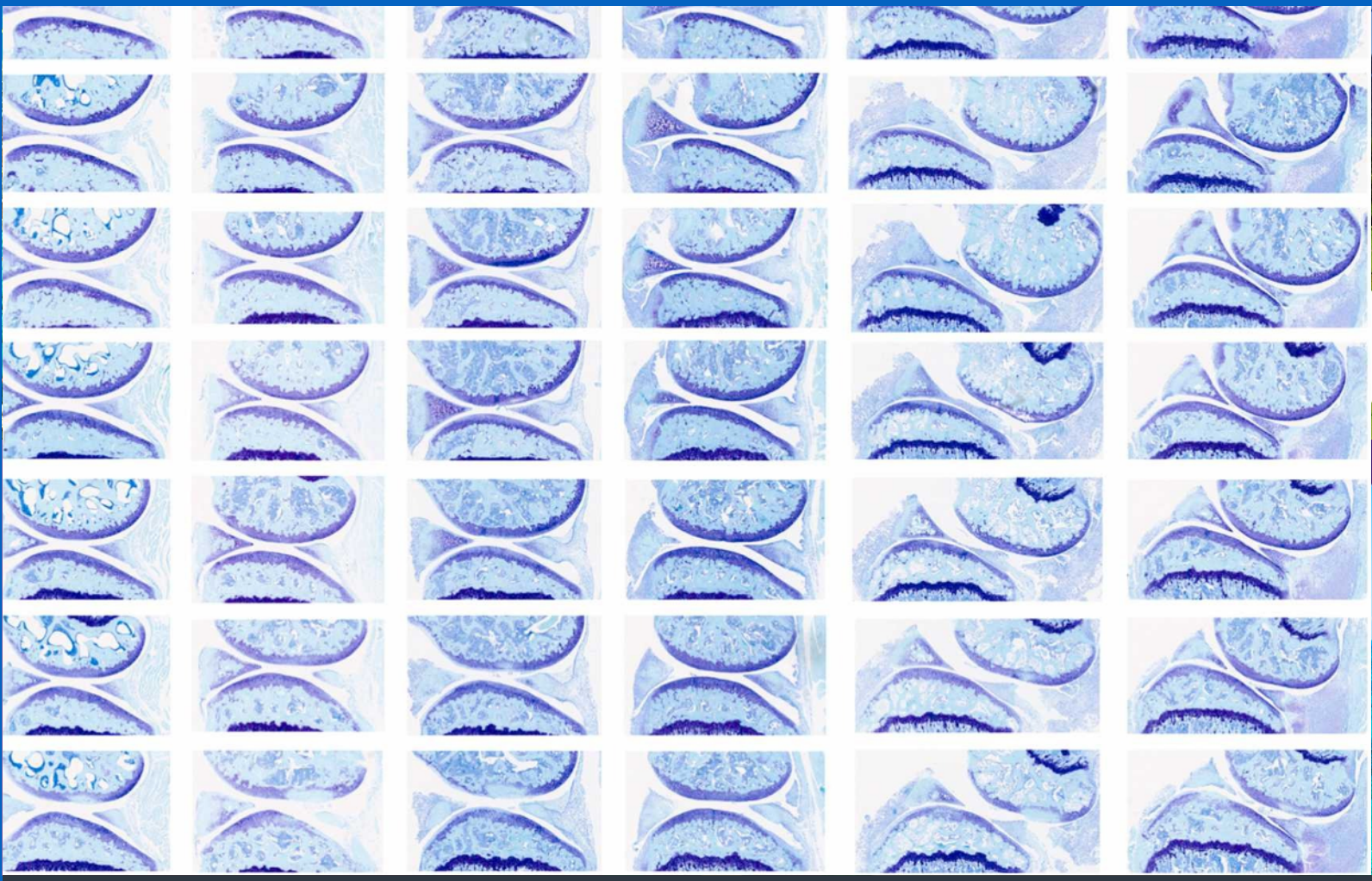
Issue 2, June 2025

ANZBMS Newsletter



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Cover image from a work by Professor Christopher B. Little, whose lab is featured in this issue, showing femoro-tibial histopathological images of mouse post-traumatic knee osteoarthritis models.
Adapted from: Haubruck et al., *Osteoarthritis Cartilage*, 2023; 31(12):1602–1611. Licensed under CC BY 4.0.

Welcome to the ANZBMS Newsletter

In this issue

Next Issue: September 2025

newsletter@anzbms.org.au
ANZBMS Early Career Investigators
@ANZBMSoc

Welcome to the second ANZBMS Newsletter of 2025!

