New injectable cell therapy could resolve osteoarthritis

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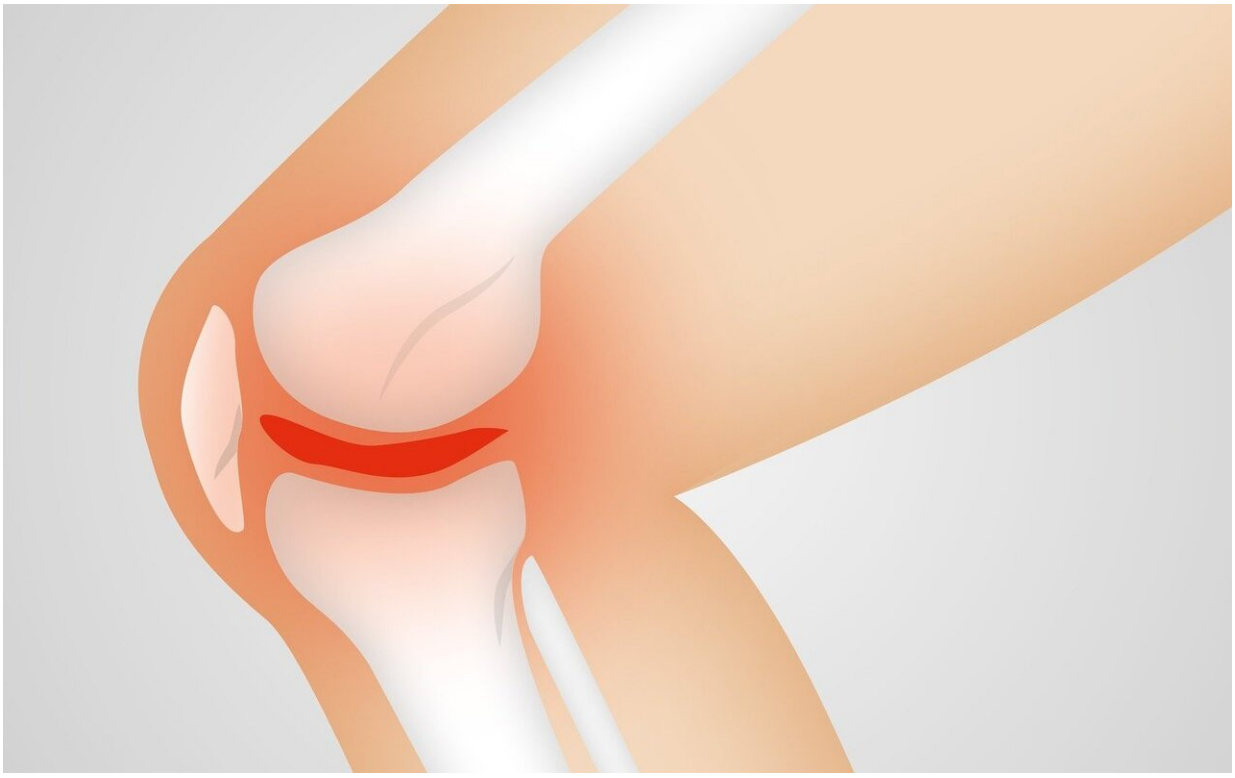

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Wake Forest Institute for Regenerative Medicine (WFIRM) scientists have created a promising injectable cell therapy to treat osteoarthritis that both reduces inflammation and also regenerates articular cartilage.

Recently identified by the Food and Drug Administration as a public health crisis, osteoarthritis affects more than 520 million people worldwide who deal with pain and inflammation. Osteoarthritis is typically induced by mechanical or traumatic stress in the joint, leading to damaged cartilage that cannot be repaired naturally.

"Without better understanding of what drives the initiation and progression of osteoarthritis, effective treatment has been limited," said lead author Johanna Bolander of WFIRM. "Initially, we studied what goes wrong in osteoarthritic joints, compared these processes to functional environments, and used this information to develop an immunotherapy cell treatment."

Osteoarthritis is a disease of the joint system. The joint includes a synovial membrane—a connective tissue that lines the inner surface of the joint. The membrane functions to protect the joint and secretes a lubricating fluid filled with cell elements needed to maintain a healthy environment and to provide friction free movement.

In healthy joints when an injury occurs, the body recruits an army of inflammatory cells and sends them to the injury site to contribute to cleaning of the damaged tissues. In the osteoarthritic joint, however, a traumatic injury leads to inflammation of the synovial membrane and cartilage damage.

"With time, the inflammation worsens, leading to degradation of the cartilage lining the joint bones and chronic inflammation in the surrounding tissues. For patients, this causes severe pain, swelling and often limits daily activities," said co-author Gary Poehling, MD, an orthopedic surgeon at Atrium Health Wake Forest Baptist.

For this study, published in *Science Advances*, the journal of the American Association for the Advancement of Science, the research

team set out to investigate what is taking place in the osteoarthritic joint environment that keeps the healing process from happening.

"We evaluated whether the cell population present in the joint fluid environment lacked the capability to contribute to functional tissue repair, or if there is something in the environment that impairs their ability to do so," said Gustavo Moviglia, Ph.D., a WFIRM researcher.

The team isolated cells from the joint fluid of osteoarthritic patients, separated the cells from the fluid and investigated them alone, but also in the presence of the autologous fluid. Separated from the fluid, they saw that the cells had the ability to undergo processes required for functional tissue repair. When they added a small percentage of the fluid back into the cell culture assay, the cells' abilities were impaired—they couldn't do their job—suggesting that the specific osteoarthritic environment stops them.

Based on these findings and what is known about functional tissue repair, a cell therapy was designed that can overcome the inflammatory environment and also regenerate cartilage.

"Cartilage activated immune cells that target inflammation, combined with progenitor cells aid tissue regeneration," said Anthony Atala, MD, senior author and director of WFIRM. "It's really a dynamic communication between these two cell populations that are crucial for the efficacy of the treatment."

The combination of cells leads to simultaneous treatment of several of the aspects involved in osteoarthritis: synovial inflammation, cartilage degradation, subchondral bone sclerosis and innervation of pain sensory neurons.

The therapy was tested in a pre-clinical model and was found to have the

ability to reverse cartilage damage in the synovial membrane and diminish the inflammation as well. To evaluate clinical efficacy, a compassionate use study was conducted in nine patients with confirmed osteoarthritis who each received one or two injections. Efficacy was evaluated through scoring of pain and functional living, MRI scans pre- and post-treatment and a biopsy from one patient was obtained.

Once treated, the patients experienced improved quality of life, ability to participate in recreational activities, and reduced pain. Additionally, MRI studies confirmed cartilage regeneration. Additional clinical studies are required to evaluate the outcome in a larger patient population as well as to evaluate potential differences in patients in specific subgroups.

More information: Johanna Bolander, The Synovial Environment Steers Cartilage Deterioration and Regeneration, *Science Advances* (2023). DOI: 10.1126/sciadv.ade4645.
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Provided by Atrium Health Wake Forest Baptist

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