New research could extend life of arthritic joints

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A medication already approved to build bone mass in patients with osteoporosis also builds cartilage around joints and could potentially be repurposed to treat millions of people suffering from arthritis, according to orthopaedic research at the University of Rochester Medical Center.

The study authors hope their laboratory findings, published in the current issue of *Science Translational Medicine*, will set the stage for the first human clinical trials to test human parathyroid hormone (brand name: Forteo) in this growing patient population.

Since 2005, arthritis has been ranked as the leading cause of disability in the United States by the Centers for Disease Control and Prevention. And by 2030 an estimated 67 million people, or 25 percent of the adult population in this country will have osteoarthritis (OA), a painful, degenerative joint disease that often begins with an injury and results in the progressive loss of cartilage. Current treatments for OA do not help improve the cartilage in the diseased joint, they only make the pain more bearable. Examples include oral anti-inflammatory agents (such as Advil or Naproxen), narcotics, or steroid injections into the affected joint. Surgical replacement of the joint and cartilage is usually required, although this major intervention often carries its own set of complications.

"We believe that a potential alternative to this cycle of pain and reduced quality of life has gone unnoticed for the past decade," said study co-author Michael J. Zuscik, Ph.D., associate professor, Department of

Orthopedics & Rehabilitation, Center for Musculoskeletal Research at URMC. "Given that Forteo is already FDA approved, our experimental findings make a compelling case for further clinical study of this drug in the context of arthritis."

The Food and Drug Administration approved Forteo a decade ago as a bone-building therapy for osteoporosis patients with severe bone loss. Although Zuscik and co-author Randy N. Rosier, M.D., Ph.D., professor of Orthopaedics & Rehabilitation, lead a laboratory that investigates osteoarthritis, through collaborative clinical work their group made an interesting observation: Occasionally, when a patient suffered from both disorders – osteoporosis and osteoarthritis – the symptoms of arthritis would improve after taking Forteo for osteoporosis.

This observation led the OA researchers to question whether the drug would have an impact on the molecular pathways that govern chondrocytes, the cells responsible for maintaining cartilage, and the changes that take place during joint degeneration. The team used a mouse model for post-traumatic knee osteoarthritis and demonstrated in several laboratory experiments that when Forteo was given daily for one month, the injured cartilage became as much as 32 percent thicker, cell production was enhanced, and genes and molecules associated with the degeneration of cartilage were suppressed.

The study was designed to mimic a common clinical situation in which injury to the meniscus and collateral ligaments result in the development of osteoarthritis later in life. Since the hallmark problem in osteoarthritis is the progressive and irreversible loss of cartilage, Zuscik said, the ability of parathyroid hormone to add new cartilage while blocking its degradation makes it a viable therapy.

In addition to the laboratory research, Zuscik and Rosier reviewed OA patient information from government databases. Of 4,000 people

diagnosed with knee arthritis, they found 14 who were also taking Forteo for osteoporosis. This small group of people reported less arthritis pain and a higher ability to function than a matched population of patients who were not taking Forteo.

Although this data involved a very small number of people and is therefore not conclusive, Rosier said, it does confirm observations made by him and other URMC orthopaedic specialists.

Future studies are still needed to address several important questions. There is some concern, for instance, about the safety of Forteo, which is made by Eli Lilly and Company and carries a black-box warning because it has been found to cause an increased risk of the bone cancer osteosarcoma, in rats. Due to this potential long-term risk in humans, Forteo is prescribed for short-term use up to two years. Thus, researchers will need to determine how long the protective/regenerative effect on cartilage persists after treatment is stopped.

Provided by University of Rochester Medical Center