This issue highlights the energy and achievements of our vibrant community. You'll find a thoughtful comment from ANZBMS President, Professor Mark Cooper, alongside updates from the Clinical Practice Committee and the Program Organising Committee. We also feature exciting initiatives from the ECIC co-chairs and the IFMRS HubLE, including a major platform redesign and new ECR-focused programming.

We are especially pleased to spotlight the work of Professor Christopher Little's on our cover and his lab in this issue's Lab Spotlight. The Member Publications section features important contributions from ANZBMS researchers on topics ranging from teriparatide/denosumab dual therapy for osteoporosis to the safety of immune checkpoint inhibitors on bone health, and long-term fracture prevention strategies in older women - highlighting the breadth and impact of bone research across clinical, molecular, and population levels.

We would also like to extend our warmest congratulations to Professor Richard Prince on his Officer of the Order of Australia (AO) appointment. As always, we are proud to celebrate our members' achievements and share opportunities for connection, funding, and engagement, so please feel free to let us know whenever there is something to celebrate. We hope this issue informs, inspires, and encourages continued collaboration for everyone.

Finally, if you're keen to help shape future editions or share your achievements, we'd love to hear from you—just drop us a line at newsletter@anzbms.org.au.

Happy reading!

ANZBMS Newsletter Editorial Board

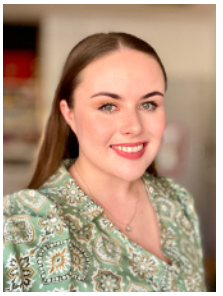

Dr Pholpat Durongbhan


Dr Haniyeh Hemmatian


Jacob Harland


Dr Kai Chen


Dr Kaitlyn Flynn


Mackenzie Skinner


Dr Chelsea Tan


Dr Karen Van

From the President

Recent events made me reflect on the phrase 'May you live in interesting times'. I see on Wikipedia that this is not actually an ancient Chinese proverb but it seems an apt phrase for our current epoch. I suspect most of us are concerned and distressed by a range of current world events. Most directly relevant to ANZBMS is the disruptions to science, scientific institutions and student education that we are seeing in countries that have traditionally been considered world leading in these areas. It is probably beyond the scope of ANZBMS and its partners to redress these issues, but our society is trying to do what it can to support our colleagues through these times. I talked in the last Newsletter about our work in hosting a regional Herbert Fleisch meeting with our regional partner societies and the International Federation of Musculoskeletal Research Societies (IFMRS). We are currently well placed to support the work of early and mid career researchers through this meeting in a way that other societies might not be able to in the current environment.

We are also working with IFMRS in other ways to support regional bone research and clinical practice. For example, through an IFMRS partnership, we are working to provide subsidised access to some of our high quality educational meetings to colleagues who work in resource limited settings in nearby countries. As a society we aim to create links and support our international colleagues rather than introducing barriers or working in isolation.

Finally, in the clinical setting we have been informed that the World Health Organization is undertaking a consultation relating to the definition of osteoporosis. We have circulated the WHO request for input to our members. As the process moves forward we intend to directly contribute to this important and timely consultation and will also work with IFMRS as part of their response.

Let me know if you have any questions about these issues, we are keen for your suggestions.

Mark Cooper
BMBCh PhD FRCP (London) FRACP, GAICD

ANZBMS President
Head of Clinical School,
Concord Clinical School
Faculty of Medicine and Health
Patyegarang Precinct

Clinical Practice Committee

The Clinical Practice Committee is pleased to share recent updates with our colleagues. A key highlight has been the successful coordination of the *Advanced Postgraduate Clinical Meeting*, held on March 15 and 16. With over 200 registrants, the event brought together clinicians from multiple medical and surgical disciplines for two days of engaging, evidence-based content and interactive case-based discussions. Feedback from attendees has been overwhelmingly positive, reflecting the relevance, depth, and practical value of the program. The strong turnout and level of engagement affirm the importance of continued postgraduate learning opportunities, and we thank all speakers, participants and contributors for helping to make the meeting a resounding success.

We have several other practical educational activities planned for later in the year and at the ASM in Cairns.

In parallel, the committee has remained actively engaged in a number of policy and industry-facing initiatives. We continue to contribute to national and local discussions on evolving prescribing frameworks. Our collaboration with pharmaceutical stakeholders remains focused on ensuring ethical alignment and scientific integrity, particularly as new agents in metabolic bone disease, menopause management, and rare bone conditions come to market.

We're always happy to hear your suggestions on how we can better engage with clinicians. If you'd like to hear more or have ideas around clinician engagement/education, please feel free to email Dr. Jasna Aleksova on jasna.aleksova@hudson.org.au.

