Docket #: S19-076

Activating skeletal stem cells to induce cartilage regeneration in osteoarthritis

Stanford scientists have developed an innovative microfracture surgery method that significantly enhances cartilage repair. By combining this surgery technique with targeted delivery of specific growth factors (e.g. BMP2 and VEGFR1) to the site of tissue degeneration, they were able to stimulate skeletal stem cells to regenerate cartilage. This process involves both mechanical stimulation from the surgery and biochemical stimulation from the growth factors to encourage stem cells to transform into cartilage.

Osteoarthritis is a degenerative disease that results in irreversible and progressive loss of cartilage lining joints and is the most common form of musculoskeletal disorder. Currently, surgeons commonly use the microfracture surgery technique in an attempt to regenerate cartilage in osteoarthritis. But, although the surgery results in 'fibrocartilage' that provides some symptomatic relief, the mechanical properties compared with normal articular cartilage are significantly reduced. Concurrently, BMP2 has been shown to be a potent bone growth factor and inhibition of VEGF signaling has been shown to reduce osteoarthritis progression and fibrosis *in vivo*. A combination therapy using both mechanical and biochemical stimulation at the site of tissue degeneration can be a powerful approach to treating osteoarthritis.

Concomitant microfracture surgery and delivery of BMP2 and VEGFR1 results in robust and stable regeneration of cartilage in models of osteoarthritis. Importantly, these findings were validated in both mouse and human tissues using pure, functionally defined skeletal stem cells. Consequently, growth-factor-enhanced microfracture surgery can serve as a first-in-class treatment for patients suffering from osteoarthritis.

Stage of Development:
Preclinical – *in vivo* (xenograft) data

Applications

- Treatment of osetoarthritis and focal chondral defects in joints
- Cartilage formation in the craniofacial skeleton

Advantages

- Cell-specific mechanism
- Robust and stable cartilage formation
- Reduction in fibrosis

Publications

- Murphy, M. P., Koepke, L. S., Lopez, M. T., Tong, X., Ambrosi, T. H., Gulati, G. S., ... & Chan, C. K. (2020). Articular cartilage regeneration by activated skeletal stem cells. Nature medicine, 26(10), 1583-1592.

Patents

- Published Application: WO2021222298
- Published Application: 20230158111

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