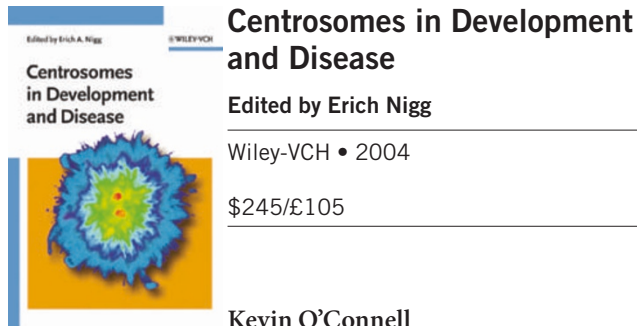


A new tome for the centrosome



Centrosomes in Development and Disease

Edited by Erich Nigg

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The centrosome is a small, non-membrane-bound organelle endowed with the remarkable capacity to nucleate and organize microtubules. It consists of a pair of centrioles — structures analogous to the basal bodies of cilia and flagella — surrounded by pericentriolar material from which microtubules are nucleated and anchored. Although scientists have long appreciated the importance of the centrosome in organizing the cytoplasm and mitotic spindle, molecular descriptions of its replication and function have remained elusive. In recent years, however, the development of powerful genetic model systems and new technologies coupled with the availability of genomic sequence data have fuelled a resurgence in centrosome research. As a result, new roles for the centrosome have come to light while old roles have been called into question. At the same time, the centrosome has emerged as an important element of human genetic and infectious diseases.

Clearly, this is a pivotal moment in the long history of this field and the new book *Centrosomes in Development and Disease*, edited by Erich Nigg, provides a comprehensive view of our current state of knowledge. The book begins with a historical perspective, revisiting the pioneering work of Van Beneden, who first described the centrosome in 1876, and Boveri who later named the organelle. Many of the chapters pay homage to these early cytologists whose keen insights still influence the field today.

The most striking property of the centrosome is its ability to organize the linear polymers of α - and β -tubulin that constitute microtubules. Microtubule nucleation at the centrosome is directed by γ -tubulin, which acts as part of a large protein assembly, the γ -tubulin ring complex or γ TuRC. Precisely how the γ TuRC accomplishes this task is not known, but Chapter 3 on microtubule nucleation contains an excellent discussion of this subject and a compelling model drawn from kinetic and structural data.

At mitosis, centrosomes organize the poles of the spindle. To ensure a bipolar structure, the centrosome must be duplicated precisely once before mitosis. Although this process has long captivated scientists, it is still largely mysterious. Chapter 9 on centrosome duplication provides an excellent discussion of this subject, describing the individual steps, the factors known to regulate these steps, and evidence for centrosome intrinsic and extrinsic controls of duplication.

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Recent insights into the mechanism of centrosome duplication and function have been fuelled by work in a variety of model genetic systems. Centrosome morphology varies widely across species, but as argued in Chapter 6 — an intriguing discussion of their evolution — all centrosomes seem to be derived from the same ancestral organelle, the flagella basal body/axoneme. This theory is supported by the strong correlation between the presence of motile flagella/cilia within a species and the conservation of centriole structure. Thus, work in these simple but genetically pliable organisms has produced important results that are universally relevant. Budding yeast contain one such centrosome analogue, the spindle pole body. This organelle, which lacks centrioles, has been extensively analysed by genetic and proteomic means. Likewise, *Caenorhabditis elegans*, *Drosophila melanogaster* and *Chlamydomonas reinhardtii* have all proved to be potent model systems for addressing questions relating to centrosome biology. There are chapters on each of these important model organisms, and the book makes it clear that each of these systems has unique advantages that make them complementary systems rather than redundant.

One of the most exciting revelations to recently emerge is that the centrosome seems to function in many important cellular processes independent of its microtubule-organizing function. These processes, which include cytokinesis and several major cell-cycle transitions, might utilize the centrosome as a rendezvous point for critical regulatory factors. In addition, the centrosome appears to have a role in the cellular response to heat shock and DNA damage. All these issues are exceptionally well covered in this volume, as are the technologies — such as mass spectrometry and laser microsurgery — that have been used to define these new functions. In fact, as discussed in Chapter 10, laser microsurgery has also been used to demonstrate that centrosomes are not absolutely required for bipolar spindle assembly, one of its oldest attributed roles.

Although its absolute value to the cell is still uncertain, the centrosome is now known to have a role in a variety of human diseases ranging from infertility to cancer. Many tumours have been found to show structural and/or numerical centrosome aberrations, lending credence to Boveri's early hypothesis that such defects could drive oncogenesis. There are several outstanding chapters on this subject, which explore a question of central importance: are centrosome anomalies a cause or consequence of cancer? In addition, several chapters detail the interactions between intracellular pathogens and the centrosome. Study of these pathogens, which include viruses that interfere with centrosome structure and copy number control, has led to insights into both the mechanisms of viral pathogenesis as well as centrosome replication and function.

Centrosomes in Development and Disease thoroughly covers a rapidly expanding field. Perhaps the only obvious omission is a treatment of the growing list of human diseases linked to cilia and basal body dysfunction such as Kartagener and Bardet-Biedl syndromes. Nonetheless, the book is well written and provides clear, concise and informative reviews of key topics. Both experts and novices alike will find this book to be an indispensable source of information on an organelle that is becoming less mysterious but more fascinating.