

# Preface

The accurate segregation of replicated chromosomes (sister chromatids) during cell division guarantees a correct number of chromosomes in subsequent generations of cells. Importantly, errors made during this process lead to aneuploid progeny with abnormal chromosome numbers, which can either cause genetic diseases, or, in the case of somatic cells, cause diseases such as cancer. For example, virtually all solid tumors known to date are aneuploid, suggesting that chromosome missegregation underlies or contributes to the initiation and/or progression of cancer.

Kinetochore are highly conserved multi-protein structures that form on the centromeric regions of sister chromatid pairs. Kinetochore orchestrate sister chromatid segregation and ensure that cellular ploidy is maintained. Following the identification of the first three kinetochore proteins in 1985 by one of us, 80–100 proteins (depending on the species) have now been localized to centromeres. These proteins act either as structural kinetochore or centromere components, or as regulators of centromere establishment, and kinetochore formation or activity. Arguably, the kinetochore is one of the most dynamic and complex protein structures known to date.

Recent years have witnessed an outpouring of studies on kinetochore components and centromeres. During the last five years alone, a yearly average of 200 and 500 papers cite the kinetochore and centromere, respectively (Pubmed). This research avalanche has resulted in an almost unmanageable amount of data. Unfortunately, since the publication of his outstanding book by Andy Choo over a decade ago (K. Choo, *The Centromere*, Oxford University Press, New York, 1997), so much has been discovered and written that the non-expert is once again overloaded and bewildered. We therefore decided to create an up-to-date reference that provides a firm basis for understanding the past, current, and also future research on kinetochores and centromeres. To do this, we decided to bring together leading researchers in kinetochore and (neo)centromere biology to share their past experiences during development of the field, to summarize the current state of the art, and to offer hypotheses and predictions that will set the framework for future research.

Chapter 1 gives an historical account of how kinetochore proteins and centromeric regions were discovered. Chapter 2 details the chromosome segregation process and the players involved in it. Chapters 3–5 discuss the chromosomal regions onto which kinetochores assemble (Chapter 3: centromeres, Chapter 4: neocentromeres, Chapter 5: artificial centromeres). Chapter 6 summarizes the composition, formation, and organization of kinetochores, while Chapter 7 reconstructs how kinetochores and centromeres developed during evolution. Chapter 8 discusses the mitotic spindle with which kinetochores interact and within which they segregate into the daughter cells. Chapter 9 describes how kinetochores establish firm contact with and bi-orient on the spindle. Chapter 10 details essential enzyme activities that regulate kinetochore assembly and function. Chapter 11 describes how the proof-reading mitotic checkpoint ensures that incorrect attachments of kinetochores to spindle microtubules are detected and corrected prior to sister chromatid segregation at anaphase. Chapter 12 explains how certain kinetochore complexes (most notably the chromosomal passenger complex) relocate to the spindle midzone at anaphase onset, thereby regulating sister chromatid segregation and triggering cytokinesis. Chapter 13 concentrates on the roles of kinetochores and centromere-bound cohesin in meiosis. Chapter 14 describes the ongoing efforts of mapping mutations in genes encoding kinetochore proteins and measuring kinetochore protein expression levels in tumor tissues. Last, but surely not least, Chapter 15 outlines how kinetochore proteins and their regulators can be turned into targets of anti-mitotic anti-cancer drugs.

We hope that with this book we have created a useful reference that will benefit experienced researchers in the field and provide an inspiration for those younger aspiring scientists and students who may wish to understand how kinetochores and centromeres orchestrate the fascinating processes of chromosome segregation that form a crucial underpinning for the continuation of life.

We would like to express our gratitude to the panel of international experts who donated their valuable time to help us review the contents of this book:

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