This year TORU is delighted to announce the development of a new laboratory (PC2 lab) in Building 10 of the Canberra Hospital. Professor Paul Gatenby, Director of Research at the Canberra Hospital and former Dean of the ANU Medical School, has strongly supported the development of the new laboratory.

The new laboratory for TORU at the Canberra Hospital will be formally opened in November, to coincide with the Australian Orthopaedic Association ACT Branch meeting.

These two laboratories will provide avenues to access sources of tissue specimens, collaborate with orthopaedic surgeons, apply cutting-edge technology for mechanisms studies, and accommodate national and international collaborations. This structure is characterized by strong interactions between clinical and basic research.

Canberra Hospital

TORU develops new laboratory at Canberra Hospital

Retreat at ANU campus Kioloa focuses research ideas

In April 2008 the research team spent three days secluded away at ANU’s Kioloa campus on the beautiful NSW south coast. We were delighted that we could be joined by Associate Professor Paul Smith, our Director, Professor Paul Gatenby, the Director of Research at the Canberra Hospital and former Dean of the ANU Medical School, as well as the team from ADFA, Dr Heiko Timmers, Associate Professor Mark Pickering and Dr Laura Gladkis, and the orthopaedic registrars working on their M. Phil Surgery degrees. We were able to review the achievements of TORU, and our directions and vision for the future. Some key strategies were put in place for the future development of collaborations and research ideas. A huge thank you goes to Dr Tom Ward for facilitating the event.
There are a variety of methods of fixing such fractures, including bicolumn plates or locking plates. The disadvantage of plating both medial and lateral sides of the tibia is that bone is stripped, increasing soft tissue trauma and compromising bone vascular supply. In the proximal tibial it has been demonstrated that a single fixed angle plate is biomechanically inferior to bicolumn non locked plates, however, no such evidence exists for the distal tibia.

This project aims to compare the biomechanical strength of fixation of tibial plafond fractures by an anterolateral locked plate against bicolumn plates.

This project is a collaboration between TORU and materials engineer Dr Zbigniew Stachurski at the Department of Engineering at the Australian National University. The ANU has made available an Instron materials testing station for this project.

Synthetic tibiae will be used, to control for bone density, elastic modulus, size and anatomical variation. Fractures lines will be stimulated. Half will be plated with bicolumn plates, and half with locking plates. Loading protocols will include a cyclical loading protocol and a load to failure protocol. Artemis dual optical registration will record deformation and stresses in the constructs.

Dr Anil Nair has commenced research towards a Master of Philosophy (Surgery) at TORU. Anil is also continuing in the Orthopaedic Registrars training program.

**Title:** Biomechanical analysis of fracture fixation in tibial plafond fractures: Single anteromedial locked plate versus bicolumn plates

Plafond or Pilon type distal tibial fractures are caused by high-energy trauma and are often associated with significant soft tissue trauma. Complications include those due to soft tissue trauma, failure to unite due to limited vascular supply or extent of comminution, and subsidence of the articular surface and subchondral bone.

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Dr Sivashankar Chandrasekaran has commenced research towards a Master of Philosophy (Surgery) at TORU. Siva will perform this research while continuing the Orthopaedic Registrars training program.

**Title:** MRI Kinematics of the PCL Deficient Knee

Description: There is controversy surrounding the operative indications for acute and chronic posterior cruciate ligament injuries. There are contradictory conclusions on the outcome of these injuries following operative intervention.

We are conducting a prospective study comparing the kinematics of the knees of 10 healthy control subjects with 20 PCL deficient subjects. Participants will perform a simulated squat in the loaded and unloaded conditions at varying degrees of knee flexion, and the position of the knee will be captured by MRI.

In particular, we will compare the tibiofemoral contact points, and the position of the femoral flexion facet centre between the two groups. We will also examine associations between the kinematic patterns and validated functional knee scores and KT-1000 arthrometry.
Heparanase stimulates osteoblasts—Pu Han (Florina) Lo

TORU is proud to present the abstract of the recent Master of Science Thesis of Ms Florina Lo.

Millions of fractures occur every year worldwide and are a major cause of morbidity and mortality. Osteoporosis is rising as a major cause of fractures. Bone anabolic therapies for patients, who have fractures or osteoporosis have been aimed primarily at increasing and restoring bone mass as well as molecular properties. Heparanase is a heparan sulfate (HS)-degrading endoglycosidase and has been implicated in fracture repair and bone formation in mice. However, the precise role of heparanase in human bone remodeling is unknown.

