OTTAWA MUSCULOSKELETAL RESEARCH PROGRAM

Introduction

Our vision is to be a model for excellence in care and education of musculoskeletal health, and in clinical outcomes and basic science research for individuals ranging from childhood to adulthood. This goal includes the development of strategies for the prevention, maintenance, and restoration of bone, joint, and muscle pathology. At the core of our research program, is a multi-disciplinary approach bringing together engineers, basic scientists, rehabilitation specialists and clinicians, and a collaboration between three faculties within the University of Ottawa and Carleton University: Medicine, Health Sciences, and Engineering, as well as the Ottawa Hospital Research Institute (OHRI), Bruyere Research Institute, Children's Hospital of Eastern Ontario (CHEO), and Institut du Savoir Montfort (Figure 1).We seek to continue to expand our current research programs with national and international scope.

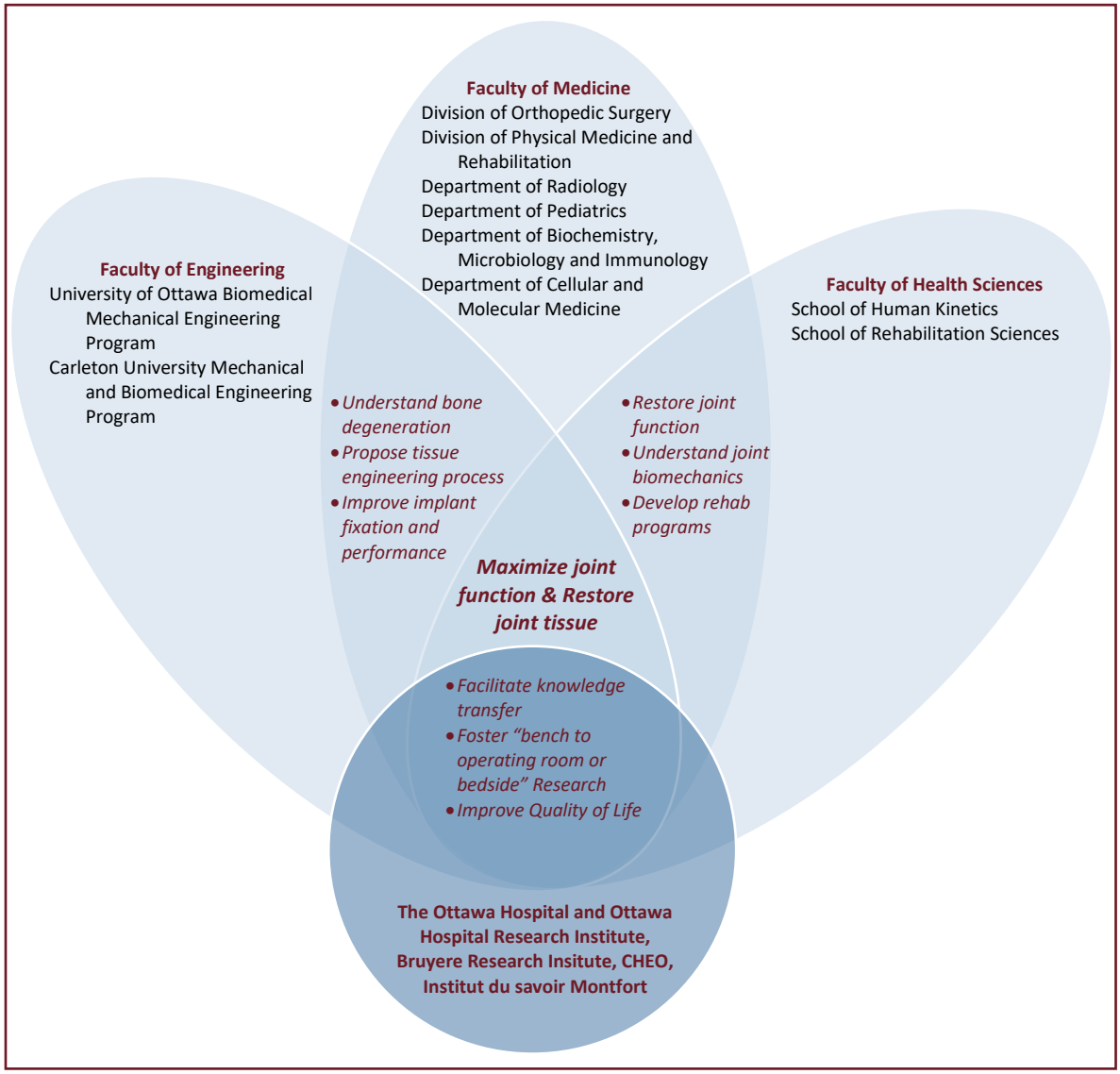

Figure 1. Research synergy amongst the three uOttawa faculties and Research Institutes

