Issue 1, March 2023

ANZBMS Newsletter

Member Achievements

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ANZBMS ECI Spotlight

ANZBMS Member Publication Highlights

Cover Image by Dr Lena Batoon, University of Michigan and The University of Queensland. Lumbar vertebra from a 3-week-old male Osteocalcin-Cre$^{+/-}$iCaspase9-EGFP$^{+/+}$ mouse showing EGFP (green) expression not just in osteocalcin+ (red) bone-lining osteoblasts but also in some bone marrow stromal cells, osteocytes and chondrocytes. More information about this mouse model can be found in here.

Welcome to the ANZBMS Newsletter

In this issue

Next Issue: June 2023

Please send us your scientific images and the best will feature on the front page of our next issue!

newsletter@anzbms.org.au
@ANZBMSoc

Welcome to 2023! We are excited to present the first issue of our merged ANZBMS Newsletter!

In this issue, we thank our exiting editorial board members (pg 5), highlight available funding opportunities for ECIs (pg 14) and celebrate the achievements of our ANZBMS members (pg 15). Recent publications, both basic and clinical, from our membership are highlighted (pgs 16 - 18), celebrating the breadth of techniques and approaches taken by bone researchers throughout Australia and New Zealand, to further our knowledge in the field.

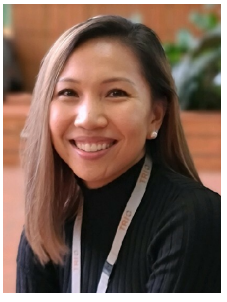
We also bring to you news and updates from different research labs from across Australia (pgs 10 - 13), so that we can all get to know each other and our research better. We hope that this will help with developing new collaborations and inform our junior members of opportunities available throughout Australia and New Zealand.

Best wishes for a fantastic 2023 from the ANZBMS Newsletter Editorial Board!

ANZBMS Newsletter Editorial Board

Dr Madhuni Herath

Laura Trainor



Dr Lena Batoon

Emma Cheney

Dr Martha Blank

Dr Shanal Kumar

Dr Jakub Mesinovic

Tian Nie

Dr Jason Talevski

Dr Yinghong Zhou

President's Comments

Professor Mark Forwood

ANZBMS President
Chair of Anatomy, School of Pharmacy and Medical Sciences
Griffith University, Gold Coast

"There ain't no cure for love
There ain't no cure for love
All the rocket ships are climbing through the sky
The holy books are open wide
The doctors working day and night
But they'll never ever find that cure for love
There ain't no drink no drug
(Ah tell them, angels)
There's nothing pure enough to be a cure for love.
(**Leonard Cohen, 1988**)

ANZBMS Colleagues, welcome to a new year. The year of the rabbit is meant to symbolise longevity, positivity, auspiciousness, wittiness, cautiousness, cleverness, deftness and self-protection. I might have some of these covered but deftness and self-protection failed in early January. While walking my dogs, I fell and dislocated my ankle and fractured the malleoli, requiring internal fixation. There may be nothing pure enough to be a cure for love, but at least good orthopaedic skills and fracture healing have my ankle on the mend. It's a timely reminder of how incapacitating even simple fractures can be, but I should be good for the dance floor in Newcastle! Speaking of Newcastle, planning for the 33rd Annual Scientific Meeting of the society is now well under way. The POC is organising an outstanding scientific program across basic, clinical and allied health topics. The conference secretariat will start sending regular updates about the meeting, so please keep an eye out for those. The first key date to put in your diaries is Friday 21st July, which will be the closing date for early bird registration, abstract submission and award applications. Our international and national speakers are being finalised and will be announced on the ANZBMS Conference website soon.

Following a successful Postgraduate Course for Advanced Trainees in October, the Clinical Practice Committee are planning, 3-part virtual program titled "The ANZBMS Osteoporosis Series" to take place over 3 evening sessions in 2023. This will be advertised in the near future. I want to thank Fran Milat who represented ANZBMS on the Council of the Adult Medicine Division of the RACP for the past two years. Fran has stepped down from this role and Jackie Center has agreed to represent ANZBMS for the next period. With the leadership of Richard Prince, the Therapeutics committee made several important submissions to the PBAC in 2022 regarding therapies. We are pleased to report that the PBAC recommended the inclusion of burosumab (Crysvita) for PBS Listing on the Pharmaceutical Benefits Scheme (PBS) for children and adults. Richard and Cherie Chiang are now working towards other initiatives to support diagnosis and treatment of hypophosphataemia.