Since previous results from our laboratory have shown that heparanase is present in the nucleus of human osteoblasts, this thesis aimed to investigate the role heparanase plays in bone formation by studying the effect of heparanase on human osteoblasts from patients with osteoporosis and healthy individuals. To examine this, an in vitro osteoblast cell model was developed to assess the effect of exogenous heparanase on cell proliferation, differentiation, and mineralization, using a cell count method, ATPlite assay, ALP assay, and an Alizarin Red-S (AR-S) stain method. The exposure of heparanase to cultured osteoblasts significantly increased cell density, ATP content, ALP production, and calcium mineral content in cultures, indicating heparanase stimulates osteoblast proliferation, differentiation, and mineralization.

To further elucidate the underlying mechanisms by which heparanase exerts its stimulatory effect on human osteoblasts, quantitative RT-PCR array was performed to profile the expression of 84 osteogenesis pathway related genes, while histone modifications were investigated using enzyme-linked immunosorbent assay (ELISA) and flow cytometry.

A number of genes were either up- or down-regulated by heparanase, including genes encoding bone morphogenetic proteins (BMPs), collagens, alkaline phosphatase (ALP), a variety of growth factors and their receptors, cytokines, cell adhesion molecules, and extracellular matrix (ECM) molecules as well as proteases.

The exposure of heparanase to cultured osteoblasts caused increased phosphorylation of histone H3 at S28. However, the amount of phosphorylated histone H3 at S10 or acetylated histone H3 was not altered by heparanase treatment. This result demonstrates that phosphorylation of histone H3 at S28 may contribute the stimulatory effect of heparanase on human osteoblasts.

This study suggests that heparanase possesses a stimulatory effect on osteogenesis of human osteoblasts.

New approaches to reaming for femur fractures

Long bone fractures, such as the tibia, femur are commonly fixed by intramedullary nailing. The technique was developed by Kuntschner in Germany to get WWI fighter pilots back into the air sooner.

Reaming for intramedullary nails raises intramedullary pressure and causes extravasation of medullary contents. This extravasation can result in a clinical picture of fat embolus in the lung. Clinically, fat embolism produces respiratory distress, chest pain and falling oxygen saturation levels and can be fatal, just like pulmonary embolism from blood clots, except that it is not amenable to treatment by anticoagulation. It is unclear yet how many post-operative fatalities are due to fat embolism.

TORU has been exploring methods to reduce the surge in intramedullary pressure during reaming. Initial in vitro studies demonstrated reamer designs and sharpness of tools could not reduce pressure below the critical 40mmHg. Application of suction through distal portals was more effective.

In recent in vivo studies in sheep, application of suction has demonstrated improved haemodynamic status in terms of improved PaCO2 and SaO2 at reaming and at 50 minutes following reaming. No differences were found in heart rate, MABP and PAP in the suction group. Importantly NEFA’s were significantly lower in blood samples from the sheep reamed using suction. Lung tissue showed a lower fat embolus count, and lower fat percentage in the tissue samples.

Like the human lung, sheep lungs show pathological physiological changes under the high pressures induced by reaming. By monitoring pressures, and using suction portals a surgeon can reduce the embolisation of fat during surgery and potentially offer safer and earlier definitive management to injured patients.


Dr Rachel Li, Prof Nick Glassgow and Pu Han (Florina) Lo, celebrate her graduation

The exposure of osteoblasts to heparanase results in a positive correlation with bone formation markers, up-regulation of osteogenic gene expression, and activation of histone H3 phosphorylation. Importantly, heparanase appears to play critical roles in bone formation beyond the regulation of BMP, vascular endothelial growth factor (VEGF) and ALP. Thus, heparanase holds a great potential as a new biopharmaceutical agent for the treatment of fractures and osteoporosis.

Fat emboli trapped in lung tissue during femur reaming

When suction is used, lung histology shows fewer emboli
Conference Papers


Li RW, Smith PN, Lo PH, Chen M, Freeman C. Angiogenic and osteogenic therapy in bone remodelling. Australian Pharmaceutical Science Association Conference, Canberra, December 6-9, 2008

Sample RR, Smith PN, Leditschke A, McMahon D, Chinnan NK, Li RW. Prevention of fat embolism using intramedullary suction system (ISS) on fractured long bone sheep model. ANZORS. Brisbane, November 2008

Pickering MR, Scarvell JM, Smith PN. A new technique for registration of 2D x-ray fluoroscopy to 3D CT data for the analysis of knee kinematics. ANZORS. Brisbane, November 2008

Gladkis LG, Li RW, Scarvell JM, Smith PN, Timmers. Direct characterisation of UHMWPE wear particles using atomic force microscopy. ANZORS. Brisbane November 2008

Fearon AM, Smith PN, Scarvell JM. Minimum one year outcomes and satisfaction following gluteal tendon reconstruction. 68th Australian Orthopaedic Association Annual Scientific Meeting. Hobart, October 2008

Pickering MR, Scarvell JM, Smith PN. A new technique for registration of 2D x-ray fluoroscopy to 3D CT data for the analysis of knee kinematics. 68th Australian Orthopaedic Association Annual Scientific Meeting. Hobart, October 2008


