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First-ever study: lack of critical lubricant causes wear in joints

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Mice that don't produce lubricin, a thin film of protein found in the cartilage of joints, showed early wear and higher friction in their joints, a new study led by Brown University researchers shows.

This link between increased friction and early wear in joints is a first; no other team of scientists has proven this association before. The finding, published in Arthritis & Rheumatism, sheds important light on how joints work. The discovery also suggests that lubricin, or a close cousin, could be injected directly into hips, knees or other joints inflamed from arthritis or injury – a preventive treatment that could reduce the need for painful and costly joint replacement surgery.

In an editorial that accompanies the journal article, orthopedics researchers from Rush University Medical Center in Chicago call the research an "important contribution to the field" and note that the use of biomolecules like lubricin to prevent joint wear "could have a substantial clinical impact, if successful."

Gregory Jay, M.D, a Rhode Island Hospital emergency physician and an associate professor of emergency medicine and engineering at Brown, led the research. For 20 years, Jay has studied lubricin's role as a "boundary lubricant" by reducing friction between opposing layers of cartilage inside joints. In this new work, Jay and his colleagues set out to answer the next question: Does reducing friction actually prevent wear, or surface damage, in joints?

To find out, Jay and his team studied cartilage from the knees of mice that don't produce lubricin. Directly after birth, the cartilage was smooth. But in as little as two weeks, researchers found, the cartilage began to show signs of wear. Under an electron microscope, scientists could see that the collagen fibers that cartilage is composed of were breaking up, giving the surface a rough, frayed appearance. This damage is called wear, an early sign of joint disease or injury.

Jay and his team then took the work a step further. To better understand how lubricin works, they tried to see the structure of the film. So they put a tiny bit of the protein under an atomic force microscope. At the nanoscale, the molecule appeared as a mesh – row upon row of interlocking fibers – that could repel a microscope probe. This repulsion, created with water and electrical charges, shows how lubricin acts as a buffer, keeping opposing layers of cartilage apart.

"We demonstrated that lubricin reduces both friction and wear and also showed how, on a molecular level, it does this work in the body," Jay said. "What's exciting are the clinical implications. Arthritis and sports injuries damage the joints of thousands of people in the United States and millions of people worldwide each year. Our aim is to make a treatment that can actually prevent wear in the joints."

Through Rhode Island Hospital, Jay has filed two patents on the protein and its sequences and, in 2004, helped form Tribologics, a biotech company formed out of Rhode Island Hospital. The Massaschusetts-based business is developing an injection treatment for inflamed joints that contains lubricin.

Source: Brown University