The Early Career Investigator Committee (ECIC) has been active in maintaining the ANZBMS profile on social media and promoting the careers of our members. Dr Cassandra Smith was elected as Co-Chair with Dr Bridie Mulholland for the next 2 years. I want to thank Dr John Kemp for his leadership during his term as Co-Chair and his active support for early and mid-career researchers. Anoohya Gandham, Ye Cao and Lena Batoon were supported to

President's Comments

attend the Herbert Fleisch meeting in Bruges in November 2022 – read more about their presentations in the ECIC December Newsletter. Dr Dzenita Muratovic was selected as the Bridging Overseas Network and Exchange (B.O.N.E) recipient and will attend the ECTS conference in Liverpool (UK) in April this year; and Dr Natalie Wee has also been invited by the Japanese Society of Bone and Mineral Research to present at a symposium on "Hot Topics in Musculoskeletal Research" at the annual meeting in Tokyo in July. Congratulations to these members. As a Council, we have a number of initiatives being developed to support our members in bone and mineral research in 2023 through funding, education and advocacy. We look forward to announcing these in the near future. Wishing all of our members a productive and successful year in 2023.

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ANZBMS ASM Abstracts Now Open!

There will be many opportunities for scientific and social networking and we encourage you to take full advantage of the program. Newcastle is situated in a beautiful region of NSW on a working harbour and offers many attractions to enjoy before or after the meeting, including the Hunter Valley wine region.

Whether you are an early or mid-career investigator, clinician, basic scientist, or allied health professional, we know that you will reconnect with peers, drive new collaborations and learn from an exciting program of cutting-edge musculoskeletal science.

KEY DATES

Earlybird Registration Deadline: Friday 21st July 2023
Abstract Submissions Deadline: Friday 21st July 2023
Clinical Cases Submission Deadline: Friday 21st July 2023

The ANZBMS Newsletter Editorial Board is changing!

Thank you to our outgoing members!

Mei Lin Tay

PhD Candidate, University of Auckland

Being on the ANZBMS ECIC team for the last 18 months has been a great experience. While on the board I developed a better understanding of what ANZBMS and the society members have been up to, plus a better understanding of research opportunities within the field. I also picked up worthwhile skills and made good connections during this time, which will no doubt be useful in my future career. I really enjoyed working with a productive and cohesive team, and look forward to your future issues.

James Smith

PhD Candidate, Garvan Institute of Medical Research

Alas, all good things must come to an end! Working as part of the ANZBMS Newsletter Editorial Board over the past 18 months or so has been very rewarding and enjoyable! Working on the committee has been a novel experience for me and a great learning curve, as well as being a fantastic way to keep up with the latest news and developments in the field. As an international PhD student, I have particularly enjoyed having the opportunity to meet and engage with other bone biologists from this part of the world, and I look forward to continuing those relationships into the future!

