Preface

THE ENDOPLASMIC RETICULUM IS ONE OF THE MOST INTRIGUING and fascinating organelles. It is found in all eukaryotic cells and performs an amazing number of different functions. The organelle was named by Keith Porter in 1953 on the basis of observations made with the electron microscope of tissue culture cells. Porter distinguished the exoplasm, a peripheral region devoid of organelles, from the adjacent endoplasm. In the endoplasm, he detected a fine network of interconnected tubules, a reticulum—hence, the name "endoplasmic reticulum" (ER). With the subsequent invention of the microtome and improved fixation methods, it became possible to look at real tissues. The collaboration between Keith Porter and George Palade led to the conclusion that the ER exists in all eukaryotic cells and that it consists of distinct but continuous domains, the smooth and rough ER, the abundances of which differ between cell types. Palade realized that the dots on the surface of the rough ER were ribosomes synthesizing secretory proteins. This was not only the first function assigned to the ER, but also a revolutionary idea: secretory proteins would cross an intracellular membrane, rather than the plasma membrane. The extension of this idea led to the discovery of the secretory pathway and the notion of intracellular protein targeting to different organelles.

This volume is the second monograph our team has assembled on the ER. In the nine years since the first volume, much has advanced in our understanding of the structure and function of the ER in normal and disease states. We have attempted to include all new material with little overlap to the previous monograph. To do so, we have invited many new authors and topics that were not included in the 2013 monograph. As in the previous volume, much of the discussion focuses on the mechanism of protein insertion into and translocation through the ER membrane. Numerous new insights have come from atomic resolution structures of the proteins that organize insertion and translocation. This includes the rapidly advancing subject of nucleocytoplasmic translocation, where atomic resolution structures of most of the subunits of the nuclear pore have now been obtained. As before, several chapters deal with processes that happen once proteins have translocated into the ER lumen, including new insights into the process of ER-associated degradation (ERAD) and ER protein quality control with specific reference to regulated degradation controlled by the covalent modification of biosynthetic enzymes and a transcription factor. The turnover of ER membranes by an autophagic process called ER-phagy has also advanced our understanding of ER quality control.

The ER, the major site of phospholipid synthesis in the cell, not only generates its own lipid but also exports lipids to other organelles. Chapters therefore cover lipid synthesis pathways, the transport of lipids between the ER, mitochondria, lipid droplets, and the autophagic isolation membrane, as well as the role of membrane contact sites that connect the ER to other organelles and the disease consequences of the failure of contact site function.

Once proteins are correctly folded, they are packaged into vesicles and transported to the Golgi apparatus. Several chapters deal with the mechanism by which coat complexes facilitate vesicle budding from the ER, with specific reference to the various receptors that mediate the selective capture of cargo proteins and lipoproteins into COPII transport vesicles. Finally, ER morphology and its role in cell health and disease are discussed. As indicated by the early discovery of smooth and rough ER by Porter and Palade, the structure of the ER is adjusted to its function. In recent years and since our last volume, superresolution fluorescence microscopy and focused ion beam milling for standard and cryo-electron microscopy have emerged to offer superior resolution and imaging of tissues, adding to our basic understanding of the organization of ER tubules and sheets in normal and disease conditions.

We hope this book makes it clear that the ER remains an exciting research area with many unresolved questions. We have seen dramatic progress on a number of fronts and yet it remains clear that more is in store for the future, particularly with the revolutionary advances in visual, genomic, and proteomic approaches to protein and membrane structure and function.

We are grateful to our colleagues who have agreed to contribute to this book. They are all leaders in the study of the ER. We believe their contributions are both educational and cutting-edge, and convey the excitement we all share on elucidating the many aspects of the multifunctional ER. We are indebted to our fellow co-authors for taking time from their busy schedules to contribute reviews of their areas of specialty. Although we tried to cover the ER as widely and deeply as possible, it is inevitable that there are omissions and errors. We apologize sincerely to the many investigators whose valuable work we were unable to cite or include. A book of this kind could not have succeeded without the excellent editorial staff of Cold Spring Harbor Laboratory Press; special thanks to Richard Sever and Barbara Acosta for initiating the project and guiding it expertly to completion.

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