

ABOVE: Fluorescent images of neural precursor cells and dopaminergic neurons generated from human embryonic stem cells.

Global Leader in Revolutionary Stem Cell Technology

One of the most tantalizing prospects in biomedical research is the possibility of using stem cells to replace cells in our brains and other organs that have been damaged by the diseases of aging. From her lab at the Buck Institute, Xianmin Zeng, PhD, is leading a global charge to get a stem cell treatment for Parkinson's disease ready for clinical trials.

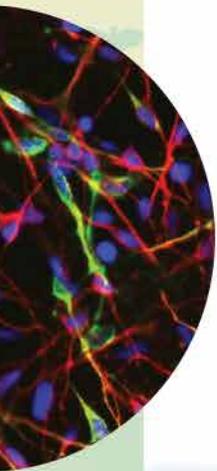
Parkinson's slowly destroys the dopamine-producing neurons in the brain that control movement. Zeng says the initial challenge in the search for a stem cell treatment for Parkinson's was getting the right stem cells to use to replace the

destroyed cells. Zeng had already generated dopamine-producing neurons from human embryonic stem cells when she came to the Buck from the National Institutes of Health (NIH) in 2005. When technology was developed in 2006 to reverse-engineer adult stem cells to become embryonic-stem-cell-like cells, she jumped on the opportunity.

But it's one thing to generate dopamine-producing neurons in a lab dish. It's another matter entirely to generate a sufficient quantity of clinical-grade neurons for human trials. In the past 2 years, Zeng developed a method to reproduce the required neurons. Also, she

proved that the method could be scaled up and the cells produced in a good manufacturing practice (GMP) manufacturing facility, which is a core requirement for clinical trials.

Zeng's manufacturing partner is the City of Hope's GMP manufacturing facility near Los Angeles, California. They have already produced some of the cells, which the Zeng Lab is currently testing to validate that they have the same function as those the lab has produced. In parallel with long-term safety studies, including a 9-month test in mice to ensure that the cells do not produce tumors, the design of the clinical trial is under way.



“We are planning and hoping to file an investigational new drug application in the near future. I cannot really tell when we can expect such a therapy, but my hope is for a Phase I trial within the next 5 years.”

—Xianmin Zeng, PhD
Associate Professor

Two years ago, the California Institute for Regenerative Medicine awarded a grant to Zeng and her long-time collaborator Dr. Mahendra Rao, the director of the Center for Regenerative Medicine at the NIH, to prepare the trial and to work on the basic biology of the disease. With clinician and manufacturing partners at University of California, San Francisco (UCSF), the City of Hope, Johns Hopkins University, and the NIH, the two are engaged in defining the criteria that will be used to determine the type of patients most likely to benefit from the new stem cell therapy.

Zeng’s work is receiving international attention. She has been globe-

trotting this past year to coordinate stem cell manufacturing procedures so that clinical trials can be run in different countries, including Japan, China, Argentina, and Sweden. Argentina’s stem cell consortium, which has an agreement with the California Institute for Regenerative Medicine, has asked Zeng to serve on its scientific advisory board to advise them on the stem cell protocol she developed.

“My collaborators want to be able to work with their own manufacturing facilities, and to decide which protocol to use. My goal this past year has been to show everyone that we

are one of the first to have verified our data and our protocol in a GMP manufacturing facility.”

At the end of the day, Zeng hopes that the new source of cells will lead to more rapid development of cell replacement therapies for Parkinson’s disease, to better understanding of the mechanism of the disease, and to testing new drugs that may help Parkinson’s patients in the future. “The global collaboration we are doing will get others the tools they need so that they don’t have to start from the beginning. This should speed up the search for new therapies.”