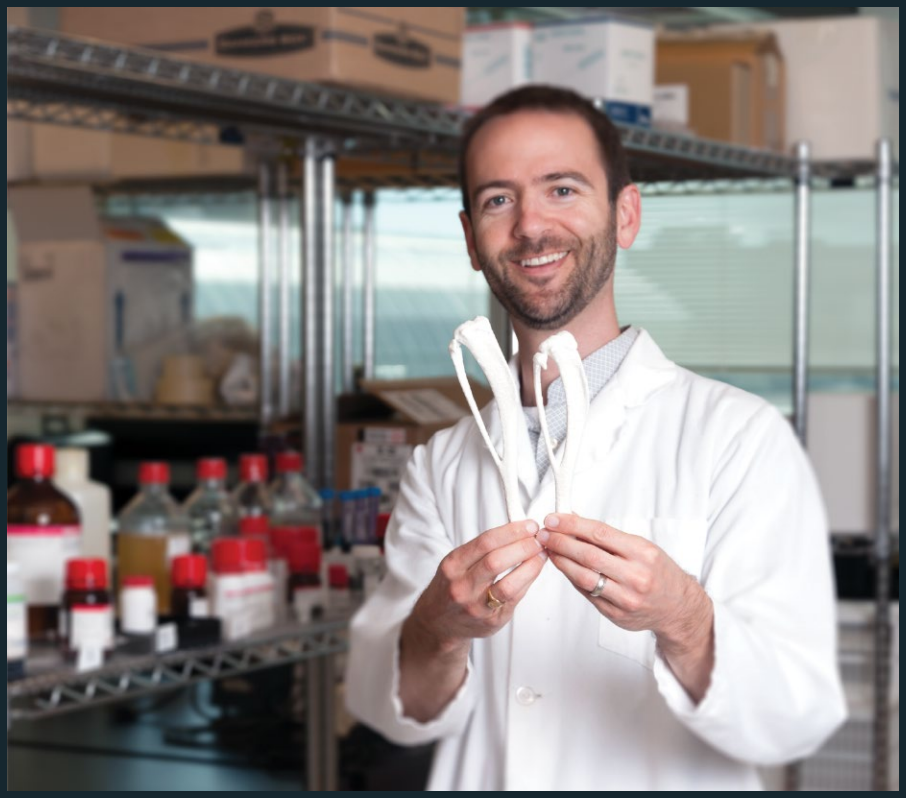
McCAIG INSTITUTE
FOR BONE AND JOINT HEALTH

WINTER 2016

RESEARCH IN MOTION

The long and the short of bone development

Understanding stature and bone growth



Campbell Rolian holding enlarged 3-D bone models of a regular mouse shinbone compared to a Longshanks shinbone

Photo by Don Molyneaux

How did you get so tall?

People of tall stature have been asked this throughout their lives. Oftentimes the answer is obvious – "oh, my parents are really tall." But how come one person's bones grow longer and faster than another's?

"Sure, our genes are largely responsible for our stature," says evolutionary biologist Campbell Rolian, a researcher in the McCaig Institute who studies skeletal variation in size and shape between individuals. "But we still don't have a complete grasp of how genetic variation is translated into height variation – you versus me – at a cellular and developmental level," he says.

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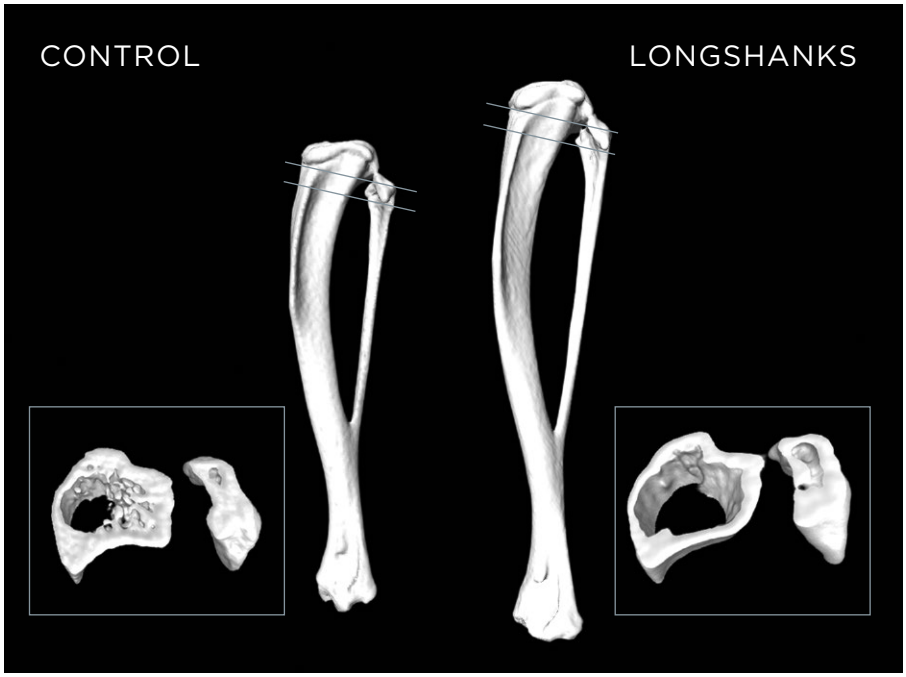

