Profile

Patrik Brundin: life on the river

> "A dream is like a river ever changing as it flows, and a dreamer's just a vessel that must follow where it goes."
>
> *Garth Brooks*

Things have to start somewhere. Not necessarily at a single point, of course. Do rivers really have a single source, or lots of beginnings? How far a river runs, now that's altogether another thing.

Things started in two places for Patrik Brundin, renowned researcher of Parkinson's disease who now heads the Center for Neurodegenerative Science at Van Andel Research Institute in Grand Rapids (MI, USA). One was the moment in 1974 when he was told his father had been diagnosed with the condition. Patrik was 12 years old, and he was scared. "Both for my father and for what was awaiting us as a family", he recalls. "My mom and I saw a documentary on TV about 'awakenings' just after my dad's diagnosis, and we were shocked at the state of the patients. I remember when I was about 15, I secretly bought a *Reader's Digest* because it had an article on Parkinson's disease. I read it, and then threw the magazine away, and told no one about it." The other was in a room in St Donat's Castle in south Wales, the home of Atlantic College, where Patrik had won a scholarship to leave his native Sweden and study for his International Baccalaureate. It was October, 1979, time to think about the qualification's dreaded extended essay, for which students formulate an original question and undertake research in an attempt to answer it. He managed to find himself a spot on a laboratory bench at Cardiff University, trying to develop a rat model of the Parkinson's disease-like symptoms suffered by manganese miners. "I wanted to do something that might help us understand this disease that was taking my father away", he explains. The outlandish expectations of a kid with no appreciation of the size of the problem? Sure. But his rats did develop motor problems, and the river began to flow.

Having now spent some 40 years researching the disease, Patrik can today appreciate the size of the problem better than most. In the 1980 and 1990s, he became known for his work on developing neural transplantation technology, figuring out how to promote the survival of brain tissue grafts, taking part at age 25 in running the first clinical trials of brain cell transplants, and eventually contributing to the determination that such grafts do survive. Later, he and his colleagues reported the effects of mutant α-synuclein on dopamine homoeostasis, describing how their interaction might cause neurotoxicity in Parkinson's disease. When these two branches of the river met, the waters began to flow deep. "Back in 2008, my laboratory and that of a colleague simultaneously discovered that some patients with Parkinson's disease who had received cell transplants a decade or more before, now had aggregated α-synuclein, or Lewy bodies, in their grafted cells; we had basically discovered that α-synuclein can move from sick to healthy cells, seeding further α-synuclein aggregation in them", he explains. "We think it helps explain how the disease progresses." All this work he performed at Lund University in Sweden, his alma mater, where he became Professor of Neuroscience in 2000. But then came a bend in the river's course.

In January, 2012, Patrik and his family moved from Sweden to Michigan where he took up his current position in what is fondly known as the River City. "The move to Grand Rapids was an amazing opportunity to build a world-class Parkinson's disease research programme from the ground up and to bring together investigators with complementary and diverse expertise," he explains. From the helm, Patrik began recruiting scientists and forging collaborations around the world. Today the team has nine professors, including his wife Lena, a psychiatrist and neuroscientist.

The work coming from the Institute continues to reveal the complexity of Parkinson's disease—the prion-like propagation of α-synuclein, how different forms of misfolded α-synuclein cause different pathologies in affected cells, and the prodromal involvement of tissues outside of the brain. "We now think inflammation in peripheral tissues, coupled with environmental factors, such as pollutants, may trigger the disease process. All of which needs to be investigated against the backdrop of genetic disposition."

His laboratory is also deeply involved in producing animal models of Parkinson's disease on which to test hypotheses and possible therapeutic agents. Does that remind him of a former time? "I suppose in some ways I am still working on that extended essay," he admits.

But we remain with no way to prevent, delay, or cure Parkinson's disease. Is that still just a dream, or is the river nearing the sea? "I have a sense that the floodgates are creeping open, thanks in part to a growing understanding of disease mechanisms and clinic-focused collaborations, such as Linked Clinical Trials [a drug repurposing initiative of which Patrik has chaired the scientific committee since The Cure Parkinson's Trust started the programme in 2012]", he says. "We are riding a wave of progress and that gives me tremendous hope." Wave. It's a word used carefully by a survivor of the 2004 Asian tsunami.

Where things end, and how, you never know until they do. But some things are certain. All rivers have their rapids, sometimes even Grand, and on one is a vessel, going where the river planned.

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For the **Linked Clinical Trial Partnership** see https://www.cureparkinsons.org.uk/linked-clinical-trial-partnership