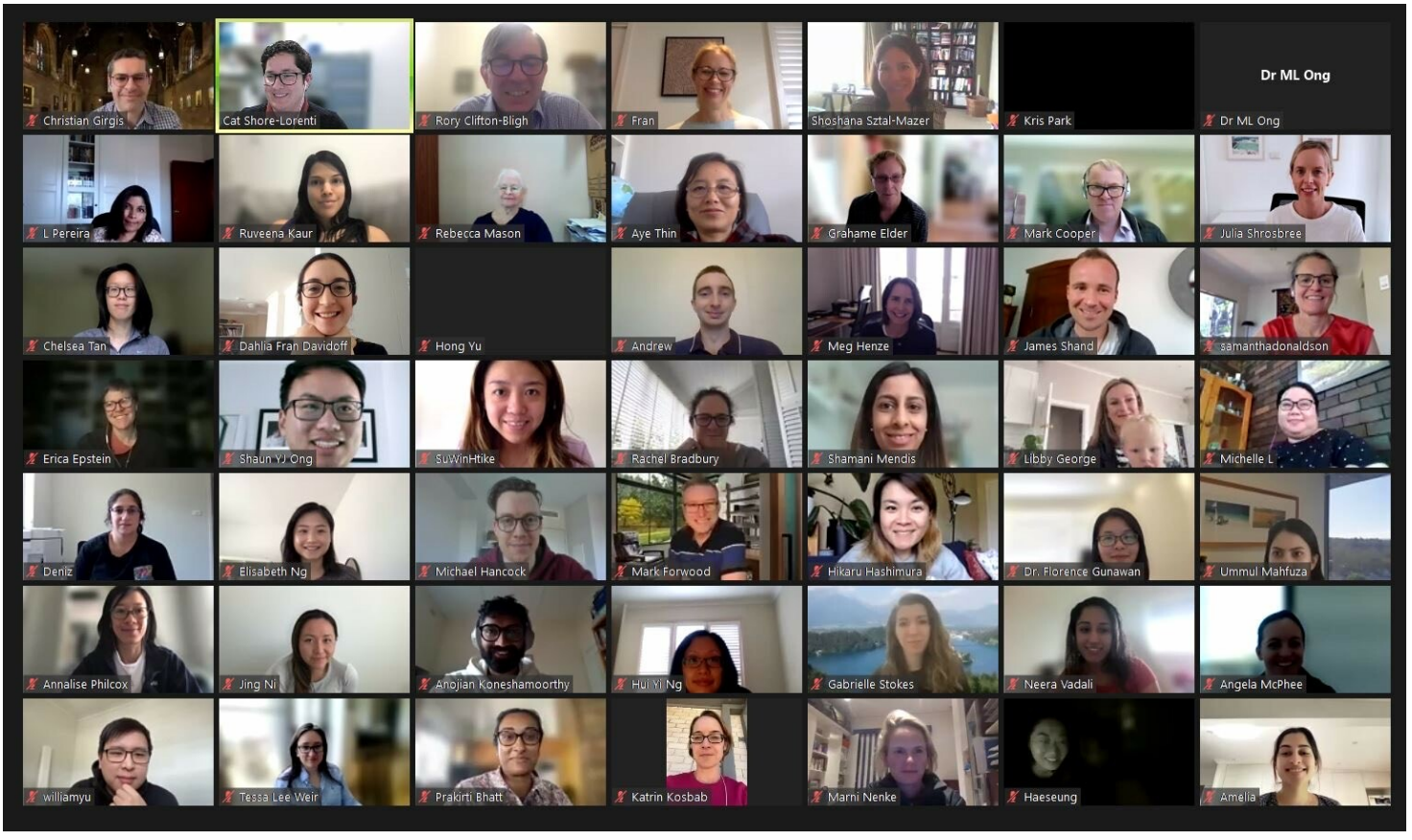
ANZBMS Committee Updates

Clinical Practice Committee

On the weekend of 29th and 30th October 2022, the Clinical Practice Committee hosted its annual Clinical Postgraduate Seminar. This was the second time the seminar was held entirely online, and we had more than 90 participants ranging from advanced physician trainees to senior clinicians dialing in.

Held over two half-day sessions, the seminar covered broad themes with case-based discussions on osteo-anabolic therapy initiation, the concept of high imminent fracture risk and considerations in sequential therapies, and treatment of osteoporosis in the very elderly and those with declining kidney function. Concise updates in the areas of vitamin D, assessment of patients with hyphosphotaemia and hypercalcaemia and radiology conundrums in patients presenting with metabolic bone disorders were discussed.

In addition to again hosting the Clinical Postgraduate Seminar this year (planned for November 2023), the Clinical Practice Committee will also be hosting a 3-part osteoporosis series throughout the year which will be available to all members of the society (online, details to follow shortly). The committee hopes that through these educational activities, the society remains the primary go-to place for clinicians to remain updated and engaged in bone and mineral medicine. If you'd like to hear more or have ideas around clinician engagement and education, please feel free to email Christian on christian.girgis@sydney.edu.au



The ECI Report is included in the ECI Section on page 8

ANZBMS New Member Spotlight

Rhiannon Healy

PhD Student, Victoria University

Research category: Clinical (exercise physiologist)

Research interests: Improving treatment and management options for low sex hormones in patients with Type 2 Diabetes

What you hope to gain from joining ANZBMS: Networking with like-minded individuals as well as updates about upcoming conferences and trainings.

Follow me **@rhiannon_healy**

Dr. Tomasz Block

2nd Year Endocrinology Advanced Trainee, Royal Hobart Hospital, Tasmanian Department of Health

Adjunct Research Associate, Department of Diabetes, Monash University.

Research category: Clinical

Research interests: I have an interest in metabolic bone disorders, especially secondary and idiopathic osteoporosis. My other research interest involves novel biomarkers and therapies targeting vascular diabetic complications, particularly nephropathy and cardiovascular disease.

What you hope to gain from joining ANZBMS: Joining ANZBMS will allow me to engage, network and collaborate with other researchers and hopefully assist me towards my future aspiration as a clinician researcher.

ECIC Co-Chairs Report

Welcome to the first update from the ANZBMS ECIC for 2023. We hope you all enjoyed some well-deserved time off over the end-of-year break and have returned to work feeling refreshed. The ECIC is looking forward to another productive year supporting and promoting our ECIs and has been busy planning our events and initiatives for 2023, including a revitalised schedule for Coffee Catch-Ups.

Currently, much of our time is being dedicated to planning our events for the upcoming ANZBMS Annual Scientific Meeting to be held from the 22nd-25th October 2023 at the Newcastle City Hall. The ASM always presents a fantastic opportunity for ECIs to disseminate their research, network, and build long-lasting collaborative relationships. The ECI events at the ASM continue to be popular and highly successful, and we expect this year to be no different. We are excited to be bringing you another year of Speed Networking and Bones & Brews, and our Career Development and Clinical Cases sessions. These events are invaluable, and we strongly encourage all ECIs attending the meeting to come along.

The ECIC is committed to promoting ANZBMS ECIs and their achievements – if you have recently published an article and would like us to promote it through our platforms, please send a link to the publication and a short blurb (no more than 50 words) to ecic@anzbms.org.au.

As always, make sure you keep an eye out on our Twitter to stay up-to-date with all things ECIC!

Until the next newsletter,

Bridie Mulholland and Cassandra Smith

ECIC Co-Chairs

ANZBMS ECI Spotlight

Dr Ayse Zengin, PhD

Senior Research Fellow

Bone and Muscle Research Group, Monash University

@DrAyseZ

Can you briefly describe what your research is about/what are your research interests?

