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Developmental biologist Lorenz P. Studer

On December 10, John B. Gurdon of the University of Cambridge and Shinya Yamanaka of the Kyoto University jointly received the 2012 Nobel Prize in Physiology or Medicine for research that enabled scientists to generate stem cells — the immature cells from which various cell types and tissues develop — and clone animals.

Their findings laid the groundwork for innovative ways to study diseases and identify potential drugs, and are expected to result in cell replacement therapies — new strategies to treat disease or injury in which engineered stem cells are used to restore damaged tissue.

Memorial Sloan Kettering researchers have been at the forefront of researching stem cells and stem cell therapies for many years. The laboratory of developmental biologist [Lorenz P. Studer](#), who directs the [Center for Stem Cell Biology](#), has made significant progress in developing stem-cell-based methods for the treatment of degenerative diseases and cancer.

We asked Dr. Studer about this year's Nobel Prize in Physiology or Medicine and the promise of stem cell research.

Drs. Gurdon and Yamanaka are receiving the Nobel Prize “for the discovery that mature cells can be reprogrammed to become pluripotent.” Can you tell us what this means and why it is important?

John Gurdon's research in frogs, in the early 1960s, was absolutely groundbreaking in showing that cell differentiation — the process by which a stem cell develops to acquire specialized functions — is reversible.

This means we can take almost any of the body's mature cells — a skin cell, for instance — and reprogram it to re-create the stem cell from which the skin cell once originated. This reprogramming could be described as resetting a cell's developmental clock to a stage called pluripotency, in which the cell has the capacity to develop into any type of cell — a nerve cell, liver cell, or blood cell, for example.

But perhaps the implications of Dr. Gurdon's discovery didn't become fully apparent until decades later. Many scientists built on his work to accomplish remarkable achievements, including, in the 1990s, Dolly the sheep — the first animal to be cloned from an adult cell.

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How did the more recent findings of Dr. Yamanaka help move the field forward?

Developmental Biologist Lorenz Studer Comments on the 2012 Nobel Prize in Physiology or Medicine

Dr. Gurdon pioneered a technique to convert mature cells into stem cells called nuclear transfer, which involves the use of unfertilized egg cells, which are not easily obtained. Applying this method for widespread clinical use would therefore be impractical and expensive.

However, in 2006, Dr. Yamanaka and his colleagues reported their first experiments demonstrating that we don't need egg cells to make mature cells pluripotent. The protocol they came up with was surprisingly simple: By manipulating four genes in a skin cell, they created an induced pluripotent stem cell (iPSC), which is similar to natural stem cells found in embryos.

The discovery raised our hope that stem cell reprogramming could have a huge impact on medicine in the future. In addition, induced pluripotent stem cells provide a unique and very exciting model system for basic research. They have been used successfully by my lab and others to examine what goes wrong in a number of diseases.

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How you have used iPSCs in your lab?

My colleagues and I engineered iPSCs from people with HSV encephalitis — brain inflammation that may develop after infection with herpes simplex virus — and used these cells to pinpoint the underlying causes of the disease. We were basically able to re-create the disease process in a cell culture dish, and examine the biological events leading to its progression step-by-step. Our findings were [published in Nature in October](#) .

We have also used iPSC technology to examine the causes of familial dysautonomia, or FD — a rare genetic disorder that affects the development of the nervous system — and to identify drug compounds that potentially could be developed into effective therapies. Recently, we [published the first study](#) in which iPSCs have been used for high-throughput drug screening.

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It is hoped that methods to generate stem cells from a person's skin cells will revolutionize medicine by making it possible to replace damaged or diseased tissues. Could you tell us more about this vision?

This is actually an area in which stem cell technology could have significant applications for cancer treatment. Many patients receiving intensive radiation or chemotherapy suffer from severe side effects because these treatments, in addition to killing tumor cells, can harm normal cells in the brain and other vital organs.

Imagine that a person develops radiation-induced brain damage. In theory, we might one day be able to reverse that damage by isolating normal cells from the patient by biopsy, converting these cells into iPSCs, directing them to develop into the type of brain cells that were lost, and transplanting them into the brain. Because the replacement cells would be genetically identical to the patient's normal cells, there would seemingly be little risk of immune rejection.

However, the idea of using iPSCs in patients with cancer and other diseases is still quite new. There are many things we don't know about these cells and the way they behave that we need to learn before exploring them for clinical use. This is one of the reasons why research in other types of stem cells, including embryonic stem cells, continues to be necessary.

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Is cell replacement likely to be used in patients anytime soon?

It's on the horizon for a few diseases, but still far from being realized for most applications.

My laboratory has come quite a long way in developing stem-cell-based therapy for Parkinson's disease. We have learned how to make mature skin cells pluripotent, and then guide these cells to develop into dopaminergic neurons, the type of brain cells that are lost in Parkinson's patients.

Working in animal models, [we have shown that the disease might be treated successfully](#) by transplanting the engineered neurons into the brain. These neurons are fully functional and behave in the brain in the exact way we need them to behave. In fact, within the next few years, we hope to be able to launch the first trial in which Parkinson's patients will receive dopaminergic neurons generated by nuclear transfer.

But for many other diseases, the development of cell replacement therapy could be many years ahead — or might not even be a feasible strategy. One of the biggest challenges is being able to make the exact type of replacement cell a patient needs, which involves learning how to control the complex processes by which that particular cell type naturally develops.

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