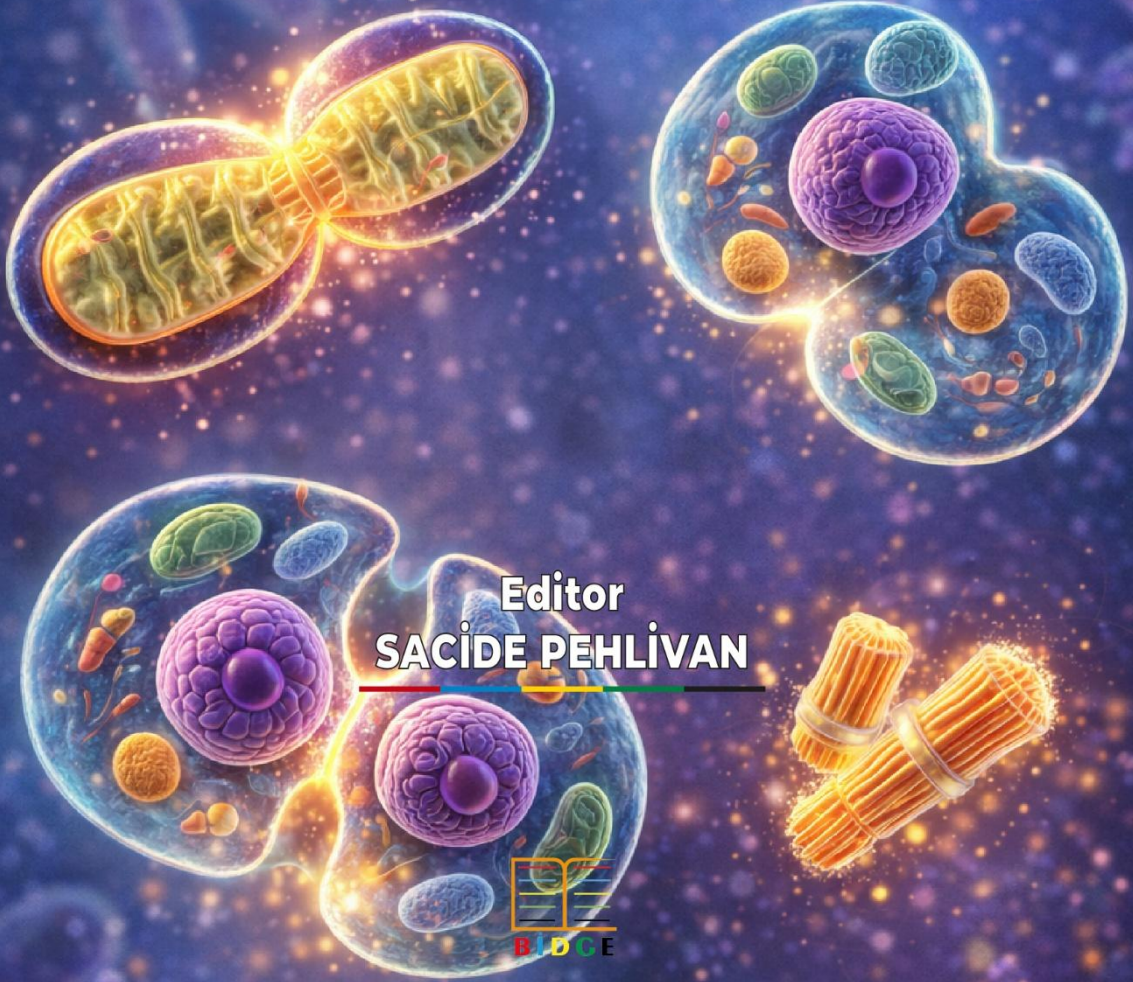
ORGANELLE DIVISION IN EUKARYOTES



Editor
SACİDE PEHLİVAN

BİDGE

BIDGE Publications

ORGANELLE DIVISION IN EUKARYOTES

Editor: PROF.DR. SACIDE PEHLIVAN

ISBN: 978-625-372-871-7

1st Edition

Page Layout By: Gozde YUCEL

Publication Date: 18.12.2025

BIDGE Publications

All rights reserved. No part of this work may be reproduced in any form or by any means, except for brief quotations for promotional purposes with proper source attribution, without the written permission of the publisher and the editor.

Certificate No: 71374
All rights reserved © BIDGE Publications
www.bidgeyayinlari.com.tr - bidgeyayinlari@gmail.com
Krc Bilişim Ticaret ve Organizasyon Ltd. Şti.
Güzeltepe Mahallesi Abidin Daver Sokak Sefer Apartmanı No: 7/9 Çankaya / Ankara

PREFACE

Eukaryotic cells are structures that reflect the complexity and order of life in their finest details. At the core of this complexity lays the structures of intracellular organelles, their functions and their division processes. Organelle division is critically important for processes like maintaining cellular continuity, ensuring growth and differentiation and adapting to environmental factors. For these reasons, division dynamics of intracellular organelles and them being distributes to daughter cells in a correct and balanced manner is a vital step for the continuation of cellular organization.

This book has been prepared as a review examining the organelle dynamics in the process of cell division in eukaryotes, in light of current literature. From double membraned organelles like mitochondria to single membrane organelles like endoplasmic reticulum, golgi apparatus and lysosomes; to cellular structures like centrosomes, cytoskeleton and endosomes are analyzed from the perspective of molecular cell biology.

This work, "Organelle Division in Eukaryotes," aims to be a reliable reference source for students and researchers in the fields of biology, medicine, dentistry, pharmacy, molecular biology, and cell biology, as well as to contribute to the understanding of the dynamics of cellular life for all readers.In the ever-evolving nature of science, it is our greatest hope that this work will inspire new questions and research.

Prof. Dr. Sacide Pehlivan
Editor

Contents

DIVISION DYNAMICS IN DOUBLE MEMBRANED ORGANELLES 5

EMİNE ZEHRA KARACA 5

SACİDE PEHLİVAN 5

DIVISION OF SINGLE MEMBRANE ORGANELLES 20

TUĞÇE KARADAĞ 20

SACİDE PEHLİVAN 20

DIVISION OF MEMBRANE-BOUND AND NON-MEMBRANE-BOUND ORGANELLES 39

ZEYNEB BERRİN KÖSEM 39

SACİDE PEHLİVAN 39

DIVISION DYNAMICS IN DOUBLE MEMBRANED ORGANELLES

EMİNE ZEHRA KARACA[1]
SACİDE PEHLİVAN[2]

Introduction

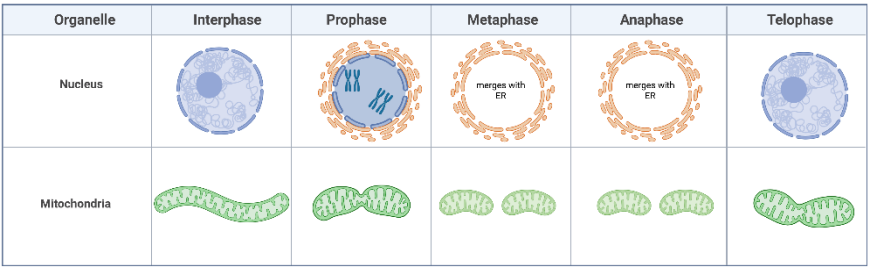
Cells are the smallest unit of life. Understanding cells and their functions completely will help us understand bigger functions, as they are the building blocks of all living organisms. Cell division is perhaps the most critical and important phase of a cell's life, and any errors occurring during that phase, either for organelle replication or the genetic material, might have deadly consequences for both the cell and the organism if it's not properly treated in time. (Cooper, 2000)

The aim of this chapter is to compile recent and relevant information about double membrane organelle division in eukaryotes with a focus on human cells, and their intracellular

[1] Istinye University, Faculty of Engineering and Natural Sciences, Department of Molecular Biology and Genetics, e-zehra-k@outlook.com - Orcid: 0009-0007-2018-0271
[2] Prof. Dr., Istanbul University, Faculty of Medicine, Department of Medical Biology, sacide.pehlivan@istanbul.edu.tr - Orcid: 0000-0003-1272-58452

mechanisms along with the diseases that might occur if any errors arise during their division.

Graphic 1 The behaviour of nucleus and mitochondria organelles during different stages of the mitotic cycle



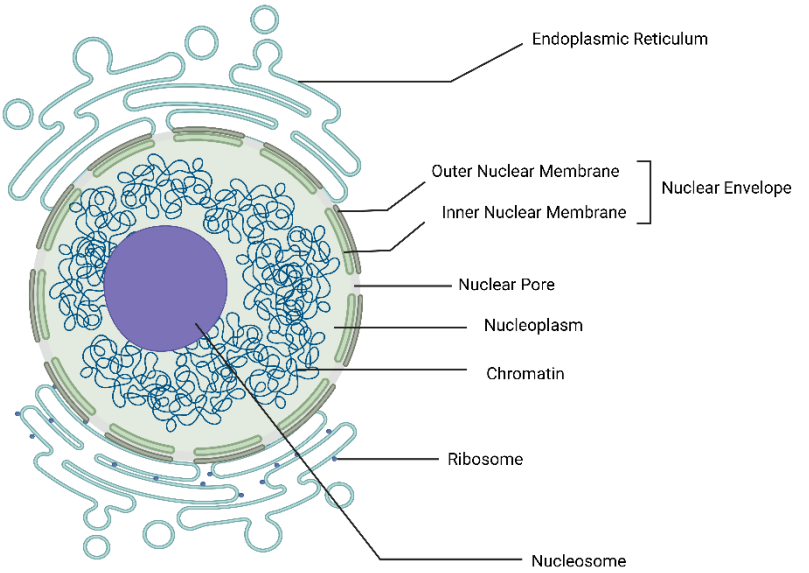
Created in https://BioRender.com

Nucleus

The nucleus is the distinguishing feature of eukaryotic cells, along with being the most important one. This large organelle is the control centre of the cell as it is responsible for generating all cellular functions. It's also the starting point of DNA transcription, splicing and the exportation of RNA (Baum & Spang, 2023). Cardiac muscle cells and skeletal muscle cells contain multiple nuclei, whereas adult red blood cells no longer contain a nucleus. Nuclei separate genetic material from the rest of the cell by covering it with a double layer membrane called the nuclear envelope (NE). The outer membrane of the NE is continuous with the endoplasmic reticulum (Dey & Baum, 2021). The two membranes are connected to each other by nuclear pore complexes (NPC) buried in the NE. These pores are selectively permeable and regulate transport of soluble material between the nucleus and the cytoplasm. The nuclear lamina, which is a fibrous meshwork under the nuclear membrane, is composed of lamin proteins. One of the primary purposes of the NE is that creates a barrier around the genetic information, protecting it from viruses that want to reach it (Lammerding, 2011). On top of being responsible

for cell homeostasis, the nucleus is the starting point of DNA transcription, splicing and the exportation of RNA (Baum & Spang, 2023).

Figure 1 The Structure of a Nucleus



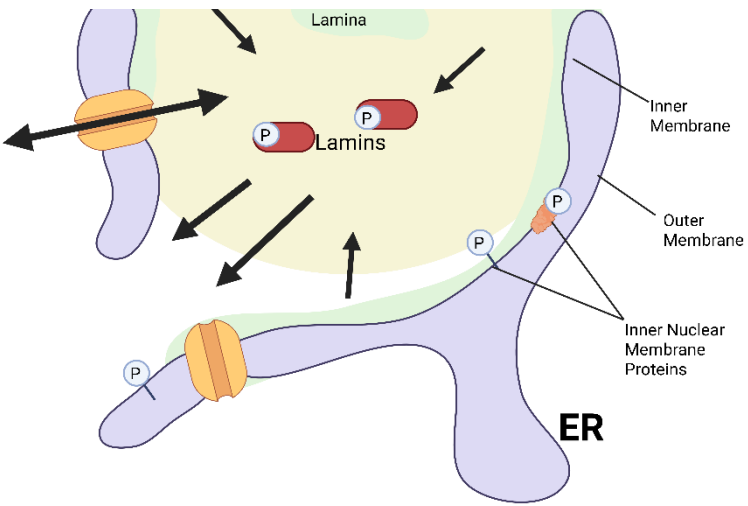
Created in https://BioRender.com

During cell division, the nuclear envelope is largely restructured in a manner that somewhat resembles that of the endoplasmic reticulum. In living organisms, there are two distinct types of nuclear division: 'open' and 'closed' nuclear division. During closed division, the NE remains intact whereas in open division, it disassembles. However, these types aren't distinct categories but rather form a spectrum. These divisions can vary from organism to organism. In humans, the 'open division' form is observed during the cell cycle (Walsh & King, 2024) During the prophase of division, the nuclear lamina is phosphorylated, causing it to disperse, and the nucleolus begins to dissolve and disappear, the NPCs dissociate and the nuclear membrane gets fragmented. The most well understood of

these mechanisms is the phosphorylation and depolymerization of the lamins, which is catalysed by the Cdc2 protein kinase. As the nuclear membrane fragments into vesicles, lamin types A and C dissociate from it, only leaving B type lamins attached to it (Zwerger & Ho, 2011).

