CAREERS

TURNING POINT Cardiologist explains move from academia to big pharma **p.301**

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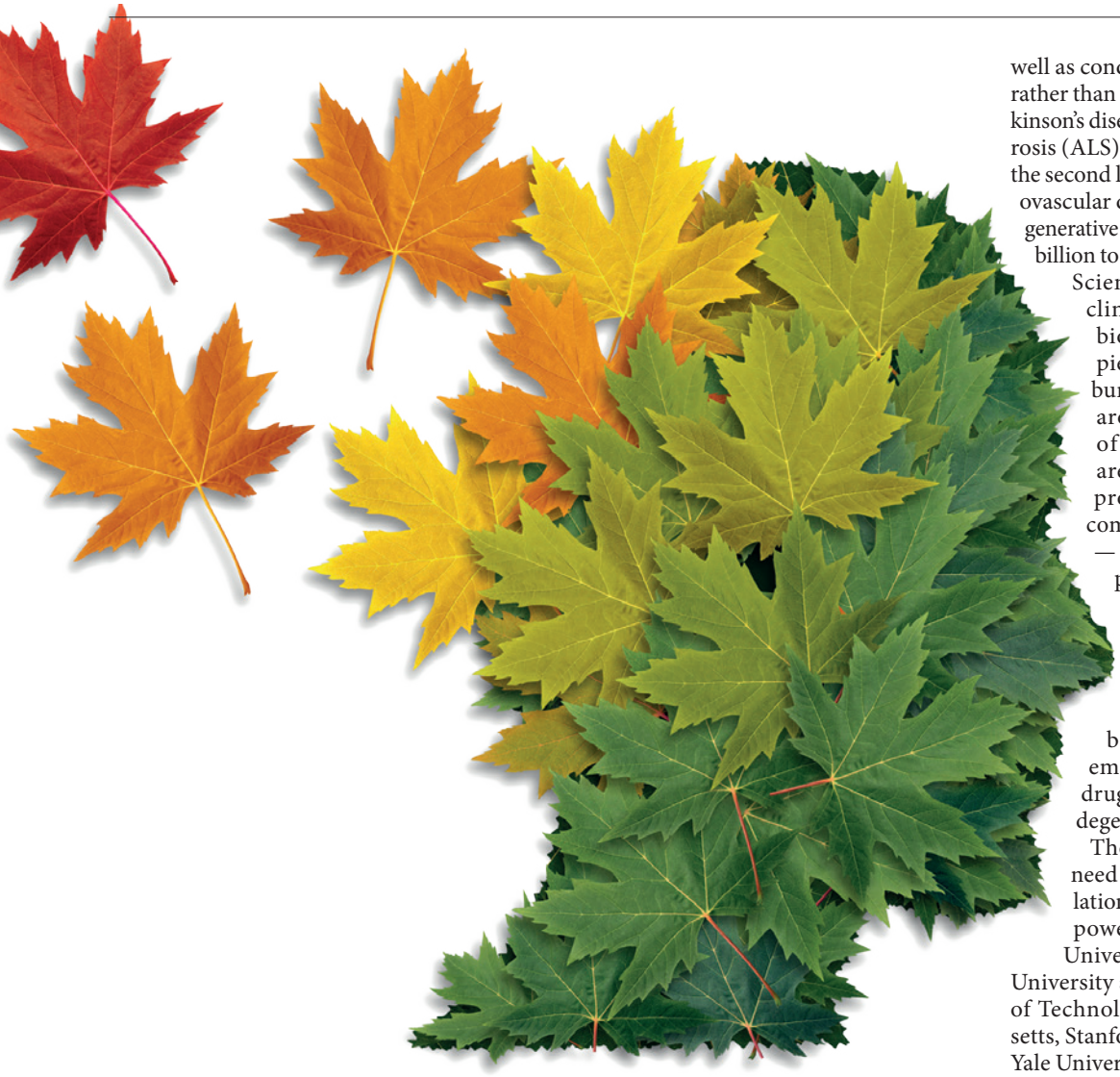

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NEURODEGENERATIVE DISEASE

Brain windfall

Diseases such as Alzheimer's and Parkinson's are rising up the research agenda, partly because of ageing populations.

