

"I DIDN'T KNOW I WAS IN CONTENTION"

After he was awarded another illustrious prize for his Alzheimer's disease research, we speak to Professor **John Hardy** about his work.

Professor John Hardy, Chair of Molecular Biology of Neurological Disease at the University College London Institute of Neurology, is no stranger to science and research prizes. The plaudits for his work on Alzheimer's disease started to arrive in the early 1990s, when he won the MetLife, Allied Signal and Potamkin prizes for first describing the genetic mutations in the amyloid gene.

Since then the awards have come with regularity, arguably peaking in 2015 when he and his team became the first UK winners of the Breakthrough Prize in Life Sciences, picking up a cool \$3 million, the largest award in the sciences, funded by Facebook, Google and other leading tech enterprises and entrepreneurs. As if that wasn't enough, he has just been named one of the recipients of the 2018 Brain Prize, winning a share of €1m for his ground-breaking research into the genetic basis of Alzheimer's disease.

More than one person

Awarded by Denmark's Lundbeck Foundation, the Brain Prize cited John and his team for formulating the amyloid hypothesis as a cause of Alzheimer's disease, and for their ongoing

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contributions to the field, from identifying a link between early-onset Alzheimer's and genetic mutations to laying the foundations for new drugs to treat the disease. It also highlighted the role John has played in helping to reveal the genetics behind other

neurodegenerative diseases, such as frontotemporal dementia, Parkinson's and progressive supranuclear palsy.

"I didn't know I was in contention for this one," says John. "It came as a big surprise. A very nice surprise." Despite the obvious delight, he admits to feeling a touch ambivalent about such awards. "Of course, it is lovely to get them. But a piece of work nearly always involves much more than just one person, while these prizes are usually given to only one or two people. To be honest, I often feel a bit embarrassed. It's good, though, that the work is highlighted and people see that science can lead to progress. They also show that science can be a good career."

Huge strides

Since the late 1980s John's career has been focused on the genetics of Alzheimer's and other neurodegenerative diseases. He began looking for the genetic underpinnings of these conditions because he believed that would uncover the best clues about the triggers and processes that drive them, eventually leading to workable and effective therapies.

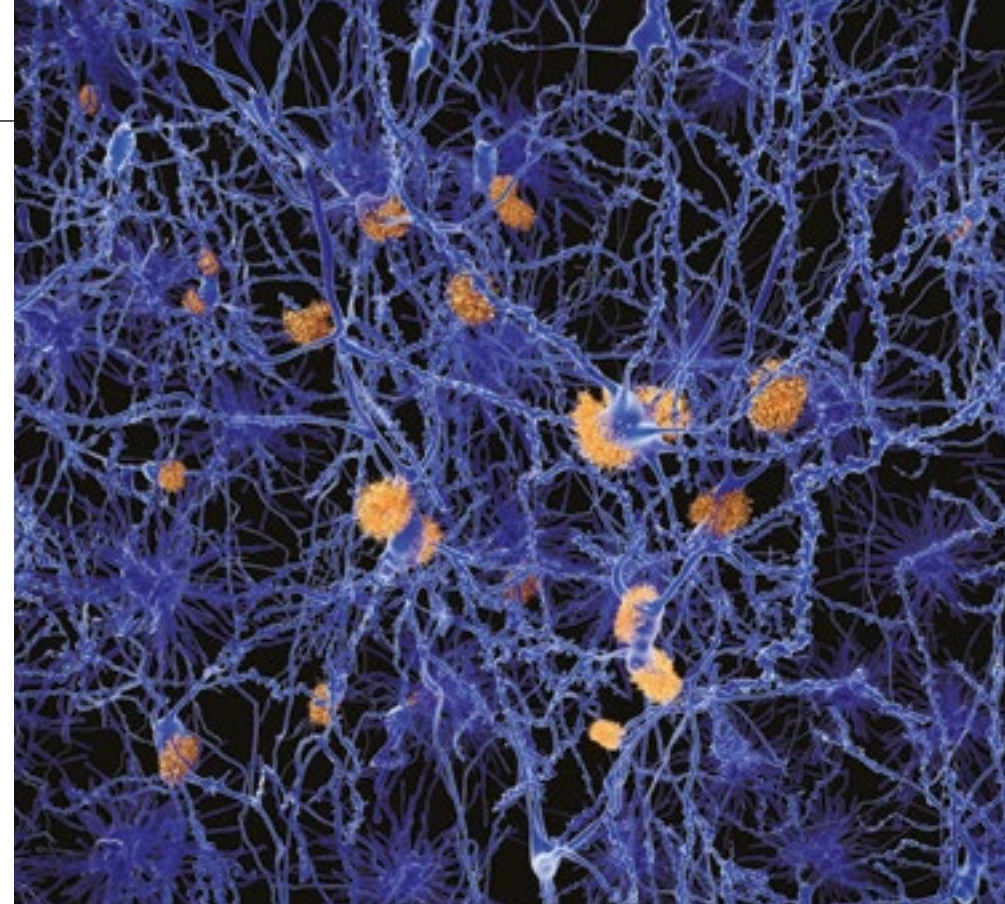
"That's really what my group has been doing since we published our first paper 30 years ago," he says. "An enormous amount of progress has been made in that

