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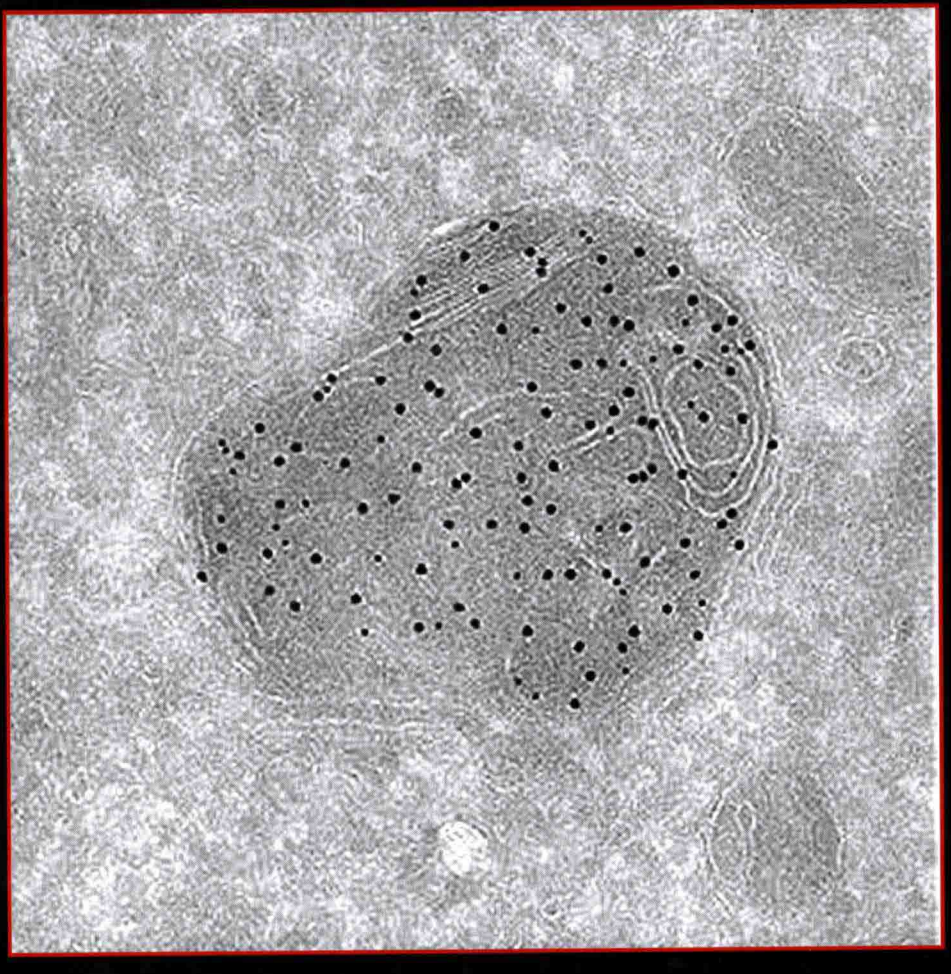
[redacted]OSOMES AND LYSOSOMAL DISEASES



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Lysosomes and Lysosomal Diseases

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Methods in Cell Biology

Lysosomes and Lysosomal Diseases

Volume 126

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Preface

Since the discovery of the lysosome by Christian de Duve almost 60 years ago, the central role of this acidic organelle in the catabolism of macromolecules, in metabolite recycling, and the elimination of infectious agents has become well established.

Mutations in genes that encode lysosomal proteins result in severe inherited diseases, termed lysosomal storage diseases. The severity of these life-limiting diseases underscores the critical importance of lysosomal function and homeostasis for the maintenance of human and animal health. Many of these diseases are associated with storage of macromolecules in neurons leading to neurodegeneration, reinforcing the critical need for normal lysosomal function for the well-being of the nervous system.

There is also now an ever expanding body of evidence suggesting that lysosomal dysfunction may also contribute to more common neurodegenerative diseases, including Parkinson's and Alzheimer's. The lysosome is already a target for therapeutic modulation, currently primarily for treating lysosomal storage diseases but no doubt will extend to more common diseases in the future in which lysosomal dysfunction is also a feature.

Over the past two decades research in lysosome biology and its role in human disease has undergone a renaissance and many new functions have been ascribed to this acidic organelle. These include regulated exocytosis, plasma membrane repair, and nutrient sensing. The lysosome has also emerged as the third regulated calcium store of the cell (in addition to mitochondria and the ER) and releases calcium in response to a potent and specific second messenger, NAADP. The lysosome is therefore a calcium signaling organelle. In addition, the transcriptional regulation of lysosome biogenesis has been discovered via the action of the transcription factor TFEB that is regulated by the nutrient sensor of the lysosome.

Through this unprecedented progress the lysosome has emerged from a mundane house keeping organelle to a major cellular signaling hub. There can be little doubt that future studies will reveal that the lysosome significantly impacts on other unanticipated aspects of cell function and we hope that some of the methods detailed in this volume will aid such discoveries.

This edition of *Methods in Cell Biology* is therefore timely as it serves as a key practical resource for those embarking on lysosome research for the first time or those in the field wanting to study different aspects of lysosome function/disease. We have therefore assembled a unique, state of the art set of methods developed by the chapter authors who are all world experts on their area of expertise.

The lysosome is not an easy organelle to study for a number of technical reasons including its acidic pH, the difficulty in purifying this organelle in healthy and diseased cells, its small size and its complex interconnections with other organelles. In this volume, we have therefore aimed to provide practical guidance on key methods that can be applied to lysosome research, with a major focus on choosing the right method and the pitfalls of applying them in practice. In addition, two

chapters are included that relate to the clinical monitoring of patients with lysosomal storage diseases.

We would like to thank all the authors for their excellent contributions to this volume and wish the readers of this volume every success in using these protocols to advance their own areas of interest. We also thank Sarah Lay for her excellent editing of this volume. We thank her for her patience with the editors during the process of assembling this new volume of *Methods in Cell Biology* dedicated to the lysosome.

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