TURNING POINT Work on genetics of twinning leads to award and post **p.401**

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REPRODUCTIVE BIOLOGY

Breeding opportunities

The reproductive sciences offer an unusual variety of career options — but some are more fertile than others.

BY CHARLOTTE SCHUBERT

Help to implant a human embryo; watch mouse eggs divide after fertilization; interview women about their experiences with emergency contraception; collect sperm from finches in the Galapagos Islands off Ecuador: specialists in reproductive biology undertake these duties and many more. The field provides a surfeit of career trajectories and research questions. "We cover everything from fertilization to death," says Dolores Lamb, director of the Center for Reproductive Medicine at Baylor College of Medicine in Houston, Texas.

The reproductive sciences also touch on human life and biology at almost every level, from molecular and cellular events such as the recognition of the egg by sperm, to whole-body processes including hormonal regulation of puberty and population-level questions such as what factors affect teenage-pregnancy rates.

"It's amazing, the diverse backgrounds that all somehow feed into reproductive medicine," says Lamb. Many researchers study reproduction as part of a doctorate in reproductive or developmental biology. Others might find their way to the field through cell biology (focusing on sperm stem cells, for example) or animal sciences (perhaps studying cattle hormones). Attendees at the annual meeting of the Society for the Study of Reproduction, which is based in Madison, Wisconsin, hail from a wide range of disciplines.

Diversity does not guarantee jobs, however, and positions are scarce in many areas of industry and academia. Richard Sharpe, who heads the graduate programme at the UK Medical Research Council's Centre for Reproductive Health at the University of Edinburgh, says that three years ago he assured students that if they excelled, they could find work. "We can no longer say that," he says. Academic opportunities have shrunk as the recession has taken a bite out of budgets and funding priorities have shifted to areas such as chronic disease, says Sharpe. (Although location does matter; see 'Renminbi for reproduction'.) In the reproductive sciences, as in most life sciences, the job market has constricted, agrees Michael Skinner, founder of the Center for Reproductive Biology at Washington State University (WSU) in Pullman.

Even so, he says, studying reproduction will give doctoral students an edge with employers from fertility clinics to animal-agriculture companies. And areas such as global health continue to grow.

LOOKING TO ACADEMIA

WSU graduates have landed academic jobs in everything from toxicology to oncology, says Skinner, who notes that much cancer research focuses on reproduction-related cancers such as breast and prostate. These days, "you have to market yourself broadly", says Tracy Clement, who earned her PhD with Skinner and is looking for an academic post. "It does not feel like a good time to be on the job market."

If she does get a university job, Clement will face funding difficulties. The major source of US research money in the field is the National Institute of Child Health and Human ▶

Development in Bethesda, Maryland, but last year only 12.5% of grant applications for major research projects to the institute were successful — less than at many other National Institutes of Health (NIH) institutions.

In the future, says Skinner, academics will require support from multiple sources — something for which the broad field is particularly suited. Skinner, for instance, has received funding not only from the NIH, but also from the Bill & Melinda Gates Foundation in Seattle, Washington, to develop a male contraceptive and from the US Department of Defense to study how exposure to environmental toxicants affects subsequent generations. He has also applied to the John Templeton Foundation, based in West Conshohocken, Pennsylvania, to study the role of epigenetics in finch evolution in the Galapagos.

MIXED OUTLOOK IN INDUSTRY

The pharmaceutical industry has shed jobs in contraception over the past 10 years, in part because of nervousness about the side effects of reproduction-related drugs, which have drawn numerous lawsuits. Companies such as Wyeth — acquired in 2009 by Pfizer in New York — and Bayer, based in Leverkusen, Germany, have cut back or dropped entire research programmes.

Daniel Johnston, a former principal research scientist at Pfizer who was laid off in 2010, could not find a job directly related to human reproduction at a pharmaceutical or biotechnology company despite more than 5 years of pharmaceutical experience in contraception and women's health. But while at Pfizer, Johnston had begun to work in oncology — and that experience helped him to find work at a company focused on liver cancer.

Johnston's lateral move is not unusual, given that reproduction overlaps with many areas (Johnston compares a testis to a tumour; both have a low-oxygen core of rapidly dividing stem cells — but one produces sperm instead of cancer cells). Susan Fisher, director of translational research in perinatal biology and medicine at the Center for Reproductive Sciences of the University of California, San Francisco, says that adaptability gives her graduates a leg up in industry. They have found jobs at biotechnology companies focused on oncology, stem cells and the rapidly expanding area of prenatal genetic testing, a market that could soon be worth more than US$1 billion yearly (see *Nature* **486,** 454; 2012). Companies competing in this area include Ariosa Diagnostics in San Jose and Natera in San Carlos, both in California. Skinner advises students and postdocs interested in an industry job to get training in the broadest possible range of lab technologies, including genomics.

