
PREFACE

Exocytosis is a fundamental cellular process that is used by eukaryotic cells to release a variety of biological compounds such as peptide hormones and neurotransmitters or to insert specific lipids and proteins in the plasma membrane. In recent years, a multidisciplinary approach, including genetics, in vitro reconstitution of vesicular transport and studies devoted to the definition of the mechanism of action of bacterial neurotoxins, promoted an extraordinary progress in the understanding of the molecular mechanisms of exocytosis. The genetic approach was pioneered in the beginning of the eighties by Peter Novick and Randy Schekman with the identification of a group of genes (SEC genes) required for post-translational events in the yeast secretory pathway. Genes fulfilling analogous functions were then found in other genetic models such as *C. elegans* and *Drosophila*. James Rothman and collaborators designed a strategy aimed at tackling the problem from a different angle and developed a method to reconstitute vesicular transport in a cell-free system. Interestingly, the SNARE and SNARE-associated proteins required for vesicular transport identified using this assay turned out to be closely related to the products of the genes isolated in the genetic screening of Novick and Schekman. The fundamental role of SNAREs in exocytosis was then beautifully demonstrated by the seminal discovery of the groups of Cesare Montecucco and Heiner Niemann that clostridial neurotoxins, the most powerful natural agents that block neurotransmitter release, exert their action by specifically cleaving neuronal SNAREs. The convergence of these findings has revolutionized our knowledge of the molecular mechanisms governing exocytosis and has emphasized the conservation of the protein apparatus driving membrane fusion from yeast to man.

Despite the impressive improvement in the understanding of the process of exocytosis, a number of important questions remain unsolved and are presently the focus of intense investigations. Thus, the cascade of events leading to the docking and fusion of secretory vesicles is still not defined in molecular terms and the mechanisms coupling second messenger generation to the activation of the secretory apparatus is only beginning to emerge. Moreover, the precise roles of lipids in the exocytotic process remain to be clarified. After all, exocytosis depends on the merging of two phospholipid leaflets and their lipid composition directly affects the physicochemical properties of the two membranes and influences the activity of the protein machinery driving fusion.

The picture emerging after more than two decades of investigations illustrates exocytosis as a complicated and finely tuned process involving a large number of components that transiently associate and dissociate. For these reasons, the understanding of the molecular basis of exocytosis has so far remained the privilege of a relatively small group of specialists. This unique collection of up-to-date reviews intends to introduce researchers and students to the forefront of this rapidly moving and fascinating field. Written by recognized experts in the field, the book aims at clarifying for a general audience the role of the key players in the exocytotic process not only in neuronal and endocrine cells but also in a variety of other cells that use exocytosis to accomplish their specialized tasks.

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