My research focuses on musculoskeletal health in underserved populations, including ethnic populations and people with conditions that you wouldn't necessarily think of their musculoskeletal health immediately, such as those with haemophilia and multiple sclerosis. I'm interested in identifying why these populations have an increased fracture risk by understanding their lifestyle (diet, nutrition, physical activity and SES). I also use various imaging devices to gain a comprehensive understanding of their musculoskeletal health e.g. bone shape, composition and structure.

Congratulations on your recent grant! Can you please tell us about it?

I was awarded $450,000 by the National Centre for Healthy Ageing (NCHA) as part of the Living Labs Program. My program aims to increase community awareness of bone health and osteoporosis among Aboriginal and Torres Strait Islander people. I am very grateful to NCHA for giving me this opportunity. I'm looking forward to working with Dr Troy Walker and the community in co-designing an educational program. The educational program will increase health literacy among Aboriginal and Torres Strait Islander people – both community members and healthcare workers. Increased knowledge among community members will enable them to take preventative measures to delay the onset of osteoporosis (e.g. with resistance and impact training) and subsequent falls and fractures. Understanding how bone health is affected by other conditions (e.g. cardiovascular disease, diabetes and chronic kidney disease) will put bone health on their radar and encourage them to query this at their next GP appointment.

What advice do you have for ECIs looking to apply for grants?

Apply for grants that fit your research area - there is too much time wasted in preparing applications and supposedly tweaking them to fit. Find schemes that target your area of research. Also surround yourself with positive like-minded people - our field is tough and soul destroying so have great people around you to make the hard times better!

ANZBMS Lab Spotlight

It takes a team to make science happen. Here's a snapshot of senior and junior lab members from two labs across Australia, and what they're up to!

1. Professor Tuan Nguyen's laboratory, University of Technology Sydney

Featuring two members: *Dr Trach S. Tran (Research Fellow) and Krisel De Dios (PhD student)*

Dr Thach S. Tran, Research Fellow

How long have you been in this lab? Approximately 2 years. However, I have been working with Tuan for approximately 10 years.

What topics are researched in your lab? The lab is engaged in a number of translational initiatives, such as creating a new tool for individualised fracture risk assessment, utilising artificial intelligence for osteoporosis risk assessment, and studying the genetics of bone loss.

What techniques are involved in your research? We are essentially a "dry lab". Our primary techniques are epidemiological methods, biostatistics or bioinformatics, and deep learning.

What was your career trajectory leading to this moment? I obtained my MD in Vietnam, and then went on to pursue a PhD in epidemiology in Thailand. Later, I completed a Master's degree in biostatistics from Sydney University. I have actively engaged in osteoporosis research for about 10 years.

What's your mentorship style? Supporter and educator.

What's a fun fact about your lab? Our lab advanced the idea of "Skeletal Age", and we asked each lab member to come up with a design that could effectively convey this idea. One week later, a member presented a design that bore a striking resemblance to a decayed animal bone. However, we decided not to use this design as it was unsuitable.

Krisel De Dios, PhD student

How long have you been in this lab? Since March 2021, I have been a part of this lab. I started off as a visiting student and later transitioned to become a research assistant at the Garvan Institute. The lab's work ethics, creative concepts, and Professor Nguyen's supervisory approach towards his students have always impressed me. I thought to myself, "If I wanted to build a robust foundation of training and skills as a researcher, this was the group where I needed to pursue my PhD".

What inspired you to choose the lab? Coming from a small lab, I was immensely impressed by the lab's diverse array of projects geared towards developing novel and applicable tools for personalised fracture risk assessment. For example, the implementation of a fracture risk assessment tool-based ongenomic profiling, or the identification of fractures using artificial intelligence. For someone who is always curious about everything and loves learning, this lab had a lot to offer and could cater to that.

What techniques do you currently use in your lab? I used to be a wet lab person, but I am now primarily using R and bioinformatic tools for my work. Recently, I've learned to use the High-Performance Computing Cluster at UTS.

What are you excited to do/achieve this year? I'm very excited to dive into the heart of my project – the genome wide analysis of bone loss and identifying genes associated with age-related loss of bone density. I'm very curious about the new genes we'll find that's related to bone loss, and by extension osteoporosis.

A fun thing you learned recently. I've had the great opportunity to learn and expand on my bioinformatics and statistics skills and knowledge from Prof. Nguyen's and Dr Tran's course and having them as mentors. It's been interesting and slightly amusing to hear about stories of how researcher's prepare their study design, plan of analysis, and their "Dos" and "Don'ts".

2. Bones and Immunology Research Group, Mater Research Institute, The University of Queensland

Featuring two members: *Professor Allison Pettit (Director of Biomedical Research and Group Leader) and Matheus de Almeida Cruz (visiting PhD student)*

Professor Alison Pettit, Group Leader

How long have you been in this lab? Since its inception in 2013.