Yours Sincerely,

Dr Jasna Aleksova

ANZBMS Clinical Practice Committee Chair 2025

Program Organising Committee

We are looking forward to the November ANZBMS ASM to be held in Cairns from 9th to 12th November 2025. We are grateful to all POC members for their support and guidance.

The POC hope to create a stimulating and engaging program with confirmed themes and speakers listed below:

International speakers:

- A/Prof John Schousboe (USA): Imaging and bone health
- A/Prof Morten Frost Nielsen (Denmark): Diabetes and bone health
- A/Prof Marc Wein (USA): Osteocyte mechano-responses. *Marc will be a faculty speaker at the Herbert Fleisch Workshop to be held following the ANZBMS 12-14th November 2025.*
- Prof Geert Carmeliet (Belgium): Metabolic regulation of bone

National speakers:

- A/Prof Dawn Coates: Dental tissue regeneration
- Dr Cassandra Smith: Exercise and bone health
- Dr John Kemp: OMICS
- Prof Bronwyn Stuckey: Menopausal hormone therapy
- Prof Rachel Davey: Transgender and bone health
- Dr Ayse Zengin: Indigenous health

We are in the process of assigning chairs for sessions and obtaining abstract reviewers. The debate topic will be:*"Nutritional therapy is better than pharmacotherapy as first line for bone loss in the older adult".* Excitingly, the debate speakers have been recently confirmed: Prof Emma Duncan, Dr Sandra Iuliano, Dr Marc Sim, and Prof Robert Blank.

Please note the Abstract Submission Deadline is the **18th of July 2025**. The ANZBMS is offering Travel Grants for eligible members to support students and early career researchers.

We look forward to an exciting 2025 meeting in Tropical North Queensland!

ECIC Co-Chairs Report

We are working on delivering some exciting initiatives this year!

The inaugural joint **ANZBMS/ESA/ADS ECR Connect workshop** is being held online on **Saturday 2nd August**. This is a brand new initiative run by the events subcommittee, in conjunction with early career committees of the ESA and ADS. The dynamic program will include interactive sessions focused on promoting career, professional and research development for early career investigators (both basic science AND clinical).

Lineup of speakers include Prof Natalie Sims, A/Prof Michelle McDonald, Dr Albert Kim and more. Planned topics include:

- Artificial intelligence
- Hacking conference presentations and promoting your research on social media
- How to design a mouse model study/investigator-initiated clinical trial
- Effective grant writing for competitive funding opportunities
- Q&A panel

Registration is open ($5 registration fee): https://events.humanitix.com/ecr-connect

The clinical subcommittee will be bringing you the **RACP-ANZBMS webinar series** between June-November. This is a six-part series of online educational talks covering a wide range of clinical topics including denosumab discontinuation, iron infusion-associated hypophosphataemia, strategies to harness osteoanabolic therapy, managing rare bone disorders and nutrition for bone health. Basic scientists are also welcome to join. We will send out registration details soon! Clinicians can access last year's webinar recordings here.

The **Clinical Cases in Metabolic Bone Disease Seminar** is back this year and will be held during the ANZBMS ASM in Cairns on Monday 10th November. This is an excellent opportunity for advanced and physician trainees to present a complex bone case. The best presentation will be awarded with a waiver of publication fee pending acceptance of the case report in JBMR Plus. The abstract submission portal is open and **submissions are due on Friday 4th July**. Click here for more information.

Keep up to speed on our latest updates through our various social channels, including our LinkedIn page and Facebook Group.

The ANZBMS ECIC is run by ECIs, for ECIs! We would love to hear from you at ecic@anzbms.org.au if you have any suggestions for how we can make navigating being an ECI better for you.

Visit the ANZBMS ECIC page if you would like to find out more about us and to connect with current committee members.

Yours Sincerely,

Dr Shejil Kumar

ANZBMS ECIC Co-Chair 2025

IFMRS
INTERNATIONAL FEDERATION OF MUSCULOSKELETAL RESEARCH SOCIETIES

HubLE

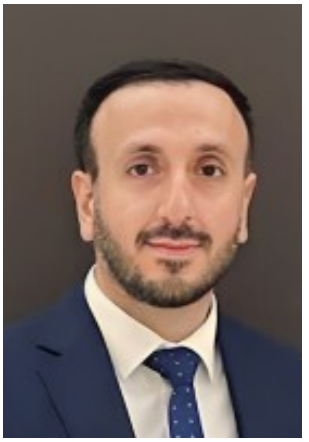
IFMRS HubLe Update

Exciting changes are underway at IFMRS HubLE! We are currently undergoing a major redesign aimed at creating a more dynamic and impactful platform. Our goal is to deliver richer content, enhanced usability, and new features that better serve the global musculoskeletal research community.

