IN BRIEF

GENETICS

GAG metabolism associated with PsA risk

A genome-wide association study in 835 patients with psoriatic arthritis (PsA) and 1,558 healthy individuals has revealed a new PsA-specific risk locus in *B3GNT2* and has highlighted the glycosaminoglycan (GAG) metabolism pathway as important in PsA. The results were validated in an independent cohort ($n = 2,847$) and the gene variants did not associate with psoriasis or rheumatoid arthritis when tested in 614 and 1,191 patients, respectively. Drug re-purposing analysis identified at least two FDA-approved drugs that target proteins encoded by genes in the GAG pathway as candidates for use in PsA.

ORIGINAL ARTICLE Aterido, A. et al. Genetic variation at the glycosaminoglycan metabolism pathway contributes to the risk of psoriatic arthritis but not psoriasis. *Ann. Rheum. Dis.* https://doi.org/10.1136/annrheumdis-2018-214158 (2018)

THERAPY

No increased risk of VTE with tofacitinib

Unlike the Janus kinase (JAK) inhibitor baricitinib, which is associated with an increased risk of venous thromboembolism (VTE) at high doses, no increased risk of VTE has been found in patients with rheumatoid arthritis (RA) using the JAK inhibitor tofacitinib compared with those using TNF inhibitors. In a cohort of 50,865 patients with RA in the USA, the occurrence of VTE was <1 per 100 patients, and although the number of reported VTEs was numerically higher in patients using tofacitinib than in those using TNF inhibitors, this difference was not statistically significant ($P = 0.13–0.70$).

ORIGINAL ARTICLE Desai, R. J. et al. Comparative risk of venous thromboembolism with tofacitinib versus tumor necrosis factor inhibitors: a cohort study of rheumatoid arthritis patients. *Arthritis Rheumatol.* https://doi.org/10.1002/art.40798 (2018)

MYOSITIS

Cancer risk associated with anti-TIF1 antibodies

Patients with dermatomyositis are more likely to develop cancer if they are positive for anti-transcriptional intermediary factor 1 (TIF1) antibodies than if they are negative (HR 3.4 (95% CI 2.2–5.4)), according to the results of a UK study of 263 patients. During a 10-year follow-up period, cancer occurred exclusively within a 3-year window either side of diagnosis in anti-TIF1 antibody-positive patients and was most common in patients over the age of 39. Patients with anti-TIF1 antibodies also had a higher risk of ovarian cancer than those without (19% of cancers versus 2% of cancers, respectively; $P < 0.05$).

ORIGINAL ARTICLE Oldroyd, A. et al. The temporal relationship between cancer and adult onset anti-transcriptional intermediary factor 1 antibody-positive dermatomyositis. *Rheumatology* https://doi.org/10.1093/rheumatology/key357 (2018)

SPONDYLOARTHRITIS

Sustained remission in PsA with secukinumab

Post hoc analysis of the FUTURE 2 study revealed that Psoriatic Arthritis Disease Activity Score (PASDAS)-based remission or low disease activity (LDA) was sustained at 2 years in patients with psoriatic arthritis (PsA) treated with secukinumab who had achieved remission or LDA at 16 weeks. Remission or LDA occurred at the highest rate in TNF inhibitor-naive patients with PsA, and patients who achieved remission or LDA had a greater improvement in patient-reported outcomes (such as physical function and health-related quality of life) at 2 years than those in whom disease activity remained high.

ORIGINAL ARTICLE Coates, L. C. et al. Secukinumab provides sustained PASDAS-defined remission in psoriatic arthritis and improves health-related quality of life in patients achieving remission: 2-year results the phase III FUTURE 2 study. *Arthritis Res. Ther.* **20**, 272 (2018)

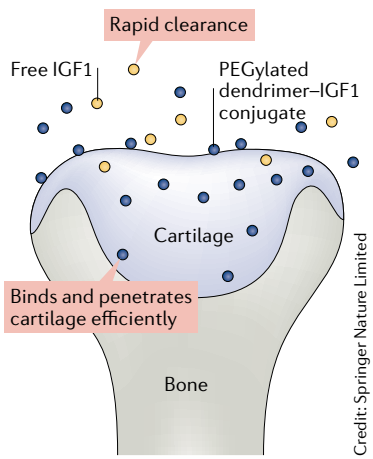
OSTEOARTHRITIS

Promising drug delivery system

Researchers have developed a new chondrocyte-targeting drug delivery system to overcome the biological barrier of dense, anionic cartilage tissue. Conjugating insulin-like growth factor 1 (IGF1), an anabolic growth factor with disease-modifying potential, to cationic nanocarriers improved the pharmacokinetics and efficacy of IGF1 intra-articular therapy in a rat model of knee osteoarthritis (OA).

"Poor drug delivery has been a cause of failure of a number of clinical candidates in OA, which is part of the reason that treatment is so limited for patients," reports Brett Geiger, first author of the new study. To develop an improved means of drug delivery, they used highly branched spherical molecules, called dendrimers, that were modified with polyethylene glycol (PEG) chains. This modification not only shielded the surface charge of the molecule, but also provided versatile branches for conjugation of other molecules, such as IGF1.

"Positively charged nanoparticles can bind to negatively charged cartilage, which keeps them concentrated in the cartilage rather than getting swept away through the venules and lymphatics," explains Geiger. "Not only does this approach enable the delivery of a wide variety of drugs of interest, but we've also shown that we can exert tight control over the dendrimer's degree of cartilage binding based on the amount of PEG we add to its surface."



Credit: Springer Nature Limited

The chosen PEGylated dendrimer–IGF1 formulation was non-toxic and could bind to cartilage for long periods, increasing the half-life of IGF1 within rat knee cartilage by a factor of 10. Furthermore, therapeutic levels of the growth factor were maintained in the cartilage for 30 days.

In a surgical rat model of OA, a single injection of dendrimer–IGF1 (2 days after surgery) rescued cartilage from degeneration more effectively than free IGF1. Treatment considerably reduced the width of cartilage degeneration and the volumetric osteophyte burden at 4 weeks compared with no treatment.

"We're very interested in studying this technology further in large animal preclinical models," says corresponding author Paula Hammond. "We intend to test our PEGylated dendrimer system in additional avascular tissues similar to cartilage and test additional disease-modifying drugs of interest."

Interestingly, in this study, the PEGylated dendrimer could fully penetrate 1 mm-thick bovine cartilage (a good representation of human cartilage in terms of thickness and structure) after ex vivo incubation, whereas the penetration of free IGF1 was limited.

"This preclinical research presents exciting signs that improving drug delivery directly to cartilage can improve efficacy of therapeutics and potentially lead to the approval of the first disease-modifying OA drug in the near future," concludes Hammond.

Jessica McHugh

ORIGINAL ARTICLE Geiger, B. C. et al. Cartilage-penetrating nanocarriers improve delivery and efficacy of growth factor treatment of osteoarthritis. *Sci. Transl Med.* **10**, eaat8800 (2018)