What topics are researched in your lab? The Team's research is centered around macrophage biology and contributions to pathology. Specifically, we investigate macrophage contributions to bone development and normal bone biology, bone regeneration after injury and fracture repair, and bone pathology (most recently osteoporosis mouse models and human total knee replacement). We're also interested in macrophage support of haematopoiesis, and whether their regenerative functions can be enhanced/mimicked to reduce cancer therapy bone marrow injury and/or improve the safety of bone marrow transplantation (collaborating with CSL to complete early phase development of a novel therapy).

ANZBMS Lab Spotlight

What techniques are involved in your research? We have heavily invested in developing/validating high quality animal models that faithfully reproduce clinical challenges and use micro-computed tomography to measure bone quality in these. Both standard and imaging flow cytometry are 'go to' techniques in the lab and we utilize FACS to bulk sort populations for either transplantation or molecular analysis. We're also skilled at quantitative histology/immunohistology (both chromogen and fluorescence based) and associated imaging.

Allison Pettit (top row middle) and Matheus de Almeida Cruz (bottom row left).

What was your career trajectory leading to this moment? With my PR hat on I'd say a constant upward trajectory, but stuttering is probably a more appropriate adjective! I got my first major CIA grant in 2008 (NHMRC Project Grant) and had been awarded repeat fellowship funding up to this point but it was still another 5 years before I formerly made independent group leader. This was somewhat by design as being wrapped by a larger group to sustain productivity during the years I was starting a family provided a productivity buffer, even though it was sometimes frustrating. It's been challenging to keep on the external fellowship track since having children and I've taken on significant leadership responsibilities to provide some job security but also because I do enjoy these duties.

What's your mentorship style? I aim to challenge my students/mentees to help them achieve their best, but make sure that this is done on a lab culture foundation that recognizes their value and always has safety nets. I try to instill research integrity and rigour as a core responsibility of researchers and that we need to continually question the caveats of the technical approaches, the weaknesses in the raw data, and the biases in our interpretation. Also, work life balance is important, so I try to encourage students/staff/mentees to make the time you are at work count so you can be 'present' in your personal life

What's a fun fact about your lab? Recently, we finally solved an itch that had been bugging us for years and proved the old proverb that seeing is believing! In bone marrow and spleen single cell suspensions, our favourite cell, macrophages, are fragmented and leave behind small parcels of themselves on other cells within the suspension. Because these parcels or remnants contain high levels of macrophages cell membrane proteins, cytoplasmic reporter molecules and RNAs, they've duped researchers, including ourselves, for years into thinking they were analyzing macrophages. This was a bit of a shock and took some getting used to! This phenomenon only became evident because of the increasing number of parameters that can be easily assessed at a single cell level and because anytime we tried to profile the 'osteomac signature' the data didn't make sense. So, dig deeper if your cell of interest is expressing what would traditionally be considered a macrophage marker or if macrophages are missing from your dataset and you were expecting them to be there!

ANZBMS Lab Spotlight

Matheus de Almeida Cruz, Visiting PhD student

How long have you been in this lab? Since December 2022.

What inspired you to choose the lab? Be able to go through an enriching sandwich doctorate experience in a relevant subject such as regenerative medicine. Additionally, having the opportunity to deepen my studies on bone tissue.

What techniques do you currently use in your lab? I've been using histology techniques for human bone samples and bead-based immunoassay for human cytokines measurement.

What are you excited to do/achieve this year? Finishing my PhD and get funding for my postdoc project in Brazil.

A fun thing you learned recently? (1) Durack in Russian, spelled dyurak, means "fool" and is a traditional Russian card game that is popular in many post-Soviet states. (2) Santos was the pioneer city in surfing in Brazil, having the first record of the sport practice in 1938.

If you and your lab want to be featured in our next issue, please email us!

newsletter@anzbms.org.au

ECI Funding Opportunities

Grant/Fellowship Scheme*	Application Period
NHMRC Investigator Grants	25 January 2023 - 22 March 2023
MRFF Early to Mid-Career Researchers Grant	Quarter 1 2023
The Australian Museum Eureka Prizes Award Program	Deadline: Friday 14 April
MRFF Rapid Applied Research Translation Grant	9 January 2023 - 12 May 2023 (5PM AEST)
ARC Industry Fellowships	TBA
Christine & T. Jack Martin Research Travel Grant	Deadline: 7 September 2023
ANZBMS Travel Grant	Deadline: 21 July 2023
The Ramaciotti Foundation Awards	Open: March 2023
Arthritis Australia (fellowships, scholarships, project grants and grants in aid)	Open: April 2023
Australian Orthopaedic Association Grant	Open: 3 April 2023 Deadline : 30 April 2023 (11:59PM AEST)
Children's Research Foundation (Channel 7) Annual Research Grant	Expression of Interest (EOI) for 2024 grant funding opportunities open
Al and Val Rosenstrauss Fellowship	Open: 3 April 2023 Deadline: 28 April 2023 (5PM AEST)
Rebecca Cooper Fellowship	Open: 1 August 2023 Deadline: 31 August 2023 (5PM AEST)
The MJA Award for Excellence in Medical Research	Deadline: 31 December 2023

