Stem cell-based cartilage regeneration technology

Harnessing the regeneration ability of stem cells, researchers are making strides in the treatment of large cartilage defects of the knee. A collaborative team including Dr Khay-Yong Saw, Dr Reza Ng, Dr Caroline Jee (Kuala Lumpur Sports Medicine Centre, Malaysia), and Dr Adam Anz (Andrews Research and Education Foundation, Florida, USA) demonstrate the safety and efficacy of peripheral blood stem cell (PBSC) injections for treating damaged articular cartilage in a recently published clinical trial. Their results showcase the potential for this innovative technology to meet a currently unmet medical need for many patients across the world suffering from joint damage.

Articular cartilage is the smooth, white tissue that covers the ends of our bones at the points where they come together to form joints. A highly specialised form of connective tissue, articular cartilage provides a smooth and lubricated surface for joints including the wrists, elbows, shoulders, hips, knees, and ankles. This slippery, shock-absorbing layer of tissue helps our bones to move against each other easily and with very little friction. Without articular cartilage, movement would be painful and difficult.

Unfortunately, articular cartilage is particularly susceptible to damage, either through injury or normal wear and tear. Cartilage is much softer and more flexible than bone, and not very good at healing itself; it has almost no potential for regeneration. Consequently, once articular cartilage is injured or gone there are very limited treatment options for patients. This is where innovative research from Dr Khay-Yong Saw, Dr Reza Ng, and Dr Caroline Jee (Kuala Lumpur Sports Medicine Centre) comes in. Years of research, including a recently published clinical trial, shows that peripheral blood stem cell injections offer exciting potential as an effective way of treating major articular cartilage damage.

CARTILAGE DEFECTS

Articular cartilage damage can lead to chronic and painful symptoms including stiffness and swelling. Moving those joints becomes very painful and this damage can lead to arthritis later in life. There are limited surgical options available for people with damaged articular cartilage. The surgical goal is to stimulate the growth of new hyaline cartilage, the specialised tissue on the joint surface. One approach, known as microfracture, attempts to encourage the growth of new articular cartilage via the creation of a new blood supply. This involves using a sharp tool to make holes in the joint surface, which brings a new blood supply, new cells, and stimulates a healing response. The same outcome is sometimes achieved through drilling or abrasion arthroplasty. Another method known as autologous chondrocyte implantation involves new cartilage cells being grown in a laboratory and then implanted back onto the joint. Some patients will also have cartilage transferred from a healthy joint. Some patients will also have cartilage transferred from a healthy joint. Some patients will also have cartilage transferred from a healthy joint. Some patients will also have cartilage transferred from a healthy joint.

CARTILAGE REGENERATION

The team’s newly developed stem cell technology is called ‘KART’ (KLSMC Articular Regeneration Technology). The aim is to achieve chondrogenesis by exploiting the natural healing qualities of a patient’s own peripheral blood stem cells (PBSC). Formed in the bone marrow, PBSC are the precursor of all the different types of blood cell. Early work carried out by Saw and colleagues identified PBSC as the stem cell of choice. Not only are they easily and safely harvested, but the researchers’ studies in animal models demonstrated their effective cartilage healing potential. Notably, PBSC can be cryopreserved for later use.

THE POWER OF STEM CELLS

Building on many years of research, a pioneering approach involving stem cell technology has been developed by Saw, Ng, Jee, and Anz. Their goal? To place stem cells at the damaged area of the joint to stimulate cartilage growth (called chondrogenesis). As Jee explains, ‘the science, surgical technique, harvesting, and storage of the peripheral blood stem cells and the postoperative rehabilitation programme that encompasses this innovative technology have been developed to enable high quality regeneration and repair’.

A stem cell is an immature, basic cell that has yet to specialise, or develop, meaning it has the potential to become any of the many types of cells in our bodies. For example, an undifferentiated stem cell may become a nerve, liver, heart, or blood cell, depending on the conditions they develop under. This of course means they have incredible regenerative potential. These methods all have their limitations, however, and fully repairing articular cartilage remains a significant unmet medical need. Consequently, many patients experience long and painful periods before undergoing a total joint replacement.

