**Option 2: Research Report on Mitosis & Disease**

Research Question: Why doesn’t chemotherapy work the same for all cancers that target mitosis?

## Introduction

Mitosis is a process where cell division takes place. Cell division results in two identical daughter cells that come from a single parent cell. The cell copies all its chromosomes during a phase that takes place before mitosis known as the interphase. This phase is responsible for making sure that the daughter cells will contain the full set of chromosomes. Making sure each daughter cell contains 46 chromosomes (23 pairs) genetically identical to their parent cell. After this phase, mitosis takes place. There are four phases to mitosis. Prophase, metaphase, anaphase and telophase. After mitosis takes place, a phase known as cytokinesis occurs which is responsible for dividing the cytoplasm, separating the daughter cells, and essentially completing the whole process of cell division.

Mitosis is very important for the growth and repair of skin tissues, muscles and organs, ensuring internal stability. Errors like chromosomal missegregation, which is when there are too many or too few chromosomes due to the incompleteness of cell division, could lead to diseases, genetic disorders and cancer. According to researchers at the University of [Amsterdam’s Center for Reproductive Medicine](https://academic.oup.com/biolreprod/article-abstract/89/2/42,%201-7/2514219?redirectedFrom=fulltext&login=false&utm_source=chatgpt.com), as a human embryo develops, the number of diploid cells which are normal cells increase indicating that some abnormal cells are lost or corrected as time passes. This indicates that embryos have the natural ability to fix errors as they grow. The research also leads on to state that mitotic errors are most frequent early on in human embryos. The errors happen the most during the first three cell divisions after the embryos fertilized. Cancer is an outcome of mitotic errors and while chemotherapy is the most known treatment for cancer patients, not all types of cancer respond to chemotherapy the same way. This leads me to state my research question: *“Why doesn’t chemotherapy work the same for all cancers that target mitosis?”*

## Molecular Mechanisms of Mitosis

As we know, mitosis is the process in which cell division takes place to produce two daughter cells which are genetically identical to their parent cell. This process goes through 4 different phases. Prophase, metaphase, anaphase, telophase and then followed by the final stage which is cytokinesis. During early stages of the first phase, prophase, which is the longest out of the four phases, the cell starts to break down and build up some structures preparing for cell division. This is where the mitotic spindle starts to form. The proteins cyclin and CDKs (cyclin-dependent kinases) activate proteins that help start the process where the spindle is formed. The spindles are made up of microtubules which as we know are strong fibers. There are three types of microtubules that make up the mitotic spindle. The kinetochore microtubules which attach to the chromosomes and pull them apart, astral microtubules, help position the mitotic spindle when in the cell. Interpolar microtubules are responsible for removing the two halves of the cell apart. The mitotic spindle's job is to position the chromosomes accordingly and move them during mitosis. Prophase is also when the chromatin condenses forming chromosomes. Once these chromosomes form, they consist of two sister chromatids which are held together by a centromere. The centromere is responsible for keeping the two sister chromatids linked and can be referred to as a magnet. Then, the nucleolus, which is a small structure inside the nucleus disappears, and the nuclear membrane which is the outer shell of the nucleus that keeps the DNA inside starts to break down. Now, the mitotic spindle starts to shape.

In the second stage, the metaphase, the chromosomes are now fully condensed and align themselves in the center of the cell. This alignment is important and is to ensure that each daughter cell will receive a full and identical set of chromosomes. A checkpoint known as the spindle assembly checkpoint makes sure the cell doesn’t progress to the next phase until each chromosome is set and ready. If anything goes wrong in this checkpoint, it could lead to the chromosomes being distributed unevenly which can cause the cell to malfunction and furtherly cause diseases.

Anaphase, which is the shortest phase of mitosis, allows the centromere which holds the sister chromatids together to split. This gives the spindle fibers the ability to pull the chromatids apart to separate ends of the cell with the help of the proteins known as dynein and kinesin. Now the chromatids are no longer chromatids but separated chromosomes. The chromosome's movement to opposite ends of the cell is due to the shortening of spindle microtubules. These microtubules retract and draw the chromosomes towards them. During this stage the cell also elongates since microtubules push against each other which only further supports the separation of the chromosomes.

