Application Note

Microscopy of Cells in Medical and Biology Studies

Basics of cell biology

ZEISS

Seeing beyond

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Single-celled microorganisms and highly specialized plants and animals have one thing in common: they consist of cells, the smallest modules within living organisms. Cell biology deals with the fascