UNIVERSITY OF BIRMINGHAM

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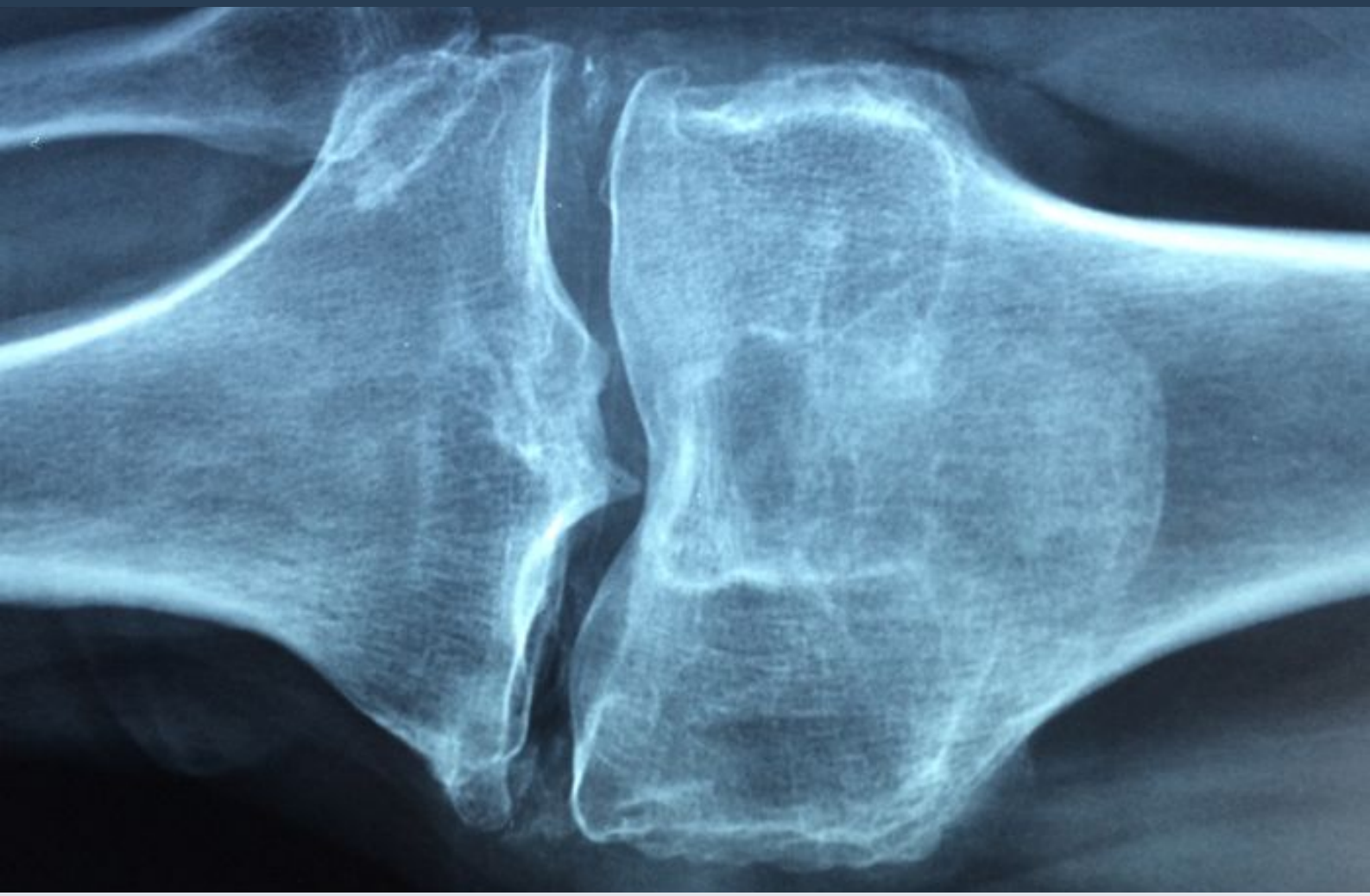
New Therapy for Bone Regeneration

A method which harnesses the regenerative capacity of extracellular vesicles that are naturally generated during bone formation.



Please note, header image is purely illustrative. Source: Pxhere, CC0

Seeking

Development partner, Commercial partner

About **University of Birmingham**

At the University of Birmingham our research leads to new inventions and fuels innovation and business growth.

