Dr Rachel Li’s interest in Osteo-molecular pharmacology

In 2006 I arrived in Canberra to work with Associate Professor Paul Smith and set up a lab with focuses on osteo-molecular pharmacology, prevention of osteoporosis and management of fractures.

Our lab is currently researching the osteogenic effects of heparanase on bone formation, in collaboration with Professor Chris Parish and Dr Craig Freeman at JCSMR. These are the pioneers in research of heparanase in angiogenesis, so that osteogenosis is a radical turn.

ACT Bone Bank reaches landmark 550 donations

The ACT Bone Bank was established in 2002 to meet the needs for bone grafting material in Canberra and the surrounding region. Prior to this, bone was transported from the Melbourne or Queensland Bone Banks. Increases in elective orthopaedic surgery in Canberra and more complicated emergency procedures increased the demand for a local and urgent supply of bone graft material.

A bone graft is similar to a blood transfusion. A piece of bone is taken from one person and after careful screening and processing, it is made available to another person. Bone can be donated when a person has a total hip replacement, as the femoral head is removed and would otherwise be disregarded. The bone is screened for specific viral diseases, and bioburden reduced by gamma irradiation. The screening process takes 180 days.

Bone graft material is used for a variety of reasons when the patients own bone stock needs augmentation. These include surgery for bone tumours, revision of total joint replacements, massive bone loss from trauma or spinal injuries. The ACT Bone Bank is licensed by the TGA. Patients from Canberra, National Capital Private Hospital, Calvary and Calvary John James Hospital can donate bone.

Research-quality bone is donated bone that has been rejected for use as donor bone. It is still biologically safe, but may have failed one of the rigorous testing procedures or is past its use-by date.

The ACT Bone Bank Coordinator is Maria Hartley, Maria is able to consent patients wishing to donate. Maria is available to liaise with the patients and facilitate the “Medical and Social History” interview required by TGA. Maria will also come to theatre and assist with tissue retrieval. All the orthopaedic surgeons need to do is ask their office staff to email Maria patient names and contact details when booking primary THR, and mention bone banking to the patients during the consultation so patients have time to consider this as an option.
Pelvic Fractures Requiring Surgery Mainly due to Motor Vehicle Accidents

Details of pelvic fractures requiring surgery are being captured to provide insight into management and outcomes.

The Canberra Hospital Pelvic Fractures Database has been set up to record all incidences of pelvic fracture that have been treated operatively after admission to Canberra Hospital. The database is administered by a committee which comprises of A/Prof Paul Smith, Dr Jennie Scarvell and the database manager Ms Roxanne Miller.

Data has been collected retrospectively using the clinical records information system (CRIS), and goes back as far as 1998. To date, a total of 1200 patients have been admitted to Canberra Hospital with pelvic fractures and of these, data from 222 operatively treated patients have been recorded and stored in the database.

We hope to compile a comprehensive bank of information so that we can make queries about certain topics of interest. For example, we will be able to determine the most common mechanisms of injury or the most frequent locations for pelvic fracture. Also, by recording all of the operative details, we will be able to measure the most common fixation method, or even make comparisons between a patient’s functional outcome and the particular fixation method used.

We already know that motor vehicle accidents are the most common mechanism of injury for people needing surgical management of pelvic fractures, followed by falls of greater than a metre, then blunt trauma, motorbike accidents, pedestrians in accidents and falls from less than one metre, and cyclists made up small groups.

The ongoing monitoring and analysis of data on clinical indicators will ultimately enable better clinical management of patients and will result in improved systems, outcomes and reduced complication and mortality rates.

TORU’s Research on Heparanase

TORU Lab has pioneered work in heparanase affecting joint diseases in collaboration with Professor Chris Parish and Dr Craig Freeman at JCSMR. Our initial results have been published in Arthritis and Rheumatism and the Journal of Orthopaedic Research.

Associate Professor Rachel Li was invited to chair the session on Molecular Pharmacology in the 7th International Drug Discovery Sciences and Technology Conference 2009. There A/Prof Li presented the first part of the research results on heparanase as an indicator of inflammatory disease activity. This gained a great deal of attention from people in pharmaceutical sciences.

The fact that heparanase exists in osteoblasts and is associated with osteogenesis may bring up a novel approach to pharmaceutical interventions for treating osteoporosis and preventing fractures by using heparanase as an anabolic factor or as a template to generate analogues of anabolic peptides.
How much do we ask of our knees?

Ideally, knee prostheses used in total knee replacement (TKR) surgery would last the lifetime of the recipient and allow the same range of motion of a healthy knee. Currently however, there is no consensus on which factors are the most important for prosthesis design: high flexion prosthesis allow a greater range of movement, but may be more susceptible to posterior polyethylene wear. One issue in determining the most important aspect of prosthesis design is a lack of evidence about the demands actually placed on the knee during everyday activities.

