

Scientists call up stem cell troops to repair the body using new drug combinations

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Scientists have tricked bone marrow into releasing extra adult stem cells into the bloodstream, a technique that they hope could one day be used to repair heart damage or mend a broken bone, in a new study published today in the journal *Cell Stem Cell*.

When a person has a disease or an injury, the bone marrow mobilises different types of stem cells to help repair and regenerate tissue. The new research, by researchers from Imperial College London, shows that it may be possible to boost the body's ability to repair itself and speed up repair, by using different new drug combinations to put the bone marrow into a state of 'red alert' and send specific kinds of stem cells into action.

In the new study, researchers tricked the bone marrow of healthy mice into releasing two types of adult stem cells - mesenchymal stem cells, which can turn into bone and cartilage and that can also suppress the immune system, and endothelial progenitor cells, which can make blood vessels and therefore have the potential to repair damage in the heart.

This study, funded by the British Heart Foundation and the Wellcome Trust, is the first to selectively mobilise mesenchymal stem cells and endothelial progenitor cells from the bone marrow. Previous studies have only been able to mobilise the haematopoietic type of stem cell, which creates new blood cells. This technique is already used in bone marrow transplants in order to boost the numbers of haematopoietic stem cells in a donor's bloodstream.

The researchers were able to choose which groups of stem cells the bone marrow released, by using two different therapies. Ultimately, the researchers hope that their new technique could be used to repair and regenerate tissue, for example when a person has heart disease or a sports injury, by mobilising the necessary stem cells.

The researchers also hope that they could tackle autoimmune diseases such as rheumatoid arthritis, where the body is attacked by its own immune system, by kicking the mesenchymal stem cells into action. These stem cells are able to suppress the immune system.

Dr Sara Rankin, the corresponding author of the study from the National Heart & Lung Institute at Imperial College London, said: "The body repairs itself all the time. We know that the skin heals over when we cut ourselves and, similarly, inside the body there are stem cells patrolling around and carrying out repair where it's needed. However, when the damage is severe, there are limits to what the body can do of its own accord.

"We hope that by releasing extra stem cells, as we were able to do in mice in our new study, we could potentially call up extra numbers of whichever stem cells the body needs, in order to boost its ability to mend itself and accelerate the repair process. Further down the line, our work could lead to new treatments to fight various diseases and injuries which work by mobilising a person's own stem cells from within," added Dr Rankin.

The scientists reached their conclusions after treating healthy mice with one of two different 'growth factors' - proteins that occur naturally in the bone marrow - called VEGF and G-CSF. Following this treatment, the mice were given a new drug called Mozobil.

The researchers found that the bone marrow released around 100 times

as many endothelial and mesenchymal stem cells into the bloodstream when the mice were treated with VEGF and Mozobil, compared with mice that received no treatment. Treating the mice with G-CSF and Mozobil mobilised the haematopoietic stem cells - this treatment is already used in bone marrow transplantation.

The researchers now want to investigate whether releasing repair stem cells into the blood really does accelerate the rate and degree of tissue regeneration in mice that have had a heart attack. Depending on the outcome of this work, they hope to conduct clinical trials of the new drug combinations in humans within the next ten years.

The researchers are also keen to explore whether ageing or having a disease affects the bone marrow's ability to produce different kinds of adult stem cells. They want to investigate if the new technique might help to reinvigorate the body's repair mechanisms in older people, to help them fight disease and injury.

Source: Imperial College London

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