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CAMBRIDGE SOCIETY FOR THE APPLICATION OF
RESEARCH

'Nature's Finest Tangle'

Protein Folding, Molecular Evolution and Human Disease

Professor Chris M. Dobson FRS

University of Cambridge, Department of Chemistry

Monday, 17th November 2003 **7.30 p.m. - 9.00 p.m.**

The Wolfson Lecture Theatre, Churchill College, Cambridge

Chair: to be confirmed

Vote of Thanks: to be confirmed

Professor Dobson writes.....

Protein folding is perhaps the most fundamental process associated with the generation of functional structures in biology. There has been considerable progress in the last few years in understanding the underlying principles that govern this highly complex process. Recently, much research has also focused on the realisation that proteins can misfold *in vivo* and that this phenomenon is linked with a wide range of diseases.

We have been investigating in particular the nature of the amyloidogenic conditions, that include Alzheimer's disease and the spongiform encephalopathies, e.g. BSE and CJD, in which protein misfolding leads to the aggregation of proteins, often into thread-like amyloid structures.

Our studies have led us to put forward new ideas concerning the origin of the various diseases associated with their formation. We have also speculated more generally that the need to avoid aggregation could be a significant driving force in the evolution of protein sequences and structures.

About the speaker:

Professor Dobson is the John Humphrey Plummer Professor of Chemical and Structural Biology. He obtained his doctorate from the University of Oxford and has been assistant professor at Harvard University, visiting professor at MIT and from 1996 - 2001 Professor of Chemistry at Oxford

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University. In 1996, he was elected a Fellow of the Royal Society, and from 1999-2001 he was President of the Protein Society. In 2001, Chris Dobson became the John Humphrey Plummer Professor of Chemical and Structural Biology in the University of Cambridge. He is based in the Chemistry Department, but has close links with the Cavendish Laboratory and the Department of Biochemistry. His research has focused on understanding the structural transitions involved in protein folding and defining the underlying mechanism of this process *in vitro* and *in vivo*. This work led him to explore the phenomenon of protein misfolding and its links to protein deposition disorders such as Alzheimer's disease, Type II diabetes and systemic non-neuropathic amyloidoses. Chris Dobson has received a variety of international honours including most recently the 2003 Stein and Moore Award from the Protein Society. He has published more than 400 papers over the last 25 years and has given a very wide range of lectures at research institutions and international meetings on the topics of his research, including the 2003 Bakerian Lecture of the Royal Society.

Organising Secretary's Notes:

Once upon a time I was a molecular biologist, and in those days long past, the matter of protein folding exercised us greatly. I remember isolating proteins with consummate care, making sure that I did not inadvertently 'unfold' the molecule, or if I did, I would attempt to *re-fold* it! I did a lot of work in protein crystallisation – an absolutely essential first step before one can elucidate its structure using X-ray diffraction. Problem was, apart from the difficulty in getting highly ordered crystals, one could make lovely crystals in which the protein *folded into the wrong form*.

This massive frustration encouraged me to plan experiments on orbiters, where the near-complete absence of gravity, and therefore convection, was thought to improve the odds for growing big, well-ordered crystals.

Thankfully, things have moved on; I look forward to Chris Dobson's lecture with great anticipation – and more than a touch of *déjà vu!*

Dr Richard Freeman FRSA

CSAR Organising Secretary

References:

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