The Trauma and Orthopaedic Research Unit (TORU) has capacity to undertake clinical and laboratory studies in the field of musculoskeletal disease. This includes clinical aspects of arthroplasty, tissue reconstruction and trauma, fracture surveillance and management, medical imaging and joint kinematics. TORU has established a laboratory facility at both Canberra Hospital and at the John Curtin School of Medical Research at the ANU. This enables us to conduct translational research within our own unit.

TORU’s mission is to conduct excellent research which meaningfully impacts on the clinical practice of orthopaedics and the well-being of patients. This includes the development of novel surgical modalities and therapeutic concepts by conducting translational medicine that bridges basic science and clinical practice. We aim to create a rich research environment by promoting active, multidisciplinary cooperation among orthopaedic surgeons, rheumatologists, physiotherapists, engineers, pathologists, biologists, mathematicians and physicists. Fundamental to our research endeavour is the provision of an educational hub for students, orthopaedic registrars and researchers.

Message from the Director

The Trauma and Orthopaedic Research Unit has once again had a productive year but it is surprising how quickly the year has gone. We have invested a great deal of time and effort with the support of Synthes in database development and have recently implemented our fracture trauma database. This has been a long term project and will provide the ACT Orthopaedic region with a wonderful resource for the future. This web-based database will enable us to collect longitudinal outcome data which has been specifically categorized by AO fracture classification and coded for comorbidities at source. Our ambition is to interest other centres in this format with the potential of creating an Australia-wide virtual registry from which we can make more informed and cost effective decisions.

The orthopaedic education and research world in Australia is changing. The Australian Orthopaedic Association has embraced this evolution and research training together with technical surgical training will be essential parts of the advanced Orthopaedic Surgical Training Program for the future. Aspiring trainees are now required to conduct research prior to being included in the program and also during their journey through the advanced programme. This emphasis on high level training in research will undoubtedly strengthen the profile of Australian orthopaedics on the world stage. With the infrastructure now in place, the ACT Orthopaedic Unit with TORU is in a great position to support the research and training agenda.

Research Highlights

- TORU has published 12 peer reviewed papers and over 40 conferences presentations over the last 12 months
- We are very pleased to welcome Joe Lynch, who has come on board as a senior research officer. Joe has come to Canberra from Canada via Sydney. He is a biomechanist with a special interest in knees who has been working with the SORI group in Sydney.
- TORU has commenced a large multicentre trial looking at the survival and patient outcomes of the ATTUNE® Total Knee Replacement System (Johnson and Johnson).
- Version 1.0 of the Canberra Trauma Fracture Database has been launched at The Canberra Hospital. This tool allows clinicians to keep a detailed record of treatments and outcomes for all patients who have sustained a fracture.
- The characterising of whiplash injuries study is progressing with the exciting development of a collaboration with both UNSW @ ADFA and the University of Canberra for image processing innovation.
- We have commenced a collaborative project with University of Canberra and Prince of Wales Hospital on the impact of dementia on access to, and outcomes from, rehabilitation following fracture related hospitalisation.
TORU Laboratory Research Report

TORU Laboratory team bridges basic and clinical sciences and facilitates communication among TORU’s collaborative institutes, universities and orthopaedic industries.

TORU team presently investigates chronic and complex bone diseases, some of which cause life-long pain and disability. These chronic conditions can be rare, such as arthritis, trauma and osteoporotic fractures. Combined, they afflict millions of Australians and cause tremendous human suffering, and cost million dollars in health care.

The team utilizes a mix of conventional molecular biology approaches as well as global methods such as next generation sequencing to study mRNA expression and its regulation by non-coding RNA e.g. microRNAs with an ultimate goal of identifying novel molecules that regulate bone resorption, formation, fracture repair and bone homeostasis.

**Key Research Areas**

**Osteoimmunology** microRNAs’ (miRNA) regulation and genetic risk factors in biomaterial related osteolysis in total joint replacement.

This research has in part supported by AOA Research Foundation. Building on the foundation laid by the dendritic cells involvement in osteolysis, the group is using off-cut tissues from the cohorts of healthy, primary and revision subjects of TJR for characterization of wear particles and identification of molecular and genetic risk factors that contribute to the osteolysis. The ultimate goals are to contribute to the development of better predictive markers, treatments, and prevention strategies.

**The third generation of magnesium (Mg): based biomaterial development**

This area addresses a need for translational research to enhance treatment and improve management of bone diseases and disorders. To advance the understanding of interaction at the interface of biomaterials and biological systems, the team is studying biocompatibility, biodegradability and bioactivity on a series of magnesium (Mg)-based biomaterials either on controlling biodegradation or osteointegration.

**Silico model of interplay and mechanism of human bone remodelling**

Integrated molecular, genetic and mathematical approaches help to identify genes that play a key role in bone homeostasis and disease process. The team is developing a multi-scale, quantitative and predictive model, which will significantly contribute to a better understanding of the intersystem crosstalk in bone remodelling including cell-cell, pathway-pathway, molecule-molecule, and gene-gene. The silico model of osteo network will hopefully facilitate recognizing biomarkers for diagnosis of rheumatoid arthritis and osteoporosis.

**Molecular pharmacological research for osteoporosis, wound and fracture healing.**

We are screening anabolic drug candidates for bone biological therapeutics that promote wound and fracture healing by directing the progenitor cells growth and differentiation. We are also exploring the use of natural extracellular matrix components as biomaterials that provide appropriate structural and stimulating properties for generating functional osteoblast and bone cells.

**Laboratory Facilities**

TORU Laboratory is located at the John Curtin School of Medical Research in the Australian National University and has established collaborations with Professor Chris Parish at the Department of Immunology and Genetics. TORU Lab has access to all the necessary high-end equipment.

**Genetic and Molecular Biology Assays:**

TORU Lab has, or has same floor access to core services for DNA and RNA sequencing, such as a complete Affymetrix GeneChip DNA array system, sequence analysis pipeline, such as SOLIDTM Small RNA Pipeline and HiSeq2000. The thermocyclers (PCR and RT-PCR machine), film processor/developer, Bio-rad gel doc system will give our students and visiting doctors an ideal working condition for catching up with frontier science and technology.

**Biochemistry and Immunohistology Assays:**

TORU Lab has, or has same floor access to, UV-VIS spectrophotometer, Infinite 200Pro (Luminescence, fluorescent and isotope spectrometer), Beckman ultracentrifuge, Packard liquid scintillation counter, Victor X3, Flow cytometer (BD’s FACScalibur with 9 colors, FACScan), fluorescent microscopy, confocal microscopy, μ-CT and Scanning electron microscopy.

