

ANZBMS Newsletter

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ANZBMS Committee Updates

ANZBMS Member Publication Highlights

Cover Image: The metaphysis of a 12-week-old female $Dmp1^{cre.Socs3^{fl/fl}}$ mouse femur, depicting **low**, **medium**, and **high** tissue density. Image courtesy of Dr Natalie Wee, Senior Research Officer and Marian and E.H. Flack Fellow at St Vincent's Institute of Medical Research. More information can be found at <https://doi.org/10.1530/JOE-22-0084>

500µm





Welcome to the ANZBMS Newsletter

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ECI Issue: December 2022

Next Issue: March 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

Hope that you are well and looking forward to end-of-year celebrations!

In this issue of the newsletter, we celebrate the success of our researchers overseas with a focus on the ASBMR award winners (pp. 5 & 6) and provide an update on the workings of the various ANZBMS committees (pp. 7 & 8)

Our publications section continues to highlight the exceptional work of ANZBMS members (pp. 10-12).

The newsletter editorial board has changed. We would like to thank Dr Niloufar Ansari (Outgoing Editor-in-Chief) for her leadership and contribution to the ANZBMS newsletter editorial board over the past two years. We also welcome Emma Cheney to the editorial board and wish her well in her role as Copy Editor. Dr Madhuni Herath has taken on the role of Editor in Chief. Our editorial board looks forward to working with the ECI newsletter editorial team, in the exciting merger planned for 2023 - our combined issue will be published in March 2023!

As the year comes to an end, we hope that you can look back and celebrate what has been a year of new beginnings, with a return to face-to-face conferences and in person networking, which has hopefully led to new collaborations and rekindling of old friendships and networks.

We wish you all a safe and joyful holiday season!

Do you have any news or successes to share or would like to provide feedback? Contact us at newsletter@anzbms.org.au

Happy reading!

ANZBMS Newsletter Editorial Board



**Madhuni
Herath**



**Emma
Cheney**



**Martha
Blank**



**Hanh
Nguyen**



**James
Smith**



President's Comments



Professor Mark Forwood

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

ANZBMS colleagues, it is unbelievable that a year has passed for the current Council and we are already close to Christmas. While the pandemic has been defeated politically, we know that it still challenges the community and the health system, and perhaps also Dickens' contention about "*laughter and good-humour*", though we welcome more of the latter and less of the former. This has been a very busy year for Council and its committees. As noted in earlier newsletters, Council and committees undertook review of their membership and terms of reference. Most recently, Dawn Coates agreed to take over Mark Cooper's role as ANZBMS Secretary. Council also reviewed our policy library and identified that ANZBMS did not have a formal Conflict of Interest (COI) policy. After reviewing examples from other organisations, we drafted a COI Policy and related guidance. That policy is now established and published on the ANZBMS webpage. The policy provides general guidance for ANZBMS members and specific guidelines for leadership on Council and Committees. In conjunction with the policy, we are developing a Register of Interests and a Register of Gifts, Benefits and Honoraria that will be available for review by ANZBMS members. This is an important development for ANZBMS governance. Council have also updated the Strategic Plan for 2022-2025, available on the

"It is a fair, even-handed, noble adjustment of things, that while there is infection in disease and sorrow, there is nothing in the world so irresistibly contagious as laughter and good-humour."

(Charles Dickens, "A Christmas Carol", 1843)

website, also a key governance and guiding document for the Society.

Our Committees continue to undertake the key work to achieve objectives in the Strategic Plan, and strengthen the reputation of ANZBMS. The Densitometry Faculty will now deliver both on-line and face-to-face densitometry courses each year to optimise availability. ANZBMS also received a request from the Emirates Osteoporosis Society to run a Clinical Densitometry course for their members. While we do get international registrations to our Australian densitometry course, this highlights its international standing. Likewise, Christian Girgis and the Clinical Practice committee have prepared a great program for the 2022 Postgraduate Course for Advanced Trainees, scheduled for late October. It has attracted 200 registrations, again highlighting the important role of ANZBMS in clinical education. As noted in the report from Richard Prince, the Therapeutics committee has made several important submission to the PBAC regarding therapies for musculoskeletal conditions. While not all applications are approved, mostly on economic grounds, feedback from PBAC indicates that they recognise the high level and standard of support via the Consumer Channel by individuals and societies including HBA and ANZBMS. I thank our committees and Chairs