As part of this transformation, HubLE will be fully integrated into the main IFMRS website—ensuring a more seamless and cohesive experience while preserving our unique identity and mission. Importantly, HubLE will continue to be the dedicated home for early-career researchers (ECRs). We remain deeply committed to amplifying the voices of emerging scientists, sharing their work, and providing valuable resources to support their growth and success.

These developments align with our ongoing initiatives, including the upcoming launch of a new podcast series, visually engaging graphical research highlights, and a feature series spotlighting outstanding ECRs we met during the leading musculoskeletal societies' annual meetings. These efforts are designed to make cutting-edge research more accessible, engaging, and visible across the community.

Stay tuned for our relaunch—and thank you for being part of the HubLE community as we move forward into this exciting new chapter!



Warmly,
Dr Mustafa Unal
Editor-in-Chief, HubLE

ECIC Events

ANZBMS-ESA-ADS ECR CONNECT - Registration now open!

The ANZBMS ECIC are excited to announce a new initiative!

ECR CONNECT is a dedicated online weekend workshop for early career researchers to gain research skills and career development advice from leading experts in the field (including Prof Natalie Sims, A/Prof Michelle McDonald, Dr Albert Kim). This is a joint initiative led by ANZBMS ECIC in collaboration with the Endocrine Society of Australia (ESA) and Australian Diabetes Society (ADS).

Date & Time: Saturday, 2nd August 2025, 9:00AM - 1:00PM AEST (online)

Topics:

- Artificial intelligence
- Fellowships and Funding
- Experimental design: from mouse models to investigator led-clinical trials
- Conference presentation skills and using social media to promote your research
- Career development Panel Q&A

Registration ($5 registration fee):

https://events.humanitix.com/ecr-connect.

The ECIC will send more details to come, so keep this date free!.

Clinical Cases in Metabolic Bone Disease Seminar

Cairns Convention Centre, Cairns
NOVEMBER 10, 2025 | 5:30 PM

Are you an Advanced Trainee with an interesting bone case? Submit your case study for the chance to present!

SUBMISSION DEADLINE: JULY 4, 2025

COVER PAGE

Name
Training hospital
Email address
Supervisor's name(s)
Supervisor's signature approving the case submission

CASE SUMMARY*

Title
Clinical case detail
Laboratory and medical imaging findings
Brief outline of the literature
3-5 take home messages (dot points)
References

**500-1000 words excl. references. Highest ranked abstracts will be selected for oral presentation.*

We are also looking for cases with a focus on the multidisciplinary management of musculoskeletal disease to stimulate discussion of both pharmacological and non-pharmacological management.

PRESENTATION PRIZE

Opportunity to submit their case report to JBMR® Plus for FREE ($2500 USD fee waived)

$30 for students/registrars/ECR, $60 for other; includes dinner and drinks

MORE INFO: https://www.anzbmsconference.org/clinical-cases

Contact details: Dr Angela Sheu (a.sheu@garvan.org.au), Dr Lucy Collins (lucy.collins@monash.edu)

anzbms.org.au @ANZBMS_ECIC

RACP Specialists. Together
EDUCATE ADVOCATE INNOVATE

ANZBMS

2025 RACP/ANZBMS Webinar Series

Speaker	Topic	Time/date
Dr Sandra Iuliano	Nutrition and bone: a clinician's guide	Monday 23rd June 6:00pm (AEST)
Prof Craig Munns	Paediatric and Adult OI	Tuesday 29th July 6:00pm (AEST)
A/Prof Christian Girgis	Management of rare bone diseases – giant cell granuloma and fibrous dysplasia	Tuesday 12th August 6:00pm (AEST)
Prof Peter Ebeling	Osteoanabolic therapy – transition/sequence/combination	Monday 25th August 6:00pm (AEST)
Dr Albert Kim	Insights into denosumab discontinuation: from bench to bedside	Monday 22nd September 6:00pm (AEST)
Dr Hanh Nguyen	Hypophosphataemia following iron infusions	Monday 17th November 6:00pm (AEST)

Register in advance for this webinar:

https://event.racpevents.edu.au/specialty-society-webinar-series-2025/anzbms

After registering, you will receive a confirmation email containing information about joining the webinar.

