SPOTLIGHT ON STEM CELLS

Stem cells: fulfilling the promise

Breakthroughs in stem cell research provide hope for patients, but it's also an optimum time for scientists in the field.

"If you're interested in the science, there's probably a skill set of yours that can be used somewhere — you don't have to be a PhD-level research scientist to be involved in this field."

Tenneille Ludwig, WiCell Research Institute

AT COLUMBIA University in New York, the circuitous route of postdoctorate scientist Sarindr Bhumiratana shows that there is no single career path in stem cell research. Bhumiratana initially studied chemical engineering, but flourished in biomedical engineering during a stint at Columbia's laboratory for stem cells and tissue engineering.

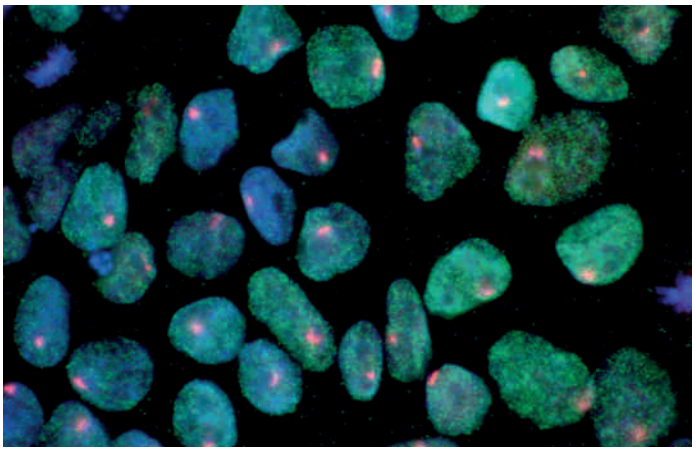
Bhumiratana went on to help develop a research programme to explore the use of stem cells to grow customized bones for patients whose heads and faces need to be rebuilt and for the healing of disfigurements that can leave psychological scars. He is now pushing this work towards clinical applications.

Bhumiratana's advisor at Columbia, Gordana Vunjak-Novakovic, describes him as a sterling example of how accessible stem cell research is as a career.

"This is a great demonstration of how you can use stem cells to solve difficult, complex problems, and how you can enter stem cell research in many different ways and go far," Vunjak-Novakovic says.

Since human embryonic stem cells were first isolated in 1998, stem cell research has provided a dazzling variety of possibilities for improving patients' lives. The multi-disciplined approaches needed to research them and the huge capacity for further discovery means the field has much potential for scientists as well.

Although some of the initial excitement around stem cells can be put down to hype, advances over the last 15 years have led many of these promises to bear fruit. Indeed, 2013 has been touted as a big year for regenerative medicine. "Now more than ever, we're on the cusp of some dramatic breakthroughs with stem cells," says Tenneille Ludwig, director of quality assurance and marketing at the WiCell Research Institute in Madison, Wisconsin.



CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

iPS cells reprogrammed from a woman's skin. These cells can be matured into other cells of the body, and used for studying models of disease.

Crucial distinctions

Most types of stem cells are specialized and can only differentiate into a certain kind of tissue — for instance, hematopoietic stem cells are the genesis of all the other blood cells.

The most valuable stem cells for research are embryonic stem (ES) cells, since they are pluripotent, capable of becoming any tissue in the body. Two clinical trials involving retinal cells derived from human ES cells for patients with Stargardt's macular dystrophy and dry age-related macular degeneration are being led by Advanced Cell Technology (ACT) in Massachusetts, and preliminary findings appear encouraging, with some vision improvements seen.

However, in recent years, breakthroughs in stem cell research have led to the development of so-called induced pluripotent stem (iPS) cells, which are typically mature cells genetically reprogrammed to become pluripotent ones using retroviruses. This year, ACT hope to launch the first human iPS cell trial, to generate blood platelets from these stem cells. If successful, it would mean a source of blood platelets for patients requiring transfusions without the need for donors.

It may also be possible to turn adult stem cells into different types of cells entirely. For instance, scientists hope to transform pancreatic ductal cells to pancreatic islet cells that can manufacture insulin for people with diabetes, says K. Lenhard Rudolph, scientific director of the Leibniz Institute for Age Research in Jena, Germany.

Acceptable alternatives

Much of the initial resistance to stem cell research focused on stem cell lines developed in the 1990s, which originate from human embryos. The development of human iPS cells in the 2000s, which gave researchers pluripotent cells without an embryonic origin, somewhat circumvented this controversy, says Thomas Hyde, chief operating officer at the Lieber Institute for Brain Development in

Stem cell surprises

Scientists are discovering many new sources of stem cells for research. Here are some of the more surprising.

BRAIN CELLS FROM URINE

Cells from the lining of the kidney are routinely shed in urine. Scientists at China's Guangzhou Institutes of Biomedicine and Health and their colleagues recently used a special brew of transcription factors to reprogram these cells into neural progenitor cells. They went on to successfully derive human brain cells that could survive in newborn rat brains.

