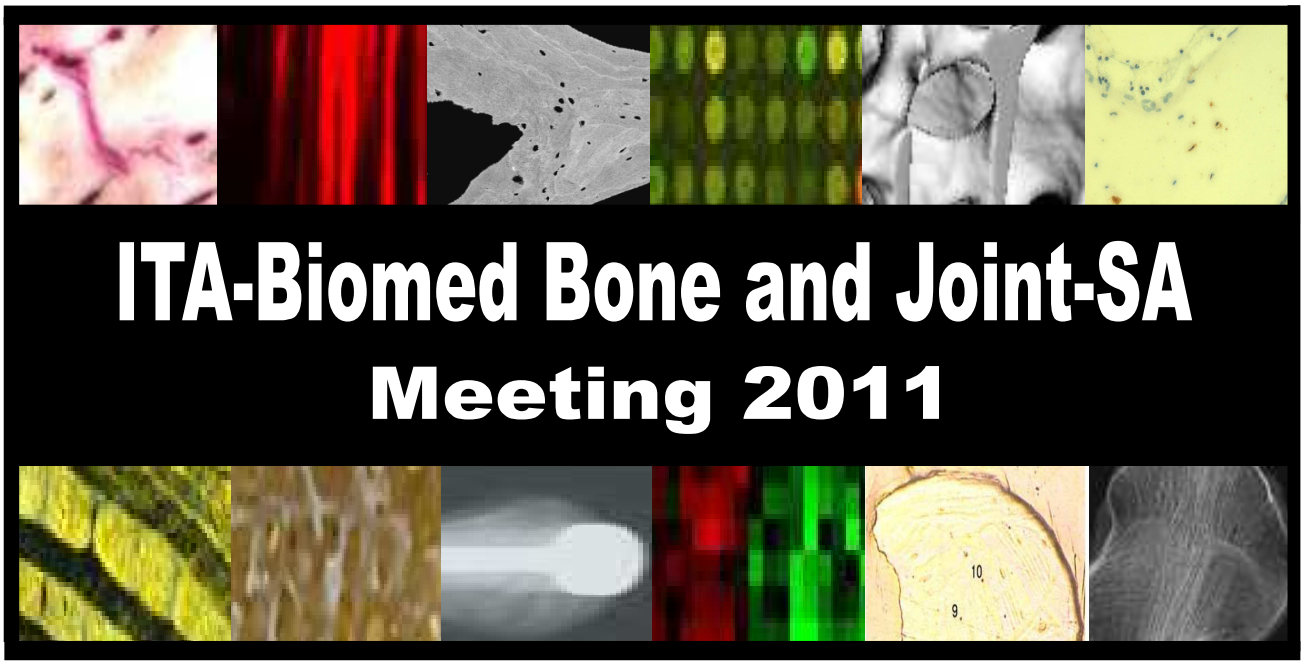

ITA-Biomed Bone and Joint-SA Meeting 2011

Promoting opportunities for scientific and commercial collaboration in biomedical bone and joint research between Italy and South Australia

21-23 February 2011

Adelaide South Australia

The University of Adelaide, Union House

Government of South Australia

Department of the Premier and Cabinet

Embassy of Italy
Canberra

BJRL

SA PATHOLOGY

ITA-Biomed Bone and Joint-SA Meeting

Adelaide, South Australia, 21-23 February 2011

The meeting organisers would like to acknowledge the support received from:

Financial Support

Government of South Australia
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SA PATHOLOGY

Australian & New Zealand Orthopaedic Research Society

Adelaide Bone and Joint Centre

From the chairman of the organising committee

Dear delegates,

Welcome to all the speakers that have accepted the invitation to attend this meeting. In particular welcome to our guests and speakers from Italy. I hope that all delegates will find their attendance a stimulating research experience and that it presents new research opportunities for collaboration with researchers in South Australia.

The **aim** of this meeting is to promote bilateral scientific and commercial collaboration in biomedical bone and joint research between leading Italian, South Australian and Australian researchers and research organisations. As leaders of research groups covering areas of biomedical research focussing on bone and joint research, you have been invited to explore your combined research capabilities, through this face-to-face networking opportunity, to promote bilateral international collaboration.

The meeting has been planned for a selected audience of about 25 participants, playing key roles in their area of research interest. Selected Italian research group leaders and scientists have been invited, along with selected research group leaders and scientists from South Australia and Australia (SA Pathology, Royal Adelaide Hospital, Women's & Children's Hospital, The University of Adelaide, Flinders University, University of South Australia, University of Sydney). We also have the participation of industry representatives from Xradia (Pleasanton, CA, USA), who will present to the audience the state of their R&D programs, and their vision or opportunities for collaboration.

The **topics** include:

- orthopaedics (fracture fixation and prevention),
- biomaterials and nanomaterials,
- multiscale imaging of bone,
- biomechanical testing,
- tissue repair,
- genes in bone disease
- animal models of bone disease.

The meeting is structured to enable two days of keynote presentations and networking sessions, followed by a third day dedicated to guided visits to research centres and laboratories in Adelaide.

Bone and joint diseases are a major concern with a high impact on the Australian and European (Italian) health systems. This is an excellent opportunity for bilateral and reciprocal insight into the latest advances and state-of-the-art in this area of research. The outcomes for Australia and Italy are potentially of high impact on a scientific, technological and commercial level. This has presented a unique opportunity for a meeting that brings together scientists and industry to foster bilateral international collaboration in the global search for identifying therapeutic targets and to create new prevention and treatment strategies in bone and joint disease. An aim of this meeting is to build on the Internationalisation of South Australia's (Australia's) research endeavours and the establishment of an effective platform for applying for international research funding.

I would like to thank the sponsors that have made this meeting possible. From the start, this meeting has been enthusiastically supported by the Department of the Premier and Cabinet, Government of South Australia (Prof Nicola Sasanelli) and by the Scientific Attache' at the Embassy of Italy in Australia (Prof Oscar Moze). Importantly, it is the sponsorship from the following: Department of the Premier and Cabinet (DPC), Government of South Australia; Embassy of Italy in Australia; Bone and Joint Research Laboratory (BJRL), SA Pathology; Ian Wark Research Institute, University of South Australia; Italian Chamber of Commerce of Adelaide (ICCI); Flinders Medical Devices and Technology (FMDAT, Flinders University); The University of Adelaide; and Xradia, that has made this meeting possible.

The meeting has been endorsed by SA Pathology, the Australian & New Zealand Orthopaedic Research Society (ANZORS) and the Bone and Joint Centre Adelaide, South Australia. Finally, I would like to thank Dr Egon Perilli for his enthusiasm for this project, who working with myself, Prof Nicola Sasanelli, Prof Oscar Moze, Dr Julia Kuliwaba, Dr Ian Parkinson and the clerical support of Ms Lisa Barrie, has coordinated the arrangements to make this meeting possible.

I wish you all a successful meeting and I am most disappointed that I will not be able to attend.