The fourth and final step is known as telophase, where cell division begins to conclude. During telophase the chromosomes begin loosening and turning into chromatins again. This is to make them less tightly packed together and easier for the cell to work with. Though it is tight during cell division to make it easier to separate genetic material correctly, once that's done the cell doesn’t need them to be so tight anymore. The change back to chromatin gives the cell the ability to function normally. At the same time, two new nuclei begin forming on the cell's opposite sides. This is because each set of chromosomes triggers the nuclear envelope. The nuclear envelope is made up of two layers of molecules that form a protective barrier around the DNA. This helps keep the DNA inside the cell separate from the rest of the cell. It surrounds the nuclei to begin rebuilding which leads to the formation of two different nuclei.

After the formation of the two nuclei during telophase, it means the start of cytokinesis, the final step of cell division. Cytokinesis is when the cytoplasm is separated and results in the two daughter cells. In humans, animal cells, the cytoplasm is separated when a cleavage furrow forms.This formation happens because a structure made of something known as actin filaments becomes tight which then leads to the pull of the membrane inward. The furrow goes in deeper and deeper until the cell splits into two separate daughter cells. Each daughter cell has its own nucleus and cytoplasm. This ensures proper replication of the daughter cells.

## Mitosis & Disease

## Cell division going wrong which causes mitotic errors are an obvious lead to why humans can develop diseases like cancer. These errors happen when the chromosomes haven’t been divided correctly between the two daughter cells. This can lead to something known as aneuploidy, when cells have one too many or one too few chromosomes. This affects the cell majorly which could lead to abnormal cell growth. This means it could turn into a cancerous cell causing it to divide abnormally eventually forming a tumor.

In the medical field, chemotherapy is the most known method to treat cancers that are products of mitotic errors. The drugs used in chemotherapy work in a way that they’re interfering at certain stages and points where cell division is happening. A study published by an author from [The Institute of Biomedical Materials and Engineering, College of Materials Science and Engineering](https://pmc.ncbi.nlm.nih.gov/articles/PMC8267727/#sec3-ijms-22-06923) in China says that the S phase (synthesis phase) which is where photosynthesis takes place as well as where the cell replicates the entire genetic material is what stage chemotherapists interfere and what they target to avoid the cancer cells from multiplying. They continue to explain that after the S phase the cell enters a phase known as the G2 phase which is the final stage before mitosis. In this stage the cell continues to grow producing the proteins needed for mitosis and checks for any errors in the duplicated DNA. This phase is responsible for ensuring the cell is ready to now divide properly. Some drugs specifically aim for the mitotic spindle which denies the chromosomes the ability to align properly in the centre of the cell which causes the cells to die. Though chemotherapy can sometimes be effective and cure cancer patients, not all types of cancers respond in the same way. Knowing what the exact mitotic error is and where or in which phase exactly it occurs would help doctors be able to target the cancerous cells better which might increase the chances of the chemotherapy being successful on the patient.

## Case Study & Data Analysis

As we know by now, cancer progresses when cell division goes wrong and loses control. These mistakes can lead to the cells gaining an abnormal number of chromosomes, leading to aggressive tumor growth and failure of treatment. My case study focuses on analyzing how mitotic errors contribute to the progression and development of lung cancer and skin cancer which is also known as melanoma and how their progression affects the success rate of chemotherapy.

Lung cancer, which is known to be one of the most common and most severe cancers, is usually linked with smoking and environmental factors that harm DNA. Mitotic errors happen when aneuploid cells which are cells with an abnormal number of chromosomes grow as a result of failed mitotic checkpoints.

MAD2 and BUB1 are malfunctioning spindle assembly checkpoint proteins that fail to allow the proper separation of chromosomes during cell division. An increased rate of chromosomal instability is caused by this malfunction. In chemotherapy, medicines like paclitaxel attack rapidly dividing cancer cells by destroying microtubules during mitosis. But because of chromosomal instability, certain cancer cells are able to get used to the stress that these medications carry within them, which helps them survive treatment and even become immune to chemotherapy.

