Reprogramming stem cells to a more basic form results in more effective transplant, study shows

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Chinese stem cell scientists have published new research that improves the survival and effectiveness of transplanted stem cells. The research led by Dr Hsiao Chang Chan, from the Chinese University of Hong Kong, is published in *Stem Cells*.

Research into differentiation has led to a variety of breakthroughs as stem cell researchers harvest cells from one part of the body and genetically adapt them to fulfill a specialized role. However, if the implanted cells are too much like the cells of the targeted area they may not have the plasticity to engraft and repair the injured tissue.

"Stem cell differentiation and transplantation has been shown to improve function in conditions including degenerative diseases and blood supply disorders," said Dr Chan. "However, the survival rate of transplanted cells in patients limits their overall effectiveness, which is a barrier to clinical use."

To overcome this issue Dr Chan's team explored de-differentiation, a process that reverts specialized, differentiated cells back to a more primitive cell.

The team focused their research on multipotent stem cells, (MSCs) which can be altered into a variety of cell types through differentiation. Bone marrow MSCs have the potential to differentiate into each of the

three basic types of lineage cells which form bone (osteocytes), cartilage (chondrocytes) and fat tissue (adipocytes).

The team first differentiated bone marrow MSCs towards a neuronal lineage, but then removed the differentiation conditions, allowing the cell to revert back to a form with more basic cellular characteristics.

Following this process the team recorded increased cell survival rates following transplants. In an animal model de-differentiated cells were found to be more effective in improving cognitive functions and in aiding recovery from strokes, compared to un-manipulated stem cells both in living specimens and in laboratory experiments.

The results confirm that de-differentiation is a workable technique for reengineering cells to an earlier, more primitive state but reprogrammed to have increased cell survival rates and therefore their potential for clinical use.

"The finding that MSCs can be reprogrammed to have enhanced survival and therapeutic efficacy in an animal model with potential application to patients is extremely exciting as it may provide a novel and clinically practical method to overcome low cell survival in cell-based therapy," concluded Dr Chan. "We are currently exploring other beneficial properties of the reprogrammed MSCs for other therapeutic applications."

"Many investigators have speculated that differentiation should improve the utility of stem cells for transplantation, but how far to differentiate the cells for the best outcome is a difficult question. Dr Chan's team have helped provide an answer by educating mesenchymal stem cells by pre-differentiating to the desired lineage before de-differentiation, making MSCs easier to manipulate and implant," said Dr Mark Pittenger, *Stem Cells* Associate Editor.

"Interesting questions still remain for future work such as which factors are expressed in the pre-differentiated stem cells that persist upon de-differentiation and can the de-differentiated cells be frozen for future use?"

Provided by Wiley

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