**Cell Culture:**

TORU Lab has a dedicated tissue culture room equipped with Class II biosafety hoods, CO2 incubators, phase contrast inverted microscope with digital photography capabilities, water bath, temperature controlled centrifuge, bench-top microcentrifuge, freezers and fridges.

**Collaborative Research**

TORU Laboratory has developed research collaborations multi- and cross-disciplinary research teams:
- ANU Research School of Chemistry
- ANU College of Engineering and Computer Science
- University of Western Australia
- Monash University
- The Westmead Hospital, University of Western Sydney

Dr Rachel Li
Laboratory Research Coordinator
The TORU clinical research unit has had a busy and successful year. Our research profile is broad and varied with topics ranging between arthroplasty, trauma, materials science and whiplash. Although successful we face many future challenges and opportunities. Attracting adequate resources is always a challenge but creating more opportunities for collaboration with other units such as ours is a rewarding way to approach the problem. In this way we hope to become more competitive with respect to NHMRC funding which, as everyone knows, is a difficult commodity to come by in surgery.

We are enjoying increased engagement from more the senior and the junior clinicians. Professor Smith, as our director, is our main source of clinical expertise but if Canberra is to achieve its potential and become a centre of excellence for orthopaedics, we need to engage all of the clinicians in a research agenda.

Canberra has many advantages with respect to research. We are small enough that the orthopaedic surgeons are able to act as a single unit across both the public and the private sectors. This enhances the opportunity for comprehensive thought exchange and collaboration. Indeed we are enjoying much more engagement with the senior clinicians who are supervising research projects in a number of areas this year. This combined with our close proximity to other large academic institutions gives us a useful edge.

TORU also has advantages over many similar units. We are embedded and supported by ACTH. At the same time our affiliation with the ANU allows us to take part in many educational opportunities and engage in supervising post-graduate degree students. We are currently supporting five MPhil students and four PhD students. In addition, six medical students per annum conduct their research under our auspices and we have projects being undertaken by interns and registrars keen to make their mark in research (and earn bonus points for their careers). Of interest is a project by Dr Jennifer Truong who is using the National Health Cost Data Collection format to properly cost two-stage revision for infection in arthroplasty which has been vastly underestimated in the past.

By virtue of our location, affiliations, and collaborations we have a rich and productive network which has allowed us to explore ideas in new and creative ways. For example our image registration technology is due to a very productive collaboration with Assoc Prof Mark Pickering at UNSW. This project has extended from the knee to the hip and we are also examining ways of automating our whiplash image data. We have two other collaborations at UNSW including the development of intrinsic bearing sensor technologies with Dr Sean O’Byrne and the exploration of trunnion wear mechanics with Dr Krishna Shankar. Our continued collaboration with Assoc Prof Jennie Scarvell at the University of Canberra includes a study of the effect of Dementia on the treatment choices for fractured neck of femur patients and the Pickles project that is using image registration to interrogate the kinematics of different knee replacement designs. At ANU we are collaborating with Dr Alex Webb in the Anatomy school on two projects: Whiplash and the blood supply of the lateral hip.

This year we have registered four industry funded fellowships with the AOA. They are administered through a number of institutions but all have a research component which we facilitate. Our Stryker Arthroplasty fellow from 2013/14, Dr Shyam Rajagopalan conducted two important studies looking at the reliability of radiologists with post arthroplasty x-ray surveillance and also a quantification of the reliability of a computer based edge matching software for assessing polyethylene wear with current clinical x-ray practices. Our other fellows include Dr Claire Bolton who is continuing her MPhil on the anatomy of the acetabulum and Dr Mitchell Kingston who is examining the blood supply of the lateral hip and the intra-tendinous supply of the gluteal tendon in particular using microCT. Our small but agile team includes Belinda Payne, our extraordinary office manager, Rui Wang our talented database architect, Mona Singhal our Whiplash Project officer and Joe Lynch our biomechanist and senior research officer. Donna Martin will soon be joining us to conduct the dementia and fractured NOF study and our many students are mentioned elsewhere in this newsletter. Although this is the clinical report it is not complete without mention of our laboratory team mates, particularly Assoc. Prof Rachel Li. Rachel attracts international admiration and we are privileged to work with her team and share some of her successes. In the future we plan to collaborate more extensively in the pursuit of exciting translational research. We are fortunate indeed to have such a close and hardworking team.

Dr Diana Perriman
Clinical Research coordinator
Prof Paul Smith, BMBS FRACS (Ortho). Director

Professor Smith is an orthopaedic surgeon at the Canberra Hospital and at Calvary John James Hospital in Canberra. He is also Co-Director of the Trauma and Orthopaedic Research Unit at the Canberra Hospital. Prof Smith is also president of the Arthroplasty Society of Australia, and Clinical Director of Orthopaedic surgery at the Canberra Hospital.

Prof Smith received his medical and surgical training in Adelaide before specialising in hip and knee joint reconstructive and replacement surgery. He was a Royal Australasian College of Surgeons Travelling Fellow in 1996 and 1997 with Fellowships in joint replacement surgery at the University of Western Ontario in Canada and at The Princess Elizabeth Orthopaedic Hospital in England. He has been honoured by The Knee Society, receiving the inaugural John N Insall Travelling Fellowship in knee surgery and has been appointed as Professor of Orthopaedic Surgery at the ANU Medical School. Prof Smith’s particular clinical interests are in reconstruction and replacement surgery of the hip and knee, complex revision joint replacement surgery and management of pelvic and acetabular injuries.

Contact: psmith.admin@orthoact.com.au

Dr Rachel W Li, MD, PhD. Laboratory Research Co-ordinator

Dr Li is a molecular pharmacologist and osteoimmunologist with interests in understanding the processes that control a ‘foreign body reaction or response’ initiated by biomaterials implanted into bone or exposed to human cells.

Dr Li received a Bachelor of Medicine and Master of Medicine, and worked as a surgeon and senior liver diseases specialist at China Medical University from 1982 to 1996. She led a number of clinical trials in anti-viral and anti-inflammatory drugs and successfully transferred an intellectual property to pharmaceutical industry.

In 2003 Dr Li completed her PhD in pharmacology at Southern Cross University and gained her postdoctoral research experience in molecular pharmacology in John A Burns School of Medicine, at University of Hawaii.

Dr Li returned to Australia in 2006 and established the TORU Laboratory which pioneered basic orthopaedic research at the ACT region. She has made some major research contributions to the fields of osteoimmunology. She has developed a range of research strengths and capabilities in orthopaedic research and biomaterial testing. Along with her focus on bone biology and immunology, she has a long-standing interest in the biomedical markers and targets that are anabolic to bone growth.

Contact: rachel.li@anu.edu.au

Dr Diana Perriman, PhD. Clinical Research Co-ordinator

Diana Perriman, BAppSc (USyd), MSc. (University of East London), PhD (ANU). Dr Perriman is currently the clinical research coordinator of TORU.

Dr Perriman is a physiotherapist who has completed her PhD at the ANU.

Her clinical career has spanned two decades in which she worked in hospitals, the community and private practice both in Australia and the UK. She has worked at the Trauma and Orthopaedic Research Unit since returning from the UK in 2003.

Her PhD research investigated the thoracic spine and kyphotic thoracic posture in aging, a suite of thoracic spine biomechanical and imaging studies culminating in a randomised controlled trial of the effect of conservative treatment for thoracic kyphosis.

Dr Perriman has also been the recipient of an NHMRC Dora Lush scholarship for this research. As clinical research coordinator Dr Perriman’s research interests lie in arthroplasty and fracture outcomes in accordance with the main focus of the Trauma and Orthopaedic Research Unit.

Contact: diana.perriman@act.gov.au
Ms Belinda Payne
Belinda is TORU's Office Manager, Belinda has been with TORU since 2013 and can be contacted at any time for queries regarding the unit. Belinda comes from a clinical background in nursing which gives her great insight into the many different aspects of orthopaedic research. Her role is diverse and comprehensive including conference and meeting organisation, financial management and administrative duties.

Mr Joe Lynch, Research Officer
Joe joined the team in mid 2014. He completed his Bachelor of Science in Exercise Science, and a Master of Science in Biomechanics at the University of Ottawa. At present Joe is involved in the running of various trials within the unit with his main interest being in functional and imaging analysis following injury and surgery.

Ms Ruidang Wang, Database Architect
Rui is a database architect who is currently designing the Fracture Surveillance Database. Rui has extensive IT experience specialising in applying database design, analytic informatics, business intelligence and online platform technologies to clinical context. Rui is currently completing her PhD at ANU.

Dr Mona Singhal, Research Officer
Dr Singhal studied medicine at Bangalore University, India. Dr Singhal has just completed the Australian Medical Council Registration Examination. She joined TORU in 2013 to work as a Research Officer on the Whiplash study.

Christine Hanranahan, Database Manager
Christine Hanranahan is a qualified nurse and has worked with both the Red Cross and the Therapeutic Goods Administration. Christine helped to develop the Arthroplasty surveillance database and continues to manage the database which is based at Orthopaedics ACT.

Ms Liz Abbott
Liz has been a physiotherapist in Canberra for over 2 decades with a special interest in orthopaedic and musculoskeletal injuries. Currently Liz coordinates the explant retrieval database.

Research Fellows

Dr Jennie Scarvell
B/AppSc Physiotherapy (Sydney), Grad Cert Higher Ed, (Canberra) Cert Health Economics (Monash) PhD (Sydney), A/Professor Department of Physiotherapy (University of Canberra). A career as clinical physiotherapist lead Jennie to a PhD on knee kinematics and the role of aberrant motion in degenerative change using a model of ACL injury. Jennie is an affiliate Senior Lecturer at University of Canberra and at ANU.

Dr Claire Bolton
Clerie is an orthopaedic registrar now based in Adelaide. She is conducting her MPhil on the morphology of the acetabulum in osteoarthritis and hip dysplasia. She is supervised by Prof Smith and Dr Perriman.

Dr Mitchell Kingston
Dr Kingston is an orthopaedic registrar at the Canberra Hospital and Research Fellow. He is currently undertaking an MPhil at the ANU looking at the anatomy of the circumflex femoral arteries.

Dr Donghai Zhang
Dr Zhang is a Chinese Anaesthetist from Shandong University who travelled to Canberra to join the TORU lab team working specifically on ‘Biocompatibility of novel sensoring materials for assessment of fracture healing.’ He has now returned to China.

Dr Maoyuan Xin
Dr Maoyuan Xin is a visiting 3rd year PhD student from the medical school of Shandong University, located in Jinan city of China. Xin’s work is supervised by Prof Paul Smith and A/Prof Rachel Li and focuses on novel sensor materials for use in medicine particularly in the field of orthopedics.

Dr Partha Palit
Dr Partha Palit won an Endeavour Postdoctoral Fellowship 2014, allowing him to join TORU’s laboratory research for 6 month. Endeavour P o s t d o c t o r a l Fellowship is internationally competitive, merit-based fellowship provided by the Australian Government that support citizens of the Asia-Pacific, the Middle East, Europe and the Americas to undertake study, research and professional development programmes in Australia. Since his arrival, Dr Palit has been actively working on our research project investigating the chemical compounds for anti-inflammatory and antiosteoporosis.

Dr Tom Ward PhD
Tom is an orthopaedic registrar, PhD and Rhodes scholar. His current research interests are in validating image registration techniques for the hip and FAI in particular.
**Medical Student Projects**

**Harrison Pickup**

**Do Volar plates lead to the best outcome in patients with distal radius fractures?**

**Background**
As the elderly population continues to grow, the incidence of DRFs is increasing. The introduction of volar plates to the repertoire of surgeons has led to an increase in their popularity over other methods of fixation. This paper looks at the functional outcomes of treating distal radius fractures in the elderly with volar plates and other fixation methods.

**Methods**
A retrospective review of patients aged 65 years or older treated for distal radius fracture during 2005, 2006, 2008 and 2009 at The Canberra Hospital was conducted. Patient outcomes were measured using the Disabilities of the Arm, Shoulder and Hand (DASH), Assessment of Quality of Life (AQoL 6D) and a Visual Analogue Scale (VAS) for patient satisfaction with wrist performance and pain. Fractures were classified from patient x-rays using the AO classification system. Fixation method, which extremity and length of stay were obtained from patients medical records.

**Results**
86 patients responded with a 38% response rate and a mean age of 73 at time of fracture. A statistically and clinically significant difference was found in the DASH scores among those with volar plates and other fixation treatment in favour of volar plates. Patients in the volar plate group had a better AQoL score. This difference was clinically but not statistically significant. In terms of satisfaction with pain and wrist performance, patients in the volar plate group once again displayed better scores than those in other treatment groups.

**Conclusion**
There was a significant difference in terms of functional outcomes from patients treated with a volar plate compared to other treatment methods. This finding indicates that the use of volar plates for distal radius fractures in the elderly leads to an overall superior outcome both in functional outcomes and patients quality of life.