Tubulin is imported into the nucleus as the nuclear envelope disassembles and the nucleolus merge with the endoplasmic reticulum, and proteins on the nuclear envelope are transferred to the mitotic endoplasmic reticulum (Okada & Sato, 2015). These changes are triggered by the nuclear pore complexes at the downstream of the mitotic kinases CDK1 and PLK1. Dynein/dynactin complexes attach to the NE and move to the ends of microtubules, and generate a tension that tears the NE. Mitotic kinases phosphorylate Lamins and Lamin binding proteins. Nuclear pore complexes partially dissociate in order to let bigger molecules pass through. (Güttinger & Laurell 2009)

Figure 2 Nuclear Disassembly



Created in https://BioRender.com

Chromosomes interact with the mitotic spindle fibres. Histone H1 phosphorylates during mitosis, as it is a substrate for Cdc2 protein kinase. The DNA inside the nucleus is replicated, and the chromatins shorten and become more distinct, forming chromosomes. These replicated chromosomes are called sister chromatids. Spindle fibres form. (Walczak & Cai, 2010)

During the metaphase, the genetic material must be completely separated from any remains of the nuclear envelope. Failure to meet this, as it might happen if the function of NE-localised REEP proteins is compromised (Schlaitz, 2013), would mean that there would be nuclear and cell defects. To make sure the cell can keep the inside of the nucleus distinct, even without a fully intact nuclear envelope, the cell uses membranes from the nuclear envelope and the endoplasmic reticulum (ER), as well as a poorly understood 'proteinaceous matrix' (Yao, 2012). This system helps maintain a separate nuclear space during cell division.

The maintenance of chromatin in the cellular environment during nuclear division is achieved through the coating of chromatin by the Ki-67 protein throughout the division process. During the chromosome separation phase, Ki-67 enables the chromosomes to move individually rather than as a whole. Additionally, during anaphase, it plays a role both in chromosome condensation and as an active carrier. The BAF protein then helps to package the chromosomes together, facilitating the formation of the reassembled nuclear envelope. Nucleoporin proteins play a role in microtubule formation and chromosome separation (Basu, 2022).

During anaphase, the nucleus has not yet reformed. The sister chromatids are pulled to opposite poles of the cell via the centromeres. Towards the end of anaphase, the nuclear envelope begins to reform at the opposite poles. In the telophase, this formation is completed and wraps around the chromosomes at the

opposite poles. This nuclear membrane is formed from the mitotic endoplasmic, signalled by inactivation of Cdc2 (Basu, 2022). The chromatins that had shortened and tightly formed the chromosomes now loosen again. In the late anaphase stage, the reformation of the nuclear envelope is carried out by proteins on the endoplasmic reticulum, and the new nuclear envelope is formed through the mitotic endoplasmic reticulum and through annual fusion. The mechanisms of annual fusion aren't yet understood but it's thought to involve the p97 AAA-ATPase complex. The sealing of the NE is carried out by the endosomal sorting complex required for transport-III (ESCRT-III). The ESCRT-III component charged multivesicular body protein 2A (CHMP2A) is directed to the forming NE through binding to CHMP4B, and provides an activity essential for NE reformation (Olmos, 2015)

Nucleus Diseases

When the integrity of the nuclear envelope, DNA, or the proteins responsible for maintaining DNA structure and function is compromised, it can lead to a variety of diseases. Improper separation of the nucleus can cause the cell to transform into a cancer cell. The stages of division are controlled by the nucleus, and its continuous uncontrolled division can lead to metastasis. Damages to proteins on the nuclear envelope, such as lamins or emerins, can cause diseases like Emery-Dreifuss muscular dystrophy (EDMD), Hutchinson-Gilford progeria syndrome (which causes premature aging), dilated cardiomyopathy, and familial partial lipodystrophy (Zwerger & Ho, 2011). Improper separation of nuclear material during division can lead to aneuploidy and chromosomal damage. Another type of damage that can occur is the pulling of sister chromatids to the same region during division, resulting in one cell with two nuclei and another without any nucleus, but these cells typically die shortly after. Dysregulation of nuclear integrity ortransport is associated with aging and neurodegenerative diseases,

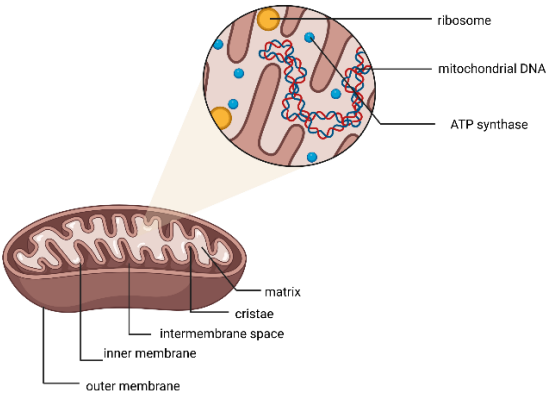
such as amyotrophic lateral sclerosis, Huntington's disease (a neurodegenerative disorder caused by mutations in the huntingtin gene, leading to progressive motor dysfunction, cognitive decline, and psychiatric symptoms), and frontotemporal dementia (Madison & Grant,). Mutations that occur in the LMNA gene encoding the nuclear intermediate filament proteins lamin A and C cause over 10 different diseases in humans. These diseases include muscular dystrophies, cardiomyopathies, lipodystrophies, and progeroid phenotypes. (Lammerding, 2011). Duchenne muscular dystrophy, while often associated with defects in muscle tissue, is also related to nuclear dysfunction as it involves the lack of dystrophin, a protein that helps stabilize the muscle cell membrane and nuclear structure. These diseases are important not only because they disrupt fundamental cellular processes but also because they can affect a wide range of tissues and systems, often leading to severe and life-limiting consequences.

Mitochondria

A double membrane organelle that's found in most eukaryotes, mitochondria are responsible for generating energy for cells using aerobic respiration for ATP synthesis. They're active organelles that frequently undergo fission and fusion in order to create the optimum energy for the cell. They possess an outer and an inner membrane (MIM), which are separated by the intermembrane space. The ATP synthesizer that is the electron transport chain (ETS) are embedded in the MIM (Al Ojaimi & Salah, 2022). Both mitochondrial membranes structurally consist of proteins and phospholipid layers, and they're very different from each other structurally. Mitochondria, unlike most other organelles, have their own set of DNAs and their own ribosomes, in a manner that is similar to prokaryotic cells. During the cell cycle, mitochondrial DNA replicates in order to prepare for the cell division, therefore the

proper replication of mitochondrial DNA and ribosomes are essential for mitochondrial health (Cooper, 2000).

Figure 3 Structure of a Mitochondrion



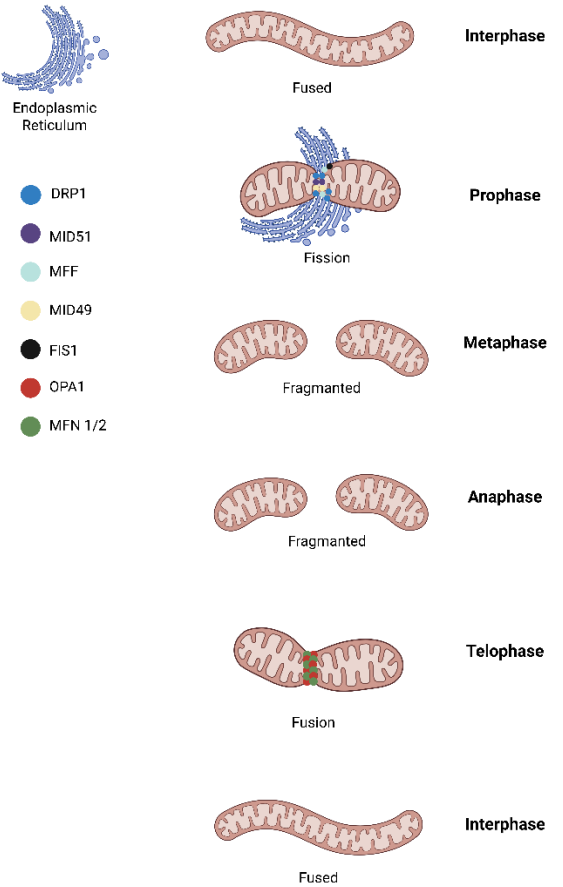
Created in https://BioRender.com

Throughout the cell cycle, mitochondria constantly undergo fission and fusion in order to properly meet the energy requirements of the cell. These dynamics are important both for meeting the energy demands for the cell's metabolic reaction requirements and also the proper inheritance of the organelle. During the G1 phase, mitochondria divide and multiply, and then fuse together to form a single, interconnected network. This provides the cell with balanced energy production and metabolic stability (Kraus, 2021). By the time the cell reaches the S phase, the mitochondrial network elongates to become more efficient at meeting the increased energy demands of DNA replication. During this time, mitochondria also replicate their own DNA in preparation for division. In the G2–M transition, mitochondria undergo fission (splitting). This fission is a critical step for the even distribution of mitochondria between daughter cells. Throughout mitosis, mitochondria remain fragmented, which facilitates their equal distribution during cell division. In cytokinesis,

the final phase of cell division, mitochondria begin to fuse again, and through fusion, a functional mitochondrial network is reformed in the new cells (Pangou & Sumera, 2022).

Mitochondrial division and fusion occur through the action of dynamin-related GTPases and it's a process that fuses the outer and the inner membrane of the mitochondria. Dynamin-related protein 1 (Drp1) and, as recent studies are indicating, dynamin-related protein 2 (Drp 2), regulate mitochondrial fission. Optical atrophy 1 protein (Opa1), which is the primary regulator of MIM fusion and cristae remodelling, and mitofusin 1/2 (mitochondrial outer membrane proteins) are involved in fusing the two mitochondrial membranes together. The basic mechanism of mitochondrial division involves the narrowing and cutting of the two mitochondrial membranes (Gandre-Babbe & van der Bliek, 2008). Drp1 protein is recruited through receptors on the mitochondrial membrane. Drp1 forms filaments that surround the mitochondrion. Through GTP hydrolysis, these filaments cut the mitochondrial membrane. In case of the loss of the Drp1 protein, it's absence would cause the mitochondria to grow and expand without being able to divide properly. Unlike Drp1, Opa1 and mitofusin 1/2 are located in segments on the mitochondrial membrane during fusion. While the loss of mitofusin 1 or 2 alone causes cell damage it would still be manageable for the cell, in case of the loss of both at the same time would result in severe mitochondrial damage that would kill the cell. Both division and fusion typically occur at regions where mitochondria contact the endoplasmic reticulum (Al Ojaimi & Salah, 2022).

Figure 4 The State of Mitochondria During Different Stages of the Cell Cycle



Created in https://BioRender.com

Mitochondrial Diseases

Mitochondrial diseases are a group of disorders caused by dysfunction in the mitochondria. These diseases are often genetic, either inherited from one's parents or arising from mutations in the mitochondrial DNA itself. Mitochondria are crucial for producing the energy that powers most cellular functions, so when they

malfunction, it can lead to a wide range of health problems These diseases are important not only because they affect basic cellular processes but also because they can impact many body systems, making diagnosis and treatment challenging. As mitochondrial diseases are often progressive and can be life-threatening, understanding them is critical for developing better therapies, improving early diagnosis, and ultimately finding potential cures. Their study also has broader implications for aging, cancer, and other complex conditions, as mitochondrial dysfunction is implicated in a range of age-related and degenerative diseases (Mitochondrial Disorders, 2025).