Shinbone of control mouse compared to Longshanks mouse. The insets are cross sections, showing less spongy bone in Longshanks, presumably as a consequence of faster growth and longer length.

"If we can understand the whole process – from cell division, to cartilage growth to bone growth, then we may be able to develop ways to modulate rates of long bone growth and improve bone health."

HOW BONES GROW

Leg bones grow from the middle out. Specialized cells in bone, called chondrocytes, divide and produce cartilage at either end – an area called the growth plate. The cartilage produced by chondrocytes serves as a "scaffold" for mineralization by bone cells (osteoblasts). During adolescence, cells in the growth plates start to die, the growth plates get smaller and smaller until they fuse, and adult stature is attained. "There's a lot that can go wrong at this point in bone development," says Rolian. "Sometimes cells continue to grow and we get limb length discrepancies or osteosarcoma (bone cancer). Sometimes the cells don't divide enough, or don't produce enough cartilage, and we get weaker bones or skeletal disorders such as dwarfism."

AN EPIC EXPERIMENT

To understand what makes one individual's limb bone grow longer than another, one can compare two extremes within the same population, while controlling variables like environment, nutrition and body mass. These factors are very hard to control in human populations, so Rolian and fellow McCaig Institute member Benedikt Hallgrimsson decided to embark on an artificial selection experiment in mice that would last five years.

They took a common white mouse stock and bred them. They then measured the length of the shinbone of the offspring with x-ray and selectively bred individuals with the longest bones. Five years and 22 generations later, Rolian has created a mouse in which shinbone length is 15 – 20 percent longer in relation to body mass, called Longshanks mice. These mice are "taller" than average and their bones grow faster. Interestingly, their bones are also weaker, having less spongy bone and breaking more easily compared with random-bred mice from the same stock. Using this mouse model, Rolian and his team can study the differences in the cells and tissues that encourage the bones to grow so much faster, and perhaps understand how the increased growth might be linked to lower bone quality. "If we can understand the whole process – from cell division, to cartilage growth to bone growth, then we may be able to develop ways to modulate rates of long bone growth and improve bone health," says Rolian.

Campbell Rolian is an associate professor in the Department of Comparative Biology and Experimental Medicine in the University of Calgary's Faculty of Veterinary Medicine, and a member of the McCaig Institute for Bone and Joint Health.

McCAIG INSTITUTE
FOR BONE AND JOINT HEALTH

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MESSAGE FROM THE DIRECTOR STEVEN BOYD

In November, we unveiled the McCaig Institute's new strategic plan, which will chart our direction for the next five years.

This strategic plan builds on the momentum of decades of research excellence, our strong integration of clinicians and research scientists, and reaffirms our commitment to better bone and joint health for Albertans. As we move forward, we will capitalize on one of our recent major strategic investments, our new Centre for Mobility and Joint Health, nicknamed the MoJo. The MoJo, which officially opened in the fall of 2016, will allow us to fulfil a new research direction for the institute — precision medicine.

Together with our partners in the Cumming School of Medicine, University of Calgary, the Alberta Bone and Joint Health Institute and the Bone and Joint Health Strategic Clinical Network, we have a highly multidisciplinary and collaborative culture to transform bone and joint health care through innovation. Working as a team, we will further the understanding of MSK conditions through basic research and discovery. We will identify and address the most important clinical challenges in MSK health to improve the delivery and effectiveness of health care in our province.

Looking ahead, I am excited about the future of our institute and the contributions we will make to ensure Albertans enjoy "Mobility for Life."

On behalf of the staff, trainees and faculty of the McCaig Institute for Bone and Joint Health, I wish you all a safe and happy holiday season.