BY KATHARINE GAMMON

For those who study neurodegenerative diseases, there is a feeling of optimism — and trepidation — about what the next few decades will bring. A flood of dementia cases lies in humanity's future as the global population ages. The non-profit group Alzheimer's Disease International predicts that there will be some 135 million cases worldwide by mid-century — up from 44 million cases today. And the World Health Organization (WHO) predicts that by 2040, as many developed countries' populations get older, neurodegenerative diseases such as Alzheimer's and other causes of dementia, as well as conditions that affect mainly motor, rather than cognitive, functions, such as Parkinson's disease and amyotrophic lateral sclerosis (ALS), will overtake cancer to become the second leading cause of death after cardiovascular disease. Treatments for neurodegenerative diseases already contribute US$20 billion to a market that is expected to grow.

Scientists who have both basic and clinical research skills in finding biomarkers and potential therapies could help to treat the rising burden of dementia. Governments around the world are well aware of the growing numbers, and are starting to invest in research programmes to understand and combat neurodegenerative diseases — which means that new research positions will emerge across the academic, non-profit and industry sectors worldwide. Opportunities are growing in work to find biomarkers that can diagnose disease long before neurological symptoms emerge, and to identify targets for drugs that might halt or slow neurodegeneration.

Those who want to enter the field need to focus their research on translational targets. Training at one of the powerhouses in the field — such as University College London, Harvard University and the Massachusetts Institute of Technology in Cambridge, Massachusetts, Stanford University in California and Yale University in New Haven, Connecticut — puts candidates in a better position when they try to get a job, says Adrian Ivinson, director of translational research at the Harvard NeuroDiscovery Center in Boston, Massachusetts. "If you've got your training in a good place and you know how to translate it into a clinical setting, the future is looking good," he says. "The next few decades will change how we tackle these diseases." He adds that there is no magic bullet for a career path in the discipline, but advises that jobseekers would do well to find themselves in a vibrant lab environment, populated by both neuroscientists and clinicians. "Generally you would say that the richer and denser that commitment to talent, the better off you're going to be as a postgraduate in terms of your qualifications," he says.

Before neurodegenerative diseases can be ▶

treated, they need to be detected — and the earlier the better. As no reliable test yet exists to spot Alzheimer's disease, Parkinson's disease or ALS before symptoms appear, publicly funded agencies and pharmaceutical companies are pooling their resources to find biomarkers — arguably the area with the biggest career opportunities for researchers interested in entering the field. Biomarkers are measurable substances that can indicate early signs of disease, infection or exposure.

PUBLIC–PRIVATE INITIATIVES

Given this interest in early diagnosis and treatment for neurodegenerative diseases, job opportunities are starting to open up in academia and industry. In February, the US National Institutes of Health (NIH) launched a partnership with ten pharmaceutical companies, including Merck, Pfizer and Sanofi, and the trade organization Pharmaceutical Research and Manufacturers of America to find biomarkers and drug targets for Alzheimer's disease (along with type 2 diabetes and autoimmune disorders). The NIH and the drug-makers are combining resources and sharing information to make the process of drug discovery move faster — a type of partnership that has not yet been tried in this field. Some of the funds will go to three trials that will test drugs to slow the progression of Alzheimer's disease, which means job opportunities for young researchers.

Canada and Europe are following similar public–private models. The Canadian Consortium on Neurodegeneration in Aging was formed in September with Can$55.5 million (US$49.4 million) in funding from the Canadian government and other partners, including Paris-based Sanofi. The consortium aims to develop ways to prevent, identify and slow the progression of neurodegenerative diseases. To do so, it is initially funding 47 principal investigators in 20 teams, across different universities, supporting about 340 scientists in all, including postdocs and graduate students. As the programme ramps up, the teams will be hiring young researchers from around the world.