Leber's hereditary optic neuropathy (LHON) affects the optic nerve and can lead to sudden vision loss, while MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) is characterized by neurological problems, muscle weakness, and episodes resembling strokes. Barth syndrome is a lipid metabolism disorder that typically affects males. It impacts cell membranes and the myelin sheaths of nerves, causing fatigue, muscle weakness, and growth retardation. Chronic progressive external ophthalmoplegia (CPEO) usually begins in adolescence or young adulthood. It is a slowly progressive disease that causes limited eye movement, general body weakness, and exercise intolerance. CPEO is also observed in patients with Kearns-Sayre syndrome. Kearns-Sayre syndrome generally begins before the age of 20 and leads to vision loss, heart problems, muscle weakness, hearing loss, and coordination difficulties. Another disease is Leigh syndrome, which begins in infancy and progresses rapidly. It is characterized by poor appetite, vomiting, irritability, loss of head control, motor skill loss, constant crying, seizures, and lactic acidosis. As the disease progresses, muscle weakness and respiratory problems arise. (Mitochondrial Disorders, 2025)

Although many patients inherit faulty mitochondria from their mothers (since mitochondria in mammals are inherited maternally), it has been determined that small amounts of pathogenic mitochondria do not damage oxidative phosphorylation. Therefore, only cells with a high percentage of mutated mitochondria are affected (cells must have 60-90% pathogenic mitochondria). Mitochondria are passed from mother to offspring through a series of purification procedures, but these mechanisms are not yet fully understood. (Mitochondrial Disorders, 2025)

Conclusion

Despite the fact that the nucleus and mitochondria are both studied extensively when it comes to cellular components, a lot of mechanisms for their division still remains unclear. Understanding these are crucial for bettering our comprehension of health as both processes are fundamental to how cells function and replicate. Mitochondria provide energy for cellular activities, and any disruption in their division can lead to energy deficits and contribute to diseases such as neurodegeneration and metabolic disorders. On the other hand, nuclear division, through processes like mitosis and meiosis, ensures the proper distribution of genetic material, which is essential for maintaining cellular integrity and avoiding mutations. Any errors in nuclear division can result in genetic diseases, cancer, or developmental disorders. Together, these processes maintain the balance of energy and genetic information that is essential for overall health, and understanding them can reveal insights into disease mechanisms, aging, and potential therapeutic strategies.

References

Al Ojaimi, M., Salah, A., & El-Hattab, A. W. (2022). Mitochondrial Fission and Fusion: Molecular Mechanisms, Biological Functions, and Related Disorders. *Membranes*, 12(9), 893. https://doi.org/10.3390/membranes1209089

Basu, S., Greenwood, J., Jones, A.W. et al. (2022) Core control principles of the eukaryotic cell cycle. *Nature* 607, 381–386. https://doi.org/10.1038/s41586-022-04798-8

Baum, B., & Spang, A. (2023). On the origin of the nucleus: a hypothesis. *Microbiology and molecular biology reviews*: MMBR, 87(4), e0018621. https://doi.org/10.1128/mmbr.00186-21

Cooper, G.M. (2000) *The Cell: A Molecular Approach*. (2nd Edition). Sunderland (MA): Sinauer Associates

Dey, G., & Baum, B. (2021). Nuclear envelope remodelling during mitosis. *Current opinion in cell biology*, 70, 67–74. https://doi.org/10.1016/j.ceb.2020.12.004

Gandre-Babbe, S., & van der Bliek, A. M. (2008). The novel tail-anchored membrane protein Mff controls mitochondrial and peroxisomal fission in mammalian cells. *Molecular biology of the cell*, 19(6), 2402–2412. https://doi.org/10.1091/mbc.e07-12-1287

Güttinger, S., Laurell, E., & Kutay, U. (2009). Orchestrating nuclear envelope disassembly and reassembly during mitosis. *Nature reviews. Molecular cell biology*, 10(3), 178–191. https://doi.org/10.1038/nrm2641

Kraus, F., Roy, K., Pucadyil, T. J., & Ryan, M. T. (2021). Function and regulation of the divisome for mitochondrial fission. *Nature*, 590(7844), 57–66. https://doi.org/10.1038/s41586-021-03214-x

Lammerding J. (2011). Mechanics of the nucleus. *Comprehensive Physiology*, 1(2), 783–807. https://doi.org/10.1002/cphy.c100038

Walsh, M. E., King, G. A., & Ünal, E. (2024). Not just binary: embracing the complexity of nuclear division dynamics. Nucleus (Austin, Tex.), 15(1), 2360601. https://doi.org/10.1080/19491034.2024.2360601

Mitochondrial Disorders, National Institute of Neurological Disorders and Stroke, (18/09/2025 reached from the website https://www.ninds.nih.gov/health-information/disorders/mitochondrial-disorders on date 18/09/2025.)

Okada, N., & Sato, M. (2015). Spatiotemporal Regulation of Nuclear Transport Machinery and Microtubule Organization. *Cells*, 4(3), 406–426. https://doi.org/10.3390/cells4030406

Olmos, Y., Hodgson, L., Mantell, J., Verkade, P., & Carlton, J. G. (2015). ESCRT-III controls nuclear envelope reformation. *Nature*, 522(7555), 236–239. https://doi.org/10.1038/nature14503

Pangou, E., & Sumara, I. (2021). The Multifaceted Regulation of Mitochondrial Dynamics During Mitosis. *Frontiers in cell and developmental biology*, 9, 767221. https://doi.org/10.3389/fcell.2021.767221

Schlaitz, A. L., Thompson, J., Wong, C. C., Yates, J. R., 3rd, & Heald, R. (2013). REEP3/4 ensure endoplasmic reticulum clearance from metaphase chromatin and proper nuclear envelope architecture. *Developmental cell,* 26(3), 315–323. https://doi.org/10.1016/j.devcel.2013.06.016

Walczak, C. E., Cai, S., & Khodjakov, A. (2010). Mechanisms of chromosome behaviour during mitosis. *Nature reviews. Molecular cell biology*, 11(2), 91–102. https://doi.org/10.1038/nrm2832

Walsh, M. E., King, G. A., & Ünal, E. (2024). Not just binary: embracing the complexity of nuclear division dynamics. *Nucleus*, 15(1). https://doi.org/10.1080/19491034.2024.2360601

Yao, C., Rath, U., Maiato, H., Sharp, D., Girton, J., Johansen, K. M., & Johansen, J. (2012). A nuclear-derived proteinaceous matrix embeds the microtubule spindle apparatus during mitosis. *Molecular biology of the cell*, 23(18), 3532–3541. https://doi.org/10.1091/mbc.E12-06-0429

Zwerger, M., Ho, C. Y., & Lammerding, J. (2011). Nuclear mechanics in disease. *Annual review of biomedical engineering*, 13, 397–428. https://doi.org/10.1146/annurev-bioeng-071910-124736

DIVISION OF SINGLE MEMBRANE ORGANELLES

TUĞÇE KARADAĞ[3]
SACİDE PEHLİVAN[4]

Introduction

One of the fundamental characteristics that distinguishes eukaryotic cells from prokaryotic cells is that they contain a variety of membrane-bound organelles with distinct functions. The ability of eukaryotic cells to maintain essential life processes depends on the precise regulation of the number of these complex and dynamic organelles. Vital processes such as maintaining cellular homeostasis, carrying out metabolic activities, growth, and cell division are carried out by these specialized cellular compartments. Single-membrane organelles—the endoplasmic reticulum (ER), Golgi apparatus, lysosomes, and peroxisomes—differ significantly from the double-membrane, semi-autonomous organelles mitochondria and chloroplasts in terms of how they replicate and are passed on to

[3]MSc (c).,Istanbul University, Faculty of Medicine, Institute of Health Sciences, Department of Medical Biology, tugceroglu22@gmail.com -ORCID ID: 0009-0004-3472-4506
[4] Prof.Dr., Istanbul University, Faculty of Medicine, Department of Medical Biology, sacide.pehlivan@istanbul.edu.tr - ORCID ID: 0000-0003-1272-5845

daughter cells during mitosis. Instead of a classical division mechanism, these organelles employ unique strategies, such as maintaining network continuity in the ER, transient fragmentation and reassembly in the Golgi, and controlled fission or de novo synthesis in peroxisomes.

Endoplasmic Reticulum

The endoplasmic reticulum is a single membrane-bound organelle that forms an interconnected network of vesicles, tubes, and cisternae that regulates the folding, processing, and transport of secretory and transmembrane proteins. It also serves as a releasable reservoir for intracellular calcium and serves as a center for lipid biosynthesis (Carlton, 2020).

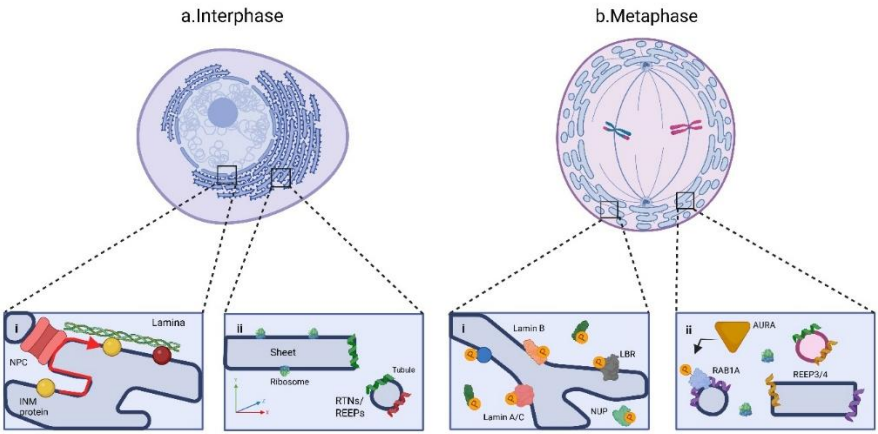
The outer membrane of the nuclear membrane structure is continuous with the endoplasmic reticulum. The nucleus is one of the most critical structures found in eukaryotic cells, and during mitosis, the "open mitosis" form is observed: during the prophase stage of division, the nuclear lamina is phosphorylated and dispersed, the nuclear membrane disintegrates, and chromosomes interact with the mitotic spindle fibers.

During cell division, the ER is not lost, fragmented, or divided by fission as in mitochondria/chloroplasts. The continuous structure of the ER during interphase is maintained by various proteins, including reticulons (RTN) and receptor expression enhancer protein (REEP), cytoskeleton-associated protein 4 (CKAP4/CLIMP-63), sigma non-opioid intracellular receptor 1 (SIGMAR1), and atlastin (Atlastin GTPase). Significant changes in ER morphology occur with the transition from interphase to mitosis. These changes are primarily due to the formation of fenestrations (holes) in the ER membrane as a result of microtubule reorganization and protein phosphorylation (Kors, 2024). Membrane holes in the mitotic ER are proposed to be critical for the efficient assembly of

nuclear pore complexes during nuclear envelope remodeling in late anaphase (Carlton, 2020; Deolal, 2024).As in many other mitotic processes, kinases serve as key regulators of nuclear membrane disassembly. Specifically, vaccinia-associated kinase 1 (VRK1) phosphorylates autointegration barrier factor (BAF); in the unphosphorylated state, BAF binds chromatin to LEM-domain proteins in the inner nuclear membrane (INM). Phosphorylation prevents this binding and weakens other interactions, thus disassociating chromatin from the membrane (Figure 1A). The absence of VRK1 prevents BAF from dissociating from DNA, resulting in prolonged mitosis and the development of abnormal nuclear membrane architecture in interphase cells. In addition, CLIMP63, a microtubule-interacting ER protein known to organize the cisternal ER, is phosphorylated during mitosis. This alteration disrupts CLIMP63 binding to microtubules and allows the ER to collapse into the cytoplasmic space, providing the necessary environment for its inheritance (Jongsma, 2015).

In 2009, Lu and colleagues obtained a different model using spinning-disk confocal microscopy and electron microscopy tomography after high-pressure freezing. They reported that in HeLa and CHO cells, mostly cisternal ER is present during mitosis, with only a few tubules associated with the spindle (Lu, 2009). Subsequent studies by Puhka and colleagues revealed that mitotic ER organization varies among cell types, suggesting that more than one form of ER remodeling may occur during cell division (Puhka, 2012).

Figure 1. Changes in the composition, distribution, and morphology of the ER during mitosis. (A) In interphase, the ER contains tubules, sheet structures, and the nuclear envelope (NE). (i) The NE associates with nuclear pore complexes (NPCs), INM proteins, and lamins. (ii) RTN and REEP proteins form the highly coiled structure of ER tubules and sheet edges. (B) In mitosis, the ER is directed toward the cell periphery and largely withdrawn from the interior of the spindle region. (i) The NE protein network is phosphorylated and dispersed; membrane-bound NUPs, INM proteins (e.g., LBR), and lamin B integrate into the mitotic ER. (ii) The ER transitions to a more highly coiled structure; this transformation is mediated by REEP3/4, RAB1A phosphorylation of AURA (which enhances RTN–REEP oligomerization), and ribosome dissociation.