McCaig Institute plots course for the next five years

McCaig Institute staff, trainees and faculty gathered in November to launch the institute's new five year strategic plan. The plan introduces our revitalized vision of "leading the improvement of musculoskeletal health for patients across their lifespan through research and education." This will shape our three strategic goals in the areas of research, education and community, and bring us closer to achieving *Mobility for Life* for all Albertans.

STRATEGIC GOAL 1

RESEARCH

Become a globally recognized centre of research excellence in precision medicine for musculoskeletal health.

The concept of precision medicine begins and ends with the patient, with clinical problems driving research. Our strength is our capacity to address research questions across the full spectrum of health research, from basic discovery through to clinical implementation.

STRATEGIC GOAL 2

EDUCATION

Provide a high-quality interdisciplinary training program in musculoskeletal health.

Training the next generation of researchers, clinicians and industry leaders in musculoskeletal health is critical for conducting innovative research. Our training program will attract the best and brightest trainees from around the world.

STRATEGIC GOAL 3

COMMUNITY

Translate research knowledge into patient care, products policies and services to improve the musculoskeletal health of Albertans.

The McCaig Institute's patient-focused research and key partnerships allow us to translate new knowledge back to the community. We will broaden our impact by building a community of provincial partners that will facilitate discovery, knowledge translation and implementation.

ALBERTA BONE & JOINT INSTITUTE HEALTH

BY CHRISTOPHER SMITH, CHIEF OPERATING OFFICER, ABJHI

With funding from the Mitacs Accelerate program and proceeds from Music in Motion fundraising events, ABJHI is pleased to announce three new internships that will look at ways to improve care for high-risk arthritis patients. This is a great example of how the philanthropy of Albertans can be leveraged to impact health outcomes.

Three projects will be conducted over a two-year period. One project, led by Dr. Elena Lopatina, will evaluate Alberta's first multidisciplinary nurse-led clinic for managing established rheumatoid arthritis (RA) patients. The clinic is a clever response to Alberta's shortage of rheumatologists and a climbing RA rate. This new approach could reduce the time rheumatologists spend managing established RA patients, freeing up time to focus on new RA cases and urgent care for people experiencing flare-ups, while improving the quality of care delivered in a traditional clinic setting.

The other two projects will shed new light on the effects of obesity on the progression of osteoarthritis (OA) in the hips and knees. They will also study additional health risks obese patients face following joint replacement and how to mitigate these risks. Despite the high prevalence of obesity among hip and knee replacement patients, there are wide gaps in our knowledge about the additional risks these patients face. Dr. Behnam Sharif will lead the work on the effects of obesity on surgery outcomes and will perform a cost-effectiveness analysis of different risk reduction approaches. Kristine Godziuk will examine the impact of different obesity types on patient outcomes.

The interns will work under the supervision of McCaig Institute member Dr. Deborah Marshall, ABJHI's Director of Health Technology Assessment and Research, and Professor, Department of Community Health Sciences, U of C, and Dr. Mary Forhan, Assistant Professor, Rehabilitation Medicine, U of A.

These projects represent the continued expansion of ABJHI's active role in research that has the potential to significantly alter traditional approaches to treatment.

WOOD FORUM 2016

ARTHRITIS & YOU

In collaboration with the University of Alberta's Faculty of Rehabilitation Medicine, the McCaig Institute hosted the 2016 Wood Forums on Arthritis and You. Hundreds attended the events in Edmonton and Calgary to learn about the latest research advances in precision medicine.

WHAT IS PRECISION MEDICINE?

Precision medicine is about making the right diagnosis and providing the right treatment, at the right time for the right patient. "There are over 100 different forms of arthritis," said Marvin Fritzler, a member of the McCaig Institute and the opening speaker at both the Edmonton and Calgary Forums. "It does not make sense that there would be a 'one size fits all' approach to arthritis care." Fritzler's talk focused on using biomarkers which provide an immune fingerprint of inflammatory diseases, helping and expediting physicians decide which treatment works best.

STEM CELL THERAPY – WHAT IS LEGITIMATE AND WHAT TO AVOID

As explained by McCaig Institute researcher and Calgary Wood Forum presenter Roman Krawetz, stem cell therapy is when stem cells are isolated from a patient or another donor, expanded in a laboratory, subjected to quality control under strict regulations and injected back into the patient. The hope is these stem cells will grow and form new cartilage. But Wood Forum presenter and University of Alberta Law professor Ubaka Ogbogu was quick to caution people about this new trend. "There is no evidence that current stem cell therapies work, and at their very worst they could be dangerous," he said. "There are clinics out there preying on people who are desperate." But, he added, there are scientists like Krawetz and his colleagues, who are working on developing safe and effective stem cell therapies for the future.

