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**News Release**



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**UAMS Bone Researcher Provides Expert Commentary
in Publication’s Controversial Reversal of Long-Held Theory**

LITTLE ROCK — The latest issue of *PLOS Genetics* includes two publications that challenge the basic assumptions behind 24 years of bone and metabolism research, and given the magnitude of the potential paradigm shift, the editors turned to Stavros C. Manolagas, M.D., Ph.D., of the University of Arkansas for Medical Sciences (UAMS) to provide expert commentary and context.

Manolagas is a distinguished professor of medicine, professor of orthopedics and director of the Division of Endocrinology and Metabolism in the Department of Internal Medicine in the UAMS College of Medicine. He is director of the UAMS and Central Arkansas Veterans Healthcare System Center for Osteoporosis and Metabolic Bone Diseases — one of the largest and longest-funded osteoporosis research centers in the world.

He has 45 years of experience in bone research and is one of the senior figures in the community, receiving the American Society for Bone and Mineral Research’s oldest and most prestigious lifetime achievement honor — the William F. Neuman Award — in 2017.

Manolagas said it is vital for science to continue to question assumptions, challenge previous theories and avoid blind loyalty to the status quo. In a wider global context when science is not trusted in all circles, Manolagas said it is more important than ever for scientists to uphold basic principles such as the reproducibility of results and the willingness to constantly question and improve.

“We have to really make every effort to make it easy for others to confirm what one scientist finds,” Manolagas said. “It is critical. It's essential for the progress of science. Whatever scientific field you’re talking about, we must deal with facts. And we can only establish facts in science by reproducibility. It can’t just be that a certain idea has become dogma.”

The debate all centers around osteocalcin, a protein that is produced by osteoblasts, which are cells involved in bone formation. While scientists historically believed osteocalcin was primarily functioning on bones, research 24 years ago became the basis for a theory that osteocalcin was actually an endocrine hormone and therefore possibly involved in everything from diabetes to fertility to mental function.

Manolagas said this expanded view of osteocalcin as an endocrine hormone resulted in countless research dollars spent on attempting to support a flawed theory. Despite the mounting evidence against the hormone idea, it persisted, in part because the original research that proposed the theory was published in leading science journals and has never been retracted.

“It should not be this way, but sometimes it can be difficult to disprove a theory that makes that big splash and appears to be backed up by so many prestigious journals,” Manolagas said.

Manolagas and his counterpart at Massachusetts General hospital at Harvard, Hank Kronenberg, published an editorial in 2014 to address the irreproducibility problem in the bone field in general and specific concerns about the “osteocalcin is a hormone” theory. Now in the current issue of *PLOS Genetics*, there are two publications, each from respected scientists on opposite sides of the globe. One is from a large collaboration between the Van Andel Institute in Michigan, Harvard University, and Boston University along with scientists in New York, and the other is from a large Japanese group from the University of Nagasaki and three Institutes and laboratories from the University of Hangzou in China.

“These are large, extensive studies that basically shatter every claim made based on this underlying false assumption,” Manolagas said. “This is a huge deal in the field of bone and endocrine research because of the pressure involved, the history of the theory, the entire subfields of research that sprung up around it — this will have implications for many years to come.”

Manolagas said that it is easy for scientists, especially when they are early in their careers and looking to establish themselves, to look at situations like these as a failure.

“Instead, the fact is that science by definition is based on mistakes, fumbles and working ever closer to honing in on truth. Science is inexorably self-correcting,” Manolagas said. “Young scientists need to trust their intuitions, but be equally prepared to disprove their own hypotheses. It is not science to build a career around simply proving that you are right about something. Sometimes we are wrong. Acknowledge mistakes, and the sooner the better.”

This applies not just to individual scientists, but to the whole field, Manolagas said.

“We have to be able to root out issues with a theory, to monitor and police ourselves, because the fact is that if we don’t do that, we’re in trouble,” Manolagas said. “The public will lose faith and trust in the insights of science, and we cannot afford that.”

UAMS is the state’s only health sciences university, with colleges of Medicine, Nursing, Pharmacy, Health Professions and Public Health; a graduate school; hospital; a main campus in Little Rock; a Northwest Arkansas regional campus in Fayetteville; a statewide network of regional campuses; and seven institutes: the Winthrop P. Rockefeller Cancer Institute, Jackson T. Stephens Spine & Neurosciences Institute, Harvey & Bernice Jones Eye Institute, Psychiatric Research Institute, Donald W. Reynolds Institute on Aging, Translational Research Institute and Institute for Digital Health & Innovation. UAMS includes UAMS Health, a statewide health system that encompasses all of UAMS’ clinical enterprise including its hospital, regional clinics and clinics it operates or staffs in cooperation with other providers. UAMS is the only adult Level 1 trauma center in the state. *U.S. News & World Report* named UAMS Medical Center the state’s Best Hospital; ranked its ear, nose and throat program among the top 50 nationwide; and named six areas as high performing — cancer, colon cancer surgery, heart failure, hip replacement, knee replacement and lung cancer surgery.UAMS has 2,727 students, 870 medical residents and five dental residents. It is the state’s largest public employer with more than 10,000 employees, including 1,200 physicians who provide care to patients at UAMS, its regional campuses, Arkansas Children’s Hospital, the VA Medical Center and Baptist Health. Visit [www.uams.edu](http://www.uams.edu) or [www.uamshealth.com](http://www.uamshealth.com/). Find us on [Facebook](https://www.facebook.com/UAMShealth), [Twitter](https://twitter.com/uamshealth), [YouTube](https://www.youtube.com/user/UAMSHealth) or [Instagram](https://instagram.com/uamshealth/).

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