Restoring Movement

The loss of movement is a frightful prospect, especially when there is scarce hope of recovery. Here, too, stem cell research offers much promise. Two lines of research at the University are exploring how to restore mobility, one focusing on the mechanics of re-building damaged tissue such as cartilage, the other on regenerating damaged nerves.

TURNING STEM CELLS INTO schwann cells

Damage to the neurons, or nerves, that carry signals to and from the brain can lead to the loss of sensation and paralysis. While the nerves can self-repair from minor injury, the ability to restore this signal-carrying ability after major damage has thus far eluded scientists.

Professor Chan Ying-shing of Physiology and Professor Daisy Shum of Biochemistry are among those who think stem cells may hold the answer to this problem. They are investigating neural regeneration in injured peripheral nerves and the spinal cord, and have had encouraging early results.

Their focus is Schwann cells, the principal support cells in peripheral nerves. Schwann cells form insulating sheaths around the axons along which nerve signals are conducted. Earlier experiments have shown that transplanting Scwhann cells into the injured spinal cords of rats could clear up the debris caused by injury and make a route for nerve fibres to grow and transmit new signals. The problem is, sourcing Scwhann cells has meant harvesting them from healthy peripheral nerves, causing new damage there.

Professor Chan and Professor Shum have managed to address this problem by deriving Schwann cells from stem cells and using them to bridge nerve defects in experimental animals.

They sourced the stem, or progenitor, cells from bone marrow and differentiated them into 'fate-committed' Schwann cells, meaning they will remain as Schwann cells and not undergo further change. They then transplanted the stem cell-derived Schwann cells into injured animals and looked for evidence that the axons were re-growing and associating with the Schwann cells. If this does not happen, the axons die and the animal may lose digits and have a contracted paw on the affected limb. In Professor Chan and Professor Shum's experiments, though, the Schwann cells did indeed bridge the gap in the injured nerve sites, resulting in a better recovery of nerve function for the animals.

"There was a great improvement," Professor Chan says. "The transplantation helped to improve their gait, which would otherwise be very distorted."

A key question is whether this approach can be used in humans. There is still some way to go in this, but the two professors have made important progress.

For one thing, they solved the problem of stem cell differentiation by ensuring the stem cells were irreversibly 'committed' to becoming Schwann cells. If the cells were transplanted before they were fate-committed, they could develop into a tumour.

Understanding the signalling process also means the professors and their team can start to address the crucial issue of timing. It takes about six weeks to direct the differentiation of stem cells into Schwann cells, which may be too long to repair the effects of some injuries. They are now trying to find a more expeditious way of differentiating stem cells, and they are thinking long-term about how to apply their findings to humans.

"We have to test if the human equivalent can be similarly directed to differentiate into Schwann cells," Professor Shum says. "If so, the derived Schwann cells will be tested first in animal models of nerve injury. If that works, then there is hope that we will be able to use the injured person's own bone marrow cells to derive Schwann cells for transplantation therapy. That's our goal." ■

Professor Daisy Shum and Professor Chan Ying-shing.

AN ENGINEERING solution

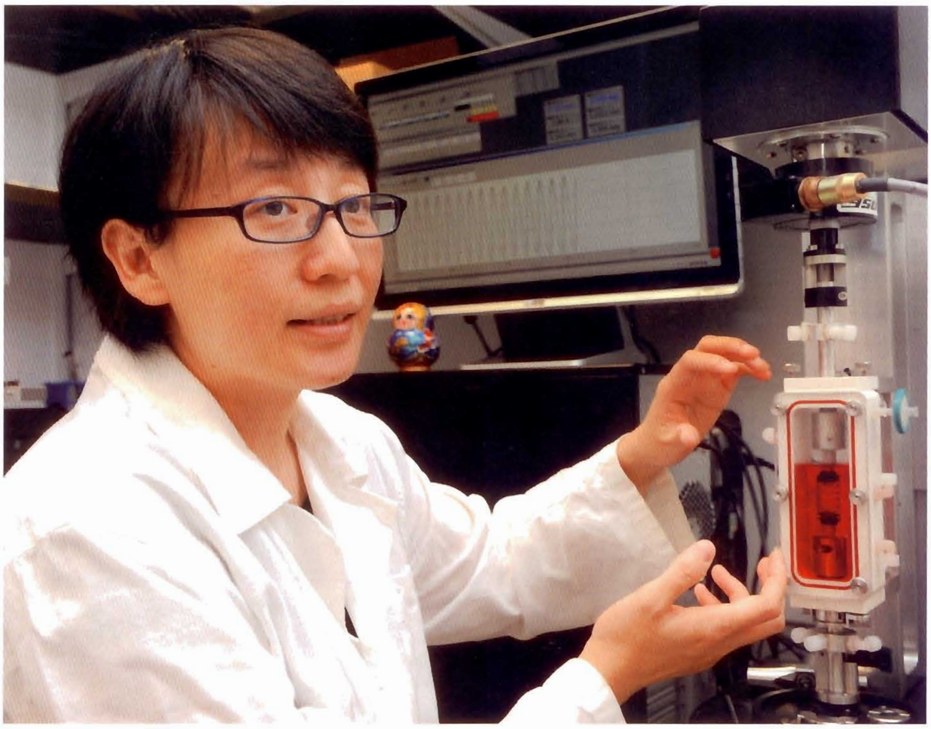
Applying engineering principles to medical problems has led to bioengineering, a field that is playing a central role in stem cell research.

Dr Barbara Chan, Associate Professor of Mechanical Engineering and her team are developing stem cells into tissues for transplant, such as cartilage, bone and inter-vertebral discs. They wrap the stem cells in tiny collagen micro-spheres, which provide a structure for the cells to develop in, and subject them to biological and mechanical signals to encourage them to differentiate, or grow, into the desired cell type.

"Stem cells are naïve cells," she says. "They don't perform any specialized function. You have to give them the appropriate 'educational programme' so they can be induced to differentiate into a particular functioning cell, such as a cartilage cell."

The 'programme' in this case involves introducing growth factors into the three-dimensional micro-sphere environment and subjecting it to mechanical loading through a bioreactor. The bioreactor is a specialized equipment that uses physical forces such as tension, torsion and compression to train stem cells to differentiate into tendons, ligaments or inter-vertebral disc cells.

In the example of cartilage cells, Dr Chan and her team were able to show that the stem cells entrapped in the microsphere underwent biological changes and developed the function, shape and structure of cartilage cells. The cartilage cells deposited new matrices in the microspheres, leading to significant mechanical changes such as increased stiffness, so that they came to resemble native cartilage tissue.



Dr Barbara Chan and a bioreactor.

To test whether the cartilage-like tissue helped in cartilage repair, the scientists transplanted thousands of the tiny microspheres into cartilage defects in rabbits, to make up one mass of tissue. While the study is not yet complete, the rabbits receiving the transplants have shown encouraging signs of repair to their cartilage, bone and the interface in between, unlike those left to self-heal. The stem cells had come from the rabbits themselves so there is no chance of rejection.

Dr Chan is now trying to secure funding to continue her studies with larger animals on the way to hopefully developing an application for humans.

"Our ultimate goal is to understand all the factors that can influence stem cell differentiation," she says. ■