radiation Oncology Branch of the National Cancer Institute, where I studied radiationinduced fibrosis of the skin and lungs under the direction of Deborah Citrin, M.D. my second post-doc with Pam Robey, Ph.D. and Kenn Holmbeck, Ph.D. at the National Institute of Dental and Craniofacial Research, which investigated the role that MMP-14 plays in regulating multipotent marrow stromal lineage plasticity and lineage commitment toward osteogenic or adipogenic fates. Ken Mann, PhD, and **Megan Oest, PhD'**s guidance has been instrumental to establishing my lab and navigating the transition from post-doc to independent scientist.

What's been the highlight of your research in the past year?

Earning the Preclinical Models Research Section Podium Award was certainly near the top of the list, but the most fulfilling moments of the past year have been seeing the first two students to join my lab - Mei Yun Lin, Ph.D. and Lisbeth Reyes-Fondeur MD - earn their doctorates. Therefore, I went into academia.

What are you currently working on?

When I returned to Upstate as faculty, I initially focused on the pathophysiology of radiation-induced bone disease, particularly the mechanisms which cause rapid and massive expansion of marrow adipose tissue after radiotherapy, and whether this change affects long-term osteogenic capacity of multipotent marrow stromal cells. A bit later we also started working on nanoparticle drug-delivery and radio sensitization strategies for pediatric musculoskeletal sarcomas. These projects are ongoing, but more recently we have broadened into delving into tissue engineering and 3D bioprinting technology in collaboration with Pranav Soman, Ph.D. at Syracuse University. The long-term goal of this line of research is to develop the technology to fabricate vascularized bone grafts that are readily perfusable upon *implantation, can be printed to match patient anatomic* deficits using medical imaging data, and are populated with autologous cells (e.g., iPS derived angiogenic and osteogenic cells).

As a young investigator, what have you found to be the greatest challenge when designing or working with preclinical models?

I'm not sure this is unique to young investigators, or if even still qualify as a young investigator - but a big challenge is adopting or replicating models published by other groups. It can feel like taking the corners off the wheel sometimes. That is not to say that others are purposely misleading or negligent, but sometimes small but important detail and nuance are lost to the word/page limits of many journals. Sometimes this information appears in the supplement or as a 'video protocol', other times it necessitates an e-mail, call, or visit to a colleague to clarify. Hopefully they are helpful. It is encouraging that a growing number of journals, including JOR, are requiring authors to include the ARRIVE checklist in studies using animal subjects among other efforts to improve rigor and reproducibility. I think it is also important to report 'negative' findings too; tell the community what didn't work, so that we don't go wasting time, effort and resources duplicating experiments.

As someone who has recently presented their preclinical study at a conference, what did you find to be the greatest challenge to communicating key elements of your model?

I think the biggest challenge for a podium presentation of 7-10 minutes is striking a balance between conveying the key findings and their translational impact, while also demonstrating the rigor of the study itself – discussing statistical power, alternative approaches etc.

When you're not in the lab, what do you like to do for fun?

The biggest source joy in my life is my family. I've just started coaching my 6yo daughter's lacrosse team, have lots of fun playing music and building towers with my 4yo son, and remodelling and maintaining an old house with my amazingly creative (and patient) wife, Liz.

What was the last book you read for fun, and would you recommend?

I've never been much of a pleasure reader, but recently it has been great fun re-discovering Shel Silverstein with my kids. We are currently working through Where the sidewalk ends' as our nightly routine. Highly recommended for a dose of silliness right before bedtime.

What is the most unusual/unexpected item sitting on your desk right now?

My desk in the lab is pretty much a fire hazard, but as I'm writing this from my home office, to my left I have the guts of an old Fender Telecaster Deluxe that I'm refurbishing. The pickups and pots still need to be polished and re-soldered, once the 'denim-blue' lacquer finish complete. Hopefully, it'll sounds as good as it looks!



Pictured: Kelsey Collins, PhD

Dr. Collins works in Dr. Guilak's lab is in the Department of Orthopaedic Surgery at Washington University School of

ORS Research Section Member Spotlight

This issue features **Kelsey Collins**, **PhD**, Washington University in St. Louis.

What is your current role(s) in orthopaedic research?

I am a research instructor in the lab of Dr. Farsh Guilak.

Where are you working currently?

Medicine and the Shriners Children's St. Louis Hospital. Dr. Guilak's lab is in the Department of Orthopaedic Surgery at Washington University School of Medicine and the Shriners Children's St. Louis Hospital.

What is your background?

I completed my BS in Exercise Biology from UC Davis in 201, and PhD in Biomedical Engineering in 2017 in Dr. Walter *Herzog's lab at the University of Calgary on diet-induced* obesity in a rat model of osteoarthritis. As a Postdoctoral Research Scholar in the Guilak Laboratory at Washington University in St. Louis, I have worked to create a niche in adipose-cartilage signaling, stem-cell biology, synthetic biology, and drug delivery to evaluate systemic contributors and novel therapeutic strategies in osteoarthritis and rheumatoid arthritis. I have had the privilege to build a skillset in pain and behavioral testing by helping with protocol development within the context of the P30 Pain and Behavior Core within our Musculoskeletal Research Center at WashU, which has been a fantastic opportunity for me to listen to advice from our clinician collaborators about how to best consider patient-relevant outcomes and pain and behavioral assays in the context of preclinical models of osteoarthritis and rheumatoid arthritis.