Smith PN, Thomas B, Duggan SM. The effect of co Morbidities on the hospital length of stay and post operative discharge destination of home residential elderly after a fracture of neck of femur. Aged Care Forum, ACT, May 2008


Fearon AM, Cormick W, Scarvell JM, Smith PN. 2007 Greater Trochanteric Pain Syndrome—where is the pathology? 6th Interdisciplinary World Congress on Low Back and Pelvic Pain. Barcelona, November 7-10


Gladkis L, Timmers H, Scarvell JM, Smith PN. Development of a constant load knee simulator to study wear in knee prostheses. AOA, ACT Branch Meeting. Canberra, November 2007


Lo PH, Smith PN, Freeman C, Li RW. Heparanase (HPSE) Up-regulates Human Osteogenic Gene Expression. AOA, Act Branch Meeting. Canberra, November 2007


Smith PN, Lo PH, Sample RR, Freeman C, Li RW. Heparanase (HPSE) is expressed in human osteoblasts and associated with bone diseases. AOA, ACT Branch Meeting. Canberra, November 2007


Journal Articles


5. Lin GD, Li RW, Myers SP, Leach DN. A Method of Selecting Plants with Anti-inflammatory Potential for Pharmacological Study. Natural Product Communications. Accepted for publishing in 2008, 3(1), 71-76


Grants Successes

TORU has been successful in the following competitive grants in 2008:

- Australian Orthopaedic Association Research Grant.
- Royal Australian College of Surgeons, CONROD Fellowship.
- Bone Growth Foundation
- Private Practice Fund of The Canberra Hospital

TORU thanks the following orthopaedic industries for their support in 2008:

- Johnson and Johnson (DePuy)
- Synthes
- Smith and Nephew
- Biomet
- Stryker

TORU Research students interpret results at John Curtin School of Medical Research
TORU's People

Assoc Prof Paul Smith, BMBS FRACS (Ortho), Director

Assoc. Prof 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. Assoc. Prof Smith is also president of the Arthroplasty Society of Australia, and Clinical Director of Orthopaedic surgery at the Canberra Hospital.

Assoc. 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 recently been honoured by The Knee Society, receiving the inaugural John N Insall Travelling Fellowship in knee surgery and has been appointed as Associate Professor in Orthopaedic Surgery at the ANU Medical School. Assoc. 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: smithadmin@co.net.au

Dr Damian McMahon, MB BS FRACS, Director

Dr McMahon is the Director of the Shock Trauma Service, Senior Staff Specialist in surgery and Co-Director of the Trauma and Orthopaedic Research Unit at the Canberra Hospital. In addition, Dr McMahon is the Director of the Clinical Skills Centre and Senior Lecturer in surgery at the Australian National University Medical School.

Dr McMahon received his medical and surgical training in Melbourne where he specialised in Trauma Surgery. He became Trauma Service Coordinator at Preston and Northcote Community Hospital in 1993 and from 1994 until 1997 he worked as Trauma and Surgical Critical Care Fellow and Attending Traumatology surgeon at the Hospital of the University of Pennsylvania, Philadelphia PA. In 1997 Dr McMahon took up his position as co-joint academic/senior staff specialist at The Canberra Hospital.

Dr McMahon was instrumental in establishing the Snowy SouthCare Helicopter retrieval service to service the region with medical and specialist support. He achieved recognition for the hospital as the first accredited Trauma Centre in Australia. Contact: damian.mcmahon@act.gov.au

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

Dr Li obtained a Bachelor of Medicine from China Medical University in 1982 and worked as a surgeon and senior infectious diseases specialist at China Medical University from 1982-1996. Dr Li’s Master project was on immune responses to viral infection. She led a number of clinical trials in anti-viral and anti-inflammatory drugs and successfully transferred an intellectual property to pharmaceutical industry. Dr Li completed her PhD in pharmacology at Southern Cross University in 2002 and gained her postdoctoral research experience in molecular pharmacology in the University of Hawaii School of Medicine. Dr Li returned to Australia in 2006 joining TORU and has established TORU laboratory with a focus on osteoimmunology. She has developed a range of laboratory capabilities to determine the effects of therapeutic, surgical and physio-therapeutic treatments on biomedical markers using human primary cell culture and large animal models.

In addition to her research work, Dr Li is an Adjunct Associate Professor at the University of Canberra teaching and supervising the students in Master of Pharmacy Program. Contact: rachel.li@anu.edu.au
Dr Jennie Scarvell, PhD, Clinical Research Co-ordinator

B(App)Sc Physiotherapy (Sydney), Grad Cert Higher Ed, (Canberra) Cert Health Economics (Monash) PhD (Sydney).