Previously, knee function and activity has been examined while subjects perform prescribed activities in a controlled environment. A study currently being undertaken by TORU research officer, Jane Wilson, will provide for the first time, information about the demands placed on the knee, outside the laboratory.

Participants are fitted with an IDEEA data recorder that has been modified to accommodate a flexible electrogoniometer. This provides a comfortable, non-invasive system for continuous monitoring of the angle, as well as rotation of the knee during a nine-hour trace of the participants’ normal, daily activities.

The study compares a group of TKR patients before and after surgery, to a group of matched control volunteers. The matched group are the same age, sex and body shape as the TKR group. A third group of twenty healthy young people aged 20-32 years have already been recruited and provide the baseline data. The coming month will see recruitment of the final four TKR participants to the study.

Results will tell us what we really ask of our knees - how much time the knee spends in a range of positions, how the knee moves during certain activities and whether this differs in TKR recipients compared to their healthy counterparts. The results will also provide an insight in to how activity and movement in the ‘normal’ knee changes with age.

Information from this research will let us predict the demands placed on the artificial joint, how these demands differ with age and gender, as well as determining how closely TKR restores normal knee function. This information will then be used to inform the design of more durable, longer lasting and ergonomic knee prostheses.

This study is proudly supported by Stryker Pty Ltd.

Building up Healthy Bone

Osteoporosis, osteoporotic fracture and non-union remain a national health concern. Therefore the continuous quest for better prevention and treatment regarding disease pathology and molecular pharmacology remains high on the agenda. Mingming Chen, a recipient of an NHMRC PhD scholarship (2009-2012) and the first PhD student in the TORU laboratory, is currently working on her thesis. A major goal of the thesis is to develop, optimize and investigate synergistic effects of our new formula on bone remodeling and fracture healing. Mingming Chen presented some of the results at the Australian Orthopaedic Association ACT Branch Annual Scientific Meeting held in November 2009 and was awarded “Best Paper and Overall Performance in the Year 2009”.

Mingming’s paper was entitled “Development of osteoclasts cell culture using poly-L-lysine coated cover slip” by Mingming Chen, Paul Smith, and Rachel Li

A model of co-cultured osteoblasts (A) and induced osteoclasts (B) in co-culture has been established in TORU to study the anti-osteoporosis drugs.
Conference Papers


Li RW*, Smith PN, ‘Heparanase –as a Drug in Bone Remodeling.’ The 7th Annual Congress of International Drug Discovery Science and Technology, Shanghai, China, Oct, 2009 (Invited speaker and section chair).


Journal Articles  (selected papers 2010-2008)


Fearon AM, Scarvell JM, Cook JL, and Smith PN 2010. Does Ultrasound Correlate with Surgical or Histologic Findings in Greater Trochanteric Pain Syndrome? A Pilot Study *Clinical Orthopaedics & Related Research* Published first on line Nov 2009.


**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

**A/Prof Rachel Wei Li, MD, PhD. Laboratory Research Co-ordinator**

A/Prof 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. Her 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. In 2002 A/Prof Li completed her PhD in pharmacology at Southern Cross University and gained her post-doctoral research experience in molecular pharmacology in the University of Hawaii School of Medicine.

A/Prof 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, she is an Adjunct Associate Professor at the University of Canberra teaching and supervising the students in Master of Pharmacy Program.
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’s recent research studied the incidence of osteoporosis in people over 40 with minimal trauma fractures. A career as a clinical physiotherapist lead Dr Scarvell to a PhD on knee kinematics and the role of aberrant motion in degenerative change using a model of ACL injury. Exciting projects currently in train include collaborations with Mark Pickering at UNSW@ADFA in imaging registration for kinematic analysis to provide 3D modelling of motion, and with Heiko Timmers for radioisotope labelling of polyethylene to measure wear in total knee replacement. Dr Scarvell was one of the inaugural Master of Physiotherapy program staff at the University of Canberra 2004-2007. She wrote and taught curriculum, and developed the clinical education program. Dr Scarvell is a registered physiotherapist and convener of the APA ACT Symposium. She is an affiliate Senior Lecturer at University of Canberra and at ANU.

Contact: jennie.scarvell@act.gov.au

Roxanne Miller B.Human Mvtt Sc. (Hons). Roxanne gained her degree from Southern Cross University in 2003. Her research was an investigation into colostomy supplementation in the elderly. Roxanne manages the pelvic fractures database and joint implant retrievals. Contact: Roxanne.miller@act.gov.au

Jane Wilson BAppSc (hons). Jane has a background in Ross River virus pathology and viral arthritis, sports science and human physiology. Jane is conducting the Journey knee and the Stryker Triathlon knee projects. Contact: jane.wilson@act.gov.au

Mingming Chen BSc, PhD. Mingming is an NH&MRC scholar in osteoclast and osteoblast coculture at JCSMR and TCH labs. Contact: Mingming.Chen@anu.edu.au

Jonathon Slater Jonathon is an MBBS/PhD student at ANU. His thesis looks at side impact motor vehicle collisions.