Kind regards,

Professor Nick Fazzalari
Head of Bone and Joint Research Laboratory
SA Pathology,
Frome Road, Adelaide 5000 SA, Australia

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Organising Committee

Prof Nick Fazzalari, Bone and Joint Research Laboratory, SA Pathology, Adelaide, Australia

Dr Egon Perilli, Bone and Joint Research Laboratory, SA Pathology, Adelaide, Australia

Adj Prof Nicola Sasanelli, Department of the Premier and Cabinet, Government of South Australia, Adelaide, Australia

Prof Oscar Moze, Scientific Attaché, Embassy of Italy, Canberra, Australia

Ms Cristina D'Alessandro, "Formit" Technology Transfer Foundation, Naples, Italy

Government of South Australia
Department of the Premier and Cabinet

Embassy of Italy
Canberra

BJRL
SA PATHOLOGY

Bone and Joint Research Laboratory (BJRL),
SA Pathology, Adelaide
Head: Prof Nicola L Fazzalari

The Bone and Joint Research Laboratory (BJRL, SA Pathology, Adelaide, South Australia, Australia) undertakes and coordinates research projects that represent collaborative efforts by BJRL faculty, clinical faculty including orthopaedic surgeons, and industrial sponsors. The Laboratory has a wide range of cross disciplinary expertise that includes project planning, study design, protocol development, Good Laboratory Practice capabilities, laboratory based tissue and biological techniques, data collection and analysis, and manuscript preparation.

The core focus of the BJRL is the analysis of tissue-level morphology during development, growth and ageing together with changes associated with adult onset bone disease such as osteoarthritis and osteoporosis. Biomaterials and tissue engineering are studied in the context of osteoporosis and osteoarthritis.

The laboratory is located in SA Pathology and is closely affiliated with other institutions including the Hanson Institute, Royal Adelaide Hospital, The University of Adelaide, and has strong collaborative research programmes with the other two universities of South Australia, the University of South Australia and Flinders University, as well as national and international research linkages.

Our Mission:

To carry out internationally competitive research that leads to a better understanding of bone and joint structure and function as well as practical patient outcomes for treatment of musculoskeletal disease.

The laboratory has cross disciplinary expertise and access to a wide range of state-of-the-art research facilities to assess the structure and quality of the bone. These include a histology laboratory, in vivo and in vitro micro-computed tomography (micro-CT) facilities, scanning electron microscope facility, confocal microscopy and an image analysis facility, a biomechanical testing facility, molecular biology, cell culture and biochemistry laboratories.

Our Aims:

- To undertake basic scientific research with strong relevance to clinical needs of patients.
- Maintain a strong focus on internationally competitive research.
- Ensure that researchers have access to necessary research infrastructure.
- Apply to government and non-government bodies to fund research.
- Support and mentor research staff, especially early career researchers.
- Support diagnostic staff development (medical, scientific, technical), and development of laboratory diagnostic capabilities in the Directorate of Surgical Pathology.
- Support teaching and training of honours, masters and PhD students.

Research Overview:

Bone quality: Matrix mineralisation; in house developed quantitative backscattered SEM-technique, which allows visualisation and quantification of degree of matrix mineralisation in human bone samples. Microdamage; in house developed novel tissue staining technique together with confocal microscopy, to study the extent, morphology and repair of microdamage of human bone.

Bone gene expression: To gain better understanding of the perturbed complex regulatory networks and molecular pathways in osteoarthritis and osteoporosis. Microarray and real time RT-PCR analyses are used to study differential gene expression.

Bone structure:In 3D; a range of micro-CT scanners, from in vitro to in vivo systems (Skyscan models 1174, 1076, 1072), are used for 3D non-destructive investigation of bone structure, for human and animal studies. After imaging of bone specimens, mechanical testing and tissue mineralisation can be assessed. In 2D; histological slides can be prepared including immunostaining.

Bone mechanical testing: Tissue level; crack propagation in human cortical bone, focusing on the effects of crack orientation, and the presence of pre-existing fatigue-induced microdamage. Organ level; compressive strength on lumbar vertebral bodies.

Intervertebral discs: Studies in our lab have demonstrated degenerative changes to the disc structure and function are linked to changes within the bone of the adjacent vertebral bodies.

Biomaterials: Engineered tissue scaffolds, resorbable bone implant screws, osseointegration.

Our advances are making a significant contribution towards the development of therapies that will slow the progression of these prevalent musculoskeletal diseases and delay if not obviate the need for expensive surgery associated with joint replacement.

Senior staff members:
Prof Nick Fazzalari (Head), Dr Julia Kuliwaba, Dr Ian Parkinson, Dr Egon Perilli

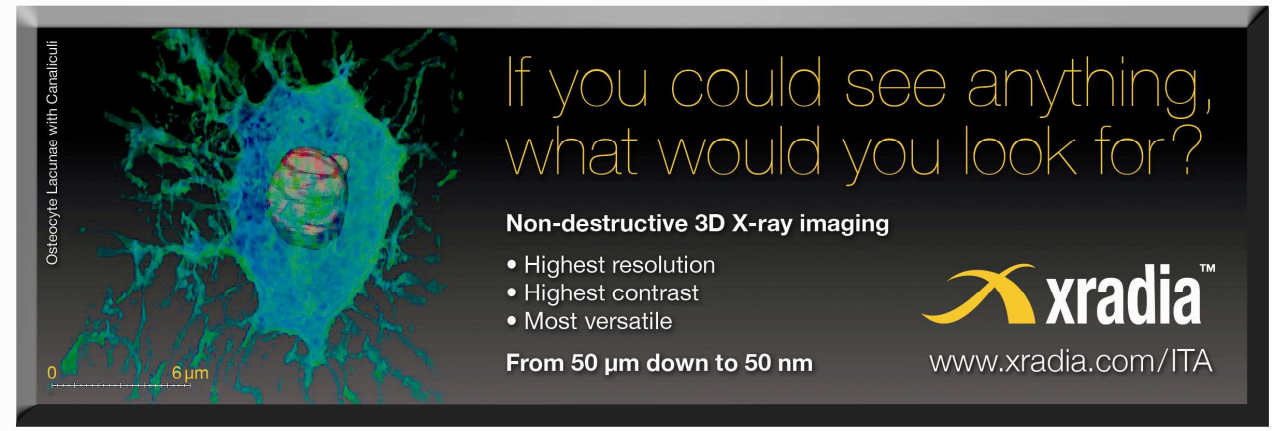
Link:

http://health.adelaide.edu.au/school_medsci/research/aandp/boneandjointimvs/

http://www.hansoninstitute.sa.gov.au/research/group.php?GroupID=4

Industry Sponsor

Topic 3: Multiscale imaging of bone: Sponsored by Xradia, USA



Meeting Program

Venue: The University of Adelaide, North Terrace Campus, L4, Union House

Monday 21 February 2011

9.00 - 9.15am	**Oscar Moze**, Scientific Attaché Embassy of Italy, Canberra, Australia Welcome speech (15min)
9.15 - 9.30am	**Nicola Sasanelli**, Australia Department of the Premier and Cabinet, Government of South Australia, Adelaide, South Australia, Australia Welcome speech (15min)
9.30 – 9.45am	**Ian Parkinson,** Australia Bone and Joint Research Laboratory, SA Pathology and Hanson Institute, Adelaide, South Australia, Australia Welcome speech (15min)

Morning session: 9.45am – 12.15pm

Topic 1: Orthopaedics (fracture prevention, fixation, healing)

9.45 - 10.15am	**Bruce K Foster**, Australia *Physeal surgery*. Women's and Children's Hospital, Department of Orthopaedic Surgery, North Adelaide, South Australia, Australia (20min talk + 10min discussion)
10.15 - 10.45am	**Mellick Chehade**, Australia DLRSA in the assessment of fracture healing University of Adelaide, Orthopaedic Trauma Consultant, Royal Adelaide Hospital, Adelaide, South Australia, Australia SA (20min talk + 10min discussion)
10.45 - 11.05am	*Morning tea break (20min)*