Created in BioRender.com

In 2009, Lu and colleagues obtained a different model using spinning-disk confocal microscopy and electron microscopy tomography after high-pressure freezing. They reported that in HeLa and CHO cells, mostly cisternal ER is present during mitosis, with only a few tubules associated with the spindle (Lu, 2009). Subsequent studies by Puhka and colleagues revealed that mitotic

ER organization varies among cell types, suggesting that more than one form of ER remodeling may occur during cell division (Puhka, 2012).

Golgi Apparatus

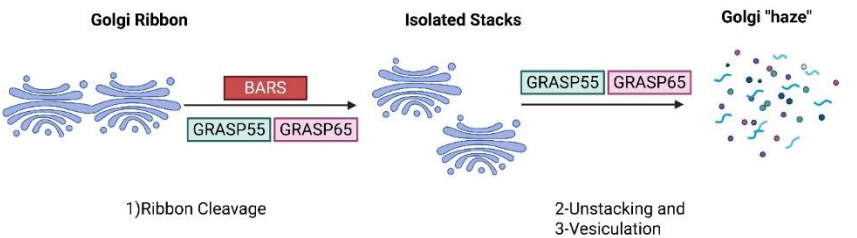
The Golgi apparatus is an organelle found in eukaryotic cells responsible for intracellular protein and lipid processing, packaging, and distribution. It regulates plasma membrane biosynthesis in three ways: protein and lipid processing, significant membrane composition modification by extravesicular lipid transport, and routing of proteins and lipids to the appropriate sites via the trans-Golgi network.

During mitosis, the Golgi apparatus undergoes a controlled remodeling process. During this process, the Golgi disassembles in the early stages of mitosis, regenerates upon completion of cell division, and becomes functional again in daughter cells. In late G2, C-terminal binding protein 1/brefeldin A and ADP-ribosylated substrate (CTBP1/BARS) proteins disrupt the bonds between the stacks of cisternae that form the Golgi ribbon structure. This process results in the Golgi becoming small ministacks. The 55/65 kDa Golgi remodeling and stacking protein (GRASP55/65), which normally holds the cisternae together, is phosphorylated by cyclin-dependent kinase 1 (CDK1), polo-like kinase 1 (PLK1), and MAP kinases. This inhibits trans-oligomerization, and the Golgi ribbon disassembles. GRASP65 also stabilizes microtubules, while weakening these bonds by phosphorylation contributes to the separation of the Golgi from the cytoskeleton. After the cisternae are separated, they disintegrate into small vesicles. Coat protein complex I (COPI) proteins continuously bud, enabling vesicle formation. Because division does not terminate during this process, the fusion of the formed vesicles is prevented by various proteins. Because fusion is inhibited, the Golgi becomes small tubovesicular clusters. The

resulting structures are called "Golgi haze" and spontaneously disperse to daughter cells by a stochastic mechanism (Cabukusta, 2018; Tang, 2013).

Golgi preparation for cell division is initiated during interphase by the mitogen-activated protein kinase kinase 1 (Mek1) and Polo-Like Kinase 1 (Plk1) kinases. These kinases disrupt the retention complexes of the noncompacted regions, leading to Golgi ribbon disassembly (Figure 2). Failure of this initiating step results in arrest in G2. Following Golgi fragmentation, the fission protein BARS is activated, likely through phosphorylation, to promote further fragmentation of the organelle into tubule reticular membranes; when these membranes are further fragmented, a dispersed Golgi “haze” forms (Jongsma, 2015) (Figure 2).

Figure 2. Schematic representation of mitotic Golgi ribbon disassembly. The Golgi ribbon first undergoes ribbon disassembly, which controls the G2/M transition, under the influence of BARS, GRASP55, GRASP65, and various MAP kinases. These stacks, isolated at the beginning of mitosis, undergo unstacking and vesiculation before completely disassembling, forming the disorganized structure known as "Golgi fog" in metaphase. This stage requires Plk1 and Cdc2, and their targets GRASP55 and GRASP65. Subsequent dephosphorylation of these kinases allows the Golgi ribbon to reconstitute in daughter cells.



Created in BioRender.com

Two models have been proposed for the complement of the Golgi apparatus; these are divided primarily according to the degree of involvement of the ER. In the first model, the Golgi remains in dynamic equilibrium with the endoplasmic reticulum (ER) during interphase. When mitosis begins, ER function ceases, the Golgi disassembles, and some Golgi proteins are imported into the ER. This rearrangement is limited to ARF GTPase 1 (ARF1)-mediated compartments. In the final stages of mitosis, ER function is restarted, and Golgi proteins are released from the ER to form new Golgi structures. This model is supported by the presence of Golgi proteins in the ER in early mitochondrial electron microscopy studies. Furthermore, inactivation of Sar1 (Secretion-Associated Ras-Like GTPase 1) and the activation of ER export lead to Golgi fragmentation and ER export of proteins. Inhibition of ARF1 with Brefeldin A (BFA) has similarly been shown to reorganize the Golgi upon absorption into the ER and subsequent BFA removal. However, after BFA treatment or Sar1 dominant-negative protein, the Golgi only migrates to the reduced ER because some matrix proteins, such as golgins and GRASP family members, remain isolated from the ER. An alternative model proposes that the Golgi is inherited independently of the ER and is distributed to the cytosol during mitosis by fragments of kinase-mediated membrane-anchoring complexes, which are then separated into vesicles and tubules and reticular structures; these fragments are then transmitted to offspring via microtubule-based transport (Valente, 2015). pp

Experimental evidence has shown that during mitosis, Golgi protein does not enter the ER, and fragments reside at the spindle pole instead of the ER. Asymmetric cell division and rescue experiments have demonstrated that both Golgi proteins and the microtubule network are required for Golgi inheritance. During cytokinesis, Golgi fragments form two "Golgi twins," which then

migrate to the centrosome and fuse, reestablishing the characteristic Golgi structure (Jongsma, 2015).

Lysosomes

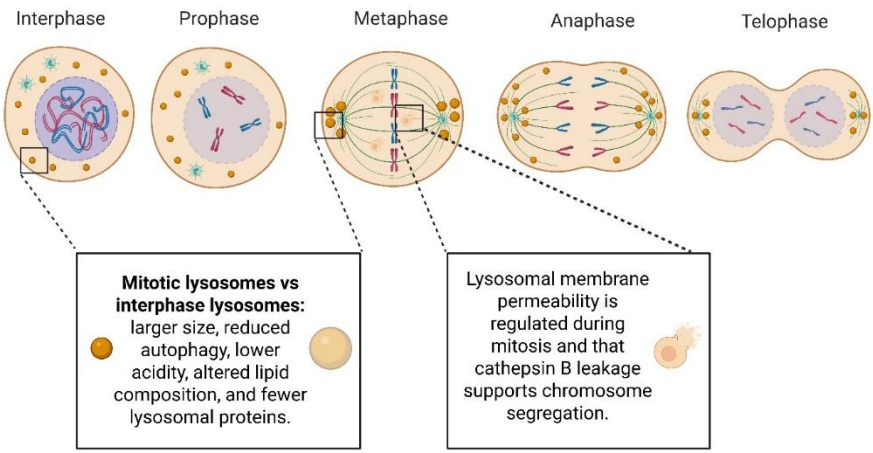
The endoplasmic reticulum is a single membrane-bound organelle that forms an interconnected network of vesicles, tubes, and cisternae that regulates the folding, processing, and transport of secretory and transmembrane proteins. It also serves as a releasable reservoir for intracellular calcium and serves as a center for lipid biosynthesis (Carlton, 2020).

During interphase in dividing cells, lysosomes are either clustered around the microtubule organizing center (MTOC) or located near the other plasma membrane. Bidirectional movement of lysosomes between these sites occurs along microtubule tracks. As cells enter early mitosis, interphase microtubules gradually reorganize to form the mitotic spindle; concurrent with microtubule remodeling, lysosomes disperse throughout the cytoplasm until they rapidly recluster around the MTOCs in telophase. Mitotic cells have less autophagic activity and fewer but larger lysosomes than interphase cells (Cabukusta, 2018). Because autophagosomes are considered lysosome-associated organelles when cells divide, they are likely partitioned among daughter cells by a mechanism similar to that used for the inheritance of lysosomes. New autophagosomes may then form de novo in daughter cells in response to autophagy-inducing signals, but the details of this process are not fully understood (Hämälistö, 2021; Jongsma, 2015).

A recent study demonstrated that cathepsin B leakage from mitotic lysosomes promotes mitotic chromosome segregation, suggesting that lysosomal membrane integrity can be regulated spatially and temporally. However, unlike many other organelles, the structural and functional changes of lysosomes during mitosis are largely unknown (Stahl-Meyer, 2022). Researches demonstrated that

mitotic lysosomes are larger, less acidic, and less deficient in lysosome-specific proteins compared to interphase lysosomes, and also undergo lipid modification (Stahl-Meyer, 2022). Lysosomal membrane integrity is considered critical for cell survival because it can be destructive if hydrolases from the lumen leak into the cytosol. However, some nonlethal functions, such as mitotic lysosomal leakage, occur near chromatin and facilitate accurate chromosome segregation (Hämälistö, 2020). Limited information is available regarding the roles and changes of lysosomes during mitosis.

Figure 3. Schematic representation of the dispersal of lysosomes in mitosis.



Created in BioRender.com

Microbodies

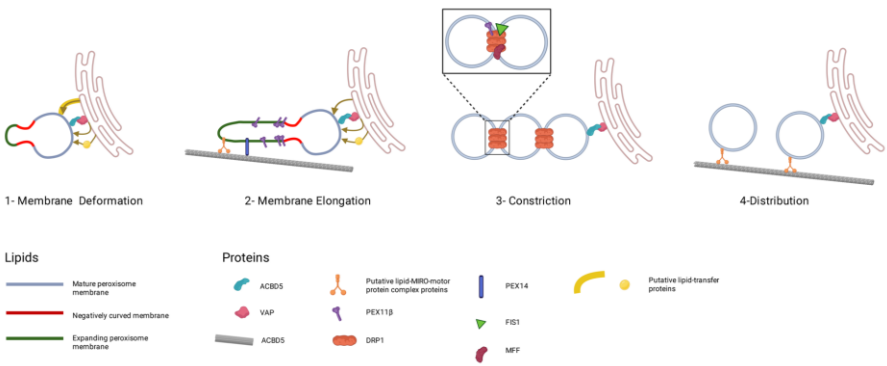
Peroxisomes are eukaryotic microbodies surrounded by a single lipid membrane. These structures, typically between 100 nm and 1 μm in size, bring together enzymes and substrates for specific metabolic pathways in high concentrations, increasing their catalytic rate or protecting the rest of the cell from the potentially harmful effects of reactive intermediates (O'Connell, 2012). Because lysosomes and microbodies operate largely independently of the

synthetic function of the cell nucleus, the division of these organelles is not directly related to nuclear division but rather to mitochondrial division. The functions of lysosomes and microbodies suggest that these organelles may have emerged later in eukaryotic evolution than the ER and Golgi apparatus (Imoto, 2011).

In general, microbody division in mammalian cells, trypanosomes, yeast, and algae proceeds in three stages: elongation, contraction, and fragmentation. Collaborative studies by several research groups have identified 32 peroxisome biogenesis factor (PEX) genes that contribute to the biogenesis or maintenance of microbodies. Microbody division involves the conserved PEX11 membrane proteins, and a dynamin-like protein has been shown to be required in yeast. PEX11 and two PEX11-related proteins are the major membrane proteins of Trypanosoma brucei microbodies, and it has been concluded that PEX11 family proteins play important roles in determining microbody membrane structure. High expression of peroxisomal biogenesis factor 11β, b isoform (Pex11pb) in mammalian cells enhanced microbody division (Imoto, 2011). Dynamin-like protein 1 (DLP1), an essential protein for microbody division (MD), was recently reported to also play a role in microbody division and to be partially directed to microbodies by PEX11. Li and Gould showed that DLP1, the human homolog of the yeast dynamin 1 (DNM1) and vacuolar protein transport protein (VPS) genes, plays an important role in microbody division in human cells (Li, 2003). Fis1p has also been found in microbodies. Together with DLP1, it appears to promote the fragmentation of not only mitochondria but also microbodies. Filamentous temperature-sensitive mutant 1 (Fts1) plays an important role in microbody division and maintenance of microbody morphology in mammalian cells, likely in coordination with Pex11pb and DLP1. However, the mechanism of division remains unclear, as PEX, dynamin-like

proteins, and fission 1 protein (Fis1p) have not been visualized at the division site of microbodies (Imoto, 2011).