In Europe, the European Union Joint Programme — Neurodegenerative Disease Research (JPND), headquartered in Paris, is the largest neurodegeneration-research initiative worldwide, involving the 29 member and third-country member countries. The consortium is funding studies on early-onset dementia, and on biomarkers and gender differences in Alzheimer's and other diseases. It funds basic-science research through to health and clinical care — which means that jobs are now opening up at institutions funded by the JPND. The idea is that no single country can have the breadth and depth of research needed to mitigate the coming avalanche of dementia cases, so teaming up is the best option.

Industry is also jumping on board. Biogen Idec in Cambridge, Massachusetts, and Genentech in South San Francisco, California, are recruiting discovery and translational scientists in neurodegenerative research as well as medical directors in development, experimental medicine and biomarkers, and global medical affairs. In the United Kingdom, GlaxoSmithKline has recently joined the UK Dementias Research Platform, a multimillion-pound public–private partnership developed and led by the UK Medical Research Council, which is focused on accelerating progress in neurodegeneration research. The platform is looking to validate biomarkers for different stages of disease progression.

Other approaches to tracking down the roots of neurodegeneration focus on neuronal synapses — the connections between brain cells. In October, the non-profit Allen Institute in Seattle, Washington, was awarded an $8.7-million, five-year grant to create a model of all the genes and proteins involved in different synapse populations in both the human and mouse brain that will be accessible to all researchers. The project aims to gain an understanding of how individual neurons in the brain connect and transfer information through synapses, says spokesman Rob Piercy. Many brain diseases and disorders ranging from Parkinson's disease to depression are rooted in abnormalities of synaptic function, he says. In the next few years, the institute will be nearly doubling its payroll from 270 to 500, and one-fifth of those hired will be brain-disease researchers.

The field has become extremely multidisciplinary, says neurosurgeon William Mack, director of the cerebrovascular laboratory in the Zilkha Neurogenetic Institute at the University of Southern California in Los Angeles. Those trained in imaging, radiology and computing have a strong chance of getting hired. Teaching hospitals are also assuming a leading role in neurodegeneration research, adds Ivinson, because they can bring basic-research findings to the clinic. "You'll see a lot of funding attention go to the groups that can demonstrate they're ready to pivot from basic mechanisms to practical questions they can address," he says.

Joseph Mazzulli, a neuroscientist at Northwestern University's Feinberg School of Medicine in Chicago, Illinois, is linking his basic research with industry to bring a potential neurodegenerative treatment to market. In 2011, he co-founded Lysosomal Therapeutics, a start-up in Cambridge, Massachusetts, that aims to market drugs to treat Parkinson's disease and Gaucher's disease, which leads to motor impairments similar to parkinsonism. He and his partners were approached by drug-makers about potential collaborations, but they chose instead to launch their own start-up to test compounds that target glucocerebrosidase, a enzyme that is involved in both Parkinson's and Gaucher's diseases. "We felt that we had a firm grasp on the mechanism that linked these two diseases," he says. "Ultimately, we thought doing it ourselves would accelerate the process and get a drug to patients more quickly." Investors seem to like the concept: the fledgling company raised $4.8 million in its first round of funding in May 2014.

"It's a 'jack of all trades' career path for sure."

MEETING OF WORLDS

Balancing research and the clinic may seem like a stretch, but for neurologist Vikram Khurana, it comes naturally. With posts at both Massachusetts General Hospital in Boston and the Whitehead Institute in Cambridge, he is studying balance disorders. Last year, Khurana and colleagues discovered a compound that can both identify and reverse some of the damage that occurs in the brain cells of patients with Parkinson's disease. He may launch a start-up to commercialize the discovery. He sees juggling his clinical and research careers as his future in the field of neurodegeneration. "It's a 'jack of all trades' career path for sure," he says, "but I recommend it to anyone who thrives on bringing different worlds together."

Ivinson adds that the field has changed since he started his career a decade ago. "We now have such an abundance of good questions to ask, be they clinical trials or fairly basic neuroscience questions or translational projects in between," he says. "Compared to when I got into this field, I'd say there's real energy that will also fuel job prospects." ■

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Vikram Khurana is working to reverse the brain degeneration associated with Parkinson's disease.

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