Scientists identify key to integrating transplanted nerve cells into injured tissue

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Scientists at the Schepens Eye Research Institute, an affiliate of Harvard Medical School, have identified a key mechanism for successfully transplanting tissue into the adult central nervous system. The study found that a molecule known as MMP-2 (which is induced by stem cells) has the ability to break down barriers on the outer surface of a damaged retina and allow healthy donor cells to integrate and wire themselves into remaining recipient tissue.

The finding, reported in the current issue (April 25, 2007) of the *Journal of Neuroscience*, holds great promise not only for patients with retinal disease, but for those suffering from spinal cord injuries and neurodegenerative disorders such as Parkinson's and Alzheimer's Diseases.

"This is a very significant finding," says Dr. Michael Young, associate scientist at the Schepens Eye Research Institute and principal investigator of the study. "We believe that it will ultimately make retinal transplantation and restoration of vision a possibility." He adds that transplantation of donor photoreceptors (in whole retina transplants) may prove to be more beneficial than transplanting stem cells alone, as these retinal transplants contain a complete organized supply of cells necessary for proper vision.

The regenerative capacity of central nervous system tissue in adult mammals, including human begins, is extremely limited. This is partly due to the formation of barriers, known as "glial" scars, which are

triggered by the body to protect the injured retina or other nerve tissue from further damage. This dense scar tissue throws up a blockade to foreign cells, including transplants meant to heal and regenerate. This is what has made previous attempts to transplant whole donor retinas so difficult, according to Young.

On the other hand, in recent years, stem cells have been shown to overcome these physical barriers, easily penetrating the scar and integrating into the injured tissue. For instance, in studies published several years ago, Young and his colleagues demonstrated this special stem-cell talent in damaged mouse retinas. In those studies cells injected into injured retinas quickly integrated into the existing retinal tissue.

Intrigued by this phenomenon, Young and his team believed that if they could identify and harness the key molecules used by stem cells to gain access into the injured retina, they could potentially improve the success of non-stem cell transplants. Based on this idea, the team conducted a series of experiments.

In their initial experiments, the team compared the chemicals that were generated when stem cells were injected into damaged retinas and those produced when they attempted to transplant whole retina tissue into the eyes of mice with degenerated retinas. They found—in the stem cell injected retinas—an increase in the amount of and the level of activity of the molecule MMP-2 in host tissue. They concluded that this molecule dissolved the scar on the outer surface of the retina. There was no increase in MMP-2 when they attempted whole-retina transplants.

The team went on to transplant a layer of stem cells between the degenerating mice retinas and healthy donor tissue (whole retina). They found that MMP-2 induced removal of the scar barrier and allowed healthy donor cells (of the whole retina) to make new connections with the damaged retinas in the mice.

"These are very powerful results," says Young. "We are convinced that the increase of this molecule is a major key to creating a permissive environment for central nervous system regeneration."

The team is now investigating therapeutic approaches that would eliminate the need for stem cells. This would involve the use of just the MMP-2 molecule, which is already available in the pharmaceutical market, to foster a receptive transplant environment in the eye, and, in other CNS tissues.

Source: Schepens Eye Research Institute