Figure 4. Peroxisomes do not arise from scratch; they proliferate by budding from existing ones (growth and fission). 1: The membrane shape changes, and a protrusion forms (supported by lipid flux from the ER). 2: The protrusion is extended by the PEX11β protein and its microtubule connections. 3: The DRP1 protein and its auxiliaries (FIS1, MFF, PEX11β) cause the membrane to constrict → the protrusion appears like beads on a string → fission occurs.4: New peroxisomes mature by importing proteins and then disperse throughout the cell via microtubules.



Created in BioRender.com

Peroxisomes form in two ways: they can derive de novo from the ER or increase their number by dividing existing peroxisomes. During mitosis, peroxisomes cluster around the spindle poles, facilitating their even distribution to both daughter cells. Studies have shown that PEX11B is a key protein involved in peroxisome division and organization. Loss of PEX11B causes peroxisomes to be unevenly distributed, misalign along the mitotic spindle, and result in abnormal cell division (Asare, 2017).

The Role of Organelle Division Defects in the Pathogenesis of Diseases

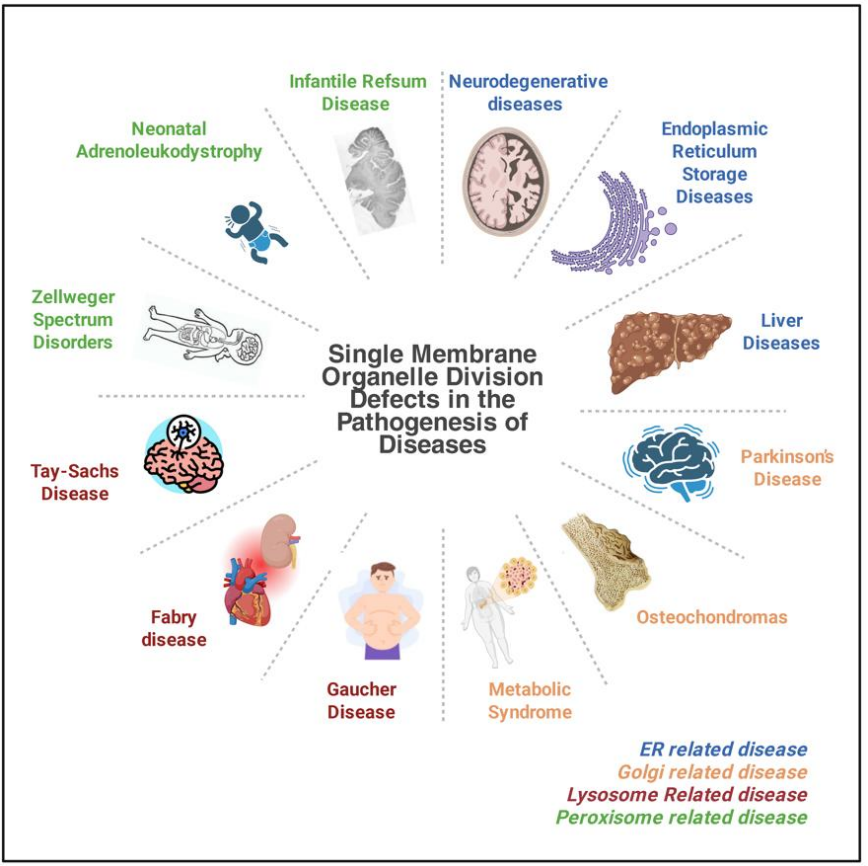
The accuracy of cell division has traditionally focused on the precise segregation of chromosomes, a process regulated by powerful checkpoints to ensure the accurate transmission of genetic information. However, an equally critical, yet less studied, aspect of cell proliferation is the inheritance of cytoplasmic organelles, particularly the endoplasmic reticulum (ER), Golgi apparatus, and mitochondria. The ER and Golgi play central roles in protein and lipid synthesis, modification, and transport, and their proper distribution to daughter cells is crucial for maintaining cellular homeostasis and viability. Failure of this process has been shown to be a major cause of cellular defects and various human diseases (Carlton, 2020; Jongsma, 2015).

The accumulation of misfolded or aggregated proteins is a fundamental theme in many diseases and can be traced to a damaged endoplasmic reticulum (ER). Endoplasmic Reticulum Storage Diseases (ERSDs) are a group of genetically based disorders characterized by the intracellular retention of mutant proteins that fail the ER's stringent quality control. While they are usually caused by a specific genetic mutation, the functional consequences of ER segregation errors, such as the transfer of an already overloaded or damaged ER to daughter cells, can exacerbate or even initiate this pathology. Examples of ERSDs include some forms of familial hypoparathyroidism, familial central diabetes insipidus, and liver disease due to α1-antitrypsin deficiency (Carmichael, 2022).

Babour and colleagues have shown that in S. cerevisiae, ER stress activates the MAP kinase Slt2 in a novel unfolded protein response (UPR)-independent ER stress surveillance (ERSU) pathway. During ER stress, ERSU modifies the septin complex to delay ER inheritance and cytokinesis. In the absence of Slt2 kinase,

the stressed ER is transferred to the daughter cell, leading to the death of both the parent and daughter cells (Babour, 2010).

Figure 5. Schematic representation of the role of single membrane organelle division defects during cell division in different diseases.



Created in BioRender.com

Errors in ER segregation underlie diseases directly linked to ER stress. The separation of the ER into daughter cells during mitosis is a highly dynamic process. A physical error in this process can lead to daughter cells inheriting a structurally damaged ER network with reduced functional capacity. This inevitably increases the accumulation of misfolded proteins by reducing protein folding

capacity, triggering chronic ER stress. In cells with limited dividing capacity, such as neurons, the inability of the UPR to withstand this constant stress can accelerate cell death, leading to neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's, as well as metabolic diseases and cancer. This suggests that maintaining the mitotic integrity of the ER is critical for maintaining cellular health and preventing ER stress-related diseases (Akaaboune, 2024; Granic, 2013).

A physical defect in the Golgi fragmentation and reassembly process during mitosis can cause daughter cells to inherit a structurally defective Golgi apparatus. This defective structure may contribute to the pathophysiology of congenital glycosylation disorders by disrupting the proper localization or function of glycosylation enzymes. Moreover, in neurodegenerative diseases (e.g., Alzheimer's), Golgi fragmentation is recognized not merely as a symptom but as an early and critical event in the pathological cascade of the disease. Golgi fragmentation can accelerate disease progression by causing severe disruptions in the processing and transport of molecules such as amyloid precursor protein (APP). These findings provide compelling evidence that a change in organelle morphology directly impacts a disease at the molecular level and how a physical segregation defect can lead to persistent dysfunction (Akaaboune, 2024; Colanzi, 2013). Disruptions in membrane traffic within the Golgi apparatus can have serious consequences for bone health and increase the risk of developing cancer. In fact, Golgi dysfunction has been linked to numerous human diseases, including metabolic syndromes, cancer, and neurodegenerative disorders (Iacobescu, 2024).

Lysosomal storage diseases (LSDs) encompass a group of more than 70 rare, inherited metabolic diseases caused by defects in lysosome function. The primary cause of these diseases is a genetic mutation that results in the deficiency of a single enzyme required

for the metabolism of certain lipids, glycoproteins, or mucopolysaccharides. When this critical enzyme is missing or defective, its substrate accumulates within the lysosome to harmful levels, ultimately impairing cellular function and leading to cell death (Akaaboune, 2024).

The clinical manifestations of LSDs are broad and highly variable, depending on the specific disorder and the age of onset. Common symptoms include developmental and intellectual delays, seizures, movement disorders, liver and spleen enlargement, bone deformities, and vision or hearing problems. While many are considered childhood diseases with a poor prognosis, some can appear later in life. Examples of LSDs include Gaucher disease, Tay-Sachs disease, Fabry disease, and Niemann-Pick disease (Akaaboune, 2024; Platt, 2018).

Peroxisome biogenesis disorders (PBDs) encompass a range of genetically heterogeneous, severe diseases inherited in an autosomal recessive manner. The underlying cause is a fundamental defect in peroxisome formation, usually due to mutations in the PEX gene family. This leads to the complete absence or structural abnormalities of peroxisomes, resulting in systemic disruption of all metabolic functions normally associated with this organelle (Argyriou, 2016).

The most severe forms of PBD are the Zellweger spectrum disorders, which include Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD), and infantile Refsum disease (IRD). These disorders share common biochemical abnormalities, such as accumulation of very long-chain fatty acids (VLCFA) and phytanic acid and deficiency in plasmalogen biosynthesis. Zellweger syndrome, the most severe prototype, is characterized by craniofacial dysmorphism, severe neurological abnormalities, including impaired neuronal migration and loss of myelination, and

liver involvement. The prognosis is extremely poor; patients rarely survive beyond the first year of life (Elumalai V, 2020).

References

Akaaboune, S. R., & Wang, Y. . (2024). Golgi defect as a major contributor to lysosomal dysfunction. . *Frontiers in Cell and Developmental Biology*, *12*.

Argyriou, C., D'Agostino, M. D., & Braverman, N. (2016). Peroxisome biogenesis disorders. . *Translational science of rare diseases*, *1*(2), 111–144.

Asare, A., Levorse, J., & Fuchs, E. . (2017). Coupling organelle inheritance with mitosis to balance growth and differentiation. *Science*, *355*(6324).

Babour, A., Bicknell, A. A., Tourtellotte, J., & Niwa, M. (2010). A surveillance pathway monitors the fitness of the endoplasmic reticulum to control its inheritance. *Cell 142*(2), 256–269.

Cabukusta, B., & Neefjes, J. (2018). Mechanisms of lysosomal positioning and movement. *Traffic*, *19*(10), 761–769.

Carlton, J. G., Jones, H., & Eggert, U. S. (2020). Membrane and organelle dynamics during cell division. *Nature Reviews Molecular Cell Biology*, *21*(3), 151–166.

Carmichael, R. E., & Schrader, M. . (2022). Determinants of peroxisome membrane dynamics. . *Frontiers in Physiology*, *13*(834411).

Colanzi, A., & Sütterlin, C. . (2013). Signaling at the Golgi during mitosis. *Methods in cell biology*, *118*, 383–400.

Deolal, P., Scholz, J., Ren, K., Bragulat-Teixidor, H., & Otsuka, S. (2024). Sculpting nuclear envelope identity from the endoplasmic reticulum during the cell cycle. *15*(1). https://doi.org/2299632

Elumalai V, P. D. (2020). Zellweger Spectrum Disorder. In *StatPearls [Internet]*. StatPearls Publishing.

Granic, A., & Potter, H. . (2013). Mitotic spindle defects and chromosome Mis-segregation induced by LDL/cholesterol—implications for Niemann-pick C1, Alzheimer's disease, and atherosclerosis. *PloS one*, *8*(4).

Hämälistö, S., Stahl-Meyer, J., & Jäättelä, M. . (2021). They Might Cut It—Lysosomes and Autophagy in Mitotic Progression. . *Frontiers in Cell and Developmental Biology*(9), 727538.

Hämälistö, S., Stahl, J. L., Favaro, E., Yang, Q., Liu, B., Christoffersen, L., ... & Jäättelä, M. (2020). Spatially and temporally defined lysosomal leakage facilitates mitotic chromosome segregation. . *Nature communications*, *11*(1), 229.

Iacobescu, G. L., Corlatescu, A. D., Popa, M., Iacobescu, L., Cirstoiu, C., Orban, C., & Iacobescu Sr, G. L. (2024). Exploring the implications of Golgi apparatus dysfunction in bone diseases. *Cureus*, *16*(3).

Imoto, Y., Yoshida, Y., Yagisawa, F., Kuroiwa, H., & Kuroiwa, T. . (2011). The cell cycle, including the mitotic cycle and organelle division cycles, as revealed by cytological observations. . *Journal of electron microscopy,*, *60*(suppl_1), 117–S136.

Jongsma, M. L., Berlin, I., & Neefjes, J. (2015). On the move: organelle dynamics during mitosis. *Trends in cell biology*, *25*(3), 112–124.

