Proteostasis or protein homeostasis is the process by which cells control the abundance and folding of the proteome. Proteostasis appears to be involved in many diseases and aging. For example, retinal dystrophies, neurodegenerative diseases, inflammatory diseases, infectious diseases, and cancer are broad categories of diseases already linked to proteostasis. For instance, several genes related to the ubiquitin pathway are implicated in retinal dystrophies. Retinal dystrophies are a group of rare diseases that affect individuals worldwide. Protein misfolding, aggregation, and accumulation are a common hallmark in various neurodegenerative diseases. The autophagy-lysosomal pathway and the ubiquitin-proteasome system, the two main intracellular degradation machineries, are essential for cell survival under stress conditions, for clearance of intracellular pathogens, for the maintenance of cellular homeostasis and play an essential role in cancer survival upon drug treatment. In addition, proteasome inhibitors, which typically target protease subunits of the proteasome, have been shown to reverse liver cancers in xenograft models and prolong time of survival of patients with certain blood cancers (e.g., multiple myeloma and multiple myeloma).

The importance of proteostasis in diseases has fostered the development of a large number of technologies to obtain deep insight into the underlining mechanistic events. The technologies are based on fluorescence/confocal microscopy, expression arrays, mass spectrometry, and diverse range of transfection models combined with biochemical assays. The methodologies target the proteins in a stationary quantitative way but also protein turnover rate can be estimated in vivo by pulsed labeling and novel technologies like bioorthogonal click chemistry. Protein homeostasis is regulated by a broad range of posttranslational modifications of which ubiquitin and SUMO are the most frequently studied. Posttranslational modifications of human proteins do not exclusively influence human health. For example, proteins from pathogens can also be heavily ubiquitinated and thereby targeted for degradation. Furthermore, interaction between the adenoviral capsid protein VI and Nedd4.2, a cellular ubiquitin ligase, is essential for virus infection highlighting the role of proteostasis in host–pathogen interactions.

This book highlights the role of proteostasis in human health and associated disease model systems. It provides state-of-the-art protocols to study and target proteostasis for therapeutics. This book is designed and written mainly by proteostasis experts with the ambitious aim to become the future reference book on proteostasis in human health.

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The left part of the cover image depicts the ubiquitin coating of Salmonella bacteria inside an infected epithelial cell (as part of the autophagy process). Bacteria are in red, ubiquitin in green, nuclei of infected cells in blue (image kindly provided by Professor Rudi Beyaert). Center image displays the structure of ubiquitin (kindly provided by Simona Polo).
Top right depicts Human ARPE-19 cells transfected with the human deubiquitinating enzyme ATXN3. Green: ATXN3, Red: Actin fillaments stained with phalloidin, Cyan: acetylated alpha-tubulin. Nuclei are stained with DAPI (Photo by Vasileios Toulis from Gemma Marfany’s group).

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