President's Comments

for these submissions that clearly make a valuable contribution to PBAC and other regulatory decision making. Finally I want to recognise the Communications (Mel Cantley as Chair), ECIC and Editorial Committees for the important work of promoting ANZBMS, members and issues across a range of media. Most recently, the social media team (lead by Sarah Hosking and Rouha Granfar) were active in promoting World Osteoporosis Day and the #StepUpForBoneHealth campaign on behalf of ANZBMS. We also supported Musculoskeletal Australia in their #RattleYaBonesDay campaign on Oct 31st. This is a National Day of

Awareness for all muscle, bone and joint conditions. I thank Niloufar Ansari for her leadership as Editor-in-Chief of the newsletter and wish her well in her new career, and welcome Madi Herath as the new EIC from this edition onwards. Thanks to all members of our Communications Committee, newsletter and social media teams for this work. As the end of year approaches, please take time to enjoy the break in whatever ways you find relaxing and rewarding; and have a safe, healthy, successful and rewarding New Year. I look forward to working with you to progress the ANZBMS mission in the new year.



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Last Call To Attend The 2022 H Fleisch Workshop

The International Federation of Musculoskeletal Research Societies (IFMRS, www.ifmrs.org) is happy to announce that **The 2022 H Fleisch Workshop** will be held on 20-22 November in Brugge, Belgium. Registration for this meeting is ongoing and we warmly encourage you to attend.

| | | |
|---|--|---|
|  IFMRS <small>INTERNATIONAL FEDERATION OF MUSCULOSKELETAL RESEARCH SOCIETIES</small> | 4th Herbert Fleisch Workshop |  |
| KU LEUVEN | 20-22 November 2022 Brugge, Belgium | |

The Herbert Fleisch Workshop is a 3-day residential workshop for young and mid-careers scientists working in musculoskeletal research. It's a few days of learning, discussion and great networking with the top scientists in the field.



ANZBMS Member Achievements

The Gideon A. Rodan Excellence in Mentorship Award



The Gideon A. Rodan Excellence in Mentorship Award is given annually by ASBMR in recognition of outstanding support provided by a senior scientist who has helped promote the independent careers of young investigators in bone and mineral metabolism. The award includes a \$2,000 honorarium and a plaque which is presented at a morning plenary session at the Annual Meeting.



Congratulations to Prof Ego Seeman, M.D.

The 2022 Gideon A. Rodan Excellence
in Mentorship Award Recipient

This award was presented during the ASBMR 2022 Annual Meeting at the Austin Convention Center in Austin, Texas, USA.

Dr. Ego Seeman is Professor and Endocrinologist in the Departments of Medicine and Endocrinology, Austin Health, University of Melbourne, Melbourne, Australia. He has worked in the field of bone biology for 40 years studying the epidemiology, pathogenesis and treatment of bone fragility.

"I thank the ASBMR Society for this recognition and great honor. I have mentored several students and thank Dr Sabashini Ramchand for nominating me for this award. Sabashini is completing her postdoctoral training and is now an independent investigator who now teaches me using her wonderful sense of bone biology. I express my deep gratitude to two giants of the field who supported my nomination, Professor TJ Martin who mentored me in my youth and continues to inspire me with his scholarship, and Professor John Bilezikian, first among equals at the round table of mentors. I have been privileged to be guided by luminaries, Professor Austin E Doyle, a man who electrified a room with his wit, intelligence and knowledge, by Professor B Larry Riggs, the Master of the Never-Ending Challenge of osteoporosis who has mentored over 50 leaders of our field and the great A Michael Parfitt, who blessed us all with his insights. If I have passed on only a tiny amount of the courage, intellectual rigor, imagination and scholarship given to me by my teachers, then I feel truly blessed. I hope I have honored work that now honors me. I thank Natalie, my wife, who makes everything possible and everything worthwhile." ~ Ego Seeman, M.D.



ANZBMS Member Achievements

ASBMR Young Investigator Award Recipients

We would like to congratulate our ANZBMS Early Career Investigators who received a Young Investigator Award at the recent American Society of Bone and Mineral Research Annual Scientific Meeting. This award recognises young investigator members who submit top-ranking abstracts to an ASBMR Meeting.



