Stem Cells for Research and Therapy: Developments Proceed Quickly on Multiple Fronts

Research Webinar: February 10, 2015
Speaker: Clive Svendsen, Ph.D., Cedars-Sinai Hospital
Host: ALS Association Chief Scientist Lucie Bruijn, Ph.D., M.B.A.

By Richard Robinson

Understanding stem cells, and developing them for therapy, has been the focus of the career of Clive Svendsen, Ph.D., of Cedars-Sinai Hospital in Los Angeles. That same focus is now the driving the development of The Neuro Collaborative, a major new project funded by The ALS Association that will develop stem cell technology, provide a repository for ALS-related stem cell lines, and spur new therapeutic approaches for ALS. Dr. Svendsen outlined the state of stem cell research for ALS in a webinar sponsored by The ALS Association.

“Dr. Svendsen has been partnering with The Association for many years,” said Dr. Bruijn, “and his research has been critical especially for understanding the therapeutic potential of cells derived from stem cells.”

Up until the past decade, most stem cells for research were obtained from very early-stage human embryos. Federal restrictions tightly limited their use. All that changed beginning in 2006, with the discovery that a simple “cocktail” of growth factors could transform skin cells to become “induced pluripotent stem cells,” or iPS cells. “We can now take cells from any adult, including from any ALS patient, and make the cells ‘go back in time’ to make stem cells. We don’t need embryos to do this anymore,” Dr. Svendsen said.

iPS cells can then be converted into any other type of cell, including motor neurons or neuronal support cells called astrocytes. The ability to quickly and easily create very large numbers of such cells has revolutionized research on the cells involved in ALS.

The potential for drug development is significant since motor neurons can now be made abundantly and used to screen thousands of compounds for their potential to slow neuron death. That work is being carried out by the laboratory of Steven Finkbeiner, M.D., Ph.D., of the Gladstone Institutes at University of California at San Francisco, which is part of the Neuro Collaborative.

The Neuro Collaborative also includes the laboratory of Don Cleveland, Ph.D., of the University of California at San Diego. His work is focusing on using iPS-derived neurons from people with ALS due to the C9orf72 gene to develop antisense therapy that will prevent expression of the mutant gene. A clinical trial of this approach is being developed.
Dr. Svendsen, meanwhile is developing a stem cell “core” devoted to collecting, developing, maintaining and distributing high-quality iPS cells from people with ALS, making them available to researchers worldwide. “This will be an open source for researchers, so they don’t have to create them again on their own.”

One goal of the Neuro Collaborative is the “Avatar Project,” which will pair each cell line with detailed (but confidentiality-protected) clinical data from the person donating the cells, including disease progression and symptoms. “We will see if we can mirror the clinical outcome in the cell line,” Dr. Svendsen said. “In this way, we may be able to use motor neurons to predict how fast your disease will progress and what drugs will slow it down. This is personalized medicine. Testing drugs on your own motor neurons—that will be our ultimate goal.”

Another major project Dr. Svendsen is developing is a stem cell-based therapy. He has engineered cells to make and release the protein GDNF (glial cell-derived neurotrophic factor), which protects motor neurons. A clinical trial of this therapy is in the final planning stages with the hope of beginning enrollment in early 2016. The trial will test whether injection of cells into one side of the lower spinal cord can improve motor neuron function on that side, compared to the non-injected side. “This design allows us to perform a very powerful analysis on a small number of patients,” he said.

The ALS Association will provide more details on this trial as soon as they become available. Those interested in more scientific detail about stem cell therapy may wish to read this scientific review article by Dr. Svendsen and colleagues: “The past, present and future of stem cell clinical trials for ALS” at http://www.sciencedirect.com/science/article/pii/S0014488614000739.

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