Topic 2: Biomaterials and nanomaterials

10.05 – 11.45pm	**Mario Malinconico**, Italy *Biodegradable composites for bone regeneration* Institute of Polymers Chemistry and Technology, National Research Council (CNR), Pozzuoli (Naples), Italy (30min talk + 10min discussion)
11.45 -12.15pm	**Clive A Prestidge**, Australia *Nanostructured materials: from bioimplants to drug delivery systems* Ian Wark Research Institute, University of South Australia, Mawson Lakes, Adelaide, South Australia, Australia (20min talk + 10min discussion)
12.15 – 1.00pm	*Lunch break (45min)*

Afternoon session: 1.00 - 4.00pm

Topic 2: Biomaterials and nanomaterials

1.00 - 1.30pm **Hala Zreiqat**, Australia
Newly developed nanocomposite scaffolds for effective skeletal tissue integration and vascularisation
Tissue Engineering & Biomaterials Research Unit, Biomedical Engineering, School of AMME J07 and Bosch Institute, University of Sydney, New South Wales, Australia
(20min talk +10min discussion)

1.30 – 2.00pm **Robert D Short**, Australia
The importance of material surface chemistry on cell attachment, spreading and growth, and relevance in tissue engineering
Mawson Institute, University of South Australia, Adelaide, South Australia, Australia
(20min talk + 10min discussion)

2.00 – 2.20pm *Afternoon tea (20 min)*

Topic 3: Multiscale imaging of bone: Sponsored by Xradia, USA

2.20 – 3.00pm **Fabio Baruffaldi**, Italy
Multiscale modelling technology to predict the risk of bone fracture: the osteoporotic virtual physiological human project
Laboratorio di Tecnologia Medica, Istituto Ortopedico Rizzoli, Bologna, Italy
(30min talk + 10min discussion)

3.00 – 3.30pm **Ian H Parkinson**, Australia
Micro-CT Imaging: Towards the clinic
Bone and Joint Research Laboratory, SA Pathology and Hanson Institute, Adelaide, South Australia, Australia
(20min talk + 10min discussion)

3.30 – 4.00pm **Tiffany Fong**, USA
Application of Advanced Multiscale 3D X-ray Microscopy in the Study of Osteocyte Lacunar Properties
Xradia, Pleasanton, USA
(20min talk + 10min discussion)

4.00 - 5.00pm ***Networking session, wine and nibbles***

5.00pm ***Closure of the 1st day of the meeting***

Tuesday 22 February 2011

Morning session 9.00am – 12.30pm:

Topic 4: Biomechanical testing of bone

9.00 - 9.30am	**Karen J Reynolds,** Australia *Medical device research and development in South Australia* Flinders Medical Devices & Technologies, Flinders University, Adelaide, South Australia, Australia (20min talk + 10min discussion)
9.30 -10.00am	**John J Costi,** Australia *Multi-scale biomechanical testing and modeling of biological tissues* Biomechanics and Implants Research Group, School of Computer Science, Engineering & Mathematics, Flinders University, Adelaide, South Australia, Australia (20min talk + 10min discussion)
10.00 - 10.20am	*Morning tea break (20min)*
10.20 -10.50am	**Egon Perilli**, Australia *Strength of whole human vertebral bodies: prediction using BMD assessed via DXA and microarchitecture via micro-CT* Bone and Joint Research Laboratory, SA Pathology and Hanson Institute, Adelaide, South Australia, Australia (20min talk + 10min discussion)
10.50 -11.20am	**Nico Voelcker,** Australia *Mechanical and material quality of fragile bone* School of Chemical and Physical Sciences, Flinders University, Adelaide, South Australia, Australia (20min talk + 10min discussion)

Topic 5: Tissue repair

11.20 – 12.00pm	**Francesco Grassi**, Italy *Novel strategies in bone and cartilage repair* Laboratory of Immunorheumatology and Tissue Regeneration, Rizzoli Orthopaedic Institute, Bologna, Italy (30min talk + 10min discussion)
12.00 -12.30pm	**Cory J Xian**, Australia *Bone growth regulation, injury repair, growth defects and prevention* Sansom Institute for Health Research, School of Pharmacy & Medical Sciences, University of South Australia, Adelaide Australia (20min talk + 10min discussion)
12.30 -1.15pm	*Lunch break (45min)*

Afternoon session 1.15 -4.15pm

Topic 6: Genes in bone disease

1.15 -1.55pm **Simone Cenci**, Italy
New homeostatic mechanisms and molecular targets against osteoporosis and multiple myeloma
San Raffaele Scientific Institute & Università Vita-Salute San Raffaele, Milano, Italy
(30min talk + 10min discussion)

1.55 -2.25pm **Julia Kuliwaba**, Australia
Molecular histomorphometry of human bone tissue: insights into the pathogenesis of osteoporosis and osteoarthritis
Bone and Joint Research Laboratory, Directorate of Surgical Pathology, SA Pathology and Hanson Institute, Adelaide, Australia
(20min talk + 10min discussion)

2.25 -2.55pm **David Findlay**, Australia
The cells and molecules involved in pathological bone loss
The University of Adelaide, Discipline of Orthopaedics and Trauma, Royal Adelaide Hospital, North Terrace, Adelaide South Australia, Australia
(20min talk + 10min discussion)

2.55 – 3.15pm *Afternoon tea break (20min)*

Topic 7: Working with animal models of human disease in Adelaide

3.15 - 3.45pm **Tim Kuche**l, Australia
Large Animal Models of Human Disease – facilities at the IMVS for Research and Translational orthopaedic projects
Veterinary Service Division, Large Animal Research Imaging Facility (LARIF), IMVS/SA Pathology, Adelaide, South Australia, Australia
(20min talk + 10min discussion)

3.45pm ***Closure of the meeting***

4:00-5.00pm **Laboratory visits: Adelaide Microscopy**,
University of Adelaide
Host: John Terlet

7.00pm ***Meeting Dinner***
Regattas Bistro, Adelaide Convention Centre
North Terrace, Adelaide South Australia 5000
7:00pm, Welcome Reception
7:30pm, Dinner

Wednesday 23 February 2011

Laboratory visits: 8.30am - 4.30pm

8.30 - 9.30am	**Bone and Joint Research Laboratory**, SA Pathology, Frome Road, RAH site Hosts: Dr Ian Parkinson, Dr Julia Kuliwaba, Dr Egon Perilli
09.30 -10.15am	**Cell and Molecular Laboratory,** SA Pathology, Frome Road, RAH site Host: Prof David Findlay
10.15 - 11.00am	*Transfer to Ian Wark Research Institute*
11.00 - 12.15pm	**Ian Wark Research Institute** University of South Australia - Mawson Lakes campus Host: Prof Clive Prestidge
12.15 - 1.00 pm	*Lunch (45min)*
Option 1	Ian Wark Research Institute to **Flinders University** Hosts: Prof Karen Reynolds, Dr John Costi Host: Prof Nico Voelcker
Option 2	Ian Wark Research Institute to **Large Animal Research And Imaging Facility** (LARIF, Gilles Plains) Host: Dr Tim Kuchel
4.30pm	***Closure of laboratory visits***
4.30pm-5.00pm	***Transfer to Hotel in Adelaide***

Abstracts

O1

Physeal Surgery

Foster BK

Women's and Children's Hospital, Department of Orthopaedic Surgery, North Adelaide, South Australia, Australia

20% of all bony injuries occur at the level of the growth plate or physis in children. Up to 20% may lead to alterations of growth with subsequent shortening and or angular deformity. Accurate reduction has been the main method of prevention of these events.

