



# 2012-13 Willard Lectures

**Professor David Eisenberg**

***University of California, Los Angeles***

*Departments of Biological Chemistry and Chemistry & Biochemistry*

## ***An Idea Before Its Time***

**Monday, April 22**

**2:00 pm**

**Room 1315 Chemistry**

**Please join us for a reception on Monday, April 22 in the Shain Atrium after the seminar.**

In the early 1950s, a female medical student at Yale, writing a thesis under the supervision of a brilliant and ambitious young faculty member, carried out a fundamental experiment in protein science. The supervisor found the results not of sufficient interest to publish, and there was never any discussion between student and supervisor about publication. The student's thesis has long lain dormant in the Yale library. Two years after the student's experiment, essentially the same results were obtained in another laboratory and published. This work was soon celebrated and described in all the textbooks. Then about 15 years later the work was awarded the Nobel Prize in Chemistry. How could a brilliant student and her brilliant faculty supervisor fail to grasp the significance of a hugely important finding, which is now one of the pillars of protein science? What can we learn from this series of events about how we should interpret our own experiments?

## ***Structural Studies of the Amyloid State of Proteins***

**Tuesday, April 23**

**11:00 am**

**Room 1315 Chemistry**

**On Tuesday, Graduate Students may meet with the speaker at 1:00pm in Room 8335.**

Amyloid diseases, including Alzheimer's, Parkinson's, and the prion conditions, are each associated with a particular protein in fibrillar form. These amyloid fibrils were long suspected to be the disease agents, but evidence suggests that in the neurodegenerative diseases, smaller, often transient and polymorphic oligomers are the toxic entities. We have identified a segment of the amyloid-forming protein, alphaB crystallin, which forms an oligomeric complex exhibiting properties of other amyloid oligomers: beta-sheet-rich structure, cytotoxicity, and recognition by an anti-oligomer antibody. The X-ray-derived atomic structure of the oligomer reveals a cylindrical barrel, formed from six anti-parallel, out-of-register protein strands, which we term a *cylindrin*. The cylindrin structure is compatible with sequence segments from the A $\beta$  protein of Alzheimer's disease and from other amyloid proteins. Cylindrins offer models for the hitherto elusive structures of amyloid oligomers, and are distinct in structure from amyloid fibrils. The spines of amyloid fibers are built from pairs of interdigitated in-register beta sheets. The beta sheets from toxic amyloid entities appear to have strands that are out-of-register.