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# The Endoplasmic Reticulum

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# The Endoplasmic Reticulum

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A subject collection from *Cold Spring Harbor Perspectives in Biology*

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## 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 on 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 abundance of which differs 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.

During the following 59 years, tremendous progress was made in understanding the various functions of the ER. This book attempts to capture in a single volume our current knowledge of this organelle and highlights many unresolved questions. One chapter deals with the mechanism by which secretory and membrane proteins move across or integrate into the ER membrane, a process called translocation. Another chapter covers the mechanism by which tail-anchored membrane proteins are inserted into the ER membrane. This mechanism is distinct from classical translocation and has received much attention recently. Several chapters deal with processes that happen once proteins have translocated into the ER lumen. These processes include glycosylation, disulfide bond formation, and chaperone-mediated protein folding. Other chapters are concerned with situations in which proteins cannot reach their native folded state or are unfolded under stress conditions. This includes the “unfolded protein response” (UPR), a transcriptional program that leads to the increased synthesis of chaperones, and “ER-associated protein degradation” (ERAD), a process in which proteins are transported back into the cytosol and degraded by the proteasome. ERAD is also hijacked by certain viruses and toxins, another topic covered in this book.

The ER, the major site of phospholipid synthesis in the cell, not only generates its own lipid, it also exports lipids to other organelles. Chapters therefore cover lipid synthesis pathways, the transport of lipids between the ER and mitochondria, and our current understanding of contact between the ER and other organelles.

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 and with retrograde traffic from the Golgi back to the ER. Genomic and proteomic approaches are also reviewed in this book, as they have provided important insight into understanding vesicular trafficking. Finally, ER morphology is also 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. Over the past years, a basic understanding has been obtained on how ER tubules are generated and connected into a network.

We hope this book makes it clear that the ER remains an exciting research area with many unresolved questions. Although essentially all ER functions are incompletely understood, some topics are

Preface

less understood than others. For example, the ER contacts a number of different organelles, yet we do not fully understand the role of these contacts. Lipid is known to be transported through inter-organellar contacts; however, the mechanism of lipid transfer at these sites remains to be defined. How the elaborate shape of the ER is generated and how ER shape relates to its many functions are also unclear. Another timely problem is the biogenesis of organelles that are at least in part derived from the ER, including the generation of peroxisomes, a topic that is also covered in this book.

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, Barbara Acosta, and Inez Sialiano for initiating the project and guiding it expertly to completion.

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