Who have been your mentors?

Farsh Guilak PhD; Christine Pham MD; Walter Herzog PhD; David Hart PhD; Cy Frank MD; Deborah Marshall PhD; Raylene Reimer PhD; Jen Neugebauer PhD; and many others in our ORS community who actively help me navigate my path within Orthopaedic Research.

What's been the highlight of your research in the past year?

As we have returned to in-person work, it has been a privilege to be able to spend more time with my lab mates and our community within orthopaedic surgery and our collaborators in other Divisions and Departments at WashU. I also have enjoyed recent on campus visits at other institutions where I can learn about their departmental culture and exchange ideas in person. It is energizing to get diverse feedback on the models and ideas we are developing, especially after a long absence of in person meetings and visits.

What are you currently working on?

We are currently working on a variety of projects around the mechanisms of fat-cartilage crosstalk. One of our most fun projects is a collaboration with Ron June's Lab at Montana State, with lots of help from PhD Students, Ayten Ebru Erdogan, and Hope Welhaven, where we are defining the secretome of fat constructs explanted from our fat free lipodystrophic mice to define metabolites and proteins that might be involved in the conversation between fat and cartilage in post-traumatic OA. In another arm of work, we are developing tissue engineering protocols for designer fat derived from mouse induced pluripotent stem cells, with the help of a very talented PhD Student Erica Ely, which allow us to perform precise mechanistic studies of how fat might be talking to cartilage. Using this approach, we will be able to determine new targets in a way that will reduce the numbers of animals needed to perform these studies without the use of complex transgenic mice.

As a young investigator, what have you found to be the greatest challenge when designing or working with preclinical models?

Many of the problems we are interested in studying in the realm of obesity and musculoskeletal health are complicated, with many factors involved that must be intentionally disentangled to understand the relative contribution of each factor. Because of this, there is a need for a team of interdisciplinary individuals to support the work. I enjoy the challenge of brainstorming ways to separate and precisely evaluate these factors with our existing in vitro and mouse models, within models we are currently developing, and new techniques or collaborations we may need to integrate to address these issues in the best way we can. Our goal is to always follow the science and listen to the story the data are telling us. As all preclinical models have inherent limitations, balancing the pros and cons of each model or approach can also be a challenge in this context. However, as many tools and techniques are evolving rapidly for more precise evaluation of tissues, cells, and spatial context, it's exciting to think about how much we can learn from each other and from our models as we integrate these approaches.

As someone who has recently presented their preclinical study at a conference, what did you find to be the greatest challenge to communicating key elements of your model?

My goal with all presentations is to tell a compelling story that can be understood by individuals from diverse backgrounds and knowledge, as the field of fat-cartilage crosstalk is a niche area within the broader context of orthopaedic research. Dr. Guilak is a master storyteller, and it has been a privilege to learn from him about how to present and explain the complex phenomena we study so that readers and people listening to presentations can connect with the ideas we are sharing. The other challenge for me is to not speak too fast, which I tend to do when I get excited about the data.

When you're not in the lab, what do you like to do for fun?

I enjoy traveling and spending time with friends and family across North America and enjoy gastronomic and oenophilic pursuits with my friends and neighbors around the many restaurants in St. Louis. I love to spend time outside, but lately most of my activity has been on a Peloton bike. If you ask my husband, my new hobby is fly fishing, which he has promised to teach me upon his upcoming immigration to the US from Canada.

What was the last book you read for fun, and would you recommend?

At our recent Musculoskeletal Biology and Regeneration Meeting, Dr. Ben Levi from UTSW gave up half of his talk time to recommend a book called Positive Intelligence by Shirzad Chamine, which he has used in his department to promote mindfulness and improve productivity. It was compelling to learn about the impact the book had made within his ecosystem, and it motivated me to start working through the text with some friends outside of the lab. I have really enjoyed learning about mindfulness through this book and would highly recommend it as a toolkit for both personal and professional growth. It's exciting to see the culture within our academic community shift to support resilience, mental health, and mindfulness.



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<u>Analgesic effects and arthritic changes following tramadol</u> <u>administration in a rat hip osteoarthritis model</u>

Keijiro Kanno, Miyako Suzuki-Narita, Yuya Kawarai, Shigeo Hagiwara, Satoshi Yoh, Junichi Nakamura, Sumihisa Orita, Kazuhide Inage, Takane Suzuki, Seiji Ohtori

Pages: 1770-1777

<u>Sex-specific biomechanics and morphology of the anterior</u> <u>cruciate ligament during skeletal growth in a porcine model</u>

Danielle Howe, **Stephanie G. Cone**, Jorge A. Piedrahita, Bruce Collins, Lynn A. Fordham, Emily H. Griffith, Jeffrey T. Spang, **Matthew B. Fisher** Pages: 1853-1864

<u>The effect of mechanical stress on enthesis homeostasis in a</u> <u>rat Achilles enthesis organ culture model</u>

Taichi Saito, Ryo Nakamichi, Aki Yoshida, Takaaki Hiranaka, Yuki Okazaki, Satoshi Nezu, Minami Matsuhashi, Yasunori Shimamura, Takayuki Furumatsu, Keiichiro Nishida, Toshifumi Ozaki

Pages: 1872-1882



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