Medical Xpress

Promising novel treatment for osteoarthritis revealed by new research

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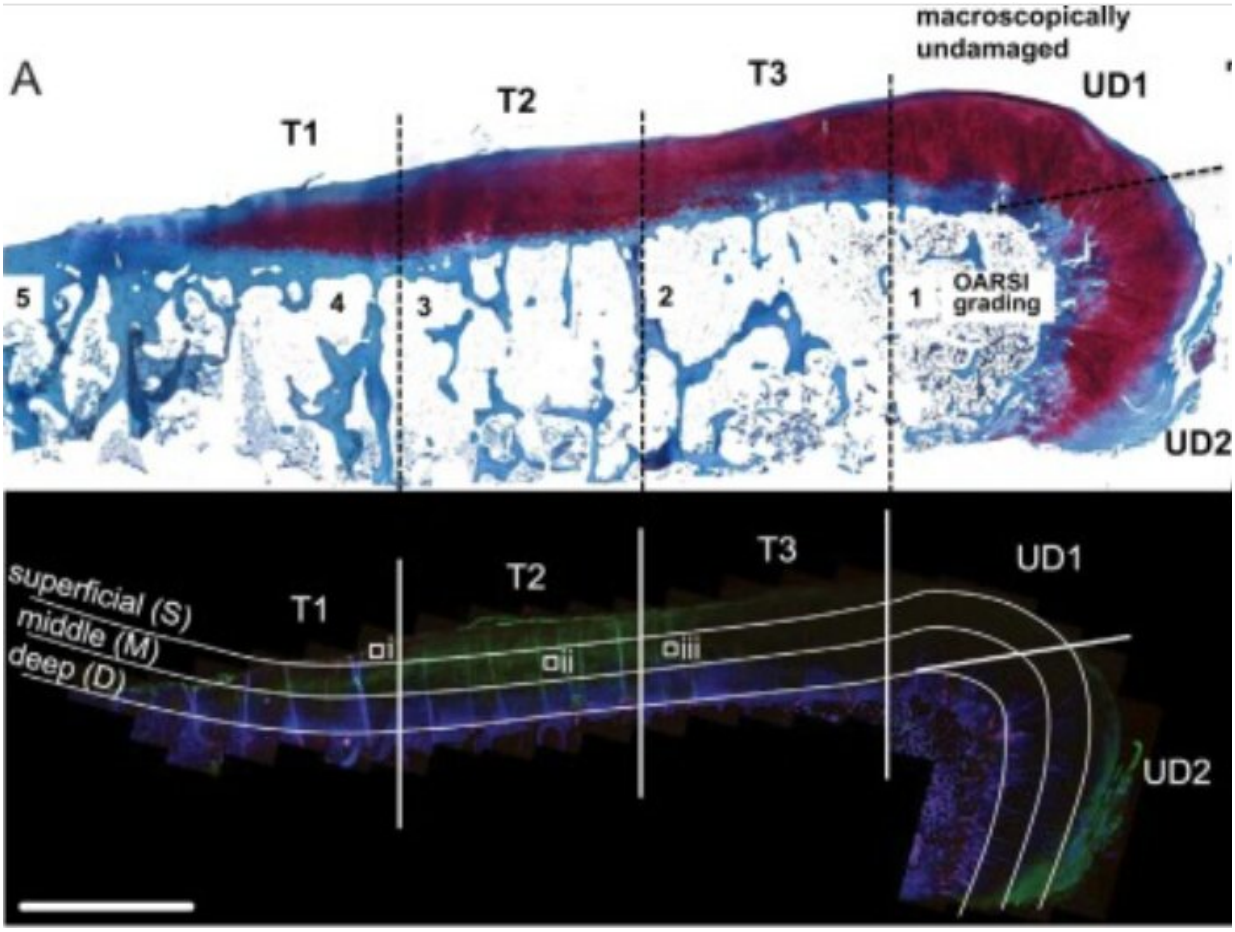

Localization of TSG-6 protein and mRNA in OA cartilage. (A) Representative section of medial tibial plateau (5 μm) from a patient with AMG stained with (upper panel) Safranin O and Fast Green or (lower panel) a TSG-6-specific antiserum RAH-1 (red) and HA-binding protein (green, for visualization of cartilage matrix). Sections stained with Safranin O/Fast Green were graded according to the OARSI scale and divided into regions for analysis: full-

thickness cartilage was denoted 'undamaged' (UD1 and UD2) and cartilage between UD and full-thickness lesion was segregated into T1, T2 and T3; all regions were subdivided longitudinally into superficial (S), middle (M) and deep (D). Scale bar = 4 mm. Credit: *Osteoarthritis and Cartilage* (2023). DOI: 10.1016/j.joca.2023.05.013

Osteoarthritis (OA) is the most common form of joint disease, affecting more than 250 million people worldwide and representing a major and growing cause of long-term disability. OA is a complex disorder where multiple factors such as obesity, joint injury and genetics contribute to structural deterioration, and potentially failure, of synovial joints. Despite a high burden of disease there are no approved disease-modifying OA drugs (DMOAD) and current strategies for pain relief are inadequate. Eventually many patients progress to late-stage OA and undergo joint replacement surgery with unsatisfactory outcomes in a significant proportion of cases.

A newly published study in the journal *Osteoarthritis and Cartilage* explores the role of the human TSG-6 protein in osteoarthritis (OA), and evaluated the disease modifying potential of Link_TSG6 (a fragment derived from the TSG-6 protein) in cell, rodent and human cartilage explant models of OA. Results from the study showed that Link_TSG6 suppresses the production of enzymes implicated in cartilage damage—a hallmark of OA. Furthermore, administration of Link_TSG6 reduced cartilage breakdown, underpinning its potential as a DMOAD, and also reduced touch-evoked pain behavior supporting a possible analgesic effect.

Caroline Aylott, Head of Research Delivery at charity Versus Arthritis, who co-funded the research, said, "There is a critical need for treatments that slow down the progression of osteoarthritis to delay or avoid joint

replacement surgery and to reduce the pain that so many experience. The data is promising and while the research is in its early stages, it shows that Link_TSG6 has the potential to offer a new class of disease modifying drugs to treat osteoarthritis."

The study revealed that Link_TSG6 mimics the intrinsic anti-inflammatory and chondroprotective properties of the full-length TSG-6 protein, as well as having greater potency. In addition, it was found that a substantial proportion of cartilage explants from OA donors undergoing knee-replacement surgery were responsive to Link_TSG6 treatment suggesting that this protein biologic may have therapeutic utility for a large number of OA patients.

"This study has identified a potential new treatment for OA with disease modifying and analgesic properties," said Professor Tony Day, a co-corresponding author, from the Wellcome Center for Cell-Matrix Research, University of Manchester, and Chief Scientific Officer of Link Biologics. "It is extremely rewarding to obtain such compelling preclinical data and we intend to progress this work by advancing Link_TSG6 towards human clinical trials over the next few years."

More information: Sheona P Drummond et al, The recombinant Link module of human TSG-6 suppresses cartilage damage in models of osteoarthritis: a potential disease-modifying OA drug, *Osteoarthritis and Cartilage* (2023). DOI: 10.1016/j.joca.2023.05.013

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