

Monocyte reprogramming for Rheumatoid Arthritis

The novel therapy offers a rapid and simple approach using a proprietary molecule to transform patient monocytes, providing them with anti-inflammatory and tissue regenerative properties. This innovative method not only identifies companion biomarkers for cell benchmarking but also holds promise for treating inflammatory conditions and reprogramming other therapeutic cells

Background

Rheumatoid arthritis (RA) is an autoimmune disease that leads to the progressive destruction of joints. The cause(s) of RA is currently unknown, but several modifiable lifestyle-associated and non-modifiable risk factors have been identified. Rheumatoid arthritis is not curable and requires life-long treatment. The global RA drug market was estimated to be ~\$28B in 2021.

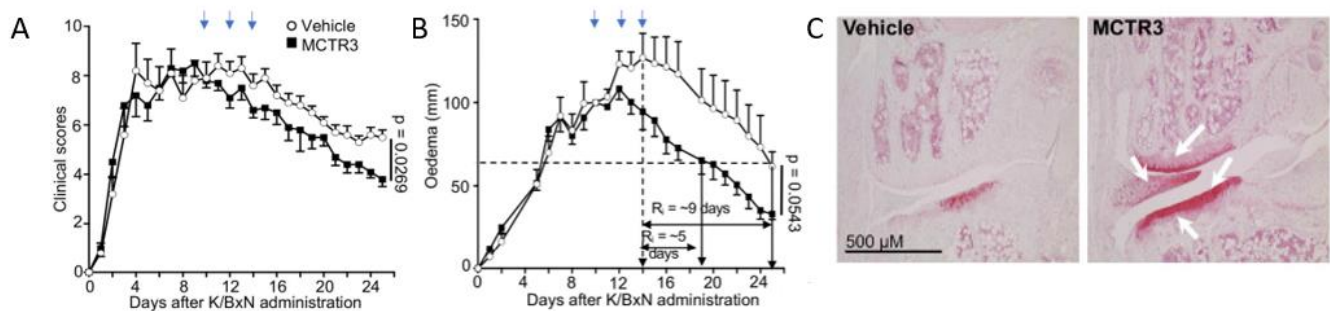
The Problem

The management of RA presents significant challenges as current treatment strategies primarily focus on inflammation control, offering little in the way of joint repair. This approach leaves the majority of patients, approximately 80%, unable to achieve low disease activity, and even fewer attain drug-free remission, necessitating lifelong treatment with its associated risks of drug-related side effects. Nearly 40% of patients prove refractory to existing treatments, underscoring the urgent need for innovative therapies that not only address inflammation but also promote joint repair.

Invention: Benefits & Application

QMUL researchers recently uncovered a novel family of specialised pro-resolving lipid mediators (SPM), termed as maresin conjugates in tissue regeneration (MCTR). MCTRs actively promote the resolution of inflammation by downregulating the production of pro-inflammatory soluble mediators and upregulating the formation of pro-resolving mediators. MCTRs also exert tissue reparative and regenerative activities. In recent studies the researchers found that the tissue protective actions of MCTRs, and in particular MCTR3, extend to models of joint damage, including inflammatory arthritis. Intriguingly our researchers observed that a short-term ex vivo incubation of monocytes with MCTR3 was able to confer the same protective activities to these cells as the systemic delivery of MCTR3. Importantly, the investigators also observed that this reprogramming can also be achieved with RA patient-derived monocytes.

The findings were validated *in vivo* on inflammatory arthritis animal models and confirmed the findings in patient-derived monocytes.



The anti-inflammatory and cartilage protective activities of MCTR3-reprogrammed monocytes

Disease course was evaluated by assessing (A) clinical scores, (B) paw oedema (C) regeneration of cartilage

The use of monocytes as the target cell population allows to leverage the natural biology of these cells, which when administered systemically will migrate to all the inflamed joints. This offers an advantage to many of the other cell-based therapeutics being developed that need to be delivered directly into the tissues and will therefore be only useful to treat a small subset of joints.

Patent

A UK patent has been filed and is currently in the PCT stage: WO 2022/263805 A1

Publication

Pistorius K, Ly L, Souza PR, et al. MCTR3 reprograms arthritic monocytes to upregulate Arginase-1 and exert pro-resolving and tissue-protective functions in experimental arthritis. *EBioMedicine*. 2022;79:103974. doi:10.1016/j.ebiom.2022.103974

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