The Division of Orthopaedic Surgery's research structure can be classified under four pillars: 1) Translational, 2) Continuous Quality Improvement, 3) Education, and 4) Surgical Clinical Outcomes. Our Clinical Research portfolio encompasses our clinical trials and quality improvement initiatives which span nine Clinical Practice Units (CPUs). To enable this we have established six research laboratories: CHEO Bone Health & Pediatric Ortho, Periprosthetic Joint Infection Lab, Ortho Biomechanics Lab, Biomaterials & Tissue Engineering, Gait/Motion Lab, and Regenerative Orthopaedic Surgery (Figure 2).

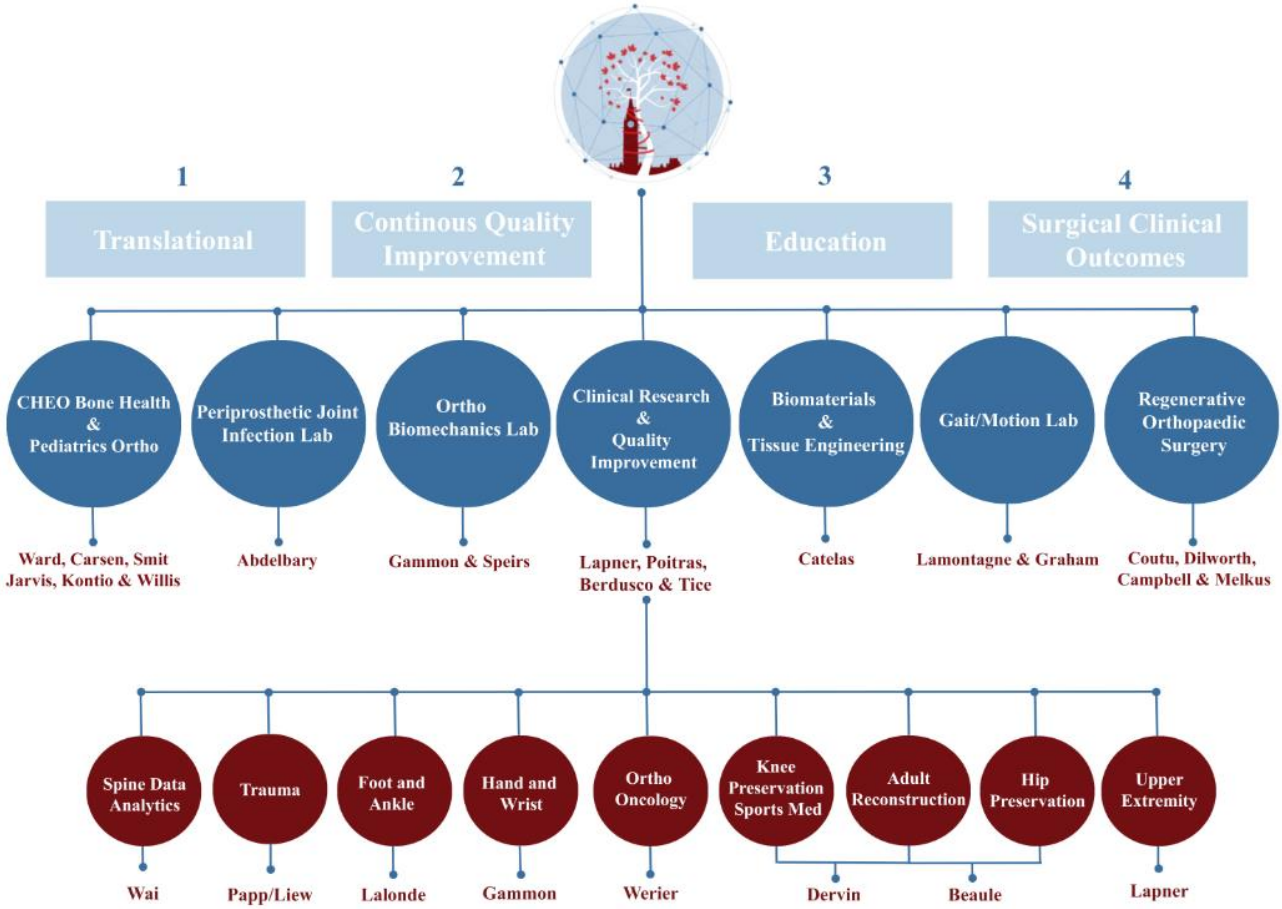

Figure 2. Structure of the University of Ottawa Musculoskeletal Research Program

Continuous Quality Improvement

As the demand for accountability and transparency surrounding the supply of increasingly expensive medical services grows, healthcare providers have put continuous quality improvement (CQI) programs in place to optimize care and improve efficiencies and its development was a key component of our 5-year Strategic Plan(2015-2020). CQI programs that rigorously evaluate healthcare services can lead to informed decisions about the direction of planned improvements through evolving knowledge translation. Successful outcomes may include better patient satisfaction, improved patient-reported outcomes, highly-efficient care pathways, and overall cost-savings. There are numerous steps involved in implementing CQI programs that require collaboration and cooperation from physicians, allied health care workers, support staff, and hospital management in order to achieve desirable goals. The Division of Orthopaedic Surgery has initiated a CQI program at both The Ottawa Hospital (TOH) and CHEO, which is designed as a classic Donabedian Construct with a triple aim framework of: 1. improving care, 2. improving patient experience, and 3. lowering cost. This is in keeping with the goal of TOH becoming a top 10% performer in quality and safety of patient care in North America. In addition, this is well-aligned with the new bundle payment initiatives initiated by the Government of Ontario which requires the prospective collection of patient reported outcome measures (i.e PROMs). To accomplish this, the Division of Orthopaedic Surgery has partnered with Consensus Medical Systems in developing a web-based platform called ConEHR which facilitates PROMs collection as well as outcome analysis of various surgical procedures.

As part of our CQI program, adverse event (AE) data collection has been streamlined through an online AE reporting form. We have introduced the validated OrthoSAVES tool. The AEs reported by Physicians, Residents, and Fellows are analyzed for themes and discussed with members of the Division of Orthopaedic Surgery as part of Morbidity and Mortality rounds (Figure 3).

