

Chris Dobson (1949–2019)

Chris Dobson passed away on September 8th, leaving a wide-reaching legacy. He is best known for revealing the generality of the phenomenon of protein misfolding and aggregation and has provided inspiration for generations of researchers.

Chris loved to tell stories, particularly those with a lesson in them. One of his favorite ones concerned a conversation that he had as a young student in Oxford with David Phillips, who at the time had recently solved the atomic structure of the first enzyme using X-ray crystallography. Seeing Chris absorbed in his work in the lab, David asked him whether he was working on an important problem. Chris responded that he was trying to understand the protein folding problem, prompting David to nod and concede that that was indeed important enough.

Chris did indeed devote the first part of his career to elucidating the problem of protein folding, making important contributions that earned him widespread scientific recognition, including the election to a Fellowship of the Royal Society. What distinguished him even more, however, was his work on a second problem, which was initiated by the observation that, in fact, proteins often do not fold correctly, but instead misfold and aggregate. Initially, this phenomenon was largely considered a nuisance in the lab that would typically spoil an experiment. With his characteristic perspicacity, however, Chris started investigating this behavior more deeply, realizing that “most proteins, if not all,” as he liked to say, can end up as insoluble aggregates. Textbooks had to be rewritten, he thought, as proteins are only metastable in their native states, while in the cellular environment they are effectively supersaturated, and so possess an inherent tendency to aggregate.

He devoted the last 25 years of his scientific life to uncovering the generality of this phenomenon. By establishing novel methods to study it and by applying these tools and understanding, his goal was to discover therapies for the wide range of human disorders associated with protein misfolding and aggregation, which include Alzheimer’s and Parkinson’s disease and type 2 diabetes. This work was underpinned by the vision that the key to controlling protein aggregation was to focus on the chemistry and physics of this process rather than its biology. His insight was that aggregation represents a deviation from biological function, which happens when proteins revert to their fundamental nature as rather insoluble polypeptide chains.

We had the great privilege of establishing the Centre for Misfolding Diseases in



Credit: Fran Monks

Cambridge with him. There is a special atmosphere at the Centre, where for nearly two decades we have shared ideas, students, space and resources in a truly collaborative manner. More recently, the Centre moved into the new Chemistry of Health building in Cambridge, which Chris was instrumental in establishing and securing funding for, and which was designed to bring together academic and translational research through hosting an incubator space to promote industrial collaborations, as well as shared laboratories to promote academic collaborations. This initiative resulted in the launch of Wren Therapeutics, a drug discovery company based on the technological innovations following Chris’s original vision about the fundamental nature of protein misfolding and aggregation. It is sobering to think that Chris will not have the opportunity to follow this story until its full promise will be realized, but his vision will live on through these activities.

The direction that Chris’s scientific activities took clearly illustrates how he understood the role of researchers in our society. He recognized that it is a great privilege to have the opportunity to follow one’s own creativity and that it is important to direct these efforts toward goals that could benefit the welfare of people. He thus divided his time between doing research

and building a network of connections with the different sectors of our society. In so doing, he took the role of ambassador for the field of protein misfolding and aggregation, devoting a significant fraction of his time to traveling and giving lectures, which was an activity that he particularly enjoyed. His talks were inspiring both for other scientists and for members of the general public, as he was able to articulate wonderfully both the basic science and its impact and to establish a close connection with his audience.

Perhaps the greatest achievement of Chris, however, has been in promoting other people, as he was a uniquely inspiring and dedicated mentor. Time and again, we heard from people how transformational their encounters with Chris were. Despite being very busy, he always devoted his undivided attention to the person in front of him and spent what seemed as all the time in the world with them. Most remarkably, he did so completely independently of the seniority of the people concerned, from the janitors and gardeners of St John’s College, at which he had been Master for 12 years, to Nobel prize winners and members of the royal family, whom he also hosted for visits at St John’s College. His ability to help people understand their own talents and strengths, as well as the route to fulfilling them, resulted in some 100 of his former students and postdocs taking up independent positions at academic institutions in all parts of the world. He always thought that his success was inextricably linked to that of the people that worked with him.

Chris has been an inspiring figure for generations of scientists. With his unique kindness and attention, and his ability to provide stability and confidence, he has touched and transformed the lives of so many of those who had the opportunity to meet him through mentoring, advice, inspiration and above all else his enduring passion for science and its ability to solve major societal problems. □

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Published online: 23 January 2020
<https://doi.org/10.1038/s41589-019-0456-6>