**Mathew Lim**

**Non-invasive measurement of pelvic tilt**

**Background**
Acetabular component orientation is fundamentally related to the degree of pelvic tilt. The position of the acetabular component is an important risk factor for dislocation after total hip replacement but current pre-surgical imaging of the hip is done in supine only. As a result the degree of change in orientation which takes place as a result of changes in pelvic tilt during function is not assessed. This can potentially result in suboptimal acetabular component positioning, and increased dislocation risk. This study evaluated the validity of using of a skin-mounted accelerometer to measure relative pelvic orientation.

**Methods**
An accelerometer customized to measure tilt relative to gravity was verified in two ways. Firstly accelerometer measurements were compared against a rotating model of a pelvis. Five repeated sets of measurements were made from this model at 19 positions to assess accuracy and repeatability. Secondly, a cadaveric section was x-rayed at five angles of tilt to assess measurement of tilt with the accelerometer compared to sacral-slope measurements taken from lateral x-ray.

**Findings**
Relative measurements of pelvic tilt from the accelerometer agreed with sacral slope measurements to within two degrees. Measurement of pelvic tilt using an externally placed accelerometer was repeatable to within 2.6 degrees.

**Interpretation**
The use of an accelerometer, mounted over the sacrum, reliably measured relative pelvic tilt with a clinically acceptable degree of accuracy. This method could therefore be used as a pre-surgical screening tool to identify patients with hypermobile pelvises', or as an aide in post-surgical dislocation risk mitigation.
New 2014 Medical Students

Mike Van Alphen

Patient-reported outcomes following mid-clavicular fractures: Non-operative vs Operative Management

To fix or not to fix – that is a question which has caused some heated exchange in our clinical meetings. This project aims to ascertain whether the 5 year outcomes for patients who have had surgical fixation for a displaced mid-clavicular fracture are better than those treated non-operatively. Mike is an ANU medical student with a keen interest in sports and orthopaedic injuries, having come from a physiotherapy background.

Sarah Jane Meresfield

Life After Arthroplasty – when will I have to have another joint replacement?

For 10 years TORU has been collecting outcome data from patients who have had their knees and hips replaced in the ACT. This data is now being plundered for a study which aims to examine and describe the effect of having an arthroplasty on the likelihood of having another and how soon. This data will enable both patients and clinicians to better understand what their orthopaedic future is likely to be. Sarah Jane Meresfield is former public servant/ Antarctic zoology student, and entered medicine in 2014 to find out why my knee always hurts.

Billy Xian

Distal Femoral Fracture Repair: Which Construct results in better Patient Reported Outcomes?

Intramedullary (IM) nails are old technology and LISS plates are new, but which is better? The evidence is divided. Some clinicians are not convinced that the LISS plate is strong enough for this application, but does the IM nail lead to early OA and joint destruction? Short and medium term follow-up studies have not shown a difference between groups. We are investigating this question by surveying the comparative outcomes at 5-6 years post operatively. Before medicine, Billy completed his Bachelors and Masters degree in Canada, specifically looking at Deep Brain Stimulation in Parkinson patients.

Stephanie Baddock

Does hip impingement planning software improve outcomes at 1 year for patients who have had surgery for FAI

Femoroacetabular Impingement (FAI) is a condition which may lead to the osteoarthritic changes which predispose us to needing a hip replacement. For this reason corrective surgery is becoming commonplace but the area is new and evolving. We are systematically collecting hip outcome (iHOT) scores for all of Dr Alexander Burns’ FAI patients. In this study we aim to ascertain the predictive power of the various x-ray signs and scores which are used to diagnose FAI (cam and pincer deformities). Sarah completed a Bachelor of Science majoring in anatomy and physiology at the University of Melbourne with an interest in FAI after having surgery for this condition.

Jason Szezepanski

What is the most effective strategy for treating pelvic discontinuity in revision THA – a systematic review.

When hip arthroplasty fails or after severe trauma, the pelvis can become divided and therefore intrinsically unstable. In these circumstances complex pelvic surgery is required. The problem is that the condition is relatively rare and the even rarer surgeons who undertake these procedures each have their own methodologies. This project involves a systematic review of all of the literature published on outcomes following pelvic repair. Jason is a former physiotherapist from Melbourne.

Sarah Ellis

Radiographic techniques in predicting the severity of femoroacetabular impingements

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Is there a relationship between hamstring and quadriceps strength, and the knee joint kinematics which predict anterior cruciate ligament injury?

Ben Serpell began working at TORU as a research assistant after completing his studies in Occupational Therapy and Human Movement in Victoria on projects related to knee kinematics following knee arthroplasty. He has been a part-time PhD candidate at the Australian National University and remains an affiliated of TORU while he completes his study for the last few years. Ben’s research remains concerned with knee joint kinematics and kinetics as he tries to establish if there is a relationship between musculotendinous stiffness and traumatic lower limb injury with special reference to anterior cruciate ligament injury. To do so Ben is upskilling in the use of technology including electromyography, force plates, and the novel CT- Fluoroscopy algorithm used for measuring knee joint kinematics originally developed by Mark Pickering and others at TORU. Ben is in the final stages of his PhD and will be submitting within the next few months.

Andrew has begun a PhD investigating injury in competitive kayak and ocean paddlers. This study will investigate injury type, injury rates and their contributing factors as well as biomechanical investigations.

The purpose of the PhD is investigating injuries in competitive Ocean, Ultra-Marathon and Sprint kayak and Ocean-ski paddlers. There is very little published data about injury in these groups, and none in relation to Ocean-ski paddlers. With ocean racing growing rapidly in popularity, and ocean skis being used more commonly in flat-water racing, the altered biomechanics and impact on injury is generally unknown.

Andrew is graduating this year from Medicine (ANU) and has a background in Sports Physiotherapy and Exercise Science with elite athletes including having worked at the English Institute of Sport.

Catherine, initially an electrical engineer, started her PhD with TORU midway through the year. Following a number of years in this field Catherine decided to make career change into health by first completing and undergraduate degree in Sport and Exercise Science at University of Canberra and now a PhD in the same place under the supervision of Dr Jennie Scarvell. Catherine has found a real passion for biomechanics and has the ability to share that passion with undergraduate students as an Assistant Lecturer in Biomechanics. Catherine has presented some of her work at the ACISC Sports and Medicine Conference in Phuket last year and submitted her first paper to Journal of Applied Biomechanics.