Inter-positional materials have also been used to prevent arrest and also reverse such deformity when it occurs. Fat is the most widely used in clinical practice. Our experimental data suggest that up to 20% of the area of the physis post injury can be successfully reversed by the mechanism of establishing a non union at the level of the physis.

There is limited ability of the growth plate to repair. It does so with fibro cartilage rather than cartilage capable of endochondral ossification.

Mechanistic studies in our Laboratory have centred on understanding the process of healing the injured physis. There are 3 phases; the inflammatory response, the infiltrative response and then boney repair. The long term aim is to prove a method of mobilising the mesenchymal stem cells to provide an intrinsic repair mechanism. Understanding the cascade of events post injury is the key to future progress.

O2

DLRSA in the assessment of fracture healing

Mellick Chehade

University of Adelaide, Orthopaedic Trauma Consultant, Level 4 Bice Building, Royal Adelaide Hospital, Adelaide, South Australia, Australia

O3

Biodegradable composites for bone regeneration

Malinconico M[1], Laurienzo P[1], Gomez d'Ayala G[1], Calandrelli L[1], Oliva A[2]

[1] *Institute of Polymers Chemistry and Technology, CNR, Via Campi Flegrei 34, 80078 Pozzuoli (Naples), Italy*
[2] *Department of Biochemistry and Biophysics, Faculty of Medicine, Second University of Naples, Via L. De Crecchio 7, Naples, Italy*

Osteoinductive materials are strongly searched in reconstructive surgery. Polymer based composites are ideal candidate, as they couple the ease of processing of polymers (by melt or by injection and hardening) with the mechanical reinforcement of fillers, once interfacial adhesion is assured. Moreover, an appropriate choice of the filler may enhance the bone regeneration activity, through cell adhesion or osteoinduction. In this respect hydroxyapatite and calcium sulphate are good candidates. As organic binder, a wide choice of different polymers is possible: biocompatible and biodegradable natural polymers such as polysaccharides and, in more recent years, biocompatible and biodegradable synthetic polyesters are normally employed, with processing methodologies which depend on the intrinsic properties of the polymers (paste injection or injection molding).
In the present communication, after briefly summarizing recent literature concerning modification and applications of these materials, several recent developments of biocomposites containing silica nanoparticles or calcium sulphate intended for bone regeneration are reported. The composites are characterized with respect to their chemical-physical and mechanical properties. Their biocompatibility and capacity to induce the osteoblastic phenotype in human bone marrow mesenchymal stem cells have been assessed. A focus will be given on two particular systems based on either natural or synthetic biopolymers with different biofillers: alginate/chitosan blends with calcium sulphate and poly(ε-caprolactone) with silica nanoparticles.

O4

Nanostructured materials: from bioimplants to drug delivery systems

Prestidge CA, Skinner WM, Thierry B, Griesser, H, Ralston, J

Ian Wark Research Institute, University of South Australia, Mawson Lakes, South Australia, Australia.

This presentation will give an Ian Wark Research Institute's (The Wark) perspective on the application of nanostructured materials for biological applications. The Wark is a nationally and internationally recognised centre of excellence in particle and material interfaces and its nanomaterials research focuses on novel biomaterials, bio-diagnostics and drug delivery systems. We specialise in advanced physicochemical methods for biomaterial preparation and characterisation, surface functionalisation of bio-implant materials, hybrid nanomaterials for the improved delivery of therapeutic molecules and tools for nanomedical applications.

In addition to our expertise and extensive equipment portfolio for surface analysis, particle/nanoparticle characterisation and probing biointerfaces, we act as the nodes for "Nano Characterisation" and "Nano Fabrication (Micro-fluidics)" in the National Collaborative Research Infrastructure Scheme (NCRIS), and are extensive users of the Australian synchrotron for characterisation of nano-biomaterials. These state of the art facilities are key in our extensive national and international collaborative network.

The Wark's capabilities in biomaterial characterisation and nano-biomaterial development will be overviewed in this presentation. Case studies will be presented, including: surface functionalisation to improve bone biomaterial performance, anti-bacterial coatings, nano-porous particles as biomaterials, hybrid Lipoceramic nanomaterials for drug delivery and microfluidic devices for cell capture and diagnosis.

O5

Newly developed nanocomposite scaffolds for effective skeletal tissue integration and vascularization

Zreiqat H

Tissue Engineering & Biomaterials Research Unit, Biomedical Engineering, School of AMME J07 and Bosch Institute, University of Sydney, NSW 2006, Australia.

Clinically available modalities for treating large bone defects are limited in their success. Significant challenges remain in the regeneration of biomechanically functional bone tissue. There is increasing demand for synthetic materials that can regenerate lost or diseased bone. Ideal scaffolds for skeletal tissue regeneration need to have the combined properties of being biocompatible, porous, interconnective degradable, osteo-inductive, osteoconductive, mechanically compatible with bone and bioactive rendering them suitable for treating large bone defects in load-bearing applications. Using the basis of “functional tissue engineering” we have developed novel nanocomposite 3D scaffolds with clinically relevant attributes for skeletal tissue and vascular ingrowth. These scaffolds exhibited mechanical properties and elasticity that are superior to the clinically available ones.
This presentation will highlight some of our newly developed ceramic composite scaffolds for effective skeletal tissue integration and vascularization. Innovative biodegradable and bioactive biomaterials for bone augmentation will provide a promising route towards individualized bone tissue regeneration.

O6

The importance of material surface chemistry on cell attachment, spreading and growth, and relevance in tissue engineering

Short RD

Mawson Institute, University of South Australia, Adelaide, Australia

In serum-containing cell culture medium, an adsorbed layer of protein forms at the solid-liquid interface. These proteins dictate whether cells attach, spread and proliferate/differentiate. The identification of how specific surface chemistries control protein adsorption, cell attachment, spreading and growth *in vitro* has been the subject of significant recent investigation, and is highly relevant to tissue engineering *ex vivo*. Over fifteen years at the University of Sheffield (UK) and the University of South Australia, molecularly-engineered surfaces fabricated by plasma polymerisation and the self-assembly of monolayer (SAMs) have been employed. These platforms have enabled us to further our understanding of how factors at the molecular level, for example, the availability of a specific surface functional group, can influence the nature of the protein layer formed, and direct events such as cell attachment, spreading and growth *in vitro*. SAMs can provide surfaces of defined chemistry (1) and are useful as model systems, but cannot been used for example in routine cell culture, nor applied to biomaterials. Plasma polymerisation (2, 3) may be used to coat most substrata, irrespective of geometry. However, whilst plasma polymerisation may be used to deposit surfaces containing predominately one chemistry, for example carboxylic acid, these surfaces also contain a 'background' concentration of alcohol and ether functionalities. Plasma copolymerisation (employing a functionalised monomer and a hydrocarbon) may be used to control the density of a specific functionality (3). In this presentation, it will be shown that surface acid functional groups promote 'osteoblast-like' cell attachment and spreading to tissue culture plastic and, semi-quantitatively (1), the relationship between surface acid concentration and cell spreading is demonstrated. ELISA experiments show how key adhesive proteins bind to acid surfaces, retaining the protein's 'functionality' (4). Work with bone cells is extended to other cell types, particularly embryonic stem (ES) cells (3), and it is shown how plasma polymerised surfaces can also be used to control the degree of cell spreading and thus maintain the capacity of ES cells for self-renewal (through many passages). It is shown how plasma surfaces may be integrated into emerging technologies that may play a pivotal role in the next generation of devices used in tissue engineering and regenerative medicine (5).