Dima A. Alajilouni, The B.O.N.E award winner for the ANZBMS/ASBMR Exchange Program

Muscle strength and physical performance are associated with risk of post fracture mortality but not subsequent fracture in men.



Tian Nie, University of Melbourne

Estradiol increases endocortical deposition, trabecular bone volume and bone strength in an adolescent male-to-female mouse model of gender affirming hormone therapy.



Dr. Renee Ormsby, Harvard University

Anti-RANKL inhibits the formation of lesions in a murine model of fibrous dysplasia.



Dr. Sabashini K. Ramchand, Harvard

Denosumab prevents bone Loss and microstructural deterioration in premenopausal women with breast cancer receiving estradiol suppression therapy: A randomized controlled trial.

Comparative histomorphometric effects of teriparatide, denosumab, or both on postmenopausal osteoporotic women: A randomized controlled trial.



Amy Ribet, The University of Western Australia

*Sugar transporter *slc37a2* regulates bone metabolism via a dynamic tubular lysosomal network in osteoclasts.*



ANZBMS Committee Updates

Therapeutics Committee

1) Current Members:

| Name | Day Job | Status on |
|-------------------------|---|----------------------|
| Richard Prince | Adult Endocrinology (Perth) | Chair 2017 - current |
| Ivone Johnson | ANZBMS Executive Officer | Executive Officer |
| Mark Forwood | ANZBMS President | 2021 - current |
| Peter Simm | Paediatric Endocrinology (Melbourne) | 2018 - current |
| Grahame Elder | Nephrology (Sydney) | 2018 - current |
| Alan Doube | Rheumatology (Hamilton, NZ) | 2020 - current |
| Belinda Beck | Director of Research, The Bone Clinic | 2020 - current |
| Christian Girgis | Adult Endocrinology (Sydney) | 2022 - current |
| Mathis Grossmann | Adult Endocrinology (Melbourne) | 2022 - current |
| Hanh Nguyen | Adult Endocrinology (Melbourne) | 2022 - current |
| Wei Wen Chen | Adult Endocrinology (Healthy Bones Australia, Sydney) | 2022 - current |

2) Current Projects:

Romozosumab and PBAC

Amgen has advised that the PBAC's decision at their July meeting was to *not recommend* romozosumab for first line use following an osteoporotic fracture in selected patients and not to expand second line listing by raising the BMD criterion from -3.0 to -2.5 and reducing the number of fractures from two to one to provide equity between primary and secondary prevention patients. However, the PBAC did make a note of the high level and standard of support via the Consumer Channel by individuals and societies including Healthy Bones Australia and ANZBMS, which seems to have helped convince them that there is a place in clinical practice for the use of romozosumab in the above patients.

Burosumab and PBAC

The PBAC noted and welcomed the input from individuals (175), health care professionals (12) and organizations (2) via the Consumer Comments facility on the PBS website. The PBAC noted the advice received from the ANZBMS and the Australasian Paediatric Endocrine Group strongly supporting the use of burosumab in clinical practice. The PBAC specifically noted the advice that the use of burosumab may reverse the serious disabilities associated with XLH and significantly improve quality of life. The PBAC noted that this advice complemented the evidence provided in the submission for paediatric and adult patients.



ANZBMS Committee Updates

Outcome: The PBAC is likely to recommend burosumab for the treatment of paediatric and adult patients with X-linked hypophosphataemia (XLH). The PBAC noted the high clinical need and strong consumer support for treatments for this condition. It should be noted that the PBAC is considering costs in the order of “ICER (incremental cost ratio) of \$355,000 to <\$455,000per QALY.”

Probable indication: It seems likely that the indication will be an S100 application accessed by the current PBS system. Patients must be treated by one of the following specialists: (i) paediatric endocrinologist, (ii) paediatric nephrologist, (iii) endocrinologist, or (iv) nephrologist.

“Patients must have a diagnosis of X-Linked hypophosphataemia by the presence of all of the following: (i) a serum phosphate concentration below the age adjusted lower limit of normal; (ii) current or historical (for those with growth plate fusion) radiographic X-ray evidence of rickets; (iii) elevated (or inappropriately normal) serum or plasma FGF-23 levels of above the mean of the assay-specific reference range; (iv) renal phosphate wasting demonstrated by a ratio of tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) according to age specific normal ranges using the second morning urine void and paired serum sample measuring phosphate and creatinine.”

