Muscles and bones in cahoots

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Traditionally, doctors and clinicians thought diseases that affect muscles or bones affected those areas specifically. For example, bone diseases only affect bones, or muscle diseases only concerned muscles. But recent evidence supports the notion that bones and muscles are more interconnected than previously thought. It seems that bones and muscles can release signals that directly affect one another's function or disease state. Even more remarkable is that these systems seem to produce secreting factors that communicate to distant parts of the body.

Dr. Marco Brotto, the director of the Muscle Biology Group at the Schools of Nursing and Medicine, University of Missouri-Kansas City (UMKC) will be discussing the latest findings about the shared communication and dependence between muscles and bones at the annual 2010 Experimental Biology conference in Anaheim, CA being held April 24-28. Brotto will deliver his presentation, "Evidence for Pathophysiological Crosstalk Between Bones, Cardiac, Skeletal and Smooth Muscles," on behalf of his team, which includes Leticia Brotto, Todd Hall and Michael Loghry, Sandra Romero, and collaborations between two other principle investigators from the University of Missouri-Kansas City, Kansas City, MO, Jon Bonewald and Mark Johnson; and Thomas Nosek, J. Shen and C-K Qu of Case Western Reserve University, Cleveland, OH.

The Cost of Aging

With new revolutions in medicine, the average lifespan in developed countries continues to increase. As a result, the incidence and cost of

treating age-related diseases has skyrocketed, particularly those that result from years of wear and tear of muscles and bones.

Every year, the cost alone in the United States of treating osteoporosis - an aging disease predominantly found in women that causes fragile bones-is $14 billion, according to The National Institutes of Health website. Other diseases, like sarcopenia - a muscle wasting disease - affects every individual over the age of 50 resulting in the loss of one to two percent of muscle mass each year. As the baby boomers get older, the trend in rising costs continues.

This is why Brotto's findings that muscle and bone diseases affect one another may have an astronomical impact when considering the long-term effects of designing new preventatives and treating age-related muscle and bone disorders.

The Lines of Communication

Brotto's collaborative group observed that mutations or defects in specific genes important for muscle function, also created changes in bones. The reciprocal effect happens when mutations are made that affect bone function. These observations led to the search for signaling components that could affect both organs, but the group has also encountered some intriguing surprises along the way.

Brotto researcher's discovered that bones act like glands to secrete hormones that are detected by muscles. Reciprocally, muscles are releasing factors, known as myokines that are detected by bones affecting bone mass and strength. And the separate muscle types, heart (cardiac), skeletal and smooth muscle (like that of the stomach and blood vessels) secrete different signals for different reasons.

The group identified multiple components of signaling systems involved

in muscle and bone communication. Specifically, they distinguished a certain type of prostaglandin released from bone cells (osteocytes). Other findings revealed that the Wnt pathway, which is important for normal development, could be linked to wasting diseases in both muscles and bones.

One area Brotto's group focused on was the regulation of calcium metabolism. Calcium is needed both to build strong bones and to make muscles contract. Researchers focused on a muscle specific phosphatase called MIP that decreases naturally as we age that may be involved the regulation of calcium levels in the body. Researchers removed the MIP protein from mice by knocking out the gene that codes for the protein. These mice had muscle weakness and faster aging, as well as reductions in bone densities. The mutant mice also had weakness in smooth muscle function of the contracting arteries and vessels. Interestingly enough, some of these results seemed to be gender specific. The female mice developed osteoporosis, but the males did not. And there was female bias for weakness in heart muscle function that was not seen in the male subjects. This data supports that calcium regulation is different between the two sexes, which may explain why women are more likely to get osteoporosis than men.

A New Approach to Bone Fractures: A Breakdown in Communication Between Muscle and Bone?

For the many diseases that target muscles diet, exercise and hormone therapy are the only treatments. Unfortunately, many patients have health conditions that prevent them from exercising limiting their treatment options. Brotto is hopeful that following the new line of research studying the communication between muscles and bones will identify novel therapies and potentially help millions of people.

When a bone is fractured, it is typically thought to be a defect in the strength of the bone. But the Bone-Muscle team at UMKC hypothesizes that it may be caused from a breakdown in communication between muscles and bones. Muscles put force on bones as they contract, which is known as mechanical loading. Perhaps the muscles put too much force on the bones at the wrong time, which results in a break.

"We would like to discover chemical factors that can bypass the issue of loading and could patch communication on the muscle side or the bone side to make the unity stronger," Brotto said.

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