(1). Daw, R. et al, *J. Mater. Chem.* 1998, *8*(12) 2583-2584
(2). Robinson, D.E. et al., *Advanced Materials*, 2008, 20, 1166-1169 (2008); Walker, R et al., *Langmuir* 2009 25 (8), 4243-4246
(3) Wells, N et al., *Biomaterials* 2009, 30 (6): 1066-1070
(4) N A Bullett, et al., *Mater Chem.* 2003 13, *(7),* 1546-1553 (2003).
(5) Priest, C et al., *Lab-on-a-Chip*, DOI: 10.1039/C0LC00339E (2010)

O7

Multiscale modelling technology to predict the risk of bone fracture: the Osteoporotic Virtual Physiological Human project.

Baruffaldi F, Baleani M, Bordini B, Cristofolini L, Schileo E, Stea S, Taddei F, Viceconti M

Laboratorio di Tecnologia Medica, Istituto Ortopedico Rizzoli, Bologna, Italy.

The Istituto Ortopedico Rizzoli is the main Italian institute of orthopaedics since its foundation in 1896, obtaining in 1981 the special status of "Scientific research hospital" from the Italian Health Ministry. The institute presents a close integration between healthcare and scientific research, which is carried out in nine laboratories at the institute employing a staff of 250 including doctors, biologists and technicians.
The mission of the Laboratorio di Tecnologia Medica is to develop, to validate and to transfer of innovative technologies to the orthopaedic clinical practice. The lab has a staff of approximately 40 people including senior and junior researchers, as well as graduate and undergraduate students.
The most representative and challenging research running in the lab is within the frame of the European project: the Osteoporotic Virtual Physiological Human (VPHOP, FP7-ICT-2008-223865, http://www.vphop.eu). The **aim** of VPHOP project is to develop multiscale modelling technology based on conventional diagnostic imaging methods that makes it possible, in a clinical setting, to assess for each patient individually, the strength of his/her bones, how this strength is likely to change over time, and the probability that he/she will overload his/her bones during daily life. The occurrence of an osteoporotic fracture is a complex multiscale event, depending on:

- the daily loading spectrum, which includes para-physiological overloading events is defined at the Body level;
- the fracture event occurs at Organ level;
- the bone elasticity is due to the tissue, which is defined at the Tissue level;
- the composition and the morphology of the bone tissue changes over time due to the metabolic activity, which is defined at the Cell activity level;
- the strength of the tissue is due to the molecular composition of the bone matrix, which is defined at the Constituents level.

By creating a patient-specific hypermodel – a model composed by many sub-models, each describing the relevant phenomena taking place at one of the many dimensional scales involved – we will be able to solve this complex problem.
Among the **expected results** for the clinical practice we can mention the patient-specific prediction of:

- the risk of femoral or vertebral fracture under low energy loading;
- the probability of developing micro-fractures at the tissue level;
- the changes over time due to the evolution of the disease and to the pharmacological treatment;
- the changes in risk due to interventional augmentation.

The VPHOP project started in September 2008 and a first hypermodel prototype made its first run in 2010. The four VPHOP hospitals are now applying it on a small cohort of patients to assess the value of VPHOP technology in a real-life clinical setting.
The Laboratorio di Tecnologia Medica (www.ior.it/tecno) is the project co-ordinator, and contributes to the VPHOP project with many different scientific competences in medical imaging, biomechanical and biological testing and modelling. The lab has a long tradition in international projects and it is open to collaborative research in the orthopaedic field.

O8

Micro-CT Imaging: towards the clinic

Parkinson IH[12]

[1] *Bone and Joint Research Laboratory, SA Pathology and Hanson Institute, Adelaide, SA, Australia.*
[2] *Discipline of Anatomy and Pathology, University of Adelaide, Adelaide, SA, Australia.*

Advances in CT-based imaging technology have resulted in convergence between laboratory-based imaging and clinical imaging, such that the ability to fully resolve all structural elements in bone without excessive radiation exposure to the patient is almost achievable. *Ex vivo* investigations of bone, at spatial resolutions below 30 microns, enable the structure and material properties to be investigated, non-destructively; hence the sample is available for further investigations. The ability to measure descriptive bone parameters at multiple scales, in the same sample, enables complex mechanistic models of the behaviour of bone under loading to be formulated.

Early work involved quantitative histological studies on samples from osteoporotic and osteoarthritic patients, which has contributed to the characterisation of cancellous bone structure in both diseases. With the availability of CT-based imaging to laboratories, our laboratory has been active in implementing 3D quantititative protocols for use in the study of osteoporosis and osteoarthritis to enable convergence between *ex vivo* and *in vivo* imaging technologies. Recent work has centered on utilising high-resolution micro-CT imaging, mechanical testing and finite element modeling to develop models for the prediction bone strength.

O9

Medical Device Research & Development in South Australia

Reynolds KJ

Flinders Medical Devices & Technologies, Flinders University, Adelaide, South Australia, Australia.

As researchers, industry and governments strive to improve the quality of life of our communities, the importance and impact of collaboration is clear. Development of new medical devices typically requires skills across many disciplines such as biology, engineering, materials science, and the relevant medical specialties. The Flinders Medical Devices & Technologies (FMDAT) research cluster brings together approximately 50 researchers and clinicians engaged in medical device research. The FMDAT cluster has dedicated facilities for product development and product testing, including: mechanical and electronic laboratories, 3D rapid prototyping and biomechanical testing facilities, clinical simulation laboratories, and surgical facilities for animal model evaluations. The co-location of Flinders Medical Centre and close links with the Repatriation General Hospital enhance collaboration in the medical space and provides additional access to resources and the ability to undertake clinical trials.

While university groups such as FMDAT have a rich resource of highly trained specialists, engagement with industry can be problematic (particularly in Australia) due to the small-to-medium enterprise nature of the industry participants, and the lack of a clear path to engagement. Companies report reluctance to approach research organisations due to pre-conceived notions that research is expensive, inefficient, and does not lead to outcomes that can be applied. As a result, medical devices are often developed through an ad-hoc process, which is largely inefficient and unfocussed.

In 2007, Flinders University led a successful bid to the State Government of South Australia for the establishment of the Medical Device Partnering Program (MDPP) in South Australia. The MDPP represents a structured approach to industry engagement and collaborative product development from early stage concepts right through to manufactured products. The MDPP has brought together a network of stakeholders in the medical device development process, facilitated new, targeted partnerships between research organisations and companies, and provided practical assistance in taking ideas closer to the market. Through its unique approach, the MDPP acts as an agent for ensuring the success of certain projects by careful project selection and development. Since the program was launched in 2008, this unique collaboration of researchers, industry, clinical end-users and government has provided assistance to almost 50 medical device companies and inventors, with benefits to researchers including increased collaboration and opportunities for research funding.

