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Aims and Scope

The series *Topics in Current Chemistry* presents critical reviews of the present and future trends in modern chemical research. The scope includes all areas of chemical science, including the interfaces with related disciplines such as biology, medicine, and materials science.

The objective of each thematic volume is to give the non-specialist reader, whether at the university or in industry, a comprehensive overview of an area where new insights of interest to a larger scientific audience are emerging.

Thus each review within the volume critically surveys one aspect of that topic and places it within the context of the volume as a whole. The most significant developments of the last 5–10 years are presented, using selected examples to illustrate the principles discussed. A description of the laboratory procedures involved is often useful to the reader. The coverage is not exhaustive in data, but rather conceptual, concentrating on the methodological thinking that will allow the non-specialist reader to understand the information presented.

Discussion of possible future research directions in the area is welcome.

Review articles for the individual volumes are invited by the volume editors.

In references *Topics in Current Chemistry* is abbreviated *Top Curr Chem* and is cited as a journal.

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Preface

Prion diseases are a group of transmissible neurodegenerative disorders including Creutzfeldt-Jakob disease (CJD) and Gerstmann-Sträussler-Scheinker syndrome (GSS) in humans, scrapie in sheep and goat, bovine spongiform encephalopathy (BSE) in cattle and chronic wasting disease (CWD) in deer. A hallmark of prion diseases is the formation and accumulation of an aberrantly folded protein denoted scrapie prion protein (PrP^{Sc}), which co-purifies with the infectious prion agent. Remarkably, the prion protein was found to be encoded by a host gene, which is constitutively transcribed under physiological conditions. We now know that not the expression of the prion protein itself is the disease-specific feature but rather its biophysical and biochemical properties. In contrast to the cellular isoform PrP^{C}, PrP^{Sc} is insoluble in non-ionic detergents, partially resistant to proteolytic digestion and characterized by a high content of β-sheet secondary structure. Furthermore, PrP^{Sc} has the propensity to form amyloid plaques in the diseased brain.

Formation of aberrantly folded protein conformers is also a hallmark of other neurodegenerative disease in humans, including Alzheimer's disease, Parkinson's disease, and polyglutamine disorders. As an unprecedented feature of prion diseases, however, the formation of non-native PrP conformers is causally linked not only to neurodegeneration but also to the formation of infectious particles. Another unique hallmark of prion diseases is that they naturally occur in some other mammalian species. Moreover, in contrast to other neurodegenerative diseases rodent models of prion diseases are available that faithfully recapitulate all aspects of human prion diseases and allow to specifically study either neurotoxic or infectious properties of PrP conformers. In combination with robust cell culture models and *in vitro* approaches it has thus been possible to decipher pathophysiological mechanisms implicated in both the formation of infectious and neurotoxic PrP conformers, a prerequisite to explore prophylactic or therapeutic strategies. While prion diseases in humans are extremely rare, the established models may help to provide new insight into common mechanisms underlying the toxic activity of misfolded protein conformers of different origins. In particular, it is plausible to assume that certain cellular components and pathways, for example the cellular

stress response, the ubiquitin-proteasome system, or molecular chaperones, play important roles in the pathogenesis of diverse protein misfolding diseases.

In this volume we have assembled a set of chapters highlighting various aspects of prion diseases in humans and animals which show the intriguing features of both physiological and pathogenic PrP conformers. In addition, a wide spectrum of methodological approaches are described, ranging from *in silico*, chemical, and *in vitro* approaches to animal models, to illustrate the elaborate and extensive technology established in the prion field, allowing the analysis of disease mechanisms and the development of diagnostic and therapeutic strategies. Finally, the reviews on shadoo, doppel and yeast prions emphasize that certain features and activities of the prion protein can also be found in other proteins and that the phenomenon of self-replicating protein conformers can be of broader biological significance.

Munich, Germany Jörg Tatzelt
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