time. It was fairly slow and steady up to about 2007, but then we had the whole human genome sequencing, and we suddenly started to make huge strides in terms of finding the genetic factors. The genome sequence has given us technologies to find all the risk genes much more easily. The last five years especially has seen things take off."

The result of this expansion is that the biological foundations of these diseases are now well understood, but it has also exposed the limits of previous thinking. "The thing we had not appreciated was that the diseases start many years before the patient comes in to see the neurologist with the symptoms. That, I think, is turning out to be the problem. Some pretty good drugs have been developed, but we are giving them too late in the disease process. A lot of these drugs should be like the statins GPs prescribe for heart disease – you don't take them when you are having a heart attack, but years before to keep your cholesterol levels down. That is the type of approach that we need to move to."

Such an approach would need a big shift in the healthcare structure, and a suite of reliable screening and diagnostic tools. "We can do that," says John. "For example, we can tell who is genetically at risk from Alzheimer's disease. Then

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Left. Alzheimer disease, neuron network with amyloid plaques

having identified those people, we can find out if they are in the early stages. But that would require a lot of healthcare organisation, which is a challenge." It's a challenge he believes Britain can meet because of a key advantage. "We have a single healthcare system and socialised medicine. That makes it easier. The US might have more money, for example, but it is also more difficult there to organise this sort of thing."

Brexit concerns

With Brexit looming he is concerned we might have to contend with new disadvantages. As he points out, Bart De Strooper, his UCL colleague and co-winner of the Brain Prize, is from Belgian, while Michel Goedert, another winner, works in Cambridge but comes from

Luxembourg: "At a simple level, anything that inhibits Europeans' ability to work here would change matters. I would not have come back if my Icelandic wife could not have worked here easily as a doctor. A lot of people in my department are Europeans, and they are worried. Will it be okay for them, their spouses and children?"

He is also concerned that the lines of communication will become more difficult, that people will find it harder to travel between labs in different countries, and that funding will become more insecure. "We get about a third of our money from Europe," he says, "a third from the UK, and a third from charities. Even if the government makes up the European part, the effect is that we get two-thirds from one source, which leaves you vulnerable if anything goes wrong. As a lab chief, I feel it is healthier to have a diversity of funding."

Only time will tell, though. "While we are seeing fewer applicants from overseas," he says, "people are not yet leaving UK universities in great numbers. But if it's a difficult Brexit, they will."

ALL ABOUT JOHN

- ✓ BSc (Hons) degree from the University of Leeds in 1976
- ✓ PhD from Imperial College, studying dopamine and amino acid neuropharmacology
- ✓ Postdoctoral training in Newcastle and Sweden, where he started to work on Alzheimer's
- ✓ Assistant professor of Biochemistry at St. Mary's Hospital, Imperial College, in 1985
- ✓ Chair of Alzheimer's research at the University of South Florida in 1992
- ✓ Professor of neuroscience at the Mayo Clinic in Jacksonville, Florida in 1996
- ✓ Chief of the laboratory of neurogenetics at the US National Institute of Aging in 2001
- ✓ Chair of molecular biology of neurological disease at UCL in 2007
- ✓ Elected a Fellow of the Royal Society in 2009.