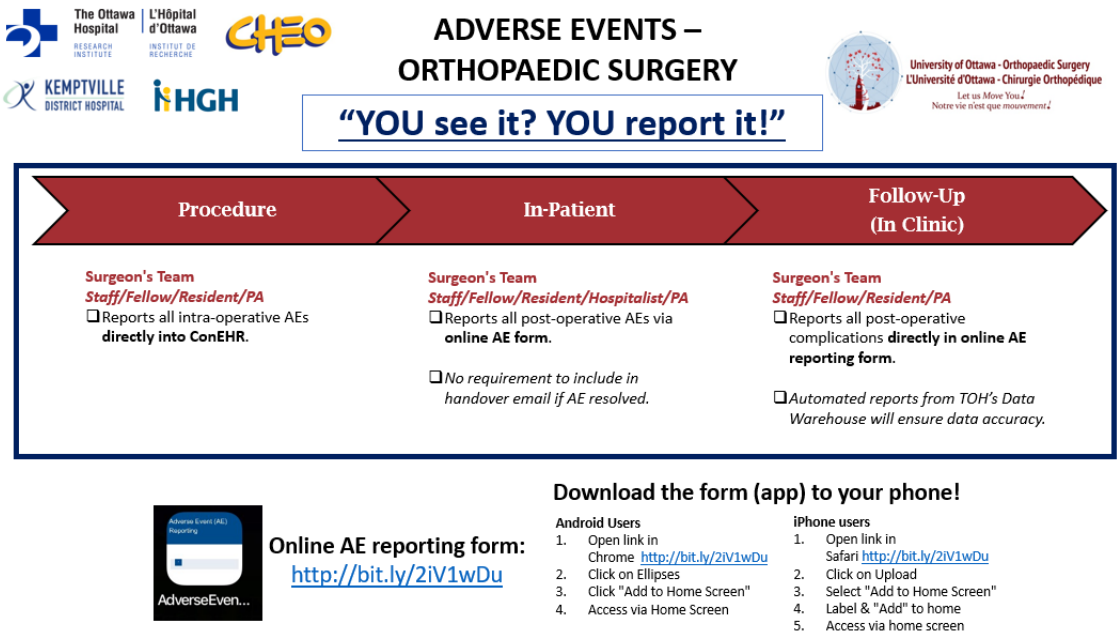

Figure 3. Adverse events reporting workflow

Research Laboratories

Pediatric Bone Health and Pediatrics Orthopedics

Vision

- The Pediatric Bone Health and Orthopedic Research units lead local, national and international initiatives in pediatric bone research, in order to effectively diagnose, monitor and treat pediatric bone disorders.
- The Unit is actively engaged in clinical and surgical intervention trials, and in the development of international, evidence-based clinical practice guidelines
- The Unit is a model of medical and surgical trans-disciplinary clinical care and research in pediatric bone diseases

Mission

- Research in the Pediatric Bone Health and Orthopedic Research unit targets the diagnosis and treatment of children with rare bone diseases including x-linked hypophosphatemic rickets, osteogenesis imperfecta and secondary osteoporosis due to cancer and muscular dystrophy. Children with sports injuries and developmental abnormalities including femoral acetabular impingement and scoliosis are also a focus.
- Our research aims at establishing a strong scientific platform and building national and international collaborations between clinicians, scientists, government and industry, to allow for the successful development of novel drug therapies and innovative surgical approaches for children with bone diseases.

Strategic Directions

1. To lead the evaluation of bone health outcomes as part of international osteoporosis trials targeting innovative disease-modifying treatments for Duchenne muscular dystrophy.
2. To test the impact of novel strategies for the prevention of vitamin D deficiency rickets, and to implement such strategies by working with government agencies to develop national policy.
3. To study the long-term impact of anti-FGF23 antibody therapy for the treatment of X-linked hypophosphatemic rickets

Periprosthetic Joint Infection (PJI) Lab

Vision

- The PJI facility fosters the establishment of multicenter clinical trials to assess the efficacy of current and novel preventative and therapeutic strategies to treat PJI patients and help combat the rising threat of antibiotic resistant biofilm infections.
- The facility nurtures the development of an internationally recognized “Center of Excellence” at TOH for managing PJIs based on innovative translational research and evidence-based medicine.

Mission