This innovative technology has been developed to enable high-quality repair and regeneration of articular cartilage.

Peripheral blood stem cell injections offer huge potential for treating damaged articular cartilage following subchondral drilling.
behind the research

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Bio
Dr Khay-Yong Saw is the founder and a consultant orthopaedic surgeon at KLSMC, Malaysia. He specialises in knee joint orthopaedic surgery with stem cells for chondrogenesis together with bone and soft tissue regeneration. He has received numerous awards, publications and patents for this pioneering technology and on his novel medical devices.

Dr Adam Anz is a consultant orthopaedic surgeon at the AREF in Pensacola, Florida, USA. His clinical and research focus has settled on knee, shoulder, and hip injuries as well as the development of innovative biologic treatments. He is one of the principal investigators on the cartilage regeneration study.

Dr Reza Ng received his education in medicine from Belgium with a specialist degree in orthopaedics. He is actively involved in stem cells research and its clinical application in treating orthopaedic degenerative diseases at KLSMC, Malaysia. He is one of the principal investigators on the cartilage regeneration study.

Dr Caroline Jee manages all applied and fundamental research and development activities at KLSMC, Malaysia. She has successfully secured a number of government grants and awards. Dr Jee holds ten international patents, is a chartered engineer (CEng), and chartered scientist (CSci).

The development of stem-cell based articular regeneration therapy for massive cartilage defects.

Detail
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Personal Response
How long do you think it will take for articular regeneration treatment to be the ‘go-to’ treatment for cartilage injury?

This will take at least the next five years following the completion of the multi-centre Phase 3 RCT with subsequent regulatory approval. The process starts with the training of orthopaedic surgeons and familiarising the treating surgeons on the principles of chondrogenesis with specialised surgical techniques and multiple post-operative PBSC injections. Educating the treating physiotherapists on the importance of post-operative weightbearing exercises with movements of the operated joints is also an essential component. PBSC harvesting centres need to be established for cell preparations, cryopreservation, storage, and delivery.

References


Behind the Research

The potential of articular regeneration therapy

Articular regeneration treatment offers a safe and highly effective way of treating patients with massive cartilage defects. The researchers are now aiming to proceed to a Phase 3 trial in 2022. Excitingly, the research team believe that their regeneration technology could be applicable to other joints.

Notably, more than 70% of patients with ‘unmet medical needs’ who received the articular regeneration treatment showed significant improvement.

Intra-Op

2nd look arthroscopy

Before

After

Cartilage regeneration treatment showed significant improvement.

The researchers used the MOCART score (Magnetic resonance Observation of Cartilage Repair Tissue) as a way to assess chondrogenesis. MRI scans revealed there were no unexpected or adverse events throughout the duration of the study.

The interim analysis yielded promising results. After just six months following articular regeneration treatment, patients showed statistical improvement in pain scores compared to the HA control group. Only 12 months following treatment, the regeneration treatment group showed significant improvement across all measures: knee pain, knee function, and cartilage repair. Notably, more than 70% of patients who received the articular regeneration treatment showed significant improvement.

THE POTENTIAL OF REGENERATION THERAPY

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Research Objectives

The development of stem-cell based articular regeneration therapy for massive cartilage defects.

Receiving traditional treatments (of HA injections and physiotherapy), patients with large cartilage knee defects (classified as ≥3 cm) were recruited to a 24-month dual-centre, open-label phase IIb randomised controlled trial (RCT). A group of 69 patients were studied over the course of two years, with half randomly receiving HA and PBSC injections following arthroscopic subchondral drilling, and the other half receiving the HA injections to act as a control group. Both patient groups also received post-treatment physiotherapy. After 24 months, the patients’ knee pain was scored, and the rate of cartilage repair was recorded.

Dr Saw, Dr Reza and Dr Jee were involved in the cartilage regeneration study.


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