Queen Mary Innovation

Opportunity 2019094

Investment opportunity

Agrin for the treatment of osteoarthritis

Novel polypeptides, which are derived from a human agrin, are a promising therapeutic approach for osteoarthritis treatment by promoting chondrocyte differentiation and chondrogenesis.

Background

Osteoarthritis (OA) is a debilitating joint disease which is characterized by breakdown of the articular cartilage and bone changes. Bone changes include the thickening of the bone supporting the cartilage and excessive bone formation at the margins of the joint (osteophytes). Isolated cartilage defects are found in 61% of all arthroscopies e.g inflammatory arthritis such as rheumatoid arthritis can result in irreversible cartilage loss. If cartilage defects are left untreated, they tend to extend to the healthy cartilage and result in osteoarthritis. Cartilage regeneration in these patients will restore quality of life and revert disability.

The Problem

There are no disease modifying therapies to treat the cause of osteoarthritis. Current treatment consists of symptom management with non-steroidal anti-inflammatory drugs with patients eventually needing joint replacement. Hence, there is an urgent unmet need for a new therapeutic approach targeting and resolving the aetiology of the disease. Isolated cartilage defects are also very frequent and if left untreated they induce further cartilage loss. The current treatment for isolated cartilage defects includes microfracture and autologous chondrocyte implantation. The outcome of the former is only transient, and the latter involves the manufacturing of each individual patient's cells, thereby leading to high production costs, small revenues and poor upscalability.

Invention: Benefits & Application

Agrin supports cartilage repair by modulating various molecular mechanisms, including Wnt signalling. QMUL researchers have identified modified, soluble polypeptides derived from human agrin or its variants and shown that they are capable of promoting chondrocyte differentiation and chondrogenesis. The small, soluble polypeptides overcome potential rejection issues, induce the recruitment of mesenchymal stem cells for cartilage repair, and support the formation of stable cartilage without bone transformation, making it a promising therapeutic approach. A single intra-articular administration was shown to be sufficient to induce regeneration of osteochondral defects in mice and sheep with structural and symptomatic improvements for at least 6 months.

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Agrin induces cartilage regeneration in models of acute osteochondral defects

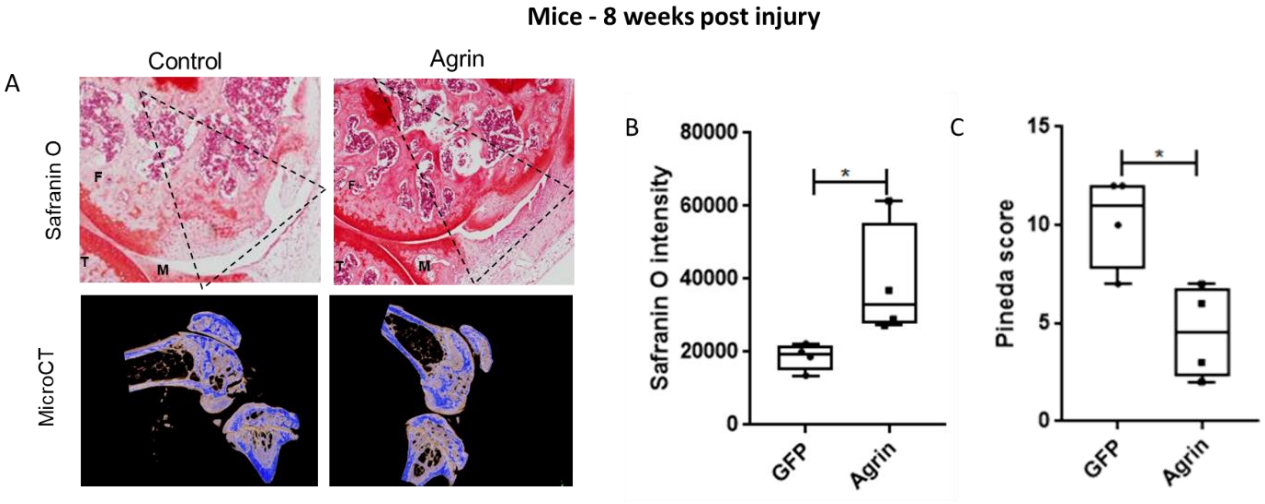

Fig. 1. A single delivery of Agrin into a large defect of the femoral condyle spanning the cartilage and the bone repairs both cartilage (A top, Safranin O staining) and bone (A bottom, microCT). Agrin produced higher quality cartilage when compared to control (B) and resulted in a higher level of repair of the joint surface (C, Pineda score).

Agrin induces immediate (post-traumatic) and sustained (up to 6 months) pain relief in sheep post-injury

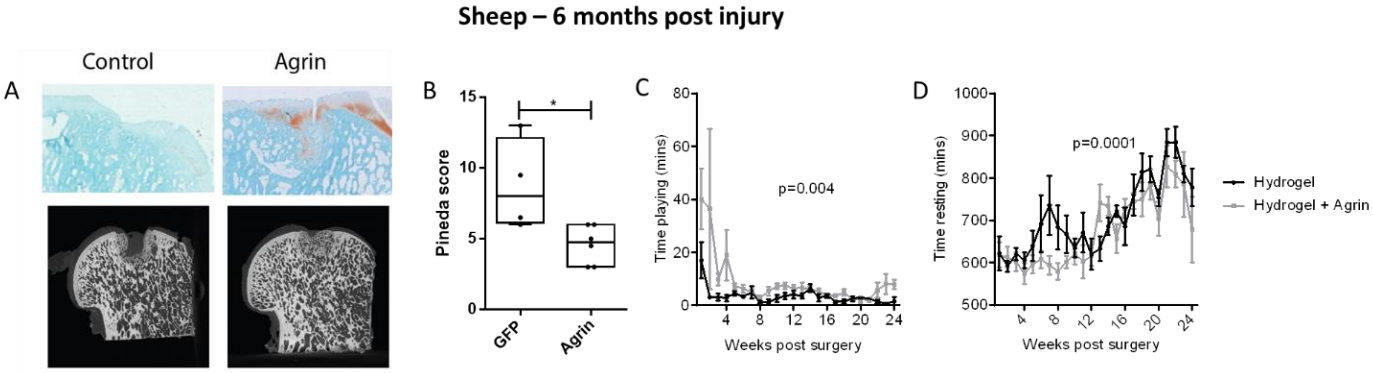

Fig 2. Agrin induces substantial cartilage (A top, Safranin O) and bone repair (A bottom, microCT) in a critical size (8mm diameter) defect in sheep 6 months post-surgery and resulted in an improved repair score (B, Pineda score). Measuring the sheep activity using locomotion-monitoring (similar to a fitbit), Agrin reduces pain immediately following surgery and this was prolonged throughout the experiment for up to 6 months, as shown by their increased time playing (C) and reduced time resting (D).

Patent

A PCT patent application has been filed.

Lead Inventor

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Publications

Eldridge SE, Barawi A, Wang H, Roelofs AJ, Kaneva M, GUAN Z, Lydon H, Thomas B et al. (2020) . Agrin induces long term osteochondral regeneration by supporting repair morphogenesis . Science Translational Medicine vol. 12 , (559)

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