Hypophosphatemia working party - developing advice for diagnosis and treatment

The first meeting of 2022 was held on 18 August.

Theramex Risedronate EC PBAC application to November 2022 meeting

ANZBMS advice submitted to the PBAC public advice portal as previously advised to members.

Aromatase inhibitor treated women post breast cancer

PBAC Secretariat reported on 14 Sept 2022:

“The PBAC deferred the consideration of alendronate, risedronate, and zoledronic acid for the treatment of osteoporosis in patients diagnosed with breast cancer who are taking an aromatase inhibitor, and in patients aged under 70 who have not had a prior fracture due to minimal trauma. The PBAC was of a mind to recommend alendronate and zoledronic acid for both populations, but deferred consideration pending a review of the Medical Benefits Scheme (MBS) implications, to ensure that the bone densitometry MBS items could be aligned with the PBAC recommendations. The PBAC was also of a mind to recommend risedronate for both populations on a cost-minimisation basis to alendronate. The PBAC did not recommend denosumab for either population.”

Prof Richard Prince, Chair of Therapeutics Committee

The ANZBMS Newsletter is merging with the ECI Newsletter in 2023. Watch out for our next issue in March 2023!



Isojima T, Walker EC, Poulton IJ, McGregor NE, Wicks IP, Gooi JH, Martin TJ, Sims NA. **G-CSF Receptor Deletion Amplifies Cortical Bone Dysfunction in Mice with STAT3 Hyperactivation in Osteocytes.** *J Bone Miner Res.* 2022. doi: 10.1002/jbmr.4654

What is the background of the study?

This study started from an unexpected finding in our main study of cortical maturation. We found that global knockout of the G-CSF receptor in mice with delayed cortical maturation due to deletion of a STAT3 inhibitor in osteocytes resulted in a very seriously delayed formation of cortical bone. This surprised us because, even though G-CSF induces STAT3 signalling, its receptor is not expressed in osteocytes. The distinctive bone phenotype, and the potential relevance to mechanisms that promote cortical bone development, made us study the new mouse in detail.

What did you find and what message do you want readers to take away?

We found that STAT3 hyperactivation in osteocytes induced a very high level of cortical porosity due to elevation of bone formation, bone resorption and vascularization. This means the STAT3 signalling pathway must be suppressed for good quality cortical bone to form. It also showed that mouse bone, like human bone, is capable of intracortical resorption and formation. This means mice could be a better model for studying human cortical bone than previously thought.

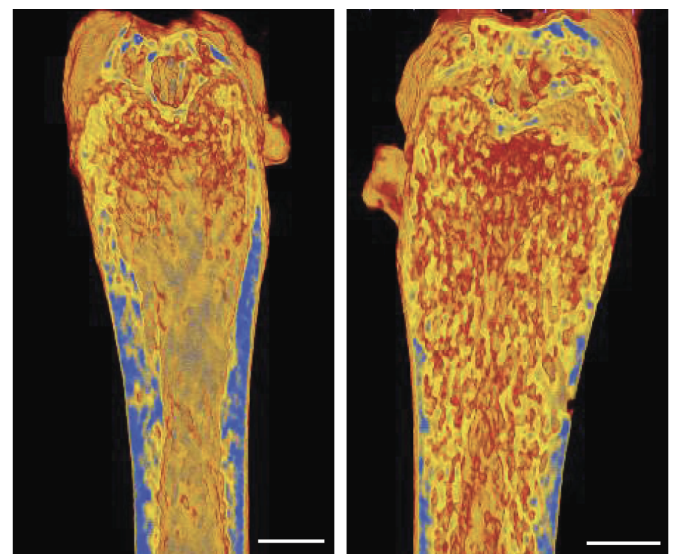
What is an application of your findings?

Our goal is to uncover the molecular mechanisms for cortical bone development, maintenance, and degeneration. We think that

our new finding should open the new research area for understanding cortical bone. Our finding suggests that STAT3 hyperactivation in osteocytes could be involved in conditions of high cortical porosity, such as in inflammatory conditions or during ageing. This is what we are now working on.

Did you face any challenges during the study?