This webinar is part of the Specialty Society Webinar Service that is being undertaken by the Royal Australasian College of Physicians in partnership with its affiliated Specialty Societies.

ecic@anzbms.org.au anzbms.org.au

ECIC Funding Opportunities

Grant/Fellowship Scheme*	Application Period
Phillip Sambrook Young Investigator Travel Award	Deadline extended to 28 June 2025
BMAS-IFMRS Future Global Leaders Awards	Applications open until 31 July 2025
ANZBMS/Bone Health Foundation Grant-In-Aid	Applications close 30 June 2025
Rebecca Cooper Fellowship	Applications open 1 August 2025, closing 29 August 2025
Christine and T.Jack Martin Research Travel Grant	TBC

With thanks to

THE INTERNATIONAL BONE MARROW ADIPOSITY SOCIETY
AT THE CROSSROADS OF FAT, BLOOD AND BONE

IFMRS
INTERNATIONAL FEDERATION OF MUSCULOSKELETAL RESEARCH SOCIETIES

Rebecca L. Cooper
Medical Research Foundation

bone health
FOUNDATION

*Clicking on the scheme name will redirect you to the grant/fellowship website.

It takes a team to make science happen. Here's a snapshot of members from a research lab, and what they're up to!

Raymond Purves Bone & Joint Research Laboratory (RPRL)

Kolling Institute, University of Sydney

Featuring: Prof Christopher Little (Lab Head), Dr Cindy Shu and Dr Carina Blaker

Professor Christopher Little, Lab Head

How long have you been in this lab/group? This time around about 21 years ..... but I actually spent 5 years in this lab "in the last century" when I did my PhD here (1992-96).

What topics are researched in your lab? We are focused on a number of common and debilitating musculoskeletal (MSK) diseases: osteoarthritis, tendon and ligament injury and disease, and intervertebral disc disease. We are a fundamental science and discovery group, but with a strong translational focus. So that means we explore the cellular and molecular mechanisms of MSK disease with regard to both structural pathology and symptoms, with a goal to translate that into better therapies that will make a difference to patients. A big part of our work is developing, using and improving pre-clinical models for both discovery and translational research, with grant funding from industry as well as Gov't and philanthropy.

What was your career trajectory leading to this moment? I completed a Bachelor of Veterinary Medicine & Surgery at Murdoch University then did specialist large animal surgery residency training and a Masters at the University of Minnesota. I received specialist certification by the American College of Veterinary Surgeons while on faculty at the University of Guelph, before leaving clinical work and coming back to do a PhD at Sydney University. I did a post-doc for 5 years at the University of Cardiff and a 2 year research Fellowship at the University of Melbourne, before being hired in my current role. Its been a long and winding road but I wouldn't change any of it, as my clinical background continues to inspire and influence the labs discovery science.

What's your mentorship style? I hope what I do is to inspire passion for research and discovery in the students and staff that work in RPRL. What we do in medical research is such a privilege - every day you might get to see something and discover something that no one has seen before, and that might make a huge difference to how we treat a disease and help patients in the future. If that doesn't get you excited and want to come to work, then I'm not sure any other mentorship from me will help. I do try and mirror my own mentors who delighted in seeing their team succeed, so I encourage everyone in the lab to be innovative, adventurous and independent. Beyond mentoring you also need to be a sponsor - make sure credit is given to the people that actually do the work, push team members into the spotlight and highlight their achievements. Finally, one of the great things about lab-based research is that its open to everyone, so I try and foster an environment of inclusion, acceptance and diversity.

What's a fun fact about your lab? While we have "bone" in our lab name, we mainly focus on the soft MSK tissues .... but we appreciate the support that bone provides :-)

It Takes a Village .....

"Meeting of the minds" - Raymond Purves and and Murray Maxwell Labs X-mas gatherings

Dr Cindy Shu, Research Fellow

How long have you been in this lab/group? 17 years! Same lab since after my PhD!

What topics are researched in your lab? Connective tissue matrix biology, proteoglycan biochemistry, tissue biomechanics, and disease mechanisms in tendon, intervertebral disc degeneration, osteoarthritis, and exploring potential therapeutic interventions. My current research explores the biological link between osteoarthritis and the risk of cardiovascular disease.

What was your career trajectory leading to this moment? After my PhD in biotechnology, I realised that my heart was in medical research. I started as a research assistant at the RPRL, where I was able to grow both my skills and knowledge in musculoskeletal research. The breadth and depth of work at RPRL kept me on my toes, and gave me the strong foundation in matrix biology, animal models of disease, and exposure to industry collaborations and clinically relevant research. Today, I'm a chief investigator on an NHMRC-funded project that seeks to characterise cardiovascular abnormalities in an animal model of OA, identify the molecular drives of this process, and ultimately develop potential diagnostics or therapies to help manage two of the world's most prevalent chronic diseases - OA and CVD.

