The Golgi

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

OTHER SUBJECT COLLECTIONS FROM COLD SPRING HARBOR PERSPECTIVES IN BIOLOGY

Germ Cells
The Mammary Gland as an Experimental Model
The Biology of Lipids: Trafficking, Regulation, and Function
Auxin Signaling: From Synthesis to Systems Biology
The Nucleus
Neuronal Guidance: The Biology of Brain Wiring
Cell Biology of Bacteria
Cell–Cell Junctions
Generation and Interpretation of Morphogen Gradients
Immunoreceptor Signaling
NF-κB: A Network Hub Controlling Immunity, Inflammation, and Cancer
Symmetry Breaking in Biology
The Origins of Life
The p53 Family

The Golgi

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

EDITED BY

Graham Warren

University and Medical University of Vienna

James Rothman

Yale University

COLD SPRING HARBOR LABORATORY PRESS
Cold Spring Harbor, New York • www.cshlpress.com

The Golgi

A Subject Collection from *Cold Spring Harbor Perspectives in Biology*
Articles online at www.cshperspectives.org

Printed in the United States of America

Executive Editor	Richard Sever
Managing Editor	Maria Smit
Project Manager	Barbara Acosta
Permissions Administrator	Carol Brown
Cover Designer	Denise Weiss
Publisher	John Inglis

Front cover artwork: A negative image montage of sections through the Golgi region of a HeLa cell. Image courtesy of Rose Watson, Cancer Research UK.

Library of Congress Cataloging-in-Publication Data

The Golgi / edited by Graham Warren, James Rothman.
p. cm.
Includes bibliographical references and index.
ISBN 978-0-87969-873-7 (hardcover : alk. paper)
1. Golgi apparatus. I. Warren, Graham, 1948- II. Rothman, James E.
QH603.G6G645 2011
571.6′56--dc23
2011023815

10 9 8 7 6 5 4 3 2 1

All World Wide Web addresses are accurate to the best of our knowledge at the time of printing.

All Cold Spring Harbor Laboratory Press publications may be ordered directly from Cold Spring Harbor Laboratory Press, 500 Sunnyside Blvd., Woodbury, New York 11797-2924. Phone: 1-800-843-4388 in Continental U.S. and Canada. All other locations: (516) 422-4100. FAX: (516) 422-4097. E-mail: cshpress@cshl.edu. For a complete catalog of all Cold Spring Harbor Laboratory Press publications, visit our website at http://www.cshlpress.com/.

Contents

Contents

Preface

Camillo Golgi (1843–1926) devised a stain that launched a new organelle at the end of the 1800s. Despite the beauty of these early images, it took several decades to establish a role for the Golgi in secretion and a few more for its role in glycosylation. In part, this reflected the uncertainty concerning the specificity of the silver stain, and in fact it was not until the early 1960s that the organelle's ubiquitous presence in eukaryotic cells was established.

The 1960s also saw the mapping of the secretory pathway, the route taken by cargo from the endoplasmic reticulum (ER) to the Golgi and then to secretory granules. The 1980s onward saw the molecular characterization of the cargo-carrying machinery: the COPII vesicles that ferry newly synthesized cargo from the ER to the Golgi; the COPI vesicles that help move it within the stack; the sorting signals and sorting adaptor proteins; the different GTPases; and the tethers and SNAREs that finally seal the transport process, catalyzing vesicle fusion and thereby delivering the cargo to the next compartment on the pathway.

But as the contributions here make clear, there is still much that we do not know, particularly at the mechanistic level. Although COPI vesicles mediate transport within the Golgi, as part of the process that ensures exposure of the cargo to the glycosidases and glycosyltransferases for the correct amount of time and in the correct order, it is not clear how this is achieved. Is the cargo carried in vesicles to the enzymes or the enzymes to the cargo? Or both? And to what extent is it important to keep the enzymes segregated within domains or discrete cisternae through specific retention mechanisms? The hope is that newer methods of fluorescence microscopy, which can peer below the normal resolution limit, and in real time, will allow individual vesicles to be tracked from budding to fusion so that traffic routes within the Golgi can be accurately mapped.

Achieving an understanding of the mechanics of the coated vesicle machinery is being driven by structural studies at the atomic level, backed up by biophysical and biochemical approaches that allow partial reactions to be reconstituted in cell-free systems: coat-GTPases that select cargo and abort when there is no cargo to be found; amphipathic proteins that sculpt and cut membranes, generating vesicles; phosphoinositides that regulate the sorting and bending processes; GAPs (GTPase-activating proteins) and kinases that remove the coat at the right time; tethers that capture vesicles at a distance but release them if there are no downstream SNAREs; and the zippering up of cognate SNAREs that trigger the final specific fusion step. Together these partial reactions are adding up to a complete picture of vesicle-mediated transport, the discontinuous process that lies at the heart of membrane traffic in eukaryotic cells, maintaining organellar identity in the face of high flux rates.

Newly synthesized cargo molecules share the same route up to and including the Golgi stack, until the *trans*-Golgi network (TGN) is reached. Here they are separated and sorted to their final destinations: the cell surface, the endosome/lysosome system, or secretory granules (in those cells with regulated secretion). The TGN can be considered an organelle in its own right, at the intersection of the exocytic and endocytic pathways, acting as a hub to sort and cycle fluxing proteins and lipids. A role for the Golgi as a signaling hub corroborates this idea.

More puzzling is the architecture and spatial distribution of the Golgi. Although all eukaryotes have Golgi components, not all are organized in the form of stacks. Cisternae are often tubulo-reticular and sometimes dispersed, which begs the question as to the functional role of cisternal stacking, and of the Golgi ribbon, which subsumes stacks into a branched reticulum that in metazoan

cells is often next to the nucleus and the centrosomes. One hope is that studies on the role of the Golgi during development will shed light on this organization, as well as studies of Golgi biogenesis, especially in mammalian cells where almost complete disassembly into vesicles occurs at the onset of mitosis, to be followed by reconstruction of the Golgi ribbon at the end of cell division.

A primary function of the Golgi is the modification of oligosaccharides on almost all transiting cargo molecules. For plasma membrane proteins, the Golgi determines the surface flavor, a unique oligosaccharide fingerprint. This varies enormously from organism to organism: Budding yeast is decorated with hundreds of mannose residues on all surface proteins, whereas mammals have multiple forms of sialic acid. This variety has given rise to the idea that oligosaccharides (and hence the Golgi) act as a means of defense, with hosts engaging in an arms race with pathogens, using global oligosaccharide variations to combat attack. The increasing number of human diseases that affect oligosaccharide fingerprints should aid studies of this idea.

More than 100 years after the first publication, the Golgi continues to fascinate and perplex cell biologists. There is much that still needs to be done.

Graham Warren
James Rothman