Yes, the bone was so crazy that it was really difficult to analyze! We couldn't use the standard methods for micro-CT, so we used an unbiased micro-CT method which we had recently developed to measure bone mass at multiple thresholds. This new method really made it possible to understand cortical bone development and we are applying it to other questions now.



Dmp1^{Cre}:Socs3^{ff} *Dmp1^{Cre}:Socs3^{ff}:Csf3r^{-/-}*

low density high



Reid IR, Bastin S, Horne AM, Mihov B, Gamble GD, Bolland MJ. **Zoledronate Reduces Height Loss Independently of Vertebral Fracture Occurrence in a Randomized Trial in Osteopenic Older Women.** *J Bone Miner Res.* 2022 Aug 19. doi: 10.1002/jbmr.4684.

What is the background of the study?

Height loss is measured as an endpoint in some osteoporosis studies, and has been thought to be a surrogate for vertebral fractures. This analysis of our recent trial of zoledronate in osteopenic older women studied the relationship between height loss and vertebral fractures in more detail.

What did you find and what message do you want readers to take away?

We found that most height loss is not attributable to vertebral fractures, so height loss alone cannot be used to detect vertebral

fractures. We found that zoledronate reduced height loss in both those with and those without incident vertebral fractures. Zoledronate might reduce subtle vertebral deformities that are not detected using current definitions, but might also preserve inter-vertebral disc height.

What is an application of your findings?

Height loss is an important endpoint of osteoporosis trials in its own right, since it is independently related to quality of life.

Sim M, Strydom A, Blekkenhorst LC, Bondonno NP, McCormick R, Lim WH, Zhu K, Byrnes E, Hodgson JM, Lewis JR, Prince RL. **Dietary Vitamin K1 intake is associated with lower long-term fracture-related hospitalization risk: the Perth longitudinal study of ageing women.** *Food Funct.* 2022 Oct 17;13(20):10642-10650. doi: 10.1039/d2fo02494b. PMID: 36169025.

What is the background of the study?

The dietary management of osteoporosis has been restricted to a discussion of calcium and Vitamin D. However, given our focus on improving the dietary management of musculoskeletal disease, we and others have provided epidemiological evidence for the benefits of vegetables on fracture reduction. These findings have led to us to investigate the nutraceutical constituents of foods that may be responsible, such as Vitamin K.

Vitamin K plays a critical role in the carboxylation of the Vitamin K dependant bone

protein, osteocalcin (OC). Our previous clinical trial showed that increasing daily intake of Vitamin K1-rich vegetables over four weeks significantly reduced total OC by conversion to the carboxylated form retained within the skeleton. This supports the concept that bone structural proteins may play a role in reduced fracture. This is important because studies suggest that fracture risk increases in those with inadequate Vitamin K consumption.

In Australia, dietary guidelines for Vitamin K are substantially lower compared to the USA (60-70µg/d vs. 90-120µg/d) and may be



insufficient to optimise bone metabolism. As such, we investigated the relationship between dietary Vitamin K1 intake with long-term fracture risk in community-dwelling older Australian women (age ≥ 70 years, $n=1373$). We also examined whether there were dose-dependent thresholds for dietary Vitamin K1 intakes to be associated with lower fracture risk.

What did you find and what message do you want readers to take away?

Compared to women with the lowest Vitamin K1 intake (Quartile 1, $<61\mu\text{g/d}^{-1}$), women with the highest Vitamin K1 intake (Quartile 4, $\geq 99\mu\text{g/d}^{-1}$) had 31% and 49% lower hazards for any fracture and hip fracture related hospitalisation over 14.5 years, respectively. Results were independent of lifestyle factors, fracture history and plasma 25(OH)D. Most importantly, we report a nadir in the relative hazard for any fractures at a Vitamin K1 intake of $\sim 100\mu\text{g day}^{-1}$.