What's a fun fact about your lab? Rather than "fun", I'd say we're family. The team supports and lifts each other up - we're team mates, mentors, coaches, cheerleaders, champions and colleagues all at once. It's no wonder we have an ongoing inside joke that RPRL is Hotel California - people may come and go, but somehow we all stay connected or keep collaborating over the years. Also, our Friday afternoon drinks are legendary!

Dr Carina Blaker, Research Fellow

How long have you been in this lab? I've been hanging around/affiliated with RPRL since I was an undergraduate summer intern in the Murray Maxwell Biomechanics Lab over 10 years ago but became a fully fledged member last year.

What inspired you to choose the lab? My initial affiliation with the lab was purely by chance. At the time I was looking for an Honours project that would allow me to apply and grow my skills as a biomedical engineer which happily co-incided with a new collaborative project between the Murray Maxwell Biomechanics Laboratory and RPRL. This time spent establishing a new preclinical model for osteoarthritis research subsequently set me on course for a research career in musculoskeletal disease and injury. Choosing the lab (or perhaps more accurately deciding to stick around) was an easy decision when presented with opportunities to learn new techniques, and work with industry to develop novel devices. But importantly, the lab is also embedded in a friendly culture and broader network that provides thoughtful guidance and purpose for those with an insatiable curiosity.

What are you excited to do? We've been building cross-disciplinary collaborations across research areas including cardiology, nephrology, neurology and pharmacology. I'm excited to see how the data will shape our understanding of osteoarthritis and drive advancements in integrated healthcare.

What's a fun fact about your lab? We like to celebrate achievements with cake and have a lot of fun creating themed cakes and decorations to mark big milestones such as project completions. See some recent examples below - knee anatomy cake and bone-on-bone cake (credit to Liz Clarke for leading the anatomical baking crew)

Dr Natasha Ung

Staff Specialist Rheumatologist, Royal North Shore Hospital, NSW Health

Research Category: Clinical

Research interests: Interest in the way diet, lifestyle measures and physical activity can contribute to bone health and autoimmune diseases.

What I hope to gain from joining ANZBMS: *To increase my knowledge in the understanding and management of osteoporosis and other metabolic bone disease; to connect with like minded professionals.*

Award Recipients

Professor Richard Prince, AO

THE UNIVERSITY OF WESTERN AUSTRALIA

"Officer of the Order of Australia (AO) appointment"

Professor Richard Prince, an ANZBMS Life Member, was one of 31 Australians to receive the Officer of the Order of Australia (AO) in the General Division in the King's Birthday 2025 Honours List. The award recognised his contribution to endocrinology, clinical bone and mineral sciences.

Individuals are appointed an Officer of the Order of Australia (AO) for distinguished service of a high degree to Australia or to humanity at large. The AO is the second-highest level of appointment.

Xiaojun Chen, PhD Candidate

THE UNIVERSITY OF WESTERN AUSTRALIA

"2025 ECTS New Investigator Awards"

Xiaojun Chen is currently a third-year PhD student in Dr Kai Chen's lab at The University of Western Australia. His abstract was among the highest-scoring submissions by new investigators for ECTS 2025. Xiaojun recently presented his PhD project at the 2025 ECTS Annual Congress, held in Innsbruck, Austria, from 23 to 26 May 2025.

Congratulations

Kumar S, Streeter C, McDonald MM, Clifton-Bligh RJ, Gild MT, Girgis CM. Combination or sequential teriparatide for osteoporosis treatment in denosumab-users: real-world bone mineral density outcomes. Bone Rep. 2025 Jun;25:101847. doi:10.1016/j.bonr.2025.101847

Featured author: Dr Shejil Kumar

PhD Candidate, University of Sydney
Endocrinology Fellow, Royal North Shore Hospital & Westmead Hospital, Sydney
E: shejil.kumar@health.nsw.gov.au

What is the background of the study?

The optimal osteoanabolic strategy remains uncertain in patients with persistently high fracture risk despite denosumab (Dmab). Sequential treatment using Dmab followed by i) teriparatide (TPTD) is suboptimal and ii) romosozumab only leads to modest BMD gains. Commencing treatment-naïve patients on combination Dmab/TPTD results in dramatic BMD gains at the lumbar spine and hip. However, BMD outcomes with combination Dmab/TPTD have not been reported in patients on established Dmab, which is of greater clinical relevance due to current osteoanabolic reimbursement criteria.

What did you find?