The research that Catherine will be pursuing at TORU is part of the PICKLeS project. Specifically she will be investigating the questions “Which implant configuration demonstrates the most improvement knee kinematics following a total knee replacement for osteoarthritis and how do these kinematics compare with matched healthy aging knees.”
Olympia John as a Ph.D. student joined TORU laboratory research team since February 2014 under the supervision of Dr Rachel Li, Professors Paul Smith and Chris Parish. She obtained her Masters in Pharmacy from C.U. Shah College of Pharmacy, Shreemati Nathibhai Thackersey (SNDT), Mumbai, India. She has also completed The Postgraduate Diploma in Intellectual Property Management from Academy of Intellectual Property Studies (AIPS), Mumbai, India. She began her career as a Formulator in Cosmetics (Haircare and Skincare) at Emami Ltd, India. Her last assignment involved formulating ANDA (abbreviated new drug applications) Generics for US and European markets at Glenmark Generics Limited from 2006 to 2010. She has over 6 years of experience in pharmaceutical sciences. She is currently working at TORU Laboratory located at John Curtin School of Medical Research, Australian National University. Her research involves heparanase as a potential biomarker in rheumatoid arthritis.

Song is a PhD student of ANU. Song gained his bachelor of applied physics from Shanghai JiaoTong University in China and master of engineering from ANU. He has a background in theoretical physics and computational analysis of engineering materials. Song’s PhD project is to investigate interactions at the interfaces among pathways of multiple systems in bone remodelling. His work is currently focusing on rebuilding signalling pathways in osteoblasts and osteoclasts by mathematical description and proving this description by designing the experiment to treat osteoblasts, osteoclasts and co-culture of osteoblasts and osteoclasts under physical stimulus from low frequency electromagnetic field. Song’s PhD project is supervised from both TORU and the college of engineering and computer science in ANU.

Obinna is a PhD student at UNSW Canberra. He obtained his Masters degree in 2012 at the same university. His current research interest is in the area of prosthetic devices for joint replacements. His PhD research work is on the investigation of wear of total hip replacement at the taper-trunnion junction. Recently, it’s been identified that excessive fretting wear at the taper-trunnion (head-neck) junction potentially contributes to premature failure of some total hip replacement procedures. The project aims to develop novel methods for investigating, evaluating and quantifying wear of total hip prostheses at the taper-trunnion junction by employing numerical methods via finite element modelling. In a broader sense, the principal goal is to work toward the minimization of wear debris produced in the hip joint, thereby resulting in a longer prosthetic lifetime. This work is supported by Global Orthopaedics.
Fracture Database

The fracture database is a unique tool with the capacity to make every patient admitted to the Canberra Hospital for fracture management a study participant. This cloud based tool enables remote surveillance and evaluation of longitudinal outcomes in our whole patient population. Of course complete capture will not be possible but this tool puts in place the capacity to track outcomes using current technology while providing the perfect test bed for new technology surveillance. This database went live in August of this year. After embedded testing and editing we will investigate the possibilities of making this tool available to other jurisdictions. This exciting initiative is a leap forward in data collection and patient evaluation.

Genetic Markers of OA

Nanoscale wear particle related osteolysis in total joint replacement (TJR) and genetic markers

This research has been in part supported by AOA Research Foundation and discovered that the dendritic cells is involved in osteolysis. Current work now focuses on a better understanding of the osteoimmunology, human tissue’s responses to implants, microRNAs’ (miRNA) variant expression and miRNA sequencing in the wear particle related osteolysis, as well as the translation of this knowledge to the clinical management of a variety of diseases and conditions related to TJR. TORU Laboratory has used off-cut tissues from the cohorts of healthy, primary and revision subjects of TJR for the characterization of the size and shape of wear particles and for the identification of genetic and environmental risk factors that contribute to the osteolysis. The ultimate goals are to contribute to the development of better predictive markers, treatments, and prevention strategies of the osteolysis.

Pressure Sensitive Carbon-Nanotube Film Study

This project is the first stage in the development of an innovative new pressure sensing technology which will seamlessly interface with ‘smart’ wireless data acquisition.

The specific aims of this research are to:
1. Develop pressure-sensitive plastic films doped with carbon nanotubes.
2. Test the potential for these films to be used with embedded microcomputers as sensors in knee replacements.
3. Test the applicability as shoe inserts for mapping of load patterns in running and jumping sports and in the military.
4. Secure funding with a view to commercialisation of the product all possible applications.

The project was just one of a small number which were funded by ACT health in 2013-14. Dr Sean O’Byrne at UNSW has commenced the preliminary work involved in fabrication and validation. TORU will be involved in testing the sensor in its knee simulator.

Pickles Knee Study—A prospective imaging study of cruciate retaining and substituting knee replacement, in osteoarthritis and healthy aging

This study aims to examine knee kinematics before and after knee arthroplasty and compare those to the kinematics of knees in a non-arthritic age-matched cohort. In the past the only way of measuring knee kinematics accurately in three planes was to implant RSA beads or use of bone pins. These methods are both highly invasive. In this study we aim to overcome this problem by using an image registration technology developed at TORU by Prof Smith, Assoc Prof Jennie Scarvell and Assoc Prof Mark Pickering by combining 3D CT and 2D video fluoroscopy. This study is unique because, for the first time, knee replacement patients will have their knee kinematics accurately measured both before and after surgery. Recruitment is underway for normal and osteoarthritic participants where their knee is scanned while they perform a number of loaded end-of-range activities. These movements allow us to see how the knee kinematics change following surgery. OA patients are randomised to receive one of three different design of implant. Testing is being done by the TORU staff in combination with the medical imaging department at The Canberra Hospital. Catherine McMaster has recently joined the project and this will make up the bulk of her PhD work.

This study has been funded by the Canberra hospital Private Practice Fund, the University of Canberra and Biomet.
**Characterising whiplash injury using magnetic resonance imaging**

Whiplash is a term describing a range of injuries caused by or related to sudden distortion of the neck. It is commonly associated with motor vehicle accidents, usually when the vehicle has been hit in the rear.

Injuries to the cervical spine following motor vehicle accidents (whiplash injury) are one of the most common causes of neck pain and disability in the developed world with significant numbers likely to develop long lasting symptoms. In the 2007/2008 financial year, the annual financial costs associated with whiplash injuries were approximated to be $AUD 700 million in New South Wales alone. To date there are no reliable physical markers with which to unequivocally diagnose whiplash injury or the degree of severity.

Dr Alex Webb has recently developed methods for quantifying the morphometry of the synovial folds in the cervical spine using MR imaging. These structures may represent structures of interest with respect to whiplash diagnosis and prognostication.

The purpose of this study is to investigate the use of 3T magnetic resonance imaging (MRI) to detect structural damage to synovial folds and surrounding structures in whiplash patients with neck pain caused by motor vehicle accident.

In this study, participants who have both acute and chronic neck pain following a motor vehicle accident will be compared with participants who do not have neck pain using MRI as well as clinical tools which have previously been used to determine the severity and prognosis of whiplash injury.

Dr Monah Singal has led the recruitment for this study and is currently looking for patients who have either acute or chronic whiplash symptoms and healthy volunteers. We expect recruitment to finish in early 2015.