Background

Despite the natural regenerative capacity of bone, there are instances where healing is impaired and clinical intervention necessary. Examples include when the quantity of bone required is simply beyond the body's natural regenerative capacity, such as in the skeletal reconstruction of large defects resulting from trauma or invasive surgeries (e.g. osteosarcoma excision), delayed or non-unions, or when the natural regenerative capacity is impaired due to osteoporosis or avascular necrosis.

The global market for bone and joint regeneration therapies is expected to reach £5.2billion by 2019, and the market is rapidly growing (CAGR 3.8%), due to pandemic aging and obesity. Spinal fusion alone accounts for 363,000 operations in North America, annually.

Current clinical approaches used to stimulate or augment bone regeneration when the quantity of bone required is simply beyond the body's natural regenerative capacity, include distraction osteogenesis and bone transport, autologous or allogeneic bone grafts, or the application of bone graft substitutes containing hyper-concentrated growth factors such as bone morphogenetic proteins, but none of these clinical interventions can be considered optimal and have significant limitations: autologous grafts cannot meet demand and cause patient morbidity, allogeneic bone lacks bioactive factors, and growth factor-based approaches (e.g. BMP-2) may have serious side-effects and high costs. Consequently, there is a considerable need to devise new methods for the generation of large volumes of bone without associated patient morbidity.

In recent years, attention has been focused on cell-based approaches. However, translation is frequently prevented by insurmountable regulatory, ethical and economic issues.

Tech Overview

Academics at the University of Birmingham have developed a novel solution to promote bone formation/regeneration (Figure 1 A), where osteoblast cells are stimulated to produce osteogenesis-enhancing extracellular vesicles in the presence of an osteoconductive donor substrate and bone marrow-derived stem cells (MSCs), which are then therapeutically delivered to the site of need to facilitate hard tissues regeneration.

The team have shown _in vitro _that if extracellular vesicles are applied in combination with a simple phosphate the therapy outperforms the current gold standard, BMP-2. The newly formed bone has improved bone quality, quantity and density versus current gold standard of care with BMP-2 (Figure 1B and C).

The method and composition of the invention may be also used to promote fusion of two bones or bone fragments; to promote spinal fusion, for example to treat lumbar degenerative disc disease. The composition may be administered via a spinal cage which may be used to provide load bearing support to the vertebrae.

Further Details:

Annexin-enriched osteoblast-derived vesicles act as an extracellular site of mineral nucleation within developing stem cell cultures" is published in Scientific Reports: 10.1038/s41598-017-13027-6.

YouTube

Benefits

- This technology delivers all the advantages of cell-based therapies but without using viable cells, by harnessing the regenerative capacity of nano-sized particles called extracellular vesicles that are naturally generated during bone formation.
- Enhanced mineral formation rate, quantity, and quality beyond that of the current clinical gold standard, BMP2.
- No risk of phenotypic conversion or teratogenicity upon implantation.
- EV production can be scaled up (unlike autograft).
- EVs present a more holistic biological approach when compared with the current application of hyper concentrated growth factors (e.g. BMPs).
- EVs are not subject to the same ethical considerations or government regulations as cell-based therapies.

Applications

The research team, led by the University of Birmingham, believe that the findings mark the first step in a new direction for tissue regeneration with the potential to help repair bone, teeth and cartilage.

Bone and hard tissue regeneration in:

- Bone fusion – lumbar degenerative disc disease
- Bone fracture
- Osseous defects
- Delayed unions, non-unions
- Bone trauma
- Arthrodesis including spinal arthrodesis, extremity arthrodesis and the like
- Bone deficit condition associated with post-traumatic bone surgery, post-prosthetic joint surgery, post-plastic bone surgery, post-dental surgery, bone chemotherapy treatment, congenital bone defect, post-traumatic bone loss, postsurgical bone loss, post infection bone loss, allograft incorporation or bone radiotherapy treatment.

Opportunity

Early stage technology. Currently proof of concept data demonstrates bone regeneration in-vitro using murine osteoblast-derived vesicles, human stem cells in the presence of a mineral substrate, beyond that of current clinical gold standards.

The researchers are looking to produce these therapeutically valuable particles at scale, and also examine their capacity to regenerate other tissues.

The university is seeking partners for further development and commercialisation.

ZSR1016

Patents

- Provisional application GB1621716.8, filed 20/12/2016

Appendix 1

Figure 1

(A) Proposed application of EVs as a therapy for bone regeneration. (B) X-ray fluorescence. (C) Alizarin red calcium staining showing enhanced mineralisation by human stem cells following EV treatment when compared with the current clinical gold standard (BMP2).