Stem cell-based therapeutics

The potential of embryonic and induced pluripotent stem cells to aid understanding of diseases and offer novel therapeutic strategies is providing new career opportunities in academia and industry, as highlighted by our two interviewees this month.

Clive Svendsen, Ph.D.
Director, Cedars-Sinai Regenerative Medicine Institute, Los Angeles, California, USA.

In May 2009, Clive Svendsen was named Director of the new Cedars-Sinai Regenerative Medicine Institute. "At the core of the institute will be a state of the art human embryonic stem cell and induced pluripotent stem (iPS) cell core facility for the generation and distribution of pluripotent human stem cells," he says.

Svendsen's research has focused on neurodegenerative disorders, for which he first discovered a passion as a 17-year-old intern studying Alzheimer's disease. Wanting to understand more, following his undergraduate degree, Svendsen took a 1-year position as a research technician for the neuropathologist Edward Bird at Harvard University, Cambridge, Massachusetts, USA, studying neuropsychiatric disorders.

After more than 7 years at Harvard and a year in Japan working for ESA — a US company specializing in diagnostic products and analytical laboratory services — Svendsen completed his Ph.D. at the University of Cambridge, UK, studying neural growth factors. "At this time, I became fascinated with the idea of regenerating or replacing dying tissues in the body," he says. Following his postdoctoral work, he joined the Centre for Brain Repair at the University of Cambridge.

While at the centre, Svendsen started to translate his research from the laboratory to the clinic. For example, he was a collaborator on a small pilot study showing that direct infusion of glial cell line-derived neurotrophic factor into the brains of five patients with early-stage Parkinson's disease led to increases in the storage of dopamine (*Nature Med.* **9**, 589–595; 2003).

In 2000, Svendsen became Professor of Neurology and Anatomy at the University of Wisconsin–Madison, USA, and a consulting professor at Stanford University, Stanford, California, USA. He also became Director of the National Institutes of Health-funded Stem Cell Training Program, and directed the University of Wisconsin–Madison Stem Cell and Regenerative Medicine Center with Dr Tim Kamp.

In these positions, he has pioneered iPS cell disease models for neurodegenerative disorders such as spinal muscular atrophy (*Nature* **457**, 277–280; 2009). Now, as Director of the Cedars-Sinai Regenerative Medicine Institute, Svendsen looks forward to translating this research into the clinic by providing clinical-grade stem cells to medical doctors at the hospital. "As the institute is housed in one of the top hospitals in the country, with great institutional support, it will allow us to generate many different iPS cell lines from patients with a range of diseases and start looking at specific patterns of cell death and how new drugs may prevent this," he says. "I am driven to ask the next question and try to move the field forward in a way that will eventually benefit patients."

Overall, he attributes his approach to scientific research to the result of many interactions with his mentors and collaborators over the years: Wayne Matson, Anders Bjorklund, Steve Dunnett, Michael Sofroniew and Jamie Thomson. To aspiring stem cell scientists, he offers the following advice: "Never be afraid to repeat an experiment and always trust the data, not your heart."

Scott Thies, Ph.D.
Senior Director, Stem Cell Biology, Fate Therapeutics, San Diego, California, USA.

Fate Therapeutics, founded in 2007, is an early-stage biotechnology company developing therapies that modulate the fate of stem cells. Scott Thies joined the company in 2008. "My group and I work closely with teams in medicinal chemistry and protein technology to identify small-molecule and protein modulators of adult stem cells that may be developed into therapeutics for tissue regeneration," explains Thies.

After his Ph.D. in Physiology at Duke University in Durham, North Carolina, USA, Thies completed postdoctoral research in biological chemistry at the University of California, Los Angeles, USA, and in endocrinology at the University of California, San Diego. As a postdoctoral fellow, when he was considering his career path, conversations with members of the junior faculty highlighted the difficulties of securing grant support as a new principal investigator, recalls Thies. So, when he received a job offer from Boston-based company Genetics Institute in 1989, he jumped at the opportunity.

"At that time, scientists at Genetics Institute had cloned the first bone morphogenetic proteins, and there was plenty of interesting science to explore. Working with academic collaborators and colleagues at the company, I found myself pursuing potential therapeutic applications for these proteins in a variety of tissue types. Our work, and that of many academic researchers, demonstrated significant effects of this protein family on stem and progenitor cell differentiation. These discoveries sparked my interest in stem cell biology," he explains.

When Genetics Institute was bought by Wyeth in 1998, Thies became a Senior Scientist in musculoskeletal sciences at the company. "I was extremely enthusiastic about the potential of stem cells to impact medical care and, with some colleagues, I tried to convince upper management that it was the right time for pharma to embrace this new area of biology. However, the stem cell field was considered too risky for Wyeth investment at the time," he says.

So, in 2001, he decided to leave Wyeth to join one of the small biotechnology companies that were working in stem cell biology. "I had the good fortune to contact Geron at the time that they were looking for someone to head their neurobiology group. Geron was pioneering the effort to develop cell therapeutics derived from human embryonic stem cells. I was delighted to join that effort and work with an inspiring team of people who shared my enthusiasm for using stem cells in regenerative medicine," he says.

Seven years later, attracted to the opportunity to help build an organization at its earliest stages, Thies joined Fate Therapeutics. "I was very enthusiastic about Fate's approach to regenerative medicine: modulating endogenous stem cells," he explains. "While working at Genetics Institute, I had seen the power of this approach applied to mesenchymal stem cells for bone repair. Since then, endogenous stem cell populations have been discovered in many organs, and iPS cell discoveries have shown new ways to alter cell fate, so the potential for modulating stem cells in the body for therapeutic applications has been greatly expanded."

WEB SITE
Career snapshots: http://www.nature.com/drugdisc/nj/nj_dd_arch.html