

Science Education Collection

An Introduction to Cell Division

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Abstract

Cell division is the process by which a parent cell divides and gives rise to two or more daughter cells. It is a means of reproduction for single-cell organisms. In multicellular organisms, cell division contributes to growth, development, repair, and the generation of reproductive cells (sperms and eggs). Cell division is a tightly regulated process, and aberrant cell division can cause diseases, notably cancer.

JoVE's Introduction to Cell Division will cover a brief history of the landmark discoveries in the field. We then discuss several key questions and methods, such as cell cycle analysis and live cell imaging. Finally, we showcase some current applications of these techniques in cell division research.

Transcript

Cell division is a process by which one cell produces two or more daughter cells. Unicellular organisms, like yeast, reproduce by cell division, whereas multicellular organisms, like us, use the same process to develop, grow, and maintain our tissues. Knowledge of what controls normal cell division is critical to understanding how disruption of this phenomenon can initiate pathological processes.

This video presents a brief history of discoveries in the cell division field, highlights key questions asked by cell biologists, reviews prominent tools being used, and showcases some present-day applications.

Let's start by reviewing some landmark studies that laid the foundation of cell division research.

The existence of cells was first reported in the 1600's by Anton van Leeuwenhoek and Robert Hooke. Empowered by innovations in microscopy, they pulled back the veil on the invisible microscopic world. The first observation that cells could divide was made in the 1830's by two botanists, Barthélemy Dumortier and Hugo von Mohl, who discovered that one plant cell can give rise to two by dividing. Following this discovery, in 1838, a botanist—Matthias Jakob Schleiden—and a physiologist—Theodor Schwann—observed similarities in plant and animal cells. This led Schwann to postulate the two tenets of cell theory, first: "all living organisms are composed of one or more cells"; second: "cells are the basic building blocks of all life." Nearly twenty years later, a physician named Rudolf Virchow published the third tenet of cell theory, which stated: "all cells arise from preexisting cells."

In 1876, Walther Flemming, while viewing cell division, observed separation of thread-like structures. Therefore, he coined the term "mitosis," derived from the Greek word *mitos* meaning thread. Later on, Edouard Van Beneden and Theodor Heinrich Boveri discovered that those threads are actually chromosomes, which are being divided with the help of microtubules arising from structures now known as centrosomes. Beneden, along with Oscar Hertwig and August Weismann, also explained meiosis—a different type of division that produces cells like gametes. They showed that meiosis, unlike mitosis, involves one round of DNA replication but two rounds of cell division, resulting in halving of the chromosome number from the parent to the daughter cells.

In the latter half of the twentieth century, scientists became interested in regulation of the cell cycle, a process in which a cell passes through a series of phases leading to its division. One of the most important discoveries in this field came in 1972 from Leland Hartwell and colleagues. Using yeast strains, they demonstrated that there are genes that play an important role in guiding cells through the cell cycle stages, and Dr. Hartwell named them as the cell division cycle genes or "cdc's."

Another discovery came in 1983 by Tim Hunt, who was studying sea urchins. He identified proteins that oscillate in their abundance in synchrony with the cell cycle phases. Due to their oscillatory nature, he named these proteins as "cyclins," and now we know that cyclins are key regulators of the cell cycle. Four years later, Sir Paul Nurse and colleagues showed that cdc genes, in particular *cdc2*, was highly conserved between yeasts and humans. Together, these discoveries significantly increased our understanding of cell division, and thus were well deservedly rewarded with a Nobel Prize in 2001.

Now that we've reviewed some historical highlights, let's examine a few fundamental questions facing the field of cell division today.

We'll begin with perhaps the broadest question in cell division: what genes and intracellular signaling pathways regulate the cell cycle? It is known that duplication and division are controlled by a series of biochemical switches that activate or deactivate the cell cycle processes. Researchers are working to shed more light on the molecules that influence the progression or inhibition of the cell cycle.

Biologists are also interested in identifying the extracellular factors that stimulate or inhibit cell division. Cells may increase cell division in response to external chemical cues called mitogens. Scientists are working to understand what external cues stimulate or inhibit cell division.

Abnormal cell division can lead to increased or decreased cell proliferation. Increased cell proliferation causes diseases like cancer. Researchers have discovered that mutations in certain genes known as oncogenes is involved in initiation of cancer. In addition, scientists have also discovered several proteins that play a critical role in tumor progression. However, several tumor-causing factors still remain unknown, and biologists are striving hard to reveal them.

Now that you have a feel for some of the unanswered questions, let's look at a few research tools biologists use to find answers.

In a mixture of actively dividing cells, the proportion of cells that exist in each phase of the cell cycle can be determined by cell cycle analysis. This is done with the help of special dyes, like bromodeoxyuridine or BrdU. It is a thymidine analog and incorporates itself in the newly synthesized DNA strand during DNA replication. Hence, it labels S phase cells only. On the other hand, fluorescent compounds like propidium iodide (PI) stain all of the DNA, but the amount of PI bound can help distinguish between cells in different phases. The final step is to analyze the stained cells using flow cytometry, and data obtained reveals distribution of cells amongst different cell cycle stages.

Advances in imaging techniques now facilitate direct observation of cell division. Scientists can now stain cells using fluorescein dyes, or perform genetic manipulation to induce expression of fluorescent proteins. Following this, they can directly observe live cells dividing using time-lapse microscopy.

Lastly, scientists have also devised a way to quantify the number of divisions that specific cells undergo within a mixed cell population. This is done by using “quantifiable tracking dyes.” These dyes are useful because the signal they generate becomes dimmer as it’s diluted through cell division. The diminishing fluorescence intensity can be used to identify cells in different generations. In addition, the difference between the highest and the lowest fluorescence intensity can provide insight into how many times the cells underwent division.

Now that you’re familiar with some common approaches to studying cell division, let’s look at how these methods are being applied.

As discussed earlier, genes play a major role in cell cycle control. Here, scientists studied the effect of genetic mutation on cell division in *Drosophila* larvae. They performed genetic crosses to produce flies with specific mutations, and then using cell cycle analysis observed the effects of the mutation within the developing wing tissue.

Using fluorescence microscopy, scientists can also directly observe how drugs affect cell division in cancer. In this experiment, researchers were interested in determining how a potential drug, JP-34, affected cancer cell division. Results showed that cancer cells treated with JP-34 underwent mitotic failure and cell death.

Finally, scientists use tracking dyes to identify differences in cell proliferation rates. Here, they employed a quantifiable tracking dye that labels cell membranes to study differences in cell division of various immune cells. The flow cytometry data analysis revealed that the proliferation rate differs between different types of immune cells.

You’ve just watched JoVE’s introduction to cell division. In this video we reviewed some of the major discoveries in cell division, key questions being asked by cell biologists today, prominent tools employed in cell division labs, and their current applications. As always, thanks for watching!