Reproductive biologists are also finding work in animal agriculture. "I get calls maybe two or three times a year from companies looking for a master's- or PhD-level scientist to run a lab," says Derek McLean, a biologist who studies cattle, pig and mouse reproduction at WSU.

Scientists who can store and manage animal semen and test fertility products for female livestock are in demand at companies and organizations such as Select Sires, a federation of farmer cooperatives based in Plain City, Ohio, that provides livestock-breeding services. Candidates for such posts have generally trained in a reproductive-biology laboratory and have a degree in animal science. The job market is steady in the United States, and is expanding in Brazil and other emerging countries that are moving towards a more industrialized animal-agriculture system, says McLean, who is leaving WSU this autumn for Phibro Animal Health in Teaneck, New Jersey.

"You have to prepare for option one — but have option two and three in the wings."
Tracy Clement

Genomics opportunities are also emerging at companies that are developing tests for genetic selection of farm animals; one such employer is Illumina in San Diego, California, which markets a high-density Bovine BeadChip, a genetic array that detects traits in cattle.

Fertility clinics are an option for those looking for something more applied — and perhaps more likely to have an immediate impact on people's lives. There are about 400 clinics in the United States, and they often hire PhD-level scientists to manage a staff of bachelor's- and master's-level technicians involved in tasks such as culturing and freezing human embryos and performing hormone assays. Such scientists often interact with patients — a lead embryologist, for instance, might contact patients with test results, and assist during implantation of the embryo. "It brings a lot of joy in our profession to help people to have a family," says Pierre Miron, who heads a fertility clinic near Montreal in Canada. "The interaction with patients is a great part of the job." Jobs at clinics affiliated with universities often provide more opportunities for fertility research than private clinics, says Miron.

The government of Quebec province began paying for *in vitro* fertilization in 2010 as part of the national health-care system, leading to rising demand for services. Many clinics are filling job slots with trainees from Réseau Québécois en reproduction (the Quebec Reproduction Network), a consortium of more than 80 researchers at institutions such as McGill University in Montreal. But in most of the world, jobs in fertility clinics are competitive. Strong candidates not only have the right human touch, says Miron, but also have training in a range of techniques, including sperm and egg manipulation.

GLOBAL IMPACT

Global health may be a more fruitful area for reproductive-biology graduates. "My personal feeling is that there is now a stronger market for people working at the population level than at the molecular level in the reproductive sciences," says Ward Cates, president emeritus of FHI 360, a global-health organization based

STEVEN R SHAW/IMAGE ASSOCIATES

ASIAN OUTLOOK

Renminbi for reproduction

Thirteen years after earning his PhD, and following two stints as a postdoc, Minghan Tong, a reproductive biologist at Washington State University in Pullman, has finally landed a tenure-track research position. Unable to find such a job in the United States, Tong is heading to greener pastures in his native China. In September, he will begin work at the Shanghai Institutes for Biological Sciences. Tong and others are applying for a 39-million-renminbi (US$6.3-million) grant to study the epigenetic regulation of sperm production.

China is a bright spot in the tight market for academic jobs in reproductive sciences. The sperm-production grant is part of a major funding initiative in the field by the Chinese government, which is interested in new approaches to contraception and in the reproductive impacts of environmental problems such as toxicants that may damage sperm and eggs by tweaking the epigenome to affect multiple generations.

In 2007, the Chinese Ministry of Science and Technology designated development and reproductive sciences as one of four core research areas, ramping up grant funding. This year, the ministry is expected to fund four 5-year projects in the field, each worth more than 24 million renminbi.

Other national and local agencies have also increased funding, spurring the establishment of dozens of research centres focused on reproductive sciences and creating hundreds of jobs, says Qinghua Shi, a professor of life sciences at the University of Science and Technology of China in Hefei. C.S.

in Durham, North Carolina. He points to Family Planning 2020, an ambitious initiative to roll out contraceptive services to 120 million girls and women in developing countries by 2020. Donors including the Bill & Melinda Gates Foundation and governments of both developed and developing nations have pledged $2.6 billion to the programme, which was launched last July at a meeting in London spearheaded by Melinda Gates. "This will define the future for public-health jobs in the reproductive sciences," says Cates.

He adds that the initiative will create jobs, mostly in the developing world, for researchers who know how to cost-effectively implement such services and for scientists who can evaluate their impact — by, for instance, assessing the uptake of contraception and its effects on population growth and women's and children's health. The effort will require researchers with backgrounds in areas such as demography, sociology, economics and public health.

