New drug offers hope for people with hand osteoarthritis

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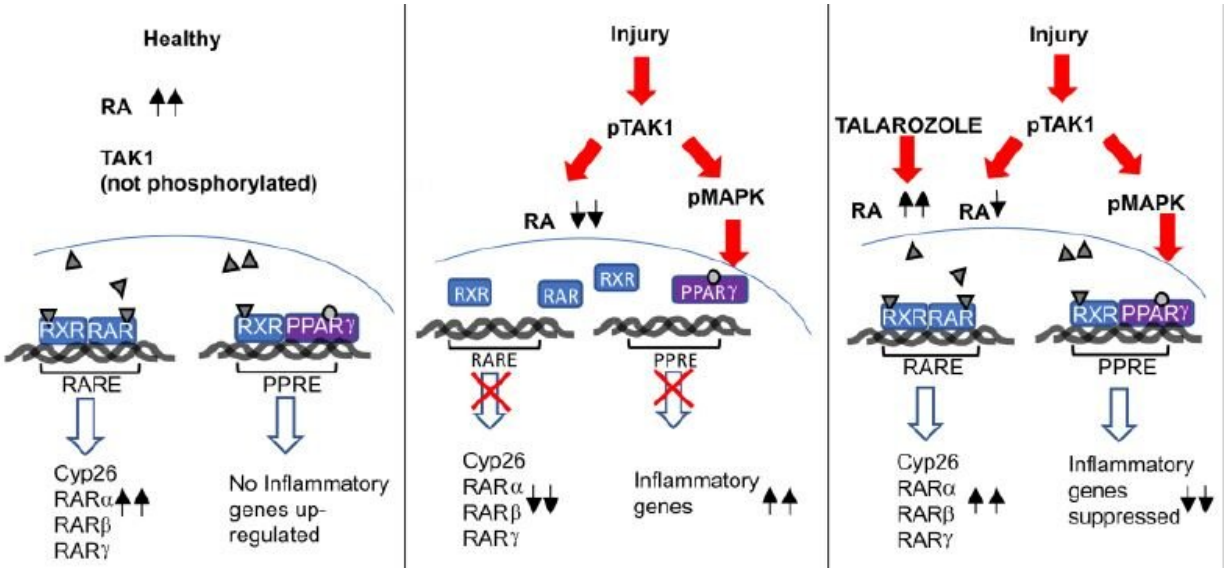

Diagram illustrating the anti-inflammatory role of all-trans retinoic acid (atRA) after cartilage injury. Credit: *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abm4054

A new study, published in *Science Translational Medicine* by researchers at the University of Oxford has identified that Talarozole, a drug that is known to increase retinoic acid, was able to prevent osteoarthritis (OA) in disease models.

Tonia Vincent, Professor of Musculoskeletal Biology & Honorary

Rheumatologist at Oxford's Nuffield Department of Orthopedics, Rheumatology and Musculoskeletal Sciences (NDORMS), said, "Hand osteoarthritis is a common and debilitating medical condition that affects mainly women, especially around the time of the menopause. We currently have no effective treatments that modify their disease."

The researchers started by investigating a common gene variant that had been linked to severe hand OA. Using patient samples collected at the time of routine hand surgery, as well as a number of experimental models, they were able to identify a key molecule that was especially low in "at risk" individuals, called retinoic acid.

More than 40% of individuals will develop osteoarthritis (OA) during their lifetime. Hand (OA) is an extremely common form of OA and there are currently no disease modifying treatments that effectively relieve symptoms or stop deformity and stiffness of the joints.

Professor Vincent added, "This project was only possible because of the multi-disciplinary approach that we took; working with our hand surgical colleagues, geneticists, data scientists and biologists."

As talarozole has an acceptable safety profile in human subjects, a small proof of concept clinical study is underway to see whether this drug might represent a new disease modifying treatment in patients.

Dr. Neha Issar-Brown, Director of Research and Health Intelligence at the charity Versus Arthritis, said, "Around 8.5 million people in the U.K. live with OA. Despite often being dismissed as just a few aches and pains, OA can have a profound and far-reaching impact on life, affecting people's ability to work, care for a family, or live independently.

"There is an urgent need for disease-modifying treatments designed to prevent or reverse the painful symptoms of OA. This study reveals a new

understanding of the causes of hand osteoarthritis, which could lead to identifying new biological targets for intervention in hand OA.

"This research is still at an early stage, but with these encouraging findings we are a big step closer in being able to develop a new class of disease-modifying drugs to treat osteoarthritis, prevent chronic pain, and enable people to live well with the condition," Dr. Issar-Brown concludes.

More information: Linyi Zhu et al, Variants in ALDH1A2 reveal an anti-inflammatory role for retinoic acid and a new class of disease-modifying drugs in osteoarthritis, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abm4054.
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