JUST KEEP MOVING

Calgary physician Preston Wiley and University of Alberta researchers Jackie Whittaker and Geoff Bostick discussed what people can do right now to live a good life with arthritis. "Osteoarthritis is the most common reason we become inactive as we age," said Whittaker. "And that inactivity leads to an increased risk of other diseases. We need to keep moving." Both Wiley and Whittaker stressed the importance exercise therapy, not only to keep fit and healthy, but also to slow down the progression of arthritis. "Cartilage doesn't have a blood supply," explained Whittaker. "The food it needs is contained in synovial fluid. When fluid swishes around, through movement and exercise, it brings in new nutrients."

THE FUTURE LOOKS BRIGHT

In Calgary, McCaig Institute Director Steven Boyd gave a presentation on the future of precision medicine in the University of Calgary's new Centre for Mobility and Joint Health. "We now have a great facility in Alberta with state of the art imaging, motion assessment and diagnostic equipment to assess individual bone and joint health on every level," said Boyd. "We are committed to finding new ways to prevent, diagnose and treat bone and joint diseases and injuries for all Albertans."

Stay tuned for more information on next year's Wood Forum, scheduled for October, 2017. The topic will be elbow and shoulder injuries.

Presented By The Arthritis Society & Beth Shalom Synagogue
Honouring tradition. Celebrating advancement.

THE JOINT AFFAIR:
An Innovative Partnership

The Arthritis Society is excited to announce the launch of The Joint Affair, a one of a kind event that will celebrate tradition and advancement within the rheumatology community.

The Joint Affair, being held on March 26th, 2017 in Edmonton, will recognize and honour Dr. Anthony S. Russell, who has been a leader in his field for almost 50 years.

Born and raised in the UK, Dr. Russell's undergraduate years were spent at Cambridge, followed by medicine at Guy's Hospital in London, the Postgraduate Medical School of London, the Canadian Red Cross Memorial Hospital, and two years research in Dallas.

Since 1971, he has been based in Edmonton, first as Assistant Professor of Medicine, then as full professor and head of the rheumatic disease unit at the University of Alberta. With over 450 peer-reviewed papers on various topics, he is a sought-after lecturer around the world.

In partnership with Dr. Russell's congregation at the Beth Shalom Synagogue, this event is about coming together to honour the rich history of his career, while profiling the advancements of arthritis research and celebrating the power of community.

A portion of the funds raised from this event will be used to establish the Dr. Anthony S. Russell Rheumatology Scholarship Fund, which is intended to encourage scholarship, advanced training, and research opportunities for members or trainees within the Division of Rheumatology at the University of Alberta.

Further details and ticketing information about The Joint Affair are available at:

thejointaffair.ca

SAVE THE DATE

SCIENCE IN THE CINEMA – HIP HOP-ERATION

THURSDAY, MARCH 16, 2017

Globe Cinema
617 – 8th Avenue SW, Calgary

The remarkable story of the world's oldest hip-hop troupe and their incredible journey from New Zealand to Las Vegas.

Join researchers from the McCaig Institute for a discussion about arthritis research at the University of Calgary and the importance of leading an active lifestyle to ensure optimal bone health.

cumming.ucalgary.ca/science-in-the-cinema

THE JOINT AFFAIR

MARCH 26, 2017

Fantasyland Hotel, Edmonton

Presented by the Arthritis Society and Beth Shalom Synagogue

A one of a kind event that will celebrate tradition and advancement within the rheumatology community.

thejointaffair.ca

TENET I2C COMPETITION

APRIL 11, 2017

Health Sciences Centre, University of Calgary

Presented by the University of Calgary, Cumming School of Medicine

TENET I2C is a "Dragon's Den" style competition that will award up to $100K to a team to transition medical research into product development.

WOOD FORUM ON ELBOW AND SHOULDER INJURIES

OCTOBER, 2017

Stay tuned for more information!

When Christina Jablonski was diagnosed with Pauci Articular Juvenile Rheumatoid Arthritis (JRA) at the age of three,

her parents' first reaction was to limit her activity. Her doctor said exercise would help so they hesitantly signed her up for hockey. In remission since she was 12, Christina credits her good health to her participation in sports and strength training.

> **"I've realized you can touch so many more people with research."**

Christina's JRA has shaped who she is and what she does. She is currently a PhD student in the McCaig Institute, studying the role of stem cells and inflammation in cartilage regeneration in the knee. "When I was younger I wanted to be a doctor, but I've realized you can touch so many more people with research," says Christina.

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Mobility for Life.

Photo by Don Molyneaux