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

ANZBMS Member Awards & Achievements

Ayse Zengin, Monash University

ANZBMS Christine and T Jack Martin Research Travel Grant

Ben Kirk, University of Melbourne

ASBMR John Haddad Young Investigator Award

David Scott, Deakin University

Elected to International Osteoporosis Foundation Committee of Scientific Advisors

Dzenita Muratovic, University of Adelaide

Selected for 2022 ANZBMS-ECTS B.O.N.E Program

Laura Trainor, University of Adelaide

Selected for IMNIS REDIConnect mentee program

ANZBMS Member Publications

Kara L Holloway-Kew, Amelia G Betson ,Kara B Anderson, Filip Sepetavc, James Gaston, Mark A Kotowicz, Wan-Hui Liao, Maciej Henneberg, Julie A Pasco. **Fracture Risk and Use of Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers.** **Calcif Tissue Int. Oct 2022. 111(4):396-408.**

What is the background of the study?

Fragility fractures are common in adults aged 50 years or older. Additionally, the National Heart Foundation of Australia guidelines indicate that primary prevention for cardiovascular disease should be targeted to individuals aged 45 years or older. Therefore, it is likely that many older adults at risk for fracture will also use an anti-hypertensive medication. Due to this overlap, it is important to understand if some of the more common anti-hypertension medications, such as angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) may affect fracture risk.

What did you find?

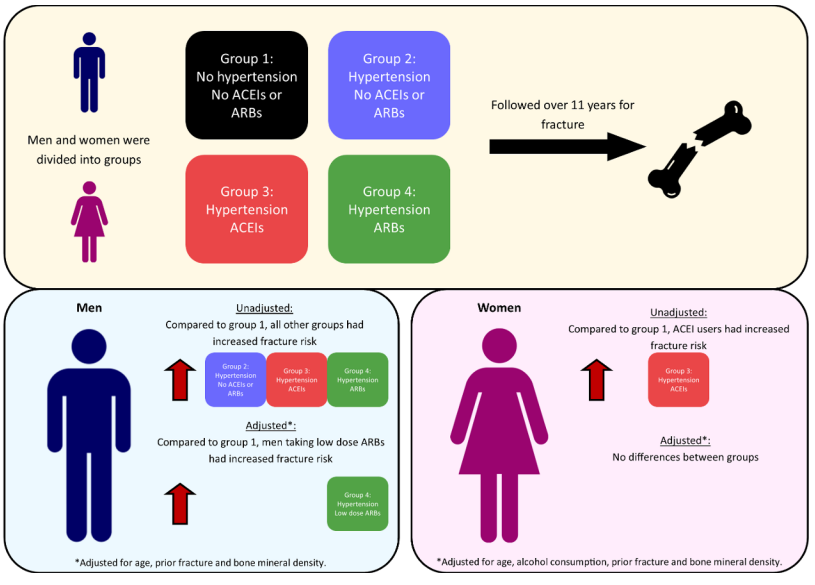
In this study, participants were followed for fractures over an 11 year period. Since hypertension has previously been identified as a risk factor for fracture, participants were divided into four groups 1) those not using ACEI/ARB and without hypertension, 2) not using ACEI/ARB, with hypertension, 3) ACEI and 4) ARB. Without adjusting for any other factors, compared to men who did not use ACEI/ARB medication and did not have hypertension (group 1), all three of the other groups had a higher risk of fracture. For women, those taking ACEI medication had a higher fracture risk. After accounting for other factors such as age, prior fracture and bone mineral density, there were no differences in fracture risk for women taking either ACEI or ARB medications. However, for men, taking a lower dose of an ARB medication was associated with an increased risk of fracture. Overall, these results indicate that ACEIs and ARBs may alter fracture risk, and the effects are different between men and women. The dosage of the medication also appears to be important.

What is the application of these findings?

These results can provide information to help clinicians decide on anti-hypertensive medication for patients who may be at risk for fracture.

What challenges did you face?

Using medication data can be challenging. For example, there are many different types of ACEI and ARB medications, and these can have different active ingredients. Managing the dosages of these is also difficult, as 300mg of one active ingredient may be standard, but could be an excessive amount for another. However, previous literature guided towards a solution, the defined daily dose criteria, which was incredibly helpful for standardising dosages.



Behnaz Azimi Manavi, Amanda L Stuar, Julie A Pasco, Jason M Hodge, Rasika M Samarasinghe, D Kavindi Weerasinghe, Lana J Williams. Evaluating use of antipsychotic medication and its relationship with bone mineral density. Front Psych, Jan 2023. DOI: 10.3389/fpsyt.2022.1004366

What is the background of the study?