The main cause of melanoma, which is skin cancer, compared to lung cancer, is UV exposure. UV exposure, which can be the ultraviolet radiation released from the sun in an excessive amount, results in genetic mutations in important mitotic regulators like BRAF. BRAF is a gene that carries a protein that is a part of the regulation of cell growth. A BRAF regulator is any factor that influences its activity, either helping it or going against it. Disregarding the possibility of chromosomal instability, melanoma cells often rely on multiple growth ways rather than severe chromosomal instability which appears in lung cancer.

A scientific paper is published in the [American Cancer Society Journal, A Cancer Journal for Clinicals](https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21820) annually. These annual reports give information on estimated numbers of cancer cases and death corresponding with that year by cancer type and U.S state. It explains symptoms, risk factors and treatment as well. The data is reliable and accurate since it is sourced from national cancer registries known as National Cancer Institute and the National Program of Cancer Registries.

After analyzing the study, it showed that lung cancer remains the deadliest cancer in both men and women. In 2024, an estimated number of 107,890 men and 109,510 women were diagnosed with lung cancer. But the number of deaths is higher in men with 67,160 deaths whereas for women it is 60,860. The number for new cases is also higher in women which could be a result of factors like increased smoking habits, being exposed to secondhand smoking alot and genetic factors too. Even when considering this information, men still have a higher death rate which can be because of historically higher smoking rates, differences in how lung cancer develops biologically between men and females, and also different responses to treatment. Detecting lung cancer early is the main reason for increased survival rates but lung cancer has one of the lowest survival rates since it's hard to diagnose at early stages and is usually diagnosed too late for prevention.

Melanoma is also one of the most common cancers especially in places with high UV radiation. In 2024, around 60,170 cases of melanoma were diagnosed in men which ended up in around 8,290 deaths. Between women, the cases are a bit lower, having 46,170 diagnoses and 3,450 deaths. Melanoma patients are well above average in states with high exposure and certain populations. Also, skin cancer is said to be 20 times more common in white people than in black. For example, one of the states in America according to the study, Utah, has a high amount of fair skinned people and also high UV exposure which might be the reason as to why there was a high number of people diagnosed with melanoma in that area in 2024. In 2021 Utah had the highest reported cases of melanoma with an estimated 46 people out of 100,000 according to a report published by [John Elflein](https://www.statista.com/statistics/663616/skin-cancer-incidence-rate-in-us-by-state/#:~:text=In%202021%2C%20Utah%20had%20the,by%20state%2C%20per%20100%2C000%20population.).

Chemotherapy effectiveness is different between lung cancer and melanoma because of differences in mitotic checkpoint failure. Melanoma is mainly caused by mutations in mitotic regulators like BRAF, whereas lung cancer is mainly caused by chromosomal instability (CIN). Identifying these differences helps in creating better suited cancer treatments, compared to chemotherapy that is meant to treat all types of cancers. The comparison between lung cancer and melanoma shows how chemotherapy that attacks mitotic errors is not effective for all cancers, highlighting the importance of personalized medicine in cancer.

## Future Applications

Mitotic therapy is a developing field of cancer treatment that focuses on cell division to avoid cancer cells from spreading uncontrollably. Researchers are developing inhibitors for mitotic regulators like Mps1 and Aurora kinases which cause chromosomal separation abnormalities and cancer cell death. Another possibility is to use spindle assembly inhibitors, including Kinesin-5 (Eg5) and Polo-like kinase 1 (Plk1) inhibitors, which interrupt mitotic processes and prevent tumor growth. Microtubule-targeting medications, like paclitaxel, are also being improved to minimize side effects. Also, mitotic therapy stimulates mitosis in cancer cells with DNA damage which leads to the cell's death when paired with drugs like radiotherapy or PARP inhibitors.

A new study published in June 2024 by [Biomed Central](https://celldiv.biomedcentral.com/articles/10.1186/s13008-024-00125-x?utm_source=chatgpt.com), involves artificial intelligence and customized medicine into mitotic treatment. Artificial intelligence helps in creating specific treatments based on a patient's genetic history which leads to improved outcomes and personalized therapy. Plus, combined medications that pair mitotic inhibitors with immunotherapy show potential for making cancer cells less resistant to immune system attacks. These improvements show mitotic therapy's potential for improving cancer treatment while reducing harm to healthy cells.

## Citations

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