In her presentation, Professor Reynolds will discuss the importance of collaboration, and highlight some recent medical device developments at Flinders University, with a focus on those relevant to bone.

O10

Multi-scale Biomechanical Testing and Modeling of Biological Tissues.

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Our group's long-term program of research is focused on developing a fundamental understanding of how biological tissues function across their hierarchical scales (nano-, micro- and macro-scopic), to develop improved computer models and experimental techniques to facilitate rigorous study of normal and diseased tissues, bones, ligaments and joints to improve human health and implant longevity.

We have been developing tools and collaborations to facilitate this research. Over the past two years, collaboration between Flinders University and The University of Adelaide has resulted in the development of a six degree of freedom hexapod robot, which represents one of the most state of the art testing systems in the world. The hexapod robot allows joints/soft tissues/materials to be subjected to complex patterns of loading (e.g. bending + twisting + shearing) to simulate the physiological forces experienced in the body. The hexapod robot has a high precision of about 1 micron (0.001 mm) and is able to deliver high forces in excess of 20 kN to study joint and implant stability and strength.

We have a number of research programs and collaborations currently underway and these are briefly summarized below:

Nano-tensile properties of collagen type I using Atomic Force Microscopy. This work is fundamental to providing an understanding of collagen at the nano-scale, which, together with the biomechanical properties of bundles of collagen at the micro-scale, will allow the development of robust computational models of the macro-scopic function of soft tissues.

Five parameter viscoelastic model of disc behavior in each of six degrees of freedom loading. In this work, we are using a viscoelastic model that is being fitted to experimental data to extract parameters that can then be used to predict the dynamic/cyclic loading behaviour of the disc, which is then validated against additional experimental dynamic data.

Development of a micro-FE model of disc lamellae and the role of translamellar bridges. A macroscopic FEA model of the disc is being developed and validated against experimental data, and this model will be used to provide the boundary conditions on a single element, which forms the basis for the micro-FE model.

Measurement of internal disc strains using stereoradiography techniques to improve understanding of how discs become injured during certain lifting activities. We will be using the hexapod robot to subject discs to thousands of repetitive loading cycles in combinations of forward and side bending and twisting. Advanced techniques to measure the internal displacements inside the disc will be used to provide a unique insight into how the disc tissue deforms as herniation injuries are created.

We strongly believe in and welcome collaboration, with the majority of our research programs built on this principle. A research group in isolation may be limited in the full spectrum of resources and expertise available, and collaboration allows a multi-disciplined approach to be adopted to more thoroughly, and broadly examine key research questions.

O11

Strength of whole human vertebral bodies: prediction using BMD assessed via DXA and microarchitecture via micro-CT

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Osteoporotic vertebral fractures constitute a serious health problem, which is increasing in incidence as the average population age rises. Current clinical imaging modalities, such as Dual Energy X-ray Absorptiometry (DXA) do not provide an individualised prediction of the risk of fracture. Significant relationships exist between bone strength and bone mineral density (BMD) derived from DXA; clinically, BMD of the spine is assessed from posterior-anterior (PA) projections. The diagnostic sensitivity of DXA in the spine may be improved by assessing BMD from lateral projections.

Trabecular bone elements have thicknesses in the order of 100 µm, and imaging techniques capable of resolving these thin elements are critical for accurate assessment of these bone structures. Until recently, bone cores had to be extracted and examined, due to limitations of the high resolution imaging techniques which were not able to examine samples bigger than 15-20 mm in length. Newly developed microcomputed tomography scanners (micro-CT) are capable to accommodate specimens of the size of human vertebral bodies. The BJRL has recently published a protocol for quantitative imaging in 3D of whole human vertebrae by micro-CT, at high resolution (18µm isotropic voxel size). Due to its non-destructive imaging nature, this allows for subsequent mechanical testing of the vertebrae, for assessing vertebral strength at an organ level.

This ongoing study is a national collaboration between three research centres in Australia. The aim was to assess BMD by lateral-projection DXA and bone volume (BV) by micro-CT, and to assess their respective capability to predict vertebral body strength determined experimentally. Eight human cadaver spines (age at death 78±10 years) were immersed in a water bath and scanned by DXA in PA and lateral projections; BMD for L2 and L3 vertebrae was determined. The L2 and L3 vertebrae were then dissected from each spine and entirely scanned by micro-CT. BV was calculated over the micro-CT trabecular bone volume of the entire vertebral bodies.

The findings highlight the higher capability of BMD assessed using lateral-projection DXA, compared to PA-projection DXA, to predict vertebral strength and variations in BV, and provide the basis for further exploring the clinical application of lateral-projection DXA analysis.

Future aims: It is suggested that a number of factors including trabecular bone microarchitecture and bone tissue properties (bone quality, i.e. bone turnover, matrix mineralisation, osteocyte lacunae), contribute significantly to bone strength. A future aim of our laboratory is to expand this investigation, by examining human vertebral bodies before and after mechanical testing to failure, in the search of variations in microstructure and bone quality being related to local failure of the bone.

O12

Mechanical and Material Quality of Fragile Bone

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Osteoporosis represents a major socioeconomic burden. Measuring bone mineral density (BMD) is currently the gold standard for diagnosing osteoporosis. But it has become evident that the strength of bone is not determined only by its mass, but by the material and structural properties of its component materials, summarised as bone quality determinants. Elements of bone quality are multifactorial, including material properties such as collagen and mineral related components (i.e. calcium, phosphorous, zinc etc.). Bone is a dynamic tissue undergoing changes in its composition, structure and functional properties with aging. It has been suggested that changes in the collagen phase of bone are responsible for bone becoming more fragile, and potentially less viscoelastic with age. Bone quality is usually mentioned as an important parameter, but investigations into bone matrix material properties are rare. Hence, research and understanding of the structure and functional relationship between bone constituents and mechanical competence is of major importance, especially for the diagnosis of osteoporotic fracture risk. Recent developments of instruments capable of exploring the hierarchical nature of bone material structure and properties enabled discrete and complementary analyses providing insights into bone quality aspects of fragile bones. A limitation of most previous studies is the fact that tissue homogenate is required. A novel and distinguishing characteristic of our investigations is the use of a combination of diverse imaging spectroscopic and microscopic techniques, which enabled us to gain insights into both the spatial distribution and the relationship of the constituents, without the need of destroying the surface.

Our studies aimed to characterise the elastic and viscoelastic mechanical properties of human fragility fractured bone and normal control bones, as assessed by atomic force microscopy-based nanoindentation and correlate outcomes with bone quality related parameters afforded by X-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion mass spectrometry (TOF-SIMS) in imaging mode. The measurements were performed as a function of tissue age, based on prior backscattered scanning electron microscopy imaging of unembedded human femoral head specimen in fragility fractures and control samples.

Our data strongly suggests a relation between the quality of the bone matrix, especially with regards to the newly formed areas, and its nanomechanical competence. We have also determined an inverse relation between the sexes in the investigated samples. The results of the present study also highlight the importance of parameters such as collagen distribution pattern and phosphorous to calcium ratio in determining bone strength.