- The research in the PJI facility is geared towards generating strong *in vitro* and *in vivo* scientific evidence to evaluate current and novel preventative and treatment strategies of PJI.

- Our research aims at establishing a strong scientific framework and building national and international collaborations between clinicians and scientists to allow for the successful clinical translation of our *in vitro* and *in vivo* findings to overcome the rising threat of biofilm and antibiotic resistant infections.

Strategic Directions

1. Improve our understanding of PJI pathophysiology and different factors contributing to PJI biofilm infection in the joint microenvironment.
2. Investigate bacteriophage as an alternative/assisting biotherapeutic strategy to enhance the efficacy of treating our patients suffering from PJI caused by resilient infections that are resistant to antibiotics.
    a. Create bacteriophage libraries with well characterized anti-biofilm activities and antibiotics interaction.
    b. Provide a novel tool to personalize PJI biofilm infection therapy.
3. Develop a representative animal model for PJI using 3D-printed implants designed to fit the bone anatomy of the animal of choice in order to test safety and efficacy of any treatment platform.
4. Evaluate current and novel irrigation, debridement and implant retention strategies using antiseptic solutions or intra-articular antibiotics.

Orthopaedic Biomechanics Laboratory

The Orthopaedic Biomechanics Laboratory (OBL) houses state of the art equipment for destructive and non-destructive mechanical testing of native biological tissues, bioengineered materials, classical engineering materials, medical devices, and implants. In addition, we offer biomedical engineering expertise and facilities to develop in-vitro testing models, cadaveric and model organism experiments, and simulations. The OBL is lead by the medical director Dr. Braden Gammon and engineering director Dr. Andrew Speirs. Dr. Gammon is an orthopaedic surgeon specializing hand and wrist reconstruction with a Masters in Biomechanics, and is an Assistant Professor in the Department of Surgery at the University of Ottawa. Dr. Speirs is an Assistant Professor in the Department of Mechanical and Aerospace Engineering at Carleton University.

Vision

Through innovative research and educational programs, to become a leader in orthopaedic biomechanics, improving the lives of all those living with musculoskeletal disease.