TORU has also partnered with Assoc Prof Mark Pickering from UNSW @ ADFA and Assoc Prof Girija Chetty from UC to develop a method of automatically segmenting specific muscle groups that surround the cervical spine using 3D MRI.

**Short, Medium and Long Term Survivorship of Attune Primary® Total Knee Prostheses**

TORU recently began a trial looking at the long term survivorship of the ATTUNE® cemented primary Total Knee Arthroplasty (TKA) system for 4 different implant configurations. Data from this study will be used to support post-market surveillance of the ATTUNE® Knee System for the 4 implant configurations, which are (1) Cruciate retaining fixed bearing (2) Cruciate retaining rotating platform (3) Posterior stabilized fixed bearing and (4) Posterior stabilized rotating platform. The study is being run in collaboration with Orthopaedic ACT, specifically, Dr Al Burns and Dr Damian Smith. Subjects who are eligible will be evaluated in clinic prior to surgery, follow-up clinic visits at less than 1 year, and at minimum 1, minimum 2, minimum 5, minimum 10, and minimum 15 years post surgery. Visit evaluations include clinical and radiographic evaluations, subject self assessment questionnaires and check for adverse events. This study is funded by Depuy Synthes.

**Arthroplasty Database**

The arthroplasty database is also an online tool which introduced in the private sector in 2009 and we hope will be taken up by ACT health in the future. The data provided by this tool serves to provide clinical surveillance reports and longitudinal outcome collection but also has some unique functions for management. The data collected has the potential to facilitate waiting list categorization and follow-up frequency management thereby improving efficiency while remaining responsive. The database is currently being streamlined.
AOA National Scientific Meeting, Melbourne 2014

- Smith PN, Li, R.W., Kirkland, N.T., Zhang, D.H., David R.N., and Birbilis, N. Biodegradable magnesium yttrium (Mg-Y) alloy promotes osteogenic differentiation of human mesenchymal stem cells.
- Perriman DM, Rajagopalan, S., Smith, P.N. How reliable is Computer Assisted THA Polyethylene Wear Measurement with Current Radiography Practices?

Australian and New Zealand Orthopaedic Research Society, Adelaide 2014

- Perriman DM, Rajagopalan, S., Smith, P.N. How reliable is Computer Assisted THA Polyethylene Wear Measurement with Current Radiography Practices?
- Lynch J, Scholes, C., Fristch, B., Ebrahimi, M., Coolican, MRJ, Smith, R., Smith, PN, Parker, DA Abnormal knee kinematics during step and turn following multiple-ligament knee reconstruction.

Australian Physiotherapy Association ACT Research Symposium, Canberra 2014

- Owers D, Webb A, Perriman D, Smith PN The evidence for cervical muscle morphometric changes after whiplash: A systematic review and meta-analysis
- Adern M, Perriman D, Smith PN. Dislocation Following Total Hip Replacement. A Descriptive Study of Common Factors and Treatment in Canberra

Arthroplasty Society of Australia Annual Scientific Meeting, Fremantle 2014

- Smith PN. I hate Clexane.
- Smith PN, Sen J, Perriman D. Reconstructive Options for Massive Acetabular Deficiencies.

36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Chicago 2014


World Congress of Molecular Medicine, 2013

- Li, R. miRNA, their target mRNA and potential personalized medicine in joint replacement
International Congress for Joint Reconstruction Sydney 2014

- Smith P. How to manage severe angular deformities when doing TKR
- Smith P. Femoral Revision: What are the options? 2014

AOA ACT Branch Scientific Meeting, Canberra 2013

- Chen S, Qin, Q., Zhang, D., Smith, P., Li, R. The influence of extremely low frequency electromagnetic field on human osteoblasts.
- Rajagopalan S, Perriman, D., Neeman, T., Smith, P. Arthroplasty Surveillance: Are radiology reports useful?
- Avakian Z, Wardle, B., Perriman, D., Smith, P. Results after one year of experience using tranexamic acid for total knee arthroplasty
- Owen D, Russell, N., Walter, W., Smith, P. Ceramic on ceramic total hip arthroplasty squeak: an estimation of the incidence of squeak and revision surgery for squeak
- Bolton C, Perriman, D., Griffin, A., Smith, P., Neeman, T. The Transverse Acetabular Ligament: Does age affect its relationship with the acetabulum?
- Selkirk A, Perriman, D., Smith, P.N. Comparison of Unicompartmental vs Total Knee Joint Replacement: Patient Reported Satisfaction, Performance and Quality of Life.

European Hip Society 11th Congress, Stockholm 2014

- Rajagopolan S, Perriman, D., Neeman, T., Smith, P. "Arthroplasty Surveillance: Are radiology reports useful?"
- Rajagopalan S. Arthroplasty Surveillance: Are radiology reports useful?

Canberra Health Annual Research Meeting, 2014

- Li RW, Smith, P.N., Birbilis, N. Biodegradable Magnesium Yttrium (Mg-Y) Alloy Promotes Osteogenic Differentiation of Human Mesenchymal Stem Cells (hMSCs).
- Perriman DM, Rajagopalan, S., Smith, P.N. How reliable is Computer Assisted THA Polyethylene Wear Measurement with Current Radiography Practices?
Gradient descent-based automatic image registration algorithms typically fail when the initial misalignment between objects is large. This is a major limitation for routine clinical applications. The registration task is even more difficult for multi-modal images because of the nonlinear relationship between the pixel intensities in the images to be aligned. In this paper, we present a fast and accurate multi-modal image registration algorithm which successfully registers three-dimensional (3D) computed tomography to two-dimensional single-plane fluoroscopy data for large initial displacements between the images. Our experimental results show that the proposed approach can increase the precision and small bias in all six 3D rigid body transform parameters.

**Background:** Tendinopathy is a common, costly condition affecting both sporting and sedentary populations. Research into tendinopathy frequently involves the evaluation of tendinosis, a pathology characterized by a lack of inflammatory cells, collagen disruption, neovascularisation, altered cell numbers and morphology and increased glycosaminoglycans. Evaluation of these characteristics can be undertaken using the Bonar histopathology score, but the characteristics are heterogeneous throughout tendon specimens with no standardized method of determining the area to be evaluated. The objective of this study was to assess whether the Bonar score varies depending on the criteria used to define the area of evaluation.

**Methods:** Two independent assessors, with a third to resolve disputes, evaluated 103 areas from 35 tendon specimens using the Bonar score. Specimens were scored once each in the area of worst collagen disruption, degree of vascularization, and cell morphological changes. The inter-tester reliability of the updated Bonar scale was good ($r(2)=0.71$).