We conducted a retrospective cohort study on patients managed in osteoporosis clinics between 2013-2023 at RNSH and Westmead. Eligible patients were managed with Dmab immediately before ≥12-months TPTD. Patients were grouped according to whether TPTD was added to ongoing Dmab (combination) or Dmab withheld during TPTD (sequential), with treatment decisions made during routine clinical care. BMD outcomes were assessed during TPTD. The total cohort (N=23; 11=combination, 12=sequential) were 77 ± 7 years old and predominantly female (87%). The cohort had prevalent vertebral (52%) and non-vertebral fractures (2.4 ± 1.5) and majority (70%) had a BMD T-score below -3.0 SD. Median Dmab exposure was 5-doses. Both groups were similar in age, sex, Dmab exposure, fracture prevalence and pre-TPTD BMD. Combination Dmab/TPTD was associated with ~10% BMD gains at lumbar spine (+0.080 ± 0.059 g/cm^2, p=0.004) with no significant change after sequential Dmab/TPTD. Hip and femoral neck BMD remained stable in both groups. No clinical vertebral or hip fractures occurred.

What is the application of these findings?

We demonstrated significant lumbar spine BMD gains (~10%) when adding TPTD to ongoing established Dmab. Hip BMD remained stable with combination Dmab/TPTD in existing Dmab-users. Although possessing several limitations, our data are of real-world clinical relevance and support the need for a prospective controlled study. Further studies should explore markers of bone turnover and skeletal microarchitecture and structure at the hip beyond DXA.

Joseph GJ, Vecchi III LA, Uppuganti S, Kane JF, Durdan M, Hill P, McAdoo AG, Tanaka H, Kell D, Searcy MB, Chen W, Rosenthal EL, Harrison DG, Nyman JS, Weivoda MM, Johnson RW. Programmed cell death protein 1 (PD-1) blockade reguates skeletal modelling in a sex- and age-depedent manner. J Bone Miner Res. doi: 10.1093/jbmr/zjaf055

Featured author: Associate Professor Rachelle Johnson

Associate Professor of Medicine, Division of Clinical Pharmacology,
Vanderbilt Centre for Bone Biology (Nashville. TN);
Program Director, Program in Cancer Biology,
Vanderbilt University School of Medicine (Nashville. TN)
E: rachelle.johnson@vumc.org

What is the background of the study?

Immune checkpoint inhibitor (ICI) therapy has revolutionized cancer care by prolonging T cell anti-tumor responses, but patients treated with ICIs often develop immune related adverse events. Recent clinical reports suggest that ICIs targeting PD-1 increase fracture risk, but limited pre-clinical studies, performed only in young male mice, suggest that ICIs have minimal effects on the skeleton. We therefore investigated the impact of PD-1 blockade on the skeleton across the lifespan and in both sexes.

What did you find?

Our recent publication by Joseph et al. indicates that global PD-1 deletion in young male mice has no effect on femoral trabecular bone and increases vertebral bone mass. In stark contrast, global PD-1 deletion reduces bone mass in adult and aged males, and in females of all ages, aligning with clinical reports of elevated fracture risk. Pharmacologic PD-1 blockade causes similar bone loss in female mice across the lifespan, and increases osteoclast activity, suggesting α-PD-1 causes excessive bone resorption. While circulating T cells are known to increase after PD-1 therapy, we report for the first time an enrichment of bone marrow T cells when PD-1 is inhibited. Given that osteoimmunological interactions can mediate bone remodeling, we investigated whether T cell enrichment in the bone marrow contributes to elevated osteoclast activity observed after PD-1 blockade. Indeed, T cell deficient mice are resistant to bone loss after α-PD-1 therapy, confirming that T cells are at least in part responsible for the pathologic bone resorption that occurs after PD-1 targeted therapies.

What is the application of these findings?

Collectively, our studies indicate that after skeletal maturity, PD-1 targeted therapy can cause bone loss due to pathologic osteoclast-mediated bone resorption that is fueled by T cells.

ANZBMS Member Publications

Nicholas Smith, Dimitrios Cakouros, Feargal J Ryan, David J Lynn, Sharon Paton, Agnieszka Arthur, Stan Gronthos. DNA hydroxymethylases Tet1 and Tet2 regulate bone aging and BMSC metabolism through the IGF-1/ mTOR signalling axis. *Stem Cells*, sxaf026, doi: 10.1093/stmcls/sxaf026.

Featured authors: Professor Stan Gronthos[1], Dr Dimitrios Cakouros[2], and Dr Agnieszka Arthurs[2]

[1]Emeritus Professor, School of Biomedicine,
Faculty of Health and Medical Sciences, University of Adelaide
[2]Lecturer School of Biomedicine,
Faculty of Health and Medical Sciences, University of Adelaide
E: stan.gronthos@adelaide.edu.au, dimitrios.cakouros@adelaide.edu.au, and agnes.arthur@adelaide.edu.au

What is the background of the study?