Cates says that researchers with a basic-science background in reproductive sciences and extra training in fields such as epidemiology often have a leg up when competing for jobs in areas including clinical-trial design, because of their understanding of biology.

Patricia Sadate-Ngatchou earned a PhD studying sperm development at WSU. But a visit home to Cameroon during a major cholera outbreak in 2010 changed the course of her career. "How do you help people on the ground?" she asked herself.

Sadate-Ngatchou is now studying for a master's degree in epidemiology at the University of Washington in Seattle. Her ultimate goal is to move into a decision-making position in government or a foundation involved in reproductive health; a suitable post might be as a programme officer overseeing grants. However, Sadate-Ngatchou thinks that she may first have to do entry-level work as an epidemiologist, for instance in disease surveillance.

The variety of questions and opportunities in reproductive biology keeps some researchers hooked on the field, despite the tough market. Some end up in niches they never expected, such as facilitating panda or reptile reproduction in zoos, or assessing toxicants for their effects on embryonic and pubertal development at government institutions such as the US Environmental Protection Agency. Clement is open to a variety of possibilities. "If you are a reproductive biologist," she says, "you have to prepare for option one — but have option two and three in the wings." ■

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TURNING POINT
Bruno Reversade

*A molecular biologist at the Agency for Science, Technology and Research (A*STAR) Institute of Medical Biology in Singapore, Bruno Reversade is the first scientist based outside Europe to win the European Molecular Biology Organization Young Investigatorship Award, which he collected last November for his work on genetics and twinning.*

Do you thrive in a competitive environment?
Yes. I realized that university would be competitive when one of my first professors said that 60% of the class would not make it to the second year. After that, I sat in the front and worked hard.

What led to your fascination with embryonic development?
I went to the University of Western Ontario in London, Canada, in my fourth year as an undergraduate and worked on early zebrafish development. The developing embryo was so beautiful and fundamental to life that I realized it was a special area. At the time, medicine and biology were all about identifying and treating disease, but I found a resonance with birth and development. I went to the Pasteur Institute in Paris for a year to work on early head development after seeing a knockout mouse with no head on the cover of *Nature* (W. Shawlot and R. R. Behringer *Nature* **374,** 425–430; 1994).

What was the biggest challenge of your PhD?
I did most of my research at the University of California, Los Angeles, where I spent the first half of my programme chasing chordin, a protein that my adviser, Eddy De Robertis, and I thought was circulating in the blood. After three years we found we were mistaken. I persevered, however, and we detailed how multiple proteins help embryos that are cut in two to self-regulate consistently. Eddy and I published the work in *Cell* (B. Reversade and E. M. De Robertis *Cell* **123,** 1147–1160; 2005).

What led you to focus on genetics in twinning?
Sitting in the lab cutting frog embryos day after day led me to a defining realization. Identical twins occur once in every 300 births, more frequently than most genetic diseases. The dogma at the time was that twinning just happens, but I started to look for evidence of a genetic trigger. Then Hanan Hamamy, a genetic clinician who at the time was at the Jordanian National Center for Diabetes, Endocrinology and Genetics in Amman, identified 13 pairs of identical twins across multiple generations of a single family — hinting at a genetic link. She kindly invited me to work with her.

How were you able to rush out to Jordan?
I wanted to test my ideas as quickly as possible, and I didn't want to do a postdoc. Perhaps that was arrogant or unrealistic, but I wanted to be independent. Fortunately, Swiss philanthropist Branco Weiss was seeking young scientists who were pursuing a biological problem with societal impact for the Society in Science fellowship. I met Branco and explained that identical twins can develop through several mechanisms, including embryonic bisection and possibly genetics, which for me calls into question the moral uproar over cloning. I convinced him that the idea was worth pursuing and he gave me the money.

Have you published this work?
Not yet. I'm now working with samples from other families with multiple sets of twins. We found a gene that is overexpressed in identical twins and encodes a protein. We are making sure it is well protected by patents.

What is your most important career move so far?
In 2008, I was the first A*STAR investigator recruited as an assistant professor at the Institute of Medical Biology. They offered me carte blanche: I have no teaching or grant-writing responsibilities. Everything was new and the country was investing so much in science. I have blossomed here because I got that freedom just as the revolution in human genetics began.

What do you plan to do next?
I want to work on rare diseases ranging from developmental anomalies to inherited cancers. If you want to understand a trait in the general population, you need to look at the outliers. ■

INTERVIEW BY VIRGINIA GEWIN