It has been reported that patients with schizophrenia have reduced bone mineral density (BMD) and increased fracture risk. However, it is not clear whether this association is due to the disease *per se* or related medications. Antipsychotics are the first-line treatment for controlling schizophrenia symptoms. Antipsychotics are among the most commonly used medications, and some of them were ranked within the top 16 bestselling drugs globally. They are commonly prescribed for patients with a variety of mental disorders such as schizophrenia, mania, and bipolar depression. Their target patient groups could be ranged from children with ADHD to the elderly with dementia. So, we planned to investigate the association between antipsychotics and bone mineral density in a population-based sample of men and women.

What did you find?

We found that antipsychotic use was associated with lower BMD at the spine and hip for women aged under 60 years compared to non-users. These relationships were sustained following further adjustment for lifestyle factors and medications known to affect bone. The association between antipsychotic use and BMD was not observed among older women or men.

What is the application of these findings?

The bone health of women using antipsychotics, mainly who are aged under 60 years, should be monitored regularly.

Heng Qiu, Christopher Hosking, Emel Rothzerg, Ariela Samantha, Kai Chen, Vincent Kuek, Haiming Jin, Sipin Zhu, Alice Vrielink, Kevin Lim, Michael Foley, Jiake Xu. ADR3, a next generation i-body to human RANKL, inhibits osteoclast formation and bone resorption. J Biol Chem, 2023. 299 (2), 102889.

What is the background of this study?

Osteoporosis, also known as "The Silent Killer", is a skeletal condition that weakens bones, making them fragile and susceptible to break. Annually, osteoporosis is affecting millions of Australians and costs billions. To date, Denosumab is the only monoclonal antibody targeting RANKL, a critical cytokine for osteoclast differentiation, in the market that is proven to prevent osteoporotic fractures. Nevertheless, Denosumab is difficult and at a high cost to manufacture and has been reported to associate with certain discomforts and side effects. To provide therapeutic alternatives, we collaborated with a biotech company, AdAlta, and developed a new class of next-generation antibodies, i-body, which mimics the shape of shark antibodies, allowing for high specificity and strong affinity against a particular disease-causing target. We later successfully screened an i-body that presents strong binding affinity against human RANKL and we named it "i-body ADR3".

What did you find?

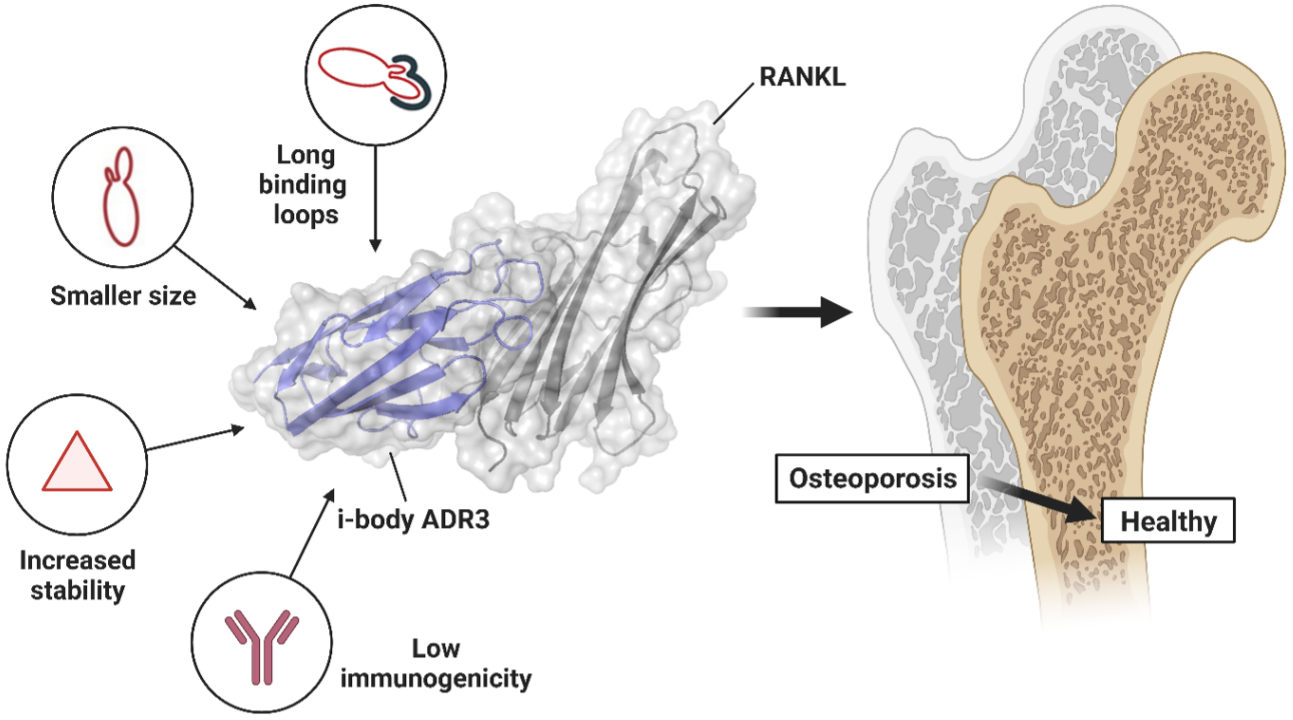
1. i-body ADR3 mimics the shape of shark antibodies, containing binding loops twice the length of human antibodies, with less than one-tenth of the size of a conventional IgG.
2. i-body ADR3 is built on a human protein, predicted to have low immunogenicity.
3. i-body ADR3 neutralizes human RANKL and suppresses osteoclast differentiation and bone resorption, with the potential to serve as a novel therapeutic for osteoporotic patients.
4. The binding loops inserted in i-body ADR3 are readily manipulated, which can further enhance the affinity against human RANKL. i-body ADR3 can also be tailored to increase the duration of the time the drug stays in the body through PEGylation or adding an Fc-Fragment.
5. Our i-body library contains over 20 billion drug candidates, holding limitless potential for other disease-causing targets.