**Results:** The Bonar score was highest in the areas of worst cell morphological (CM) changes, followed by collagen disruption (CD) and lowest for the area of most extensive vascular proliferation (VS) (regression: CD vs. CM, $p=0.008$, CM vs. VS, $p<0.001$, CD vs. VS, $p=0.013$). Suggested modifications to the Bonar score include the addition of a cellularity domain, specific definitions of hypo- and hypercellularity, and changes to the vascularity score to include pathological avascularity.

**Conclusions:** The updated Bonar score includes a standardized method of selecting the area of evaluation, which should provide increased reliability when assessing the extent of tendon degeneration.
Musculoskeletal injury causes pain and when chronic can affect mental health, employment and quality of life. This study examined work participation, function and quality of life in people with greater trochanteric pain syndrome (GTPS, n=42), severe hip osteoarthritis (OA, n=20) and an asymptomatic group (ASC, n=23). No differences were found between the symptomatic groups on key measures, both were more affected than the ASC group, they had lower quality of life score (ASC=0.68). GTPS appears to confer levels of disability and quality of life similar to OA = 0.52; and ASC=0.29; OA=0.52; and ASC=0.68). GTPS appears to confer levels associated with end stage hip OA.

Greater trochanteric pain syndrome negatively affects work, physical activity and quality of life: a case control study

Fearon, A. M., Cook, J. L., Scarvell, J. M., Neeman, T., Cormick, W., & Smith, P. N.

Journal of Arthroplasty

Increased substance P expression in the trochanteric bursa of patients with greater trochanteric pain syndrome

Fearon, A. M., Twin, J., Dahlstrom, J. E., Cook, J. L., Cormick, W., Smith, P. N., Scott A

Rheumatology International


Fisher, A. A., Martin, J., Srikusalanukul, W., Smith, P.N.

Clinical Medicine Insights: Geriatrics

Aims: To estimate age- and sex-specific incidence rates and time trends of post-stroke hip fracture (HF) in the Australian Capital Territory (ACT) and to present projections of future post-stroke HF incidence in Australia until 2051.


Results: Over the study period among 1784 stroke survivors HF was recorded in 61 (3.42%) subjects (40 women and 21 men), indicating a HF incidence rate of 6.31 per 1000 stroke person-years. The standardized annual post-stroke HF incidence rate (per 100,000 person-years) in women was 1.7 times higher in men (18.9 vs. 11.1 per, p=0.008), and in the oldest group (.80 years) compared to aged 60-69 years (47.54 vs. 4.73) and 4 times higher for men (26.65 vs. 6.50). Post-stroke HF occurred on average within the first 2.3 years, about 2 times more often in women aged ≥ 75 years (p = 0.033) and in survivors after an ischaemic stroke (p = 0.052), but age per se did not affect the time to HF. During the 11-year period the incidence rates of post-stroke HF increased annually in total by 17.9%.

Conclusions: Post-stroke HF is relatively common, prevalent in women and occurs on average within 2.3 years after the stroke. The incidence of post-stroke HF in elderly people is decreasing. However, because of population ageing and increasing number of stroke survivors, the absolute number of post-stroke patients sustaining a HF and their proportion among the total HF population could be expected to increase.
An in vivo comparison of the orientation of the transverse acetabular ligament and the acetabulum

Griffin, A. R., Perriman, D. M., Bolton, C. J., & Smith, P. N.

Journal of Arthroplasty

Aligning the acetabular component with the Transverse Acetabular Ligament (TAL) to ensure optimal anteversion has been reported to reduce dislocation rates. However, to our knowledge in vivo measurement of the TAL angle has not yet been reported in a large cohort of normal hips.

CT scans of 218 normal hips were analyzed. The TAL and four acetabular rim anteversion angles were measured (superiorly to inferiorly) relative to the anterior pelvic plane.

The mean TAL anteversion angle was 20.5° ± 7.0°, and the acetabular rim angles from superior to inferior were 11.0° ± 12.9°, 19.9° ± 8.8°, 20.9° ± 6.2° and 25.1° ± 6.2° respectively. Both the TAL and the acetabular rim were significantly more anteverted in females than in males.

The TAL anteversion angle was comparable to the predominant orientation (central rim section) of the native acetabulum while the superior acetabulum was comparatively retroverted and the inferior was relatively more anteverted.

A fast and robust technique for 3D–2D registration of CT to single plane X-ray fluoroscopy degeneration.


Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization

The application of 3D–2D image registration can be enormously helpful for different clinical purposes, such as image-guided surgery and the kinematic analysis of bones in knee and ankle joints. A limitation of this approach is the need to calculate the voxel values in the 3D volume for every iteration of the registration procedure prior to generating a digitally reconstructed radiograph. In this paper we propose a new multi-phase 3D–2D image registration algorithm which uses partial 3D volumes to estimate out-of-plane rotations.

In our proposed algorithm, only one full 3D update is used to generate a 2D projection during the registration procedure. Experimental results show that our proposed method can provide a registration accuracy similar to the commonly used approach which employs 3D updates at every iteration. As a result of reducing the number of 3D updates, the proposed approach reduces the time required to carry out the registration by a factor of 10–20 without any accompanying loss of registration accuracy.

An early intervention programme had no detectable influence on the health status of people with musculoskeletal injuries following road traffic crashes

Littleton, S. M., Hughes, D.C., Poustie, S.J., Robinson, B.J., Neeman, T., Smith, P.N., Cameron, I.D.

Injury

Aim: To compare the health status of people with minor injuries from road traffic crashes that are exposed to an early, active intervention programme (intervention group) with those receiving usual care (control group) over a 12 month period.

DESIGN: Prospective comparative study using sequential cohorts.

Subjects: People presenting to hospital emergency departments with mild to moderate musculoskeletal injuries following road traffic crashes.

Main Outcome Measures: Physical Component Score (PCS) and Mental Component Score (MCS) of the Short Form 36 (SF–36) health status measure; Hospital Anxiety and Depression Scale (HADS) and the Functional Rating Index (FRI) recorded immediately post-crash, at 6 months and at 12 months after injury.

Results: There were 95 participants allocated to the control group and 98 allocated to the intervention group. Participants were enrolled at a mean of 9.3 days following the crash. There were no significant differences in baseline health measures between the groups. Apart from a small improvement in anxiety for the intervention group, there were no significant differences in health status between the groups. Twenty percent of participants in the intervention group received treatment from external healthcare providers that was inconsistent with the recommendations of the intervention programme.