3-D PRINTED STEM CELLS

3-D printers lay down thin layers of material much like ordinary printers, except they deposit layer upon layer to create 3-D objects. A team of researchers at Heriot-Watt University and Roslin Cellab in Scotland recently showed they could print using inks containing human embryonic stem cells, which stayed alive after printing and could develop into different types of cells. Bioengineers are exploring 3-D printing as a way of creating tissues and organs for transplant.

STEM CELLS FROM CADAVERS

Last year, researchers at the Pasteur Institute in Paris and colleagues discovered that stem cells can remain alive in human corpses for at least 17 days after death. They kept cadavers at 4C to avoid decomposition and these stem cells, which normally give rise to skeletal muscle, survived without oxygen. The cells had extraordinarily reduced metabolic activity when discovered, marking the first time scientists have found that stem cells were capable of such dormancy. Another team of scientists at NIH and the Lieber Institute for Brain Development in Baltimore discovered that living cells from the scalps and brain linings of human corpses could be transformed into stem cells. Specifically, fibroblasts, the most common cells of connective tissue in animals, could be collected from cadavers and reprogrammed into induced pluripotent stem cells, which could then develop into a multitude of cell types, including neurons.

Gordana Vunjak-Novakovic, whose lab at Columbia University uses stem cells to develop tissue grafts, consults with a surgeon about implantations.

Baltimore. ES cell experiments are likely to remain necessary, however, as given the reprogramming they have undergone, it is still uncertain how useful or safe iPS cells are.

Nonetheless, plans for major projects in the next three to five years are poised to generate significant funding for iPS stem cell research, says Erik Forsberg, executive director at WiCell. He describes a programme "to generate tens of thousands of new human iPS cell lines from thousands of people from both the general population and patient groups." This will allow wide-scale comparison of healthy stem cell lines against those in patients, helping to model diseases and provide insights on their biology. The projects will be broadly funded, with investment coming from the National Institutes of Health, the California Institute for Regenerative Medicine, the Allen Institute for Brain Science based in Seattle, the StemBANCC partnership managed by the University of Oxford, and the Wellcome Trust and Medical Research Council in the United Kingdom.

Options abound

The wide range of funding bodies investing in stem cell research echoes the variety of career paths in the field in addition to the scientists and physicians who conduct the research and the technicians in the lab. Companies such as Stemcell Technologies in Vancouver develop the reagents, instruments and techniques used in stem cell research, and do much of the other specialized work required, such as DNA extraction and sequencing, epigenetic profiling, and sometimes entire preclinical studies.

Quality assurance is also essential — people who ensure labs follow good manufacturing and clinical practices and adhere to guidelines governing what might go into the human body. "You have to be passionate about getting the work done right, have a meticulous personality with a lot of attention to detail, and work with top management down to technicians and even janitors cleaning labs," says Jessica Martin, director of cell banking and distribution at WiCell.

There are jobs in stem cell research outside the lab as well. For instance, the regulatory framework around stem cell science creates a need for legal specialists to consider the issues. "There's also definitely a need for people who can write grant applications, for sales and marketing staff, and for those who can educate the general public on the politics and ethics of the work," Ludwig says. "If you're interested in the science, there's probably a skill set of yours that can be used somewhere — you don't have to be a PhD-level research scientist to be involved in this field."

Enthusiasm, however, is a must. "By now, everything that is easy to do has probably been done a long time ago. Today we're facing difficult problems, and to solve those you need excited people who never give up, who really work relentlessly toward accomplishing something," Vunjak-Novakovic says.

Given the multi-disciplinary nature of stem cell research teams, "the ability to learn the language of other disciplines is extremely important," adds Terry Thomas, senior vice president of research and development at Stemcell Technologies. When interviewing candidates, he asks questions outside a person's area of research, "to get a look at their ability to process new ideas, catch on quickly and to test intelligence and flexibility."

Experience outside science is also advantageous. "I'm looking for people with broad horizons, which matters in a frontier field like stem cell research, so I really look for things on resumes like travel, volunteer work, as well as people who were heads of student associations or ran a business. People who can make things happen," Thomas says.

Given the pace of evolution with stem cell research, Thomas says, "you will need to constantly learn and almost anticipate new developments. You need to be flexible".

There are critics who claim that stem cell research has failed to live up to its promise, but those within the field have seen the advances. "Now is probably the best time ever to work in the field of stem cells," Vunjak-Novakovic says.

Hyde agrees: "The promise of stem cells cannot be underestimated, but it's not simple work that can occur after just a week or a month." That said, " to go from initially deriving human ES cell lines to clinical trials with them in just 10 years or so is pretty impressive. It's still amazing how far we've come in so short a time."

Nature editorial staff have no responsibility for content

Leibniz Institute for Age Research
Fritz Lipmann Institute (FLI)

The Fritz Lipmann Institute for Age Research (FLI) in Jena, Germany is seeking for

Group Leaders at Assistant Professor or Tenured level

Successful candidates should strengthen the focus of the institute in molecular mechanisms of stem cell aging, organ homeostasis, age-associated disease, and old-age cancer. We encourage applications from any area of cell biology, molecular biology, DNA and protein integrity control, functional genomics, and systems biology. The use of diverse animal models including Planarians, C. elegans, Drosophila, fish or mouse is welcome.

