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crossroads; 1.2 Protein folding; 1.2.1 Protein-Folding Code; 1.2.2 Protein-Folding Models; 1.2.3 Polymer Aspects of Protein Folding; 1.2.4 Different Conformations Seen in Protein Folding; 1.3 Nonfolding; 1.3.1 Intrinsically Disordered Proteins and Their Abundance; 1.3.2 Some Functional Advantages of IDPs
1.3.3 Function-Induced Folding of IDPs1.3.4 IDPs and Human Diseases; 1.3.5 How Does an Amino Acid Sequence Encode Intrinsic Disorder?; 1.3.6 Polymer Aspects of Nonfolding; 1.4 Misfolding; 1.4.1 Molecular Mechanisms of Protein Misfolding; 1.4.2 Fibrillogenesis of Globular Proteins: Requirement for Partial Unfolding; 1.4.3 Fibrillogenesis of IDPs: Requirement for Partial Folding; 1.4.4 Conformational Prerequisites for Amyloidogenesis; 1.4.5 Multiple Pathways of Protein Misfolding; 1.4.6 Polymer Aspects of Protein Misfolding; References
2 Recruiting Unfolding Chaperones to Solubilize Misfolded Recombinant Proteins 2.1 Introduction; 2.2 Chemical Chaperones; 2.3 PPIs and PDIs are folding enzymes; 2.4 Molecular Chaperones; 2.5 The small Hsps; 2.6 Hsp90 ; 2.7 Hsp70/Hsp40; 2.8 GroEL Chaperonins; 2.9 Conclusions; References; 3 Osmolytes as Chemical Chaperones to Use in Protein Biotechnology ; 3.1 Introduction; 3.2 Protein-destabilizing conditions and counteracting mechanisms: shared or independent routes?; 3.3 Proposed molecular mechanisms for osmolyte activities; 3.4 Osmolytes and expression of recombinant proteins
3.5 Biotechnological relevance of osmolytes for preserving purified proteins3.6 Conclusions; References; 4 Inclusion Bodies in the Study of Amyloid Aggregation ; 4.1 Introduction; 4.2 Structure of IBs ; 4.2.1 Amyloid-like Nature of IBs ; 4.2.2 Detection and Characterization of Amyloid Conformations Inside IBs ; 4.3 Formation of IBs ; 4.3.1 In Vivo Formation Kinetics; 4.3.2 Molecular Determinants of IB Aggregation; 4.3.3 Sequence Specificity in IB Formation; 4.4 IBs as the simplest model for in vivo amyloid toxicity; 4.4.1 The Fitness Cost of Amyloid Aggregation
4.4.2 Citotoxicity of Amyloid IBs 4.4.3 Infectious Properties of IBs ; 4.5 Using IBs to screen for amyloid inhibitors; 4.6 Conclusions; References; 5 Protein Aggregation in Unicellular Eukaryotes ; 5.1 Introduction; 5.2 UPR: Unfolded protein response in the ER; 5.3 Removing persistent misfolded proteins with the proteasome; 5.4 Lysosomal/vacuolar proteolysis (overload UPS); 5.4.1 Autophagy; 5.4.2 Selective Types of Autophagy; 5.5 Refolding of protein aggregates in cytosol and nucleus; 5.6 JUNQ and IPOD; 5.7 Segregation of aggregates in yeast
5.8 Proteins forming nonpathological amyloid-like fibrils in unicellular eukaryotes

Sommario/riassunto

This book focuses on the aggregation of recombinant proteins in bacterial cells in the form of inclusion bodies. Recent reports revolutionized the current view of inclusion bodies from that of inert deposits of inactive proteins to reservoirs of proteins that can eventually maintain biological activity and/or be rescued by cells. Aggregation is put in the context of updated knowledge about the folding and aggregation of proteins in simple cells and new perspectives derived from the application of this knowledge are presented. The following topics are addressed: a) molecular and c