Dr Yongliang Yang Dr Yang is a PhD student in Orthopaedic Surgery at Shandong University, China. Dr Yang is here on a prestigious Chinese government sponsored scholarship. A/Prof Rachel Li, our lab unit coordinator, has been key in organisation of this project and we hope this will be the first of many such visiting scholars. The scholarship is primarily a research one but allows Dr Yang to have a day a week clinical exposure as well. Dr Yang attends theatre with consultants who are operating.

Contact: aurel.serpell@anu.edu.au

Corinne Coulter B(App)Sc, Physiotherapy. Corinne is doing her research Master’s degree with an RCT to explore efficient and effective rehabilitation post total hip replacements. Contact: Corinne.coulter@act.gov.au

Dr Jennie Scarvell, Clinical Research Coordinator

Angela Fearon BAppSc(Physio), MPhysio. Angie completed her Bachelor of Physiotherapy at Lincoln Institute of Health Sciences and her Master’s degree in 2001. She has been a clinical Physiotherapist since 1996 and established her own practice in Canberra. Ms Fearon’s PhD thesis looks at tendinosis, enthesisopathy and Greater Trochanteric Pain Syndrome. Contact: angie.fearon@anu.edu.au

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 ergonomiometry. Diana’s PhD thesis at ANU involves an investigation of kyphotic thoracic posture in normal adults and people with stroke. Diana is an NH&MRC Dora Lush Biomedical scholar. Contact: diana.perriman@anu.edu.au

SiZhu (Josie) Zhao BBioTech, MBioTech. SiZhu is an Mphil student of TORU. She gained her bachelor of biotechnology from China and Master of Biotechnology from ANU. SiZhu has a background in allergy and immunohistochemistry. She

Suzanna Littleton M/Public Health, Cert. Critical care nursing, RN. Suzanna has been a member of TORU through her work on the Accident Care Evaluation study, sponsored by the NRMA ACT Road Safety Trust. Suzanna's PhD program explores clinical pathways for people with musculoskeletal injuries following road accidents. Contact: susannah.littleton@acec.biz

Jonathon Slater Jonathon is an MBBS/PhD student at ANU. His thesis explores clinical pathways for people with musculoskeletal injuries following road accidents. Contact: susannah.littleton@acec.biz

Kylie McKay is the Office Manager for TORU. Contact 02—6244 3858 Kylie.mckay@act.gov.au

Ben Serpell, BHSc, B(App)Sc OT (hons), B(App)Sc Human Movement (hons). Ben’s PhD asks “Is there a relationship between hamstring and quadriceps strength, and the knee joint kinematics which predict anterior cruciate ligament injury?” We look forward to collaboration with the AIS and UC.
This year in Trauma and Orthopaedic Research Unit four medical students are conducting research projects as part of their medical degrees.

Jon Anderson is analysing digital x-rays to measure the difference in the orientation of the acetabulum in standing and lying films. This pre-operative planning influences the alignment of the acetabular implant. This is compared to the orientation of the acetabular implant post-operatively. This work has implications for pre-operative planning and clinical decision making, and also for post operative outcomes for total hip replacement patients in terms of dislocation risks and prosthesis wear.

Emily Sikorski is delving into the retrieved implants library to catalogue the collection and collect data. She will explore reasons and mechanisms for failure, and compare these to clinical findings and findings of the National Joint Replacement Registry reports.

Stefanie Orlick is working alongside of Research Officer Jane Wilson on the Stryker knee study. This study is entitled: Electrogoniometric analysis of Knee Range of Movement before and after Knee Replacement. This sub-study is entitled “Knee kinematics: how does our knee motion change as we age?” Stefanie will explore questions such as what are the demands on the knee in osteoarthritis and in healthy aging? Stefanie uses an electrogoniometer, which is applied to the side of the knee, to collect knee motion data using a 9 hour monitoring trace.

Phil Jaksa looking at “Outcomes post total hip replacement with 3rd generation acetabular cementing technique. 10 year follow up study.” This includes clinical outcomes data and radiological data for patients who received total hip replacements in 1998 – 2000 with the 3rd generation acetabular cementing technique perfected by Associate Professor Paul Smith.

The five medical student projects from last year’s class were all completed, and all without exception received Higher Level Performance awards for clear, well balanced representation of their studies, clearly identified aims, limitations, and presentation. Congratulations!

Three papers have already been submitted for publication from that work, and two more have gone on to form the first part of larger prospective studies.