The institute offers highly competitive funding and start up packages at international level. Successful candidates for tenured positions could be co-appointed as full W3 professor at the Friedrich-Schiller-University Jena.

The FLI is an international research institute located in Jena, Germany and is a member of the Leibniz Association. Its basic budget is supported jointly by State and Federal Government.

The FLI aims to increase the number of women in leading positions, and thus encourages qualified female candidates to apply. In case of comparable qualifications, preference will be given to female applicants.

Applications (including CV, list of publications, PDF-versions of the 5 most important original papers along with a brief outline of current and intended research, plus the contact details of two referees) should be submitted to GL-applications@fli-leibniz.de **as a single pdf file by July 15th, 2013** (code number 11/13)

Further information can be obtained by contacting Prof. K. Lenhard Rudolph, e-mail: GL-applications@fli-leibniz.de.
Please see also http://www.fli-leibniz.de/index_en.php

W237031R

Revive
Institut Pasteur

Young Group Leader Positions in Stem Cell Biology

The Institut Pasteur announces an international call for candidates wishing to establish independent research groups on its Paris, France campus. The recruitments are part of the Revive Laboratory of Excellence (LabEx) programme, recently awarded to the Institut Pasteur on "Stem Cells and Regenerative Biology and Medicine". Candidates will be integrated into the cutting edge interdisciplinary environment provided by the Department of Developmental & Stem Cell Biology. Candidates specializing in the field of stem cells in the context of developmental and cell biology, genetics, epigenetics, regeneration, translational research and ageing are encouraged to apply.

To be eligible, candidates must have defended their PhD on or after June 20, 2005 (women with children are eligible up to 10 yrs after their Ph.D). Successful candidates will be appointed as head of a group of up to 6 people for a period of 5 years. The budget (up to 1,500,000€ over 5 years) includes the salary for the group leader, a three-year postdoctoral position, a technician's position, part-time secretarial assistance, a substantial contribution to running costs and equipment, and access to on-campus facilities including state-of-the-art technology core facilities.

Candidates should send their formal applications by E-mail to the Director of Scientific Evaluation, Prof. Alain Israël, at the Institut Pasteur (g5revive@pasteur.fr). **The deadline for applications is June 20, 2013**. Short-listed candidates will be contacted for interview to be scheduled for beginning of September 2013 and recruitment decisions announced by October 2013. Further information on the Revive program can be found at http://www.pasteur.fr/revive

Applicants should provide the following (in order) in **a single pdf file**:

1. A brief introductory letter of motivation, including the name of the proposed group. Candidates are encouraged to contact the coordinator of the Revive programme Shahragim Tajbakhsh (shaht@pasteur.fr).
2. A Curriculum Vitae and a full publication list.
3. A description of past and present research activities (up to 5 pages with 1.5 spacing; Times 11 or Arial 10 font size).
4. The proposed research project (up 10 pages with 1.5 spacing; ; Times 11 or Arial 10 font size).
5. The names of 3 scientists from whom letters of recommendation can be sought, together with the names of scientists with a potential conflict of interest from whom evaluations should not be requested.

W237202R

STANFORD
SCHOOL OF MEDICINE
Stanford University Medical Center

SENIOR RESEARCH SCIENTIST IN STEM CELL BIOLOGY

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Outstanding opportunity within a cutting edge stem cell research and genetic engineering laboratory to help manage a dynamic research team. Position involves elucidating mechanisms underlying stem cell fate decisions, nuclear reprogramming, and artificial bioengineered niches with therapeutic applications (see http://www.stanford.edu/group/blau). Strong background in molecular biology and cell sorting (FACS) a must. Expertise in fluorescence and confocal microscopy, mouse models, mammalian cell culture, and retroviral and lentiviral transduction desirable. Stem cell experience (muscle, hematopoiesis, iPS) a plus. Stanford position is at the level of Senior Research Scientist in the Baxter Laboratory for Stem Cell Biology in the Center for Clinical Sciences Research under the direction of Professor Helen Blau. A good publication record is essential and demonstrated success in grant/fellowship writing desired.

The candidate must have excellent oral and written communication skills and aptitude in leading and working with research teams (including overseeing experimental design with graduate students and postdoctoral fellows) as well as coordinating work conducted with collaborators within the Stanford community and with academic and biotech collaborators.

Salary $80,000 - $110,000 p.a./commensurate with experience. Stanford offers a humane, supportive environment in which to pursue your life and your career with an excellent benefits package. Position available for candidate with three or more years of postdoctoral experience. Candidate should expect to start in the summer of 2013 for a minimum of three to six years in the position.

To apply please send a CV and list of referees to Dr. Helen M. Blau, CCSR 4215, Stanford University School of Medicine, Stanford, CA 94305-5175 (hblau@stanford.edu or fax: (650)736-0080).

NW237542R