What is the application of your finding?

1. i-body ADR3 is designated to alleviate bone loss in osteoporotic patients and improve their bone quality.
2. A small-molecule inhibitor of RANKL was reported to slow down the bone metastasis of breast cancer and melanoma cells. i-body ADR3 is more stable than small molecules and much smaller in size than IgGs with more efficient tissue penetration. Therefore, i-body ADR3 could be also a good candidate drug for bone metastasis.

Did you face any challenges?

Drug specificity is always a challenge during development, and it is almost impossible to test the off-target interactions due to the countless molecules in cells. To examine the specificity of i-body ADR3, we deliberately overexpressed RANKL in a human cell line and found that i-body ADR3 only binds to RANKL-expressing cells, which suggests a high degree of specificity in ADR3-RANKL binding .



33rd Australian & New Zealand Bone and Mineral Society Annual Scientific Meeting

SAVE THE DATE October 22 – 25, 2023

Newcastle City Hall, New South Wales

Calendar of Events

Melbourne Bone Group Meeting
29 March 2023, Melbourne, Australia
More information here

Bone Research Society Annual Meeting
14-15 April 2023, Liverpool, UK
Abstract submission closed
More information here

European Calcified Tissue Society Congress
15-18 April 2023, Liverpool, UK
Abstract submission closed
More information here

International Symposium on Paget's Disease
19-20 April 2023, Manchester, UK
Abstract submission closed
More information here

ANZBMS Osteoporosis - 3 part webinar series
'Part 1: Initiating Osteoporosis Therapies'
10 May 2023, FREE for ANZBMS members
More information here

WCO-IOF-ESCEO Congress
4-7 May 2023, Barcelona, Spain
Abstract submission closed
More information here

Cancer and Bone Society Conference
7-10 June 2023, St Louis, USA
Abstract submission deadline: 15 March 2023
More information here

KSBMR Seoul Symposium on Bone Health
18-20 May 2023, Seoul, South Korea
Abstract submission deadline: 3 March 2023
More information here

OIFE Topical Meeting: Balancing life with OI
9-10 June 2023, Stockholm, Sweden
Abstract submission deadline: 6 March 2023
More information here

ANZBMS Annual Scientific Meeting
22-25 October 2023, Newcastle, Australia
Abstract submission deadline: 21 July 2023
More information here

HubLE News

Niloufar Ansari

HubLE Editor-in chief for innovative science communication, **Niloufar Ansari,** is stepping down from HubLE after 3.5 years. The HubLE team and research community thanks her for her dedication and excellent work. She was instrumental in creating new content, including captions for our video-based content and the new structure of HubLE with five key features:

1. **HubLE Graphics:** Images, infographics, and doodles.

2. **HubLE Publications:** Published research in the form of author interviews, thesis summaries, and scientific highlights.

3. **HubLE Exchange:** Scientific exchanges and reports from scientific meetings featuring community members.

4. **HubLE Opinions:** Opinion pieces emphasizing critical barriers and topics of debate facing the community.

5. **HubLE Resources:** Innovative scientific methods and techniques, research groups, and new research.

Aline Bozec

Jonathan Gustafson

The new editor in chief for innovative science communication will be **Aline Bozec**, who will continue to work closely with **Jonathan Gustafson**, Editor-in-Chief for Scientific Content. They will be organising a range of activities with the aim of supporting the next generation of MSK scientists to shape the future of our field, providing high-quality accessible knowledge with an emphasis on innovation, and empowering early investigators to share their work with other researchers and professionals from across the world.

Join the HubLE community today!

To share your ideas and learn from our international community, visit our website **www.huble.org** and view the latest content from the HubLE community including Exchange interviews with Neharika Bhadouria (Purdue University, USA) during ORS 2022, and HubLE Publications interview with Marco Ponzetti (University of L'Aquila, Italy).

ANZBMS Researchers:

We want to share & celebrate your wins!

We are on the lookout for ANZBMS members who have celebrated success (awards and publications) to be highlighted in the Spotlight or Publication sections for the upcoming editions of the newsletter.

We would also love to highlight member's beautiful research-related images on our newsletter cover.

If you know of someone or want to self-nominate, please email us at **newsletter@anzbms.org.au**