Kors, S., & Schlaitz, A. L. (2024). Dynamic remodelling of the endoplasmic reticulum for mitosis. *Journal of Cell Science*, *137*(22), jcs261444.

Li, X. G., S. J. . (2003). The dynamin-like GTPase DLP1 is essential for peroxisome division and is recruited to peroxisomes in

part by PEX11. . *The Journal of Biological Chemistry*, *278*(19), 17012–17020.

Lu, L., Ladinsky, M. S., & Kirchhausen, T. (2009). Cisternal organization of the endoplasmic reticulum during mitosis *Molecular biology of the cell*, *20*(15), 3471–3480.

O'Connell, J. D., Zhao, A., Ellington, A. D., & Marcotte, E. M. . (2012). Dynamic reorganization of metabolic enzymes into intracellular bodies. *Annual review of cell and developmental biology*, *28*(1), 89–111.

Platt, F. M., d'Azzo, A., Davidson, B. L., Neufeld, E. F., & Tifft, C. J. (2018). Lysosomal storage diseases. . *Nature reviews Disease primers*, *4*(1), 27.

Puhka, M., Joensuu, M., Vihinen, H., Belevich, I., & Jokitalo, E. . (2012). Progressive sheet-to-tubule transformation is a general mechanism for endoplasmic reticulum partitioning in dividing mammalian cells. . *Molecular biology of the cell*, *23*(13), 2424–2432.

Stahl-Meyer, J., Holland, L. K. K., Liu, B., Maeda, K., & Jäättelä, M. (2022). Lysosomal changes in mitosis. . *Cells*, *11*(5), 875.

Tang, D., & Wang, Y. (2013). Cell cycle regulation of Golgi membrane dynamics. . *Trends in cell biology*, *23*(6), 296–304.

Valente, C., & Colanzi, A. . (2015). Mechanisms and regulation of the mitotic inheritance of the Golgi complex. *Frontiers in Cell and Developmental Biology*, *3*(79).

DIVISION OF MEMBRANE-BOUND AND NON-MEMBRANE-BOUND ORGANELLES

ZEYNEB BERRİN KÖSEM[5]
SACİDE PEHLİVAN[6]

Introduction

In eukaryotic cells, there are numerous membrane-bound and non–membrane-bound organelles, including the Endoplasmic Reticulum, Golgi Apparatus, Lysosomes, Peroxisomes, Endosomes, Ribosomes, the Centrosome, and Cytoskeletal Elements. How these organelles are segregated during cell division and transferred to daughter cells has become increasingly clear through recent research. In this section, the division mechanisms of the Centrosome, Endosomes and Cytoskeletal Components are reviewed in light of current literature, and their relevance to human disease is discussed to highlight their biological significance.

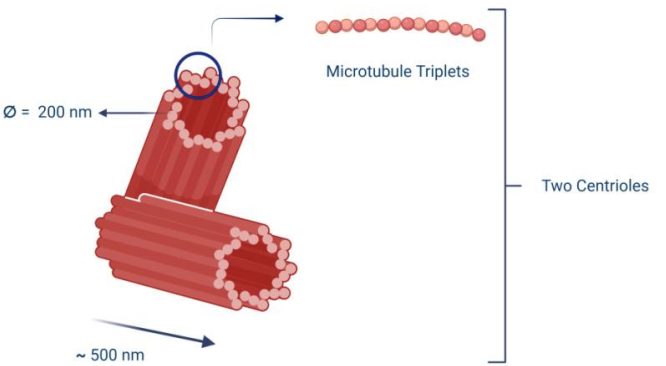
[5] MSc (c), Istanbul University, Faculty of Medicine, Department of Medical Biology, zbkosem@gmail.com - Orcid: 0009-0003-3421-7072
[6] Prof. Dr., Istanbul University, Faculty of Medicine, Department of Medical Biology, sacide.pehlivan@istanbul.edu.tr - Orcid: 0000-0003-1272-58452

Centrosome:

The Centrosome serves as the primary microtubule-organizing center (MTOC) in animal cells. It consists of a pair of orthogonal centrioles surrounded by pericentriolar material. This structure guides the proper positioning of organelles by facilitating the nucleation and anchoring of microtubules. The centrosome directs the formation of symmetric microtubule arrays, regulating the pericentrosomal localization of the Golgi Complex and facilitating the transport of endosomal vesicles to the cell center via dynein.

The Centrosome in animal cells is a non-membranous organelle composed of two connected centrioles, pericentriolar material (PCM), and some additional structures. Acting as a microtubule-organizing center, the centrosome orchestrates the steps of mitotic division. Each centrosome consists of a mature centriole and a newly formed centriole that are connected to each other. Centrioles are cylindrical structures made up of nine microtubule triplets. A centriole is approximately 200 nm in diameter and 500 nm in length, forming a cylinder composed of nine microtubule triplets. (Prigent & Uzbekov, 2022)

Figure-1: Structure of Centrosome



Created in BioRender.com

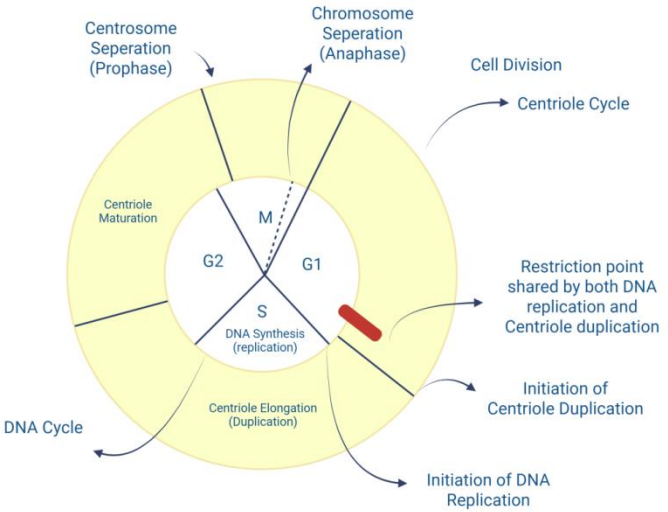
The Centriole pair is surrounded by pericentriolar material (PCM), an electron-dense matrix composed of various protein complexes that regulate protein trafficking, degradation, and nucleation. During the cell cycle, centrosomes, like chromosomes, are duplicated. Upon entering mitosis, these duplicated centrosomes undergo maturation, a process characterized by a substantial expansion of the PCM and a corresponding increase in microtubule numbers, enabling the formation of functional bipolar mitotic spindles for chromosome segregation. Centrosome maturation involves a complex interplay of components, ranging from protein scaffolds that facilitate molecular interactions to motor proteins that dynamically assemble spindle microtubules by transporting various molecules and structures. (Prigent, 2025) Centriole maturation can be described using three models: the procentriole, the new centriole, and the mature centriole. A mature centriole is one that is fully developed and at least two cell cycles old. The centriole formed in the previous cell cycle is considered the new centriole. The new centriole possesses two types of appendages, known as distal and subdistal appendages. (Prigent & Uzbekov, 2022)

Centrioles duplicate or can form de novo, although duplication is the more common mechanism. Duplication occurs only once per cell cycle. The newly formed centriole initially lacks a complete PCM and appendages, acquiring them only after mitosis, thereby maturing into a fully functional centriole for the next cycle.

During interphase, a cell contains a single centrosome composed of two orthogonally arranged centrioles surrounded by PCM. Therefore, each cell in G1 phase contains only one centrosome. In G1, the mature centriole and its appendages connect to new centrioles, severing links between daughter centrioles. Breaking these connections permits their duplication.

Centriole duplication is regulated by Polo-like kinase 4 (PLK4). PLK4 recruits SCL/TAL1 interrupting locus (STIL) to the centriole ring and activates it via phosphorylation. This activation then recruits Spindle assembly abnormal protein 6 homolog (SAS-6), which drives the formation of the cartwheel structure. Centriole duplication begins at the end of G1 and the start of S phase, continuing through G2. (Prigent, 2025)

Figure-2: Centrosome Duplication in the Cell Cycle.



Created in BioRender.com

When the cell reaches the G2–early mitotic phase, the two centrosomes separate and move to opposite sides of the nucleus. Their PCM expands, increasing microtubule nucleation and establishing the two spindle poles that will capture chromosomes. During anaphase, the centrosomes remain at the poles, and after cytokinesis, each daughter cell inherits one centrosome (a mother–daughter pair). In the subsequent interphase, the inherited daughter centriole matures, completing the cycle and preparing the cell for the next duplication event. Thus, centrosome division is a coordinated and semi-conservative process: template-based procentriole

formation occurs in S phase, followed by elongation and maturation, and finally, separation to spindle poles during mitosis generates two functional centrosomes for the daughter cells. (Nigg & Stearns, 2011)

Interphase Stage:

During interphase (i.e., the G1, S, and G2 phases of the cell cycle), the cell contains a single centrosome. The centrosome is composed of two orthogonally arranged centrioles—a mature centriole and a new centriole—surrounded by protein-rich structures known as pericentriolar material (PCM). Together, the centrioles and PCM function as the microtubule-organizing center (MTOC) of the cell.

Late G1/Early S Phase:

As the cell progresses from late G1 to early S phase, each existing centriole begins to serve as a template for a new procentriole. During G1, each cell contains only a single centriole. The new procentriole nucleates at a right angle to the existing mother centriole. This process is mediated by a structural framework known as the cartwheel scaffold, which facilitates the formation of the new procentriole.

S and G2 Phases:

The newly formed daughter centriole begins to elongate, a process that continues throughout S phase and into G2 phase. At this point, each centrosome consists of a mother–daughter centriole pair. However, the new centriole is not yet fully mature: it lacks certain PCM components and appendages, including distal and subdistal appendages. These features are acquired only after mitosis, allowing the new centriole to assume the role of a mother centriole in the next cell cycle. (Srsen & Merdes, 2006)

G2/Early Mitosis Phase:

As the cell prepares for mitosis, the two centrosomes separate and move to opposite sides of the nucleus. Following separation, the PCM surrounding each centrosome expands. This expansion enhances microtubule nucleation, establishing the spindle poles at opposite ends of the cell. These poles will form the mitotic spindle apparatus and facilitate the attachment of chromosomes.

Anaphase and Cytokinesis:

During anaphase of mitosis, the centrosomes remain at opposite poles of the cell. Upon completion of cytokinesis, each daughter cell inherits one centrosome (a mother–daughter centriole pair). This ensures that each cell possesses the necessary center for microtubule organization in the subsequent cell cycle.

Next Interphase:

In the newly formed cells, the inherited daughter centriole matures throughout interphase. By the end of this maturation process, the daughter centriole acquires the capacity to function as a "mother" centriole. Consequently, the cell becomes prepared to duplicate its centrosome again in the next cell cycle.

Centrosome Duplication as a Semi-Conservative Process:

- Template-based procentriole formation begins during S phase.
- Procentrioles elongate and develop throughout S and G2 phases.
- During mitosis, centrosomes are pulled to opposite poles, establishing the spindle poles.
- After cytokinesis, each daughter cell inherits a mother–daughter centriole pair.

- In the subsequent interphase, the daughter centriole matures, and the cycle begins anew.

Polo-like Kinase 4 (PLK): PLK4 is the key regulator that ensures the correct number of centrosomes. It initiates centriole duplication at the end of G1 phase. PLK4 levels increase during the G1–S phase transition. PLK4 forms a ring structure that binds to the PCM on the outer circumference of the centrosome. It directly phosphorylates the STIL and SAS-6 proteins. This phosphorylation triggers STIL to anchor to the PCM and induces SAS-6 to form the cartwheel structure, leading to the formation of a new procentriole.

Positive Feedback and Self-Limitation: PLK4 recognizes itself via the SCF-βTrCP ubiquitin ligase complex (SCF–βTrCP), which mediates its ubiquitination. This ubiquitination prevents excessive accumulation of PLK4, ensuring that centriole duplication occurs only once. Low levels of PLK4 are still sufficient to phosphorylate the necessary proteins and initiate a new centrosome, whereas high levels trigger its auto degradation.

In summary, PLK4 functions both as an “initiator” and a “regulator”: it phosphorylates the proteins required for centriole duplication and promotes the formation of a new procentriole, while simultaneously controlling its own levels to guarantee that duplication occurs only once and at the correct time. Centrosome (centriole) duplication is a cell cycle–linked event, beginning in late G1/early S phase and completing by the end of mitosis (telophase–cytokinesis).

Table 1: Centrosome duplication across the cell-division phases.

