

Public release date: 25-Apr-2011[[Print](#) | [E-mail](#) | [Share](#)] [[Close Window](#)]

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Scientists create stable, self-renewing neural stem cells

Abundant precursor cells can become many types of neurons without introducing tumor risk

In a paper published in the April 25 early online edition of the *Proceedings of the National Academy of Sciences*, researchers at the University of California, San Diego School of Medicine, the Gladstone Institutes in San Francisco and colleagues report a game-changing advance in stem cell science: the creation of long-term, self-renewing, primitive neural precursor cells from human embryonic stem cells (hESCs) that can be directed to become many types of neuron without increased risk of tumor formation.

"It's a big step forward," said Kang Zhang, MD, PhD, professor of ophthalmology and human genetics at Shiley Eye Center and director of the Institute for Genomic Medicine, both at UC San Diego. "It means we can generate stable, renewable neural stem cells or downstream products quickly, in great quantities and in a clinical grade – millions in less than a week – that can be used for clinical trials and, eventually, for clinical treatments. Until now, that has not been possible."

Human embryonic stem cells hold great promise in regenerative medicine due to their ability to become any kind of cell needed to repair and restore damaged tissues. But the potential of hESCs has been constrained by a number of practical problems, not least among them the difficulty of growing sufficient quantities of stable, usable cells and the risk that some of these cells might form tumors.

To produce the neural stem cells, Zhang, with co-senior author Sheng Ding, PhD, a former professor of chemistry at The Scripps Research Institute and now at the Gladstone Institutes, and colleagues added small molecules in a chemically defined culture condition that induces hESCs to become primitive neural precursor cells, but then halts the further differentiation process.

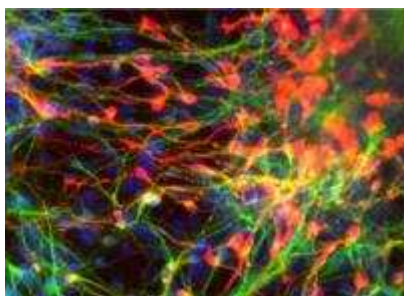


IMAGE: Depicts stained mature neurons, derived from precursor cells, expressing the neurotransmitter dopamine.

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By adding other chemicals, the scientists are able to then direct the precursor cells to differentiate into different types of mature neurons, "which means you can explore potential clinical applications for a wide range of neurodegenerative diseases," said Zhang. "You can generate neurons for specific conditions like amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), Parkinson's disease or, in the case of my particular research area, eye-specific neurons that are lost in macular degeneration, retinitis pigmentosa or glaucoma."

The new process promises to have broad applications in stem cell research. The same method can be used to push induce pluripotent stem cells (stem cells artificially derived from adult, differentiated mature cells) to become neural stem cells, Zhang said. "And in principle, by altering the combination of small molecules, you may be able to create other types of stem cells capable of becoming heart, pancreas, or muscle cells, to name a few."

The next step, according to Zhang, is to use these stem cells to treat different types of neurodegenerative diseases, such as macular degeneration or glaucoma in animal models.

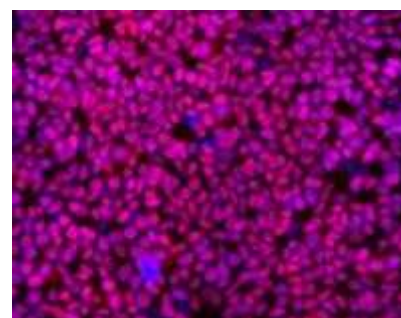


IMAGE: Depicts cultured, self-renewing primitive neural precursors derived from human embryonic stem cells using molecule inhibitors.

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Funding for this research came, in part, from grants from National Institutes of Health Director's Transformative R01 Program, the National Institute of Child Health and Development, the National Heart, Lung, and Blood Institute, the National Eye Institute, the National Institute of Mental Health, the California Institute for Regenerative Medicine, a VA Merit Award, the Macula Vision Research Foundation, Research to Prevent Blindness, a Burroughs Wellcome Fund Clinical Scientist Award in Translational Research and the Richard and Carol Hertzberg Fund.

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