

## Bad to the bone: new research to shed light on osteoporosis

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Ten million people in the United States are estimated to already have bone diseases, and almost 34 million more are estimated to have low bone mass, putting them at increased risk for osteoporosis, according to the National Osteoporosis Foundation.

Liyun Wang, assistant professor of mechanical engineering at the University of Delaware, knows the serious consequences of osteoporosis.

Two of Wang's aunts have suffered from the insidious bone-thinning disease, and one aunt died within a year after falling and fracturing her hip.

Wang is now leading research that will shed light on how osteocytes--the cells encased inside your bones--sense external stimuli and communicate with cells on the surface, signaling them to either build more bone or remove existing bone.

The five-year, \$1.6 million project, ranked in the top 5 percent of research proposals recommended for funding by the National Institutes of Health (NIH) this year, holds promise in unveiling the mysteries of bone and joint diseases afflicting people worldwide.

The results may not only help scientists home in on the cause of osteoporosis and arthritis, but also develop more effective drug therapies to treat the debilitating bone and joint diseases.



The project will involve an interdisciplinary team of investigators at UD, including Prof. Mary C. Farach-Carson and Associate Prof. Randall Duncan, who hold primary appointments in biological sciences with joint appointments in mechanical engineering, and John Novotny, assistant professor of mechanical engineering.

"Bone and joint disorders affect almost half of all people over 50 years old, at a cost of \$250 billion annually in the United States," Wang said. "A third of the people who suffer a fracture due to bone loss end up dying within a year."

The embedded bone cells, or osteocytes, that Wang is studying, act like the bone's "brain."

"The osteocytes are very smart," Wang says. "They can tell whether a person is using his or her bones or not. If the person is physically active, the osteocytes tell cells on the surface that it's okay to put on more bone. Otherwise, they signal the surface cells to remove bone at a rate that can be as high as 3 percent bone mass per month, which is the case for patients confined to long-term bed rest and for astronauts," she notes.

The osteocytes lie in tiny pits or holes, called lacunae, within the bone. These living cells have many long arms that connect them to surface bone cells and the bone's vascular system. The narrow channels housing the osteocyte's arms (canaliculi) and the lacunae form a network through which a mixture of water, nutrients and other bioactive molecules flows.

"Although it is hard as cement, bone is actually like a stiff sponge," Wang says. "It's porous and has water inside. When we have mechanical loading, when you run, for example, a part of the leg bone is compressed, and water is pushed through gaps, less than a micrometer in size, between the osteocytes and the bone cement that surrounds them."



This powerful wave of fluid keeps the osteocytes happy and functioning well, Wang says, delivering nutrients to them from nearby blood vessels and quickly dispersing signaling molecules, such as calcium ions, from one cell to its neighbors.

Using a novel microscopic imaging method that Wang developed, which is based on fluorescence recovery after photobleaching (FRAP), the research team hopes to do what no one has done before: see inside living bone and determine how rapidly these signaling and nutrient molecules are transferred between the cells when a bone is at rest and when it is at work.

A high-powered laser-scanning microscope will be used to assess the movement of molecules in the tibia of an anesthetized mouse. A harmless green fluorescent dye, tagged to various-sized proteins, signaling molecules and cell nutrients, will be injected into the animal's bloodstream.

The dyed molecules will be subjected to a flash of intense light, temporarily photobleaching them black, leaving a distinct black sector surrounded by green. Thus, if the molecules diffuse into one another's territories, they can easily be tracked by color.

Using similar techniques, Wang is investigating the communication between bone and cartilage in the development and progression of osteoarthritis, one of five projects in an \$11 million NIH grant led by Thomas Buchanan, professor and chairperson of the UD Department of Mechanical Engineering. The UD effort includes a unique mentoring program for women scientists.

Wang says she is grateful for the mentoring and support she has received from her colleagues at UD since she joined the faculty in 2005, as well as from her doctoral advisers at the City College of New York, including



Profs. Susannah Fritton, Steve Cowin, and Sheldon Weinbaum; and Dr. Mitchell Schaffler, with whom she worked as a postdoctoral researcher at the Mt. Sinai School of Medicine.

Currently, Wang's laboratory group includes Wen Li, a graduate student in biomechanics and movement science, Xiaozhou Zhou, a graduate student in mechanical engineering, and undergraduate students Ben Keller and Laura Schultz, who are both working on degrees in mechanical engineering, and Samantha Nigro, who is pursuing her degree in biological sciences. Research associate Jun Pan will join the group at the end of this year.

"My students have been excellent," Wang says, smiling. "They are wellorganized and eager to learn how to do research. They are very motivated, and that is important. We have exciting work ahead of us!"

Source: University of Delaware

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