
Preface

Eukaryotic cells have a variety of membrane-enclosed compartments termed organelles. Each organelle has unique functions, which are based on proteins that are specifically transported into each organelle according to their intrinsic “address tags”. Organelles can produce cellular building blocks as well as provide energy, both of which are required for cell survival, proliferation, and differentiation. Research from several decades, assembled in this book, shows that the specific functions of organelles are not only geographically confined within membranous compartments, but also depend on rather intimate inter-organelle communication. Historically, such communication was thought to occur via vesicular trafficking. However, studies starting in the 1970s on lipid synthesis and transport have led to the discovery of another way that organelles can communicate, generating the concept of “membrane contact sites” (MCS). The importance of MCS truly emerged by the finding in the late 1990s that the endoplasmic reticulum (ER) releases Ca^{2+} in hotspots directed towards mitochondria. Recent studies have discovered not only major MCS regulatory proteins, but also new roles of MCS, including their involvement in a number of diseases, including neurodegenerative diseases, type 2 diabetes, infections, inflammation, and cancer. Today, MCS research is one of the most rapidly developing and exciting fields in cell biology and basic medicine.

This book aims to provide a comprehensive coverage of our quickly evolving knowledge of organelle communication at MCS and the significance of MCS for disease. The book is organized into two parts in addition to the overview (Chap. 1). The first part consists of nine chapters that set forth the organization and roles of MCS. The ER plays a principal role in organelle contacts, because it forms a wide network in cells and has several unique sub-domains with distinct functions. This allows the organelle to form contacts with other organelles in a variety of ways. Four chapters deal with the mitochondria-associated membrane (MAM), a domain of the ER that faces mitochondria. Other chapters describe the contact of the ER with the Golgi apparatus, endosomes, the plasma membrane, and lipid droplets. While the Golgi apparatus at the *cis*-side accepts transport vesicles from the ER, at the *trans*-side it interacts with the ER through MCS. Lipid droplets are unique among organelles in that they are surrounded by a phospholipid monolayer. Enzymes that are responsible for the biogenesis of lipid droplets are concentrated at the MAM, highlighting that these organelles are highly

dependent on MCS formation. The second part (seven chapters) concerns viruses and pathogens (e.g., hepatitis C virus, *Chlamydia*, and *Coxiella*) whose targets are MCS and diseases that are caused by malfunctions of MCS, including Alzheimer's disease, Parkinson's disease, type 2 diabetes, and inflammation.

Given the rapidly evolving knowledge about MCS, it is inevitable that there are many controversies and conflicting reports in this field, which often prevents non-expert researchers from a deeper understanding of MCS and their significance. This book nicely summarizes the present status of MCS research for researchers who are not familiar with this field. MCS has been attracting much interest from young, talented researchers, which is reflected by the fact that several authors of this book have recently started their own laboratories. As editors, we hope that this book will stimulate graduate students and postdocs, who have the potential to energize, drive, and develop this field in the near future, and clinical fellows who may extend disease-related MCS research. The book will also be a valuable reference for established researchers who want to view their own research data and projects from the standpoint of MCS and who have so far focused on a type of cell biology that is based on "isolated organelles".

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Hachioji, Tokyo, Japan
Edmonton, Alberta, Canada

Mitsuo Tagaya
Thomas Simmen

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Tagaya, M.; Simmen, Th. (Eds.)

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