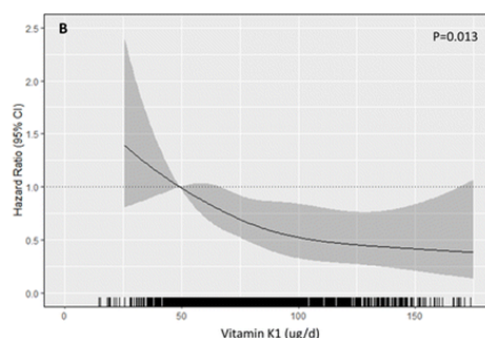
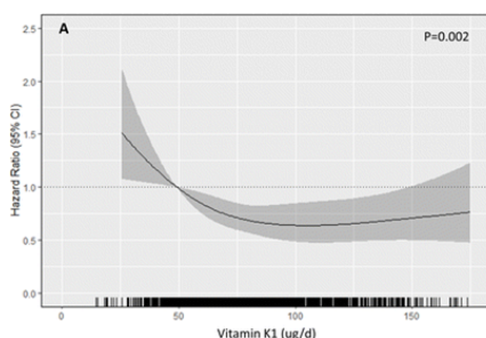
What is an application of your findings?

Approximately $100\mu\text{g}$ of Vitamin K1 can easily be achieved by consuming one to two serves per day (between 75g to 150g) of vegetables such as spinach, kale, broccoli and cabbage. These recommendations are in-line with public health guidelines advocating higher vegetable

intake (e.g. ≥ 5 serves daily), which include one to two serves of green leafy vegetables. This is a simple strategy to ensure Vitamin K needs are met, which could have long-term positive implications for musculoskeletal health. Given the large size of the association recorded, this paper should strengthen calls for an RCT of the long-term outcomes of dietary Vitamin K1 supplementation in deficient populations.

Did you face any challenges during the study?

Getting funding and analysing the Vitamin K content of Australian food was a challenge. This is essential given the absence of a database for Vitamin K in Australia, and evidence that Vitamin K content of food is known to vary substantially depending on region. It took us a couple of years to develop an analytical method to measure the Vitamin K content of commonly consumed foods in Australian supermarkets, publish our database, and finally apply it to food frequency questionnaires in this cohort. We also needed to validate our dietary estimate of Vitamin K1 against a biomarker of Vitamin K status, in this case the ratio of undercarboxylated OC to total OC (ucOC:tOC). Finally, having access to an epidemiological study with detailed food intake and fracture outcomes was essential.



Multivariable-adjusted relationship between dietary Vitamin K1 intake with any fracture (A) and hip fracture-related hospitalisations over 14.5 years. The hazard ratio compares the specific intake of Vitamin K1 to the median intake for women in the lowest quartile ($49\mu\text{g/d}^{-1}$).



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Calendar of International Events & Webinars

4th Herbert Fleisch Workshop

20-22 November 2022, Brugge, Belgium

More information [here](#)

24th Asia-Pacific League of Associations for Rheumatology Congress (APLAR)

6-9 December 2022, Hong Kong

More information [here](#)

Orthopaedic Research Society 2023

10 - 14 February 2023, Dallas, Texas, US

More information [here](#)

Bone Research Society Annual Meeting 2023

14-15 April 2023, Liverpool, UK

Abstract submission deadline 12 Dec 2022

More information [here](#)

European Calcified Tissue Society 2023

15 -18 April 2023, Liverpool, UK

Abstract submission deadline 12 Dec 2022

More information [here](#)

11th International Meeting of Paediatric Endocrinology

4-7 March 2023, Buenos Aires, Argentina

More information [here](#)

7th International Congress on Controversies in Rheumatology and Autoimmunity

16 - 18 March 2023, Turin, Italy

More information [here](#)



To support the next generation of scientists to shape the future of MSK research, we started 'HubLE Early Investigator Spotlight' to introduce early investigators and highlight their published HubLE content.

Our Early Investigator Spotlight in October was the HubLE Exchange interview with Giulia Furesi (Washington University in St. Louis, USA) at the ASBMR 2022. Check out Giulia's interview [here](#) to learn more about her research on the role of osteolineage cells in regulating breast cancer.

| | |
|---|---|
|  Early Investigator Spotlight October 2022 |  |
| RESEARCH TITLE | |
| <i>Adult-Derived Osteolineage (Osterix +) Cells As New Regulators Of Breast Cancer</i> | |
| RESEARCH CATEGORY | |
| <i>Basic</i> | |
| KEYWORDS | |
| <i>Breast Cancer, Osterix, Bone Marrow, Cancer-associated Fibroblasts, Tumor Microenvironment</i> | Giulia Furesi, PhD Washington University in St. Louis, USA. |

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