Phases of The Cell Cycle	**Stages of Centrosome Duplication**
Late G1 - Early S	PLK4 is recruited to each existing mother centriole, phosphorylates STIL, and initiates the formation of a procentriole (a new “daughter” centriole) at the proximal side of each mother centriole.
S - G2	Procentrioles elongate as SAS-6, CPAP, Cep135, and other proteins assemble the nine-armed “cartwheel” structure and microtubule singlets. The mother–daughter centriole pair remains attached to the original centrosome.
Late G2 - Prophase	The two centrosomes (each now containing a mother–daughter pair) begin to separate, driven by motor proteins (dynein/kinesin) and the elongating spindle microtubules.
Prometaphase – Metaphase	Each centrosome functions as a spindle pole and initiates the formation of the bipolar spindle that aligns the chromosomes.
Anaphase – Telophase	The two centrosomes remain at opposite poles and maintain spindle organization.
Cytokinesis (Abscission)	After cytokinesis, the centrosomes are distributed to the two daughter cells. The daughter centriole of each pair matures into a new mother centriole and becomes ready for the next duplication cycle in the following G1 phase.

Table 1: Stages of centrosome division according to the phases of cell division.

Centrosome duplication begins in late G1/early S phase and is completed by the end of mitosis, ensuring that each daughter cell inherits a complete centrosome (consisting of one mother and one newly matured daughter centriole).

Diseases Arising from Centrosome Duplication Defects:

Errors in centrosome duplication are most commonly associated with cancer and neurodevelopmental disorders, and they also play a role in kidney diseases, cilia-related disorders, and certain genetic syndromes. If centrosome duplication and separation do not occur properly, severe problems arise during cell division. Each cell must contain only one centrosome pair, and during mitosis, these must segregate correctly to the spindle poles. Failure to do so disrupts proper chromosome segregation, leading to missegregation. This can result in aneuploidy, chromosomal instability, and tumor formation. Common clinical outcomes include:

1. Cancer: Amplified or mispositioned centrosomes generate multipolar spindles, producing aneuploid or tetraploid cells. This creates a basis for tumor initiation, progression, and resistance to therapy. Increased centrosome numbers (amplification) are observed in many solid tumors, including breast cancer, colon cancer, pancreatic cancer, and glioblastoma. In hematologic malignancies (e.g., leukemia), they can also contribute to chromosomal instability. (Mc Gee, 2015: Mazzoleni, 2024: Sinha, Duijf, & Khanna, 2019).

2. Microcephaly and Developmental Delay: Mutations in centrosome-associated checkpoint genes (e.g., Budding Uninhibited by Benzimidazoles 1 (BUB1), Mitotic Arrest Deficient 1-Like 1 (MAD1L1)) disrupt spindle assembly, reduce the proliferation of neural progenitor cells, and lead to severe neurodevelopmental disorders. This condition is often associated with high tumor predisposition syndromes. In diseases such as Primary Hereditary Microcephaly (MCPH), mutations in centrosomal proteins (e.g.,

Abnormal Spindle Microtubule Assembly (ASPM), Centromere Protein J (CENPJ), SCL/TAL1 Interrupting Locus (STIL)) impair the division of neural progenitor cells, resulting in a reduced brain volume. (Milan, 2025)

3. Mosaic Variegated Aneuploidy (MVA) Syndrome: Abnormal numbers of centrosomes can lead to incorrect chromosome segregation and, consequently, aneuploidy. As a result, affected individuals may exhibit growth retardation, early-onset cancers, and infertility in males. (Milan, 2025)

4. Organ-Specific Polyploidy: If cytokinesis fails due to centrosome defects, binucleated hepatocytes, the main functional cells of the liver, or cardiomyocytes can arise. Chronic polyploidy in these tissues predisposes them to liver disease and impaired cardiac function.

5. Premature Cellular Senescence: Excess centrosomes limit tissue regeneration and contribute to age-related decline. Microtubule and centrosome abnormalities have also been reported in aging and degenerative diseases, including neurodegenerative disorders such as Alzheimer's and Parkinson's disease. (Rani & Gupta, 2022)

Overall, improper centrosome duplication disrupts genomic stability and cell cycle regulation, linking a wide range of diseases from developmental disorders to cancer.

Endosome

Endosomes are dynamic membrane compartments that sort internalized cargo. Early endosomes receive material from the plasma membrane and mature to either recycling endosomes or late endosomes; late endosomes can fuse with lysosomes or return cargo to the Trans-Golgi Network (TGN). The shape and motility of

endosomes are tightly regulated by actin polymerization and microtubule-based motor proteins (dynein and kinesins).

During mitosis, the cell must distribute its organelles, including the endosomal system, to the two daughter cells. The division of endosomes is not a true fission event. Instead, endosomes are separated through a combination of microtubule-dependent transport, membrane remodeling, and Endosomal Sorting Complex Required for Transport (ESCRT)-mediated scission.

Figure-3: Early Endosomes.

Created in BioRender.com

Figure-4: Late Endosomes.

Created in BioRender.com

a. Reorganization of the endosomal network: In early prophase, the Endocytic Recycling Compartment (ERC) surrounding the nucleus fragments into smaller vesicles that are distributed throughout the cytoplasm. This dispersion occurs as dynein-dependent minus-end transport becomes inactivated during mitosis, while the Kinesin-1 and Kinesin-3 motors, which transport endosomes toward the cell periphery, are activated.

b. Microtubule-based separation: As the mitotic spindle forms, endosomes attach to the spindle microtubules through motor proteins (e.g., kinesin-1, dynein). The spindle acts as a scaffold that directs endosomal vesicles to each daughter cell. The spindle checkpoint ensures that an adequate endosomal load has reached both poles before cytokinesis begins.

c. ESCRT-III–mediated scission: During late telophase, the midbody contains ESCRT-III complexes that not only sever the plasma membrane but also remodel peripheral endosomal membranes. ESCRT-III can generate intraluminal vesicles (ILVs) within late endosomes, thereby effectively partitioning endosomal content between the daughter cells. (Wollert & Wunder, 2009)

d. Reformation of the ERC (Endosomal Recycling Compartment): After cytokinesis, the dispersed vesicles reassemble around the newly formed centrosomes, re-establishing the perinuclear ERC in each daughter cell. Therefore, the inheritance of endosomes relies not on a dedicated division mechanism, but on fragmentation, transport along the spindle by motor proteins, and ESCRT-dependent membrane remodelling. (Elia & Sougrat,2011)

The inheritance of endosomes differs from that of mitochondria and peroxisomes, as the latter undergo fission/fusion cycles, whereas endosomal networks fragment and disperse. Proper distribution of endosomes is critical because balanced transfer of receptors, signaling proteins, and membrane trafficking to the daughter cells is required during cell division. Additionally, literature indicates that endocytosis is temporarily suppressed during mitosis, so most endosomes focus on transport and reorganization.

The division of endosomes is not a true fission process; rather, it involves the equal distribution of endosomal membranes

and their contained vesicles between the two new cells throughout mitosis. This distribution begins during the M phase (particularly at the prophase–metaphase transition) and is completed during cytokinesis (telophase–abscission). (Noureddine, 2021) When examining the stages:

Prophase/Early Prometaphase: Early endosomes (EEs) and recycling endosomes (REs) move away from the centrosome along microtubules via dynein/kinesin motors. This movement directs the endosomes toward the cell poles, bringing them closer to the two emerging spindle poles.

Metaphase/Anaphase: Endosomes are pulled toward each spindle pole by spindle-associated motor proteins, ensuring that each pole receives an equal number of endosomal vesicles and membranes.

Telophase: As the nuclear membranes reassemble, endosomes gather within the newly formed perinuclear endosomal network (ERC).

Cytokinesis (Abscission): ESCRT-III spiral structures constrict the membranes, physically separating the two cells. During this stage, endosomal membranes are fully partitioned between the daughter cells. Once cytokinesis is complete, each daughter cell possesses its own endosomal system (early endosomes, recycling endosomes, late endosomes).

In summary, endosome distribution begins during the prophase–metaphase transition and concludes at cytokinesis (abscission), ensuring that membrane and signaling traffic are equally inherited by both daughter cells.

Diseases that may arise from problems in endosome partitioning:

If endosome division malfunctions, it can lead to neurodegenerative diseases, developmental syndromes, cancer, immune system disorders, and metabolic storage diseases. Diseases caused by defects in endosome division include:

1. Neurodegenerative diseases: Conditions such as Amyotrophic Lateral Sclerosis/Frontotemporal Dementia (ALS/FTD) and Alzheimer's disease are associated with mutations in endolysosomal genes; dysfunction of these genes is a critical driver of disease pathogenesis. (Todd & Shao, 2023) In Parkinson's disease, impairment of components such as clathrin-mediated synaptic endocytosis and the retromer complex component Vacuolar Protein Sorting 35 (VPS35) leads to dopaminergic neuron loss. Huntington's disease can also be included as an example. (Vidyadhara, Lee, & Chandra, 2019)

2. Peripheral neuropathy: Mutations in Ras-Related Protein Rab-7a (RAB7A) in Charcot-Marie-Tooth type 2B (CMT2B) patients lead to increased late endosomal protein levels and lysosomal activity, ultimately causing neurodegeneration. (Romano, 2021)

3. Developmental and intellectual disorders: Sodium/Hydrogen Exchanger 6 (NHE6) loss disrupts endosomal maturation and lysosomal function; this condition is associated with Christianson syndrome.(Pescosolido & Ouyang, 2021) WASH Complex Subunit 4 (WASHC4) (SWIP) mutation leads to endo-lysosomal pathway dysfunction and cognitive-motor impairments. (Courtland, 2021)

4. Movement disorders: Loss-of-function variants in Homotypic Fusion and Protein Sorting (HOPS) complex genes Vacuolar Protein Sorting 16 Homolog (VPS16) and Vacuolar Protein

Sorting 41 Homolog (VPS41) cause early-onset dystonia and lysosomal abnormalities. (Schreglmann & Bhatia, 2022)

5. Lysine storage diseases and related conditions: Neuronal Ceroid Lipofuscinosis (NCL), Gaucher disease, and other lysine storage diseases share a common pathomechanism involving disruption of retromer-dependent endosomal trafficking. (Schreglmann & Bhatia, 2022)

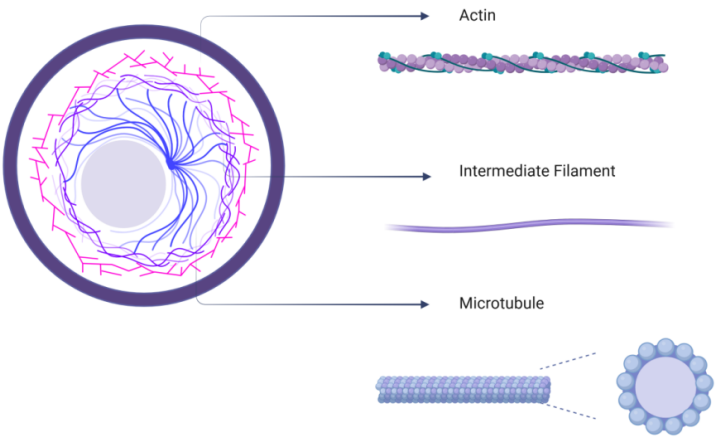
6. Muscle diseases: Early endosomal impairment and endolysosomal pathway dysfunction have been reported in the Duchenne muscular dystrophy model. (Chassagne, 2024)

These examples indicate that errors in endosome division trigger fundamental pathological processes across a wide spectrum of genetic, neurological, developmental, and metabolic disorders.

Cytoskeleton

The cytoskeleton is composed of microtubules, actin filaments, and intermediate filaments. Microtubules support long-distance transport, actin filaments facilitate short-range movements and membrane remodeling, and intermediate filaments provide structural resilience and organelle anchoring. Interactions among these filaments form a dynamic network that coordinates intracellular signaling, cargo sorting, and organelle positioning.

Figure-5: Cytoskeletal Elements.



