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EDITORIAL

Amyloid Fibrils—Common Threads in the Natural History of Proteins

The term "common threads" used in the title of this editorial was borrowed from the program materials of a recent workshop on molecular mechanisms of neurodegenerative diseases. The phrase alludes to the fibrillar shapes of amyloid fibrils while at the same time calling attention to the tantalizing connections between protein aggregation and a number of human neurodegenerative diseases including Alzheimer's disease, Huntington's disease, Parkinson's disease, amyotrophic lateral sclerosis, and prion diseases. In borrowing this felicitous construction, I wish to suggest in addition a deeper linkage of protein aggregation, including amyloid fibril formation, to more familiar topics in the history of research into the behavior of protein molecules.

Mankind's first observations about the physical properties of proteins very likely involved phase changes under the influence of thermal or other stresses—the boiling of an egg, the acid precipitation of casein, or the gelation of collagen. More recently, in the latter half of the 19th century, amyloid deposits in human tissue were described by Virchow, and the aggregation response was developed as one of the first ways of biophysically characterizing purified proteins. In an extensive review of protein denaturation published in 1944, Hans Neurath pointed out the importance of nonnative protein aggregation and lamented its neglect by the protein chemistry field. The situation began to brighten in the 1970s with pioneering work on the physical and chemical nature of amyloid fibrils and on the structures and assembly processes of *in vitro* aggregates and bacterial inclusion bodies. More recently, the past decade has seen an explosion of interest in and information on protein aggregation in general and amyloid formation in particular, and some of the most recent work is featured in this special issue of *Accounts of Chemical Research*.

This issue is roughly organized into papers on (1) amyloid structure, (2) early events in assembly and the determinants of amyloidogenicity, and (3) the elongation phase of amyloid assembly and the energetics of assembly. This collection of Accounts shows how elucidation of the common threads of protein aggregation is generating a rich tapestry of knowledge about this primordial feature of polypeptide molecules. Weaving this tapestry is both intellectually challenging and gratifying and is clearly worthwhile simply as an endeavor of basic scientific research. We should never lose sight, however, of another worthy research goal: unraveling the noose of pathological protein aggregation surrounding neurons and other cells in a large and growing number of devastating human disorders.

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