Dr Scarvell began her involvement with the Trauma and Orthopaedic Research Unit in 2000 when she commenced a PhD on the kinematics of the knee using Magnetic Resonance Imaging and the process of degeneration using anterior cruciate ligament injured knees as a model.

Dr Scarvell taught Musculoskeletal and Paediatrics units of the inaugural Master of Physiotherapy program at the University of Canberra 2004-2007.

Dr Scarvell is a registered physiotherapist, actively involved in the profession. Dr Scarvell has been convener of the APA ACT Branch Symposium the past 3 years.

Dr Scarvell took up the position of Clinical Research Co-ordinator in November 2007. Dr Scarvell's research interests include many aspects of Orthopaedics and Rheumatology, particularly knee kinematics and the development of osteoarthritis in the injured knee.

Exciting projects currently in train include collaborations with UNSW@ADFA in 2D to 3D image registration for kinematic analysis, and in measurement of wear in polyethylene.

Jennie is adjunct Senior Lecturer at ANU and at Uni of Canberra.

Contact: jennie.scarvell@act.gov.au

Ms Roxanne Sample, B.Human Movt Sc. (Hons).

Roxanne gained her degree from Southern Cross University in 2003. Her research was an investigation into colostomum supplementation in the elderly. Roxanne has been managing administration and events coordination for the unit, including the Australian Orthopaedic Association ACT Branch meeting each November. Roxanne manages the pelvic fractures database and joint implant retrievals.

Contact: Roxanne.sample@act.gov.au

Gail Cox


Contact: Gail.cox@act.gov.au

Mingming Chen

BSc, PhD. Mingming has commenced this year as a lab assistant working with Dr Rachel Li in tissue culture at JCSMR.

Ben Serpell

Is travelling and working for Gloucester Rugby club, and we look for forward to his return in June 2009

TORU’s people: Post graduate students

Ms. Angela Fearon, BAppSc(Physio), MPhysio

Ms Fearon completed her Bachelor of Physiotherapy at Lincoln Institute of Health Sciences in 1986 and her Master’s degree in 2001. She has been a clinical Physiotherapist since 1986 and established her own practice in Canberra. Ms Fearon’s PhD thesis looks at tendinosis, enthesopathy and Greater Trochanteric Pain Syndrome.

Contact: angie.fearon@anu.edu.au

Ms Diana Perriman, BAppSc (Physio), MSc.

Diana attained her physiotherapy degree from Sydney University in 1982 and her Master’s degree at the University of East London (UK) in 1995. Her Masters research investigated the effect of orthotics on the hemiplegic ankle using electrogoniometry. Diana’s PhD thesis at ANU involves an investigation of kyphotic thoracic posture in normal adults and people with stroke. Diana is an NHMRC Dora Lush Biomedical scholar.

Contact: diana.perriman@anu.edu.au

Susannah Littleton

M.Public Health, Cert. Critical care nursing, RN. Susannah has been a member of TORU through her work on the Accident Care Evaluation study, sponsored by the NRMA ACT Road Safety Trust. This year Susannah commenced her PhD program, on the clinical pathways for people with musculoskeletal injuries following road accidents.

Contact: susannah.littleton@acec.biz

Anil Nair MBBS

Anil is enrolled in the Master of Philosophy (Surgery) program at ANU, and is on the College of Surgeons Orthopaedic Program.

Sivashankar Chandrasekaran, MBBS.

M.Sports Med.

Siva is undertaking a Master of Philosophy (Surgery) at TORU through ANU, and is on the College of Surgeons Orthopaedic Program.

More on Anil and Siva’s research on page 2.

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The capital's centre for musculoskeletal research

TORU Laboratory Capacities

The Missions of TORU Laboratory are:

To provide research and educational environments for students, orthopaedic registrars and researchers via promoting active, multidisciplinary cooperation among orthopaedic surgeons, rheumatologists, engineers, pathologists, biologists, mathematicians and physicists.

To develop novel surgical modalities and therapeutic concepts by conducting translational medicine that bridge basic science and clinical practice.

TORU Laboratory provides research environment for medical students, orthopaedic registrars to be exposed to the relevant basic sciences in their training periods. TORU Laboratory has developed a line of research projects and collaboration with other universities. TORU laboratory current research focuses are

Therapeutic research on
- Bone remodeling and fracture healing
- Osteoblast and osteoclast regulation
- Skeletal muscle ischemia
- Chronic inflammatory diseases of obese, diabetes and osteoarthritis

Molecular mechanisms of inflammatory and degenerative joint diseases
- Osteoarthritis
- Rheumatoid arthritis

- Osteoporosis

Novel biomarkers for diagnosis and drug target of joint diseases
Novel surgical modalities (experiment on large animal models)

Pathway focused gene expression and signaling
- Angiogenesis
- Apoptosis
- CYP450
- Drug metabolism
- Inflammatory cytokines
- PI3
- Obesity and diabetes
- Osteogenesis

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