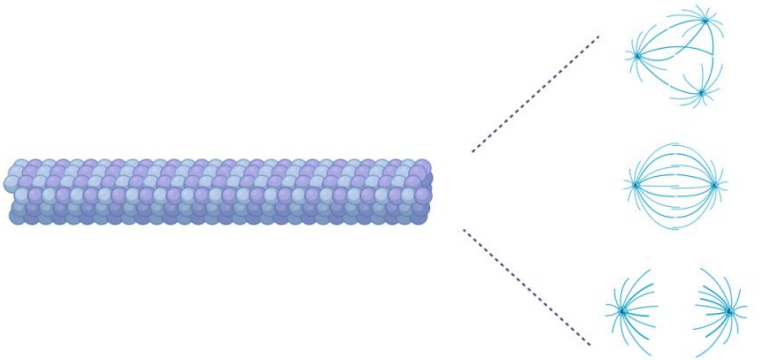
Created in BioRender.com

The cytoskeleton (microtubules, actin filaments, and intermediate filaments) is reorganized during cell division. It is not possible to speak of a complete division in the strict sense. When its subtypes are reviewed:

Microtubules: In prophase, the microtubule network disassembles and is replaced by the mitotic spindle apparatus. This structure captures the chromosomes and separates them toward the poles. Upon entry into mitosis, the interphase microtubule network rapidly breaks down, and the γ-tubulin–containing ring complexes in the centrosomes form nucleation centers for short microtubules extending toward the chromosomes. Kinesin-5 (EG5) pushes antiparallel microtubules apart, while dynein pulls them inward, thereby generating a bipolar spindle. Kinetochores capture the microtubule plus ends and convert them into kinetochore fibers, pulling chromosomes toward the poles during anaphase. After segregation, microtubules reorganize into the interphase network again in each daughter cell. In telophase, the spindle structure

disassembles and the normal microtubule network is re-established. (Alberts, 2002)

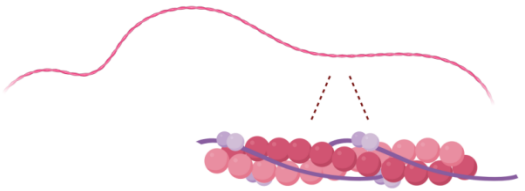
Figure-6: Microtubule Division.



Created in BioRender.com

Actin filaments: During cytokinesis, an actin–myosin ring forms at the center of the cell. This ring contracts, pulling the cell membrane inward and separating the two daughter cells (cleavage). Simultaneously, the actin cortex is reorganized: Ras Homolog Family Member A(RhoA) activation at the equatorial region recruits formins and myosin-II, generating a dense actin–myosin network just beneath the plasma membrane. Myosin-II motor activity produces tension, constricting the ring, pulling the cleavage furrow inward, and ultimately dividing the cell into two. Septin filaments and actin-binding proteins (e.g., α-actinin) crosslink the filaments and ensure the stability of the contractile structure. (Lancaster & Baum, 2014)

Figure-7: Actin Filaments.



Created in BioRender.com

Intermediate filaments: During prophase, they are phosphorylated by Cyclin-Dependent Kinase 1 (CDK1)/ Regulatory Cyclin B (Cyclin B), which causes their disassembly and allows the nuclear envelope to break down. In telophase, they become de-phosphorylated again and reassemble into a network beneath the newly forming nuclear envelope. Mitotic kinases phosphorylate vimentin, lamins, and other intermediate filament proteins, leading to filament disassembly. This permits the spindle to access the chromosomes and prevents obstruction of chromosome movements. In telophase, phosphatases dephosphorylate these proteins, enabling the filaments to repolymerize around the newly formed nuclei and within the cell cortex. (Ritter & Kreis, 2022)

As a result, the cytoskeleton is a dynamic structure that disassembles and reorganizes during cell division. It coordinates both chromosome movements and cytokinesis to separate the cell into two daughter cells. The three filament systems work together:

1. Microtubules form the bipolar spindle that separates the chromosomes.
2. Actin enables the cleavage furrow to constrict during cytokinesis.
3. Intermediate filaments provide structural stability and are reassembled after division is completed.

Prophase (early): The interphase microtubule network rapidly disassembles. The γ-tubulin ring complexes at the centrosomes nucleate short microtubules that will form the mitotic spindle. The actin cortex begins to soften, and RhoA is inactivated at the cell equator.

Prometaphase/Metaphase: A bipolar spindle forms; kinetochores capture microtubule plus ends and establish stable kinetochore fibers. The components that will form the actomyosin contractile ring (formin-derived actin filaments and non-muscle myosin-II) begin to accumulate at the future division site, but the ring is not yet active.

Anaphase: Microtubules shorten (depolymerization at the kinetochores) and slide toward the poles, segregating the chromosomes. At the same time, RhoA is reactivated at the equatorial region, initiating the assembly of actin-myosin filaments that will drive furrow formation.

Telophase: The spindle disassembles, and microtubules reorganize into an interphase-like network in each daughter cell. The actomyosin contractile ring is now fully established and begins to constrict the cleavage furrow.

Cytokinesis (Abscission): The contractile ring tightens, the plasma membrane ingresses, and the ESCRT-III complex severs the intercellular bridge. Intermediate filament networks (lamins, vimentin) are re-phosphorylated and reorganize around the newly forming nuclei.

Cytoskeletal reorganization begins in prophase (disassembly of the interphase microtubule array and initial changes in the actin cortex) and completes with cytokinesis/abscission; the actomyosin contractile ring drives furrow constriction, and spindle microtubules become fully re-established in the new daughter cells. (Alberts, 2002)

Diseases associated with improper cytoskeletal function during cell division;

They are based on genetic and cellular pathomechanisms arising from the failure to maintain the correct timing and structural integrity of the cytoskeleton during division.

1. Microtubules: Errors in spindle assembly and chromosome segregation. Cancer (chromosomal instability, tumor development), microcephaly and neurological developmental disorders (Abnormal Spindle Microtubule Assembly (ASPM), Centrosomal Protein 152 (CEP152) mutations), mosaic variegated aneuploidy (MVA) syndrome.

2. Actin-myosin rings: Cytokinesis defects, failure to complete nuclear division during cell division. Embryonic lethality and congenital anomalies (actin-associated protein mutations), cardiomyopathy (β-actin, Myosin Heavy Chain 7 (MYH7) mutations), and muscular dystrophies (loss of actin-associated proteins).

3. Intermediate filaments: Cell shape alterations and loss of mechanical stability, disruption of nuclear positioning during division. Epidermolysis bullosa (keratin mutations), neurological disorders (developmental defects associated with vimentin deficiency). (Ritter & Kreis, 2022)

Centrosome, endosome, and cytoskeletal division help us understand how cells distribute their organelles and membranes to newly forming daughter cells. This clarifies our understanding of how cellular function and vital integrity are maintained. Because disruptions in these processes can lead to cancer, neurodegenerative diseases, developmental syndromes, and immune or metabolic disorders, understanding their mechanisms contributes to the diagnosis and treatment of various diseases. In addition, detailed knowledge of these pathways can reveal potential drug targets that

correct division errors or modulate organelle inheritance. While helping us understand how cells coordinate growth, differentiation, and tissue formation, examining endosomal distribution explains how signaling proteins, receptors, and membrane components are properly transferred, contributing to the maintenance of cellular homeostasis. Therefore, studying these processes allows us to deeply understand fundamental cell biology and provides important insights into disease mechanisms and therapeutic strategies.

References

Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2002). How Cells Regulate Their Cytoskeletal Filaments. In *Molecular Biology of the Cell* (4th edition ed.). New York: Garland Science.

Chassagne, J., Da Silva, N., Akrouf, I., Cadot, B., Julien, L., Barthélémy, I., ... & Benkhelifa-Ziyyat, S. (2025). Early endosome disturbance and endolysosomal pathway dysfunction in Duchenne muscular dystrophy. *The American Journal of Pathology*.

Courtland, J. L., Bradshaw, T. W., Waitt, G., Soderblom, E. J., Ho, T., Rajab, A., . . . Soderling, S. H. (2021). Genetic disruption of WASHC4 drives endo-lysosomal dysfunction and cognitive-movement impairments in mice and humans. *Elife, 10*. doi:10.7554/eLife.61590

Elia, N., Sougrat, R., Spurlin, T. A., Hurley, J. H., & Lippincott-Schwartz, J. (2011). Dynamics of endosomal sorting complex required for transport (ESCRT) machinery during cytokinesis and its role in abscission. *Proc Natl Acad Sci U S A, 108*(12), 4846–4851. doi:10.1073/pnas.1102714108

Lancaster, O. M., & Baum, B. (2014). Shaping up to divide: coordinating actin and microtubule cytoskeletal remodelling during mitosis. *Semin Cell Dev Biol, 34*, 109–115. doi:10.1016/j.semcdb.2014.02.015

Mazzoleni, A., Awuah, W. A., Sanker, V., Bharadwaj, H. R., Aderinto, N., Tan, J. K., . . . Papadakis, M. (2024). Chromosomal instability: a key driver in glioma pathogenesis and progression. *Eur J Med Res, 29*(1), 451. doi:10.1186/s40001-024-02043-8

Mc Gee, M. M. (2015). Targeting the Mitotic Catastrophe Signaling Pathway in Cancer. *Mediators Inflamm, 2015*, 146282. doi:10.1155/2015/146282

Milan, M. (2025). Chromosomal instability in development and disease: Beyond cancer evolution. *Curr Opin Cell Biol, 95*, 102537. doi:10.1016/j.ceb.2025.102537

Nigg, E. A., & Stearns, T. (2011). The centrosome cycle: Centriole biogenesis, duplication and inherent asymmetries. *Nat Cell Biol, 13*(10), 1154–1160. doi:10.1038/ncb2345

Noureddine, A., Paffett, M. L., Franco, S., Chan, A. E., Pallikkuth, S., Lidke, K., & Serda, R. E. (2021). Endolysosomal Mesoporous Silica Nanoparticle Trafficking along Microtubular Highways. *Pharmaceutics, 14*(1). doi:10.3390/pharmaceutics14010056

Pescosolido, M. F., Ouyang, Q., Liu, J. S., & Morrow, E. M. (2021). Loss of Christianson Syndrome Na(+)/H(+) Exchanger 6 (NHE6) Causes Abnormal Endosome Maturation and Trafficking Underlying Lysosome Dysfunction in Neurons. *J Neurosci, 41*(44), 9235–9256. doi:10.1523/jneurosci.1244-20.2021

Prigent, C. (2025). Centriole Duplication at the Crossroads of Cell Cycle Control and Oncogenesis. *Cells, 14*(14). doi:10.3390/cells14141094

Prigent, C., & Uzbekov, R. (2022). Duplication and Segregation of Centrosomes during Cell Division. *Cells, 11*(15). doi:10.3390/cells11152445

Rani, B., Gupta, D. K., Johansson, S., & Kamranvar, S. A. (2022). Contribution of integrin adhesion to cytokinetic abscission and genomic integrity. *Front Cell Dev Biol, 10*, 1048717. doi:10.3389/fcell.2022.1048717

Ritter, A., & Kreis, N. N. (2022). Microtubule Dynamics and Cancer. *Cancers (Basel), 14*(18). doi:10.3390/cancers14184368

Romano, R., Rivellini, C., De Luca, M., Tonlorenzi, R., Beli, R., Manganelli, F., . . . Bucci, C. (2021). Alteration of the late endocytic pathway in Charcot-Marie-Tooth type 2B disease. *Cell Mol Life Sci, 78*(1), 351–372. doi:10.1007/s00018-020-03510-1

Schreglmann, S. R., & Bhatia, K. P. (2022). HOPS-Associated Neurological Disorders: Lysosomal Dysfunction as an Emerging Concept Underlying Dystonia. *Mov Disord Clin Pract, 9*(4), 452–453. doi:10.1002/mdc3.13405

Sinha, D., Duijf, P. H. G., & Khanna, K. K. (2019). Mitotic slippage: an old tale with a new twist. *Cell Cycle, 18*(1), 7–15. doi:10.1080/15384101.2018.1559557

Srsen, V., & Merdes, A. (2006). The centrosome and cell proliferation. *Cell Div, 1*, 26. doi:10.1186/1747-1028-1-26

Todd, T. W., Shao, W., Zhang, Y. J., & Petrucelli, L. (2023). The endolysosomal pathway and ALS/FTD. *Trends Neurosci, 46*(12), 1025–1041. doi:10.1016/j.tins.2023.09.004

Vidyadhara, D. J., Lee, J. E., & Chandra, S. S. (2019). Role of the endolysosomal system in Parkinson's disease. *J Neurochem, 150*(5), 487–506. doi:10.1111/jnc.14820

Wollert, T., Wunder, C., Lippincott-Schwartz, J., & Hurley, J. H. (2009). Membrane scission by the ESCRT-III complex. *Nature, 458*(7235), 172–177. doi:10.1038/nature07836

ORGANELLE DIVISION IN EUKARYOTES