O13

Novel strategies in bone and cartilage repair

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Regenerative medicine aims at promoting tissue repair by combining growth factors, biomimetic materials and the use of progenitor cells able to give rise to a progeny of fully differentiated cells. Focus of our laboratory is to develop novel and improved approaches to regeneration of bone and cartilage. After exploiting dedifferentiated chondrocytes for treatment of cartilage lesions, we developed a ialuronan-based scaffold for preclinical studies in cartilage regeneration. Current ongoing projects for cartilage regeneration include: treatment of osteoarthritis with adipose-derived mesenchymal stromal cells (MSC) (ADIPOA European Project), development and testing of novel biomaterials as a scaffolds for chondrocyte growth and extracellular matrix synthesis; development of innovative experimental protocols for exploiting cell-based therapy into clinical practice. Bone regeneration is approached in several projects: regulation of bone cells function by the cross-talk between osteoblast/osteoclasts and T cells, development and preclinical testing of osteogenic molecules; identification of novel markers of osteogenic differentiation of MSC into mineralizing osteoblasts (i.e. Collagen XV), investigation of the role of specific transcription factors in osteogenic differentiation of MSC. A major focus of the lab is the role of inflammation in chondrocytes and bone cells impairment; projects are ongoing regarding chemokine regulation of chondrocytes and bone cells function as well as NF-kB-mediated pathways of cartilage degradation. Furthermore, the lab holds partnership with industries in the field of biomaterials and is involved in preclinical testing of novel osteoinductive scaffolds. An industrial research branch of the laboratory has recently been launched with the objective of translating basic research into medical products or devices.

The lab is seeking collaborative opportunities in developing animal models for the investigation of candidate genes responsible of human skeletal diseases (osteoarthritis, osteoporosis), development and testing of novel compounds for bone repair as well as collaborations for structural analysis of bone and cartilage structure.

O14

Bone growth regulation, injury repair, growth defects and prevention

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Children's bone growth and bone mass accumulation are, apart from being regulated by genetic factors and hormones, also strongly influenced by environmental and lifestyle factors such as nutrition, injuries, and medical treatments. Using in vivo, ex vivo and in vitro models and a wide range of histological, cellular and molecular techniques, our lab has been conducting research related to: (1) mechanisms of bone growth, bone mass accumulation, and nutritional regulation; (2) growth plate injury responses, repair mechanisms, and growth factor and/or stem cell-based regeneration; and (3) pathophysiology for and prevention of cancer chemotherapy-induced bone growth defects. Currently, we are examining whether some micro-nutrients can be used to positively modulate bone growth, bone mass accumulation, skeletal progenitor cells and the prevention of age-related bone loss.

The growth plate is responsible for the longitudinal growth of bones in children. Growth plate trauma is a major problem in paediatric orthopaedics as 20% of childhood bone fractures involve the growth plate, and in many cases (30%) the injured growth plate cartilage is undesirably repaired by bony tissue, causing significant bone growth defects such as limb length discrepancy and angulations. Using a rat growth plate injury repair model, we have identified different phases of injury responses and some cellular and molecular events that lead to faulty bony repair. We have also found that the infiltration of progenitor cells into the growth plate injury site may be involved in the faulty repair of the growth plate.

As another significant risk factor impacting bone growth, while chemotherapy-based cancer treatment is becoming more successful, its long-term skeletal side-effects are becoming more obvious. Intensive chemotherapy may stunt bone growth and cause osteoporosis in children. Using rat chemotherapy models, our work investigates the underlying cellular and molecular mechanisms (such as apoptosis, altered bone marrow microenvironment and skeletal cell differentiation) for chemo-induced bone growth defects and the regeneration potential of bone and bone marrow. We also aim to develop supplementary preventative treatments that will preserve bone growth and bone marrow during and after chemotherapy, and so far we have already identified some micronutrients that have some protective properties for the skeleton during cancer chemotherapy.

O15

New homeostatic mechanisms and molecular targets against osteoporosis and multiple myeloma

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Our group is based at the San Raffaele Biomedical Campus. Our research is focused on the basic cell biology of osteoclasts and plasma cells, with implications for osteoporosis and multiple myeloma, the main degenerative and tumoral diseases of bone, respectively.

Osteoimmunology and osteoclast biology. Half a billion years ago, the evolutionary invention of a mineralized endoskeleton provided jawed vertebrates with superior locomotion, predatory capacity, and protection, preparing for the evolution of higher vertebrates. The parallel appearance of adaptive immunity and the subsequent relocation of hematopoiesis to the bone marrow explains why immunity and bone share extra- and intra-cellular circuits. The field of osteoimmunology is thus a powerful framework to better understand bone biology and identify therapeutic targets. In this context, we discovered new immune-mediated estrogen-dependent mechanisms contributing to post-menopausal bone loss (1-3), including a novel skeletal role for the molecular switch of antigen presentation as a regulator of osteoclast differentiation (3,4), providing novel therapeutic targets and mouse models of spontaneous osteoporosis of biotechnological value.

The opportunity of Italian Genetic Isolates. Recent genome-wide association studies have expanded our knowledge on gene variants linked to decreased bone density, but also reinforced the notion that many more variants relevant to osteoporosis remain to be identified. Italy's peculiar history and geography generated a remarkable number of genetic isolates, which, due to homogeneous genetic background, known genealogy, and limited environmental variation, offer the statistical power to complement ongoing general population studies and define gene variants critical to skeletal health. We plan to exploit the fully collected clinical, genealogical and environmental information of the Italian Network on Genetic Isolates (5) to identify new genetic determinants of bone diseases.

Myeloma and proteostasis: turning stress against cancer. With its complex microenvironment, the skeleton is a privileged site for cancer development and homing. Multiple myeloma is an incurable plasma cell malignancy (2% of all cancer deaths) that diverts the bone environment to support tumor growth. We recently demonstrated that normal and neoplastic plasma cells experience severe proteasome stress, explaining myeloma's exquisite sensitivity to the new anti-tumoral agents proteasome inhibitors, indicating that cytotoxic stress can provide novel targets against myeloma (6-9). Parallel studies on protein homeostasis in osteoclasts reveal targets shared with myeloma cells, identifying potential therapeutic synergies. By deploying hypothesis-driven and unbiased approaches, including *degradomics* and *metabolomics*, we expect to widen our current understanding of proteostasis and stress biology in myeloma, with profound translational implications, e.g. the dissection of the as yet mysterious mechanisms whereby mammalian cells cope with proteotoxicity, adapting proteasome biogenesis or activating autophagy, of prognostic and therapeutic promise (10).

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O16

Molecular histomorphometry of human bone tissue: insights into the pathogenesis of Osteoporosis and Osteoarthritis

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Osteoporotic fractures and osteoarthritis (OA) cause significant morbidity in the middle-age and elderly population. The incidence of these musculoskeletal diseases will rise as a result of population ageing. Novel treatment strategies are needed for osteoporosis (OP) and OA; currently available OP pharmaceuticals only reduce future fracture risk by ~50%, and there are no effective treatments to prevent OA progression. Current diagnostic indicators for OP, such as low bone mineral density, do not identify all individuals at risk of fracture. The risk of fragility fracture is dependent upon bone strength, which is determined by a complex interplay of cortical-cancellous bone structural and material variables, regulated by changes in bone turnover. On the other hand, cartilage alterations are critical in OA. However, the notion that OA is characterised only by the degeneration of the articular cartilage has recently been reconsidered, as subchondral bone (SCB) alterations have been found to be involved in the early phase of the disease process. Data suggest that SCB is a driving force behind the cartilage degradation observed in OA. Human OA SCB is sclerotic, yet at the tissue level the bone is hypomineralised, has increased collagen metabolism and altered bone remodelling. Several studies have shown that patients with OA may have, apart from the local changes in the affected joints, a generalised increase in bone mass. Thus, OP and OA might be considered as opposite processes, because bone mass decreases in OP, whereas it tends to increase in OA.

The Bone and Joint Research Laboratory has a long-standing research program that is focused on elucidating the molecular mechanisms of altered bone structure and material properties in OP and OA. Our research approach involves sequential analyses of human bone tissue samples utilising complementary technologies such as real time RT-PCR, microarrays, immunohistochemistry, histomorphometry, micro-CT imaging, quantitative backscattered electron microscopy, and nanoindentation. This presentation will feature examples of how our methodological approach has revealed its power to uncover interaction or dependence between molecular and histomorphometric parameters and hence establish biologically plausible mechanisms. Study data that will be presented include: (1) candidate gene studies that have identified differentially expressed genes, involved in bone remodelling, between hip OA, OP and normal bone; (2) genome-wide microarray analyses of human bone tissue and osteoblasts that have led to the identification of several groups of genes (including regulators of osteoclastogenesis, osteoblastogenesis, bone matrix mineralisation) and pathways (TGFβ/BMP and WNT) potentially involved in OA and OP pathogenesis; and (3) our recent immuno-histomorphometry studies that are investigating the role of the osteocyte-canalicular cell network in OA and OP.

O17

The Cells and Molecules Involved in Pathological Bone Loss

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Our research focuses on pathological bone loss, which may be systemic, such as in postmenopausal osteoporosis, or focal, as seen in osteolytic bone tumours, or at sites of inflammation, or around orthopaedic joint implants. We use *in vitro* cell culture, molecular biology and animal models to investigate this important clinical problem. We seek to identify the cellular and molecular drivers of these different forms of unwanted bone loss, which is needed in order to effectively address these conditions clinically. This talk will give examples of several aspects of our work, which shed light on the cells and molecules involved in pathological bone loss, in the expectation that collaborative opportunities arise from such sharing. The first example will be our work on the role of vitamin D in bone turnover and how local production of 1,25$(OH)_2$vitamin D in osteoblasts and osteoclasts may be important as a tonic regulator of this process. The second example will be regulation of bone formation, by osteoblasts and osteocytes, by the molecule sclerostin and the molecular mechanisms that we have discovered underpinning this action of sclerostin. The third example will be some of our recent work to elucidate peri-prosthetic osteolysis. The reaction of periprosthetic tissues to polyethylene (PE) wear particles from orthopaedic implants is thought to account for much of the osteolysis associated with aseptic loosening and implant failure. While cells of the monocyte/macrophage lineage are implicated, evidence suggests that osteoblastic cells may also be affected by PE. We have investigated this possibility using human osteoblasts in a novel cell culture system, which was developed to replicate the 3-dimensional (3D) environment, in which osteoblasts are exposed to PE particles *in situ*. Effects of PE particles on human osteoblasts were explored in terms of their expression of specific genes. Human primary osteoblasts underwent differentiation in 3D culture into a mature osteocyte-like phenotype over a 21-28 day culture period, acquiring increased expression of osteocalcin, E11/gp38, DMP-1 and SOST/sclerostin mRNA. In the presence of PE, the cells increased the expression of genes associated with support of osteoclast formation and activity (RANKL, IL-8 and M-CSF) and decreased their production of bone matrix proteins (eg. type I collagen). Our results suggest that human osteoblastic cells can respond to PE directly and do so in a pro-osteoclastogenic manner, which may contribute to the osteolytic effect of PE in orthopaedic implant recipients.

O18

Large Animal Models of Human Disease – facilities at the IMVS for Research and Translational orthopaedic projects.

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The scope and scale of facilities available for Orthopaedic research was given a major boost by the NCRIS funding process. This Federal Programme, with substantial State co-contribution, saw the Gilles Plains site of the IMVS expand its services to the research community. By being a part of the National Imaging Facility (NIF), the Large Animal Research and Imaging Facility (LARIF) has access to a network of Imaging specialists around Australia. The Gilles Plains node of NIF has a 1.5T Sonata MRI, DXA and digital X-ray, Imaging Intensifiers, a soon to be installed 16 slice CT, ultrasound equipment, two large operating theatres and surgical support areas serviced by experienced theatre and anaesthetic technicians, a 45 person meeting room and offices for theatre staff. A large Animal Holding Facility which should be completed by June 2011 is adjacent to the surgical facility, and this will make LARIF a complete package for GLP or research orthopaedic projects.

The Gilles Plains site has 25 acres of paddocking for the holding of sheep or goats, configured as 22 paddocks ranging from 0.2 to 2.5 hectares. This enables groups of sheep to be held under natural conditions, with hand feeding during the summer, and a substantial green pick available during the winter/spring. There are QC-1 paddocks for projects involving imported material requiring this level of containment by AQIS. Post-surgical sheep/goats/pigs will be able to progress from indoor pen holding, to undercover pens with deep litter or soil flooring, to paddocks. Where the animals are held depends on their post-op monitoring needs, their treatment regime, and the frequency with which access to them is required for measurement purposes. On-site Veterinary services and Pathology expertise is available, and a pre-clinical team is available to assist research groups with their regulatory or animal management needs.

Projects underway include a GLP pre-clinical vertebral disc augmentation study using the IMVS developed model of disc degeneration. This project also involves a revision surgery group, and follow-up MRI and X-ray during the course of the 12 month study. Bone histopathology is key to the efficacy and safety aspects of the 36 sheep study design. Just completed is a hepatic artery embolisation drug eluting bead PK and safety study. This was an II guided surgical study and required accurate PK blood sampling, and in-depth histology for safety determination. Several new projects are being initiated by the company Surgical Research Australia from Adelaide – ranging from bone deficit studies to chondral defect interventions. An NH&MRC funded project has the LARIF team as a PI on a bone plate antibacterial coating study. Nanoparticle and unique plant based antibacterial molecules will be trialled in a 'infected wound' model. Local and interstate researchers can use LARIF on a fly-in fly-out basis, or in a more traditional way, and charges are levied to cover costs on a scale which depends upon the nature of the funding for the study. Pre-clinical work attracts the highest fees, including theatre session fees, and the lowest fees apply to competitive grant funded projects.

At present the MRI is operated by radiographers from the RAH, courtesy of the Dept of Radiology. In most cases interpretations of the images is made by members of the research team, but in some cases external consultants are used.

The value of being a part of the NIF 'family' was shown recently when a set of DTI sequences were needed to create a library of images of normal sheep brains prior to screening a transgenic sheep model of Huntingtons Disease. The combination of advice from NIF node members, Siemens applications staff, and MR/neurology researchers, has optimised the quality of data which will be available to the overseas research group.

LARIF is connected to SabreNet, part of E-research, and the intention is to have data sets available to imaging clients practically in real time, and via password access, to have all their data downloadable for analysis and presentation. DICOM files from the MR, CT, digital X-ray and DXA will in future be handled in this way.

In summary, Adelaide is fortunate to have access to such a strength in Orthopaedic research, in access to a surgical research company for translational/pre-clinical research services, and to a facility like LARIF where a surgical research one-stop-shop is available and where state of the art Imaging equipment is in place.

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