Mission

The Orthopaedic Biomechanics laboratory focuses on clinically applicable engineering research aimed at understanding etiology of musculoskeletal diseases and restoring health and function to individuals with those diseases. We promote the development and pre-clinical evaluation of innovative surgical procedures, biomaterials, implants and diagnostic tools for safe and improved patient treatment options.

Strategic Directions

Research: leading discovery and practice-changing research designed to improve the lives of those with musculoskeletal disease as well as our understanding of its etiology.

Education: leading education opportunities for medical and engineering students at the undergraduate, graduate and post-graduate levels.
Sustainability: increase the number of permeant research staff positions with opportunity for professional growth and development integrating graduate students as well as securing financial support from our partners: Carleton University and Ottawa Hospital Research Institute.

Biomaterials and Tissue Engineering

Vision

'Implants that last a lifetime and bone substitutes that perform as well as natural bones' is the vision of the Biomaterials and Tissue Engineering laboratory, a state-of-the-art facility specializing in the analysis of cellular and molecular mechanisms leading to hip implant failure, as well as in bone regeneration.

Mission

The dual mission of the is to:
1. Develop new and improved methods to modulate the biological response to implant wear and corrosion in order to prolong implant survivorship and thereby improve the quality of life for large groups of patients
2. Develop vascularized bone substitutes as a treatment option for patients suffering from bone loss. This unique and multidisciplinary research lies at the interface between fundamental and clinical orthopaedic research. To achieve its mission, the laboratory brings together a team of internationally recognized researchers and clinicians with proven expertise, thereby placing the University of Ottawa and The Ottawa Hospital at the forefront of these important fields of research.

Strategic directions

Research at the Biomaterials and Tissue Engineering laboratory aims to achieve three main goals:

1. Identify the cellular and molecular mechanisms involved in the biological response to implant wear and corrosion;
2. Develop new therapeutic approaches to modulate the biological response to implant wear and corrosion;
3. Develop vascularized bone substitutes using 3D printing and bioactive agents to direct angiogenesis and bone tissue growth.

Gait/Motion Laboratory

Vision

Improve the quality of life and mobility of Canadians of all ages through a better understanding of the function of the musculoskeletal system and joints.

Mission

The Human Motion Biomechanics Laboratory is dedicated to advancing the understanding of human joint function and musculoskeletal tissues using musculoskeletal biomechanics approaches to optimize mobility and physical performance in healthy and pathological joints.

Strategic Directions

1. Improve the understanding of joint defects on motion and performance.
2. Develop musculoskeletal models to compute muscle forces and joint loading in healthy and pathologic individuals during dynamic tasks.
3. Develop and validate new innovative therapeutic approaches for patients recovering from joint reconstruction/replacement and optimize the return to normal activities.
4. Investigate the effect of physical activities on bone remodelling during bone growth and development.
5. Advance the knowledge in injury prevention of hip and knee.
6. Provide training for highly-qualified personnel from undergraduate to doctorate students as well as post-doctorate fellow in basic and clinical research.

Regenerative Orthopaedic Surgery

Vision

The Regenerative Orthopaedic Surgery Facility brings together a group of basic and clinical scientists seeking to harness the regenerative potential of stem cells to treat and/or prevent degeneration of the musculoskeletal system such that Canadians can enjoy full mobility throughout their life course.

Mission

Our mission is to fully characterize the stem cells of the musculoskeletal system such that we understand their role in maintaining healthy tissue, and how their function becomes diminished in degenerative disease states. A full understanding of the mechanisms controlling stem cell function will allow the development of novel therapeutics to improve repair of damaged tissues in the musculoskeletal system.

Strategic Directions

1. Develop new therapies that will prevent muscle degeneration in aging. As epigenetic changes in cells are dynamic and reversible, we will target epigenetic pathways in an effort to increase the regenerative potential of muscle stem cells during normal human aging. Identification of epigenetic differences in stem cells isolated from either younger or older patients will allow us to develop therapies to turn on specific genes that could rejuvenate the muscle in aged individuals.
2. Characterize skeletal stem cells from the bone growth plate for their potential to form cartilage tissue. Determining the key characteristics of skeletal stem cell populations will allow us to develop therapeutics from pluripotent stem cells that could be injected to regenerate cartilage for patients with osteoarthritis.