Conclusions: The intervention programme failed to result in a clinically significant improvement in health outcomes compared with usual care. There is some evidence to suggest that the intervention had some psychological benefits, as evidenced by the small improvement in anxiety levels. Limited adherence, frequent use of co-interventions, or other factors (such as intervention content or intensity) may have reduced its effect.
Hamstring strain injuries (HSIs) are the most prevalent injury in a number of sports, and while ACL injuries are less common, they are far more severe and have long-term implications. Given the high incidence and severity of these injuries, they are key targets of injury preventive programs in elite sport. Evidence has shown that a previous knee injury (including ACL injury) increases the risk of HSI; however, whether the functional deficits that occur after HSI result in an increased risk of ACL injury has yet to be considered. In this clinical commentary, we present evidence that suggests the link between previous HSI and increased risk of ACL injury requires further investigation by drawing parallels between deficits in hamstring function after HSI and in women athletes, who are more prone to ACL injury than men athletes. Comparisons between the neuromuscular function of the male and female hamstring has shown that women display lower hamstrings-to-quadriceps strength ratios during isokinetic knee flexion and extension, increased activation of the quadriceps compared with the hamstrings during a stop-jump landing task, a greater time required to reach maximal isokinetic hamstring torque, and lower integrated myoelectrical hamstring activity during a sidestep cutting maneuver. Somewhat similarly, in athletes with a history of HSI, the previously injured limb, compared with the uninjured limb, displays lower eccentric knee flexor strength, a lower hamstrings-to-quadriceps strength ratio, lower voluntary myoelectrical activity during maximal knee flexor eccentric contraction, a lower knee flexor eccentric rate of torque development, and lower voluntary myoelectrical activity during the initial portion of eccentric contraction. Given that the medial and lateral hamstrings have different actions at the knee joint in the coronal plane, which hamstring head is previously injured might also be expected to influence the likelihood of future ACL. Whether the deficits in function after HSI, as seen in laboratory-based studies, translate to deficits in hamstring function during typical injurious tasks for ACL injury has yet to be determined but should be a consideration for future work.

Squeaking arising from a ceramic-on-ceramic (CoC) total hip replacement (THR) may cause patient concern and in some cases causes patients to seek revision surgery. We performed a meta-analysis to determine the incidence of squeaking and the incidence of revision surgery for squeaking. A total of 43 studies including 16,828 CoC THR that reported squeaking, or revision for squeaking, were entered into the analysis. The incidence of squeaking was 4.2% and the incidence of revision for squeaking was 0.2%. The incidence of squeaking in patients receiving the Acce lode femoral stem was 8.3%, and the incidence of revision for squeaking in these patients was 1.3%.
A simple strontium phosphate (SrP) conversion coating process was developed to protect magnesium (Mg) from the initial degradation post-implantation. The coating morphology, deposition rate and resultant phases are all dependent on the processing temperature, which determines the protective ability for Mg in minimum essential medium (MEM). Coatings produced at 80 °C are primarily made up of strontium apatite (SrAp) with a granular surface, a high degree of crystallinity and the highest protective ability, which arises from retarding anodic dissolution of Mg in MEM. Following 14 days' immersion in MEM, the SrAp coating maintained its integrity with only a small fraction of the surface corroded. The post-degradation effect of uncoated Mg and Mg coated at 40 and 80 °C on the proliferation and differentiation of human mesenchymal stem cells was also studied, revealing that the SrP coatings are biocompatible and permit proliferation to a level similar to that of pure Mg. The present study suggests that the SrP conversion coating is a promising option for controlling the early rapid degradation rate, and hence hydrogen gas evolution, of Mg implants without adverse effects on surrounding cells and tissues.

The postdegradation effect of pure Mg, Mg1Y, Mg5Al, and Mg2Ca alloys on the proliferation and gene expression of human mesenchymal stem cells (hMSCs) was investigated. It was revealed that that Mg (2+) ions result in an increase in cell proliferation. However, we observed a maximum concentration (approximately 8.0 × 10(4) M) that was favourable to ATP production, above which ATP production began to decrease. In contrast to proliferation, no maximum concentration for osteogenic differentiation was observed, with increasing concentration of Mg(2+) ions resulting in an increase in osteogenic differentiation across the entire tested range. Interestingly, the Mg2Ca alloy had minimal effect on osteogenic differentiation, with Mg1Y and pure Mg having a superior effect on the proliferation and differentiation of hMSCs. This was also observed from gene expression data, where these alloys upregulated TGFβ-1, SMAD4, FGF-2, FGF-10, and BMP-2, while SOX-2, SOX-9, and TGFα were down regulated. Increased expression of TGFβ-1, SMAD4, BMPs, and COLA1 protein provided further evidence to support osteogenic differentiation and that the influence of the alloying extracts on differentiation may be via the SMAD signalling pathway.

Background: Arthritogenic alphaviruses such as Ross River virus (RRV) and chikungunya virus (CHIKV) have caused widespread outbreaks of chronic polyarthritis. The inflammatory responses in alphavirus-induced arthritis and osteoarthritis (OA) share many similar features, which suggests the possibility of exacerbated alphavirus-induced bone pathology in individuals with pre-existing OA. Here, we investigated the susceptibility of osteoblasts (OBs) from OA patients to RRV infection and dissected the immune mechanisms elicited from infection.

Methods: Primary hOBs obtained from trabecular bone of healthy donors and OA patients were infected with RRV. Infectivity and viral replication were determined using flow cytometry and plaque assay, respectively. Real-time PCR was performed to determine expression kinetics of type I interferon (IFN)-related immune mediators and osteotropic factors.

Results: OA hOBs showed enhanced RRV infectivity and replication during infection, which was associated with delayed induction of IFN-β and RIG-I expression. Enhanced susceptibility of OA hOBs to RRV was associated with a more pronounced increase in RANKL/OPG ratio and expression of osteotropic factors (IL-6, IL-1β, TNF-α and CCL2) in comparison to RRV-infected healthy hOBs.

Conclusions: Delayed activation of type I IFN-signalling pathway may have contributed to enhanced susceptibility to RRV infection in hOBs from OA patients. RRV-induced increases in RANKL/OPG ratio and expression of osteotropic factors that favour bone resorption, which may be exacerbated during osteoarthritis. This study provides the novel insight that osteoarthritis may be a risk factor for exacerbated arthritogenic alphaviral infection.
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A/Prof Alex Scott  
Dept of Physiotherapy, University of British Colombia
Interested in Studying with TORU in 2015?

TORU is affiliated with the Australian National University and works closely with UNSW@ADFA and University of Canberra as well. Prospective higher degree students are encouraged to consider possible research opportunities at TORU in 2015. Contact TORU or prepare a 1-2 page research proposal for TORU to consider. TORU is committed to progressing research in trauma and orthopaedics, and to developing young researchers.