Bone cells named for Power Rangers could morph thinking on skeletal disease therapy

By Ana Mulero

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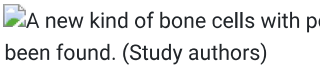

A new kind of bone cells with potential therapeutic uses has been found. (Study authors)

A newly discovered type of cell found in the blood and bone marrow is poised to reveal novel and targeted therapeutic approaches for osteoporosis and other skeletal diseases.

Researchers at the Garvan Institute of Medical Research, an Australian biomedical research institute, named the bone cells "osteomorphs," after the Mighty Morphin Power Rangers. In a study published in *Cell* on Thursday, the cells were said to play a critical role in controlling and maintaining the bone by fusing and forming cells known as osteoclasts that are specialized in breaking down bone tissue.

The research team argues that the discovery of osteomorphs could improve understanding in the field of bone resorption — through which osteoclasts break down bone tissue and release minerals — and lead to findings on underlying mechanisms of bone conditions and their treatments.

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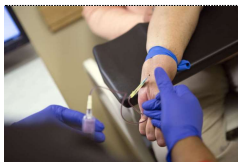

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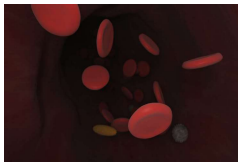

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Intravital Microscopy and Gene Expression Lab, says the discovery "is a game-changer" because it sheds light on bone biology and "presents significant new inroads for osteoporosis therapy."

In an interview with *The Academic Times*, Phan noted that anyone can get osteoporosis, which develops as bones become brittle with age, increasing the risk of fracture and mortality.

The discovery also holds potential for addressing the types of cancers that spread to the bone. That will make it important for researchers to understand the biological processes unfolding inside the bone, and particularly as old bone is continuously removed through resorption, researchers will look to study how osteoclasts reabsorb bone.

For the study, the Garvan researchers used experimental models, collaborating with Imperial College London colleagues to develop a method to study osteoclasts in live animal bone in real time. They developed single-cell RNA-sequencing technology specifically for the purposes of studying the new bone cells, then isolated the cells and sequenced the genes that they expressed.

While these cells expressed many genes in common with the osteoclasts from which they came, they also expressed some others. Many of the latter genes are involved in bone diseases, according to Phan. F[illegible]eleted 40 genes observe[illegible] osteomorphs in

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the experimental models. For 17 of them, the deletion impacted both the amount of bone and bone strength, the study shows.

The findings challenge the existing consensus that osteoclasts undergo cell death after completing their function of breaking down bone tissue. Instead of dying, osteoclasts tested in the study broke up into smaller cells that then joined back up to form large osteoclasts. This process, of breaking up and reassembly of these bone-resorbing cells, was dubbed "osteoclasts recycling."

Phan and Michelle McDonald, the study's first author and leader of Garvan's Bone Microenvironment Group, noted that osteoclasts recycling was entirely new to their team, which hypothesized that the process could increase the lifespan of the cells.

Yet another area where results provide new insights relates to a side effect associated with the osteoporosis treatment denosumab.

"Some individuals who discontinue the osteoporosis treatment denosumab experience a reduction in bone mass and an increase in so-called 'rebound vertebral fractures,'" Phan explained. Additional insights into how osteoporosis medications affect osteomorphs could inform potential improvements to these medications.

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The study has also opened multiple new lines of research. Genes that switched on in osteomorphs offer numerous leads "in terms of trying to understand what other molecules are important in the regulation of bone," Phan said.

The Garvan Institute is already looking to hire a research officer/postdoctoral researcher whose responsibilities will include performing and analyzing flow cytometry experiments of the new type of bone cell in mouse and clinical studies. The immediate next step for Phan is to understand whether osteomorphs could be significant in the activation of cancer. Researchers plan to introduce cancer models into their system to see how the observed processes play out in live animals.

“We’re putting a whole animal that is alive under the microscope and seeing how everything is moving around and interacting,” Phan said. “That will be the key thing moving forward to understand how cancer cells, for example, might interact with the cells inside the bone."

Another area for further research is the role of osteomorphs in autoimmune diseases, such as rheumatoid arthritis, as Phan says these new cells' dysregulation could be causing bone destruction in the joints.

The study, "Osteoclasts recycle via osteom[illegible]RANKL-stimulated bone re[illegible]blished in Cell

on Feb. 25. The authors of the study were Michelle M. McDonald, Weng Hua Khoo, Ya Xiao, Jad Zamerli, Peter Thatcher, Wunna Kyaw, Karrnan Pathmanandavel, Abigail K. Grootveld, Imogen Moran, Danyal Butt, Akira Nguyen, Sean Warren, Sindhu T. Mohanty, Niall Byrne, Rachael L. Terry, Marija K. Simic, Ryan Chai, Julian M.W. Quinn, Scott E. Youlten, Jessica A. Pettitt. David, Abi-Hanna, Paul Timpson, Paul A. Baldock, Michael J. Rogers, Robert Brink, Peter I. Croucher, and Tri Giang Phan, The Garvan Insitute of Medical Research; Pei Ying Ng and Nathan J. Pavlos, University of Western Australia; Maté Biro, University of New South Wales; Natalie C. Butterfield, Siobhan E. Guilfoyle, Davide Komla-Ebri, Michael R.G. Dack, Hannah F. Dewhurst, John G. Logan, Graham R. Williams, and J.H. Duncan Bassett, Imperial College London; Yongxiao Li, The Australian National University; Rohit Jain and Wolfgang Weninger, University of Sydney; Mischa Lundberg and John P. Kemp, University of Queensland; Shuting Sun and Frank H. Ebetino, Biovinc; and Woei Ming Lee, The Australian National University.