The Ten-Eleven Translocation (Tet) enzymes, particularly Tet1 and Tet2 are a family of dioxygenases involved in epigenetic regulation as they oxidize 5 methylcytosine (5mc) to 5-hydroxymethylcytosine (5hmc) . While their role in haematopoiesis, neural physiology and cancer is well studied, their function in bone aging and bone marrow stromal cell (BMSC) metabolism is less understood. This study investigates how Tet1 and Tet2 influence skeletal aging and BMSC function uncovering novel molecular drivers.

What did you find?

- Old BMSC display a decrease in global 5hmc and Tet1/2 expression.
- Tet1 and Tet2 double knockout (TetDKO) mice exhibited significant skeletal defects, including reduced trabecular bone volume and osteoblast numbers, especially in aging males.
- TetDKO BMSCs (52 week old) showed impaired osteogenic differentiation, increased adipogenesis, increased cellular senescence and reduced proliferation.
- Gene set analysis discovered negative regulators of IGF-1 signalling to be upregulated in TetDKO BMSC population (52 week old). Pappa2, a regulator of IGF-1 bioavailability, showed a dramatic decrease in 5hmc along its promoter and was significantly downregulated.
- TetDKO led to reduced IGF-1 signalling and downstream mTOR pathway activity, which are critical for bone formation, BMSC function and provide a possible aging link between Tet1/2–nutrition-bone.
- The findings suggest that Tet1 and Tet2 maintain bone homeostasis by regulating epigenetic control of IGF-1 signaling via Pappa2.

What is the application of these findings?

This study highlights a novel epigenetic mechanism linking Tet enzymes to bone aging and BMSC metabolism. Disruption of Tet1/2 impairs IGF-1/mTOR signaling, contributing to age-related bone loss. These insights open potential therapeutic avenues targeting epigenetic regulators or the IGF-1/mTOR axis to combat osteoporosis and skeletal aging.

Enwu Liu, Ryan Yan Liu, John Moraros, Eugene V. McCloskey, Nicholas C. Harvey, Mattias Lorentzon, Helena Johansson & John A. Kanis. Association between walking and hip fracture in women aged 65 and older: 20-year follow-up from the study of osteoporotic fractures. ***Osteoporosis International*** **doi: 10.1007/s00198-025-07508-y**.

Featured author: Dr Enwu Liu

Academic, College of Medicine and Public Health, Flinders University, Adelaide
E: enwu.liu@flinders.edu.au

What is the background of the study?

Hip fractures among older women represent a major public health concern due to their association with disability, decreased quality of life, and high mortality and healthcare costs. While pharmacological and dietary strategies are commonly used to prevent fractures, physical activity-particularly walking-has been suggested as a simple, low-cost intervention. However, the long-term association between walking and hip fracture risk remains unclear, especially in older women. This study aimed to evaluate whether walking is associated with a reduced risk of hip fractures using 20 years of prospective data from the Study of Osteoporotic Fractures (SOF).

What did you find?

The study included 9,704 community-dwelling women aged 65 and older in the USA. Over 20 years, 1419 hip fractures were documented. Women who walked for exercise had a significantly lower risk of hip fractures compared to those who did not (HR = 0.864; 95% CI: 0.762–0.980). Each additional city block walked daily for exercise (about 200 steps) was associated with a 1.4% reduction in hip fracture risk. Spline analysis revealed a threshold effect: walking ≥16 blocks daily (≈3200 steps) was significantly protective, but walking beyond 33 blocks (≈6600 steps) conferred no additional benefit.

What is the application of these findings?

These results suggest that regular walking for exercise can substantially reduce hip fracture risk in older women, independent of bone mineral density. Public health interventions and clinical guidelines should promote walking-specifically 3200-6600 steps per day-as a safe, effective, and accessible strategy for hip fracture prevention. This recommendation can inform fall-prevention programs, geriatric care strategies, and health policy targeting older populations. However, randomized controlled trials are needed to confirm causality and further explore optimal walking doses and contexts.

ANZBMS Researchers:
We want to share & celebrate your wins!

We are on the lookout for members who have celebrated success (awards and publications) to be highlighted in the Spotlight or Publication sections for the upcoming editions of the newsletter. If you know of someone or want to self-nominate, please email us at **newsletter@anzbms.org.au**

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会場 熊本城ホール (熊本市)
会長 宮本 健史
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