Gene therapy could expand stem cells' promise

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Once placed into a patient's body, stem cells intended to treat or cure a disease could end up wreaking havoc simply because they are no longer under the control of the clinician.

But gene therapy has the potential to solve this problem, according to a perspective article from physician-scientists at NewYork-Presbyterian Hospital/Weill Cornell Medical Center published in a recent issue of the journal *Cell Stem Cell*. The paper details strategies for genetically modifying stem cells prior to transplantation in order to ensure their safety.

"Stem cell therapy offers enormous potential to treat and even cure serious diseases. But wayward stem cells can turn into a runaway train without a conductor. This is an issue that can be dealt with and we have the technology to do that in the form of gene therapy," says senior author Dr. Ronald G. Crystal, chief of the Division of Pulmonary and Critical Care Medicine at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and the Bruce Webster Professor of Internal Medicine and Professor of Genetic Medicine at Weill Cornell Medical College.

Stem cells have the capacity to differentiate into any of the different tissues making up the human body, thus holding the promise of treating or curing diseases such as multiple sclerosis or spinal-cord injury by replacing diseased cells with healthy cells.

But unlike other therapies such as chemotherapy, antibiotics or aspirin,

stem cells have no expiration date, and that poses a real problem.

"Almost all therapeutics we use have a half life. They only last a certain amount of time," Dr. Crystal says. "Stem cells are the opposite. Once the future stem cell therapist does the therapy, stem cells have the innate potential to produce more cells."

The challenge takes on even more urgency with recent developments, including a federal administration now more open to exploring the potential of stem cells, the recent FDA approval of a human trial involving embryonic stem cells, as well as the reported case of a young boy who developed a brain tumor four years after receiving a stem-cell treatment for a rare genetic disorder.

As evidenced by this boy's experience, one of the biggest potential problems with stem cell therapy is the development of tumors.

But there are other problems as well.

Stem cells directed to become beating heart cells might mistakenly end up in the brain. Or insulin-producing beta cells which can't stop means the body can no longer regulate insulin levels.

"You've totally lost control," Dr. Crystal says. "What do you do?"

The best chance of circumventing these issues is genetic modification of the stem cells prior to actually transplanting them, Dr. Crystal says. Theoretically, this is similar to how gene therapy is used to treat cancer, but with important improvements.

"Instead of gene therapy being done in the patient, as is the case in cancer, it's being done in the cells in a laboratory before doctors use them for therapy so that they still have control of these cells," Dr.

Crystal explains.

Therapists would rig certain genes to respond to a "remote control" signal. For instance, giving a certain drug could prompt a "suicide" gene to kill a budding tumor.

But gene therapy also needs to be carefully done and, ideally, two independent gene-manipulation systems would be used to ensure that stem cells remain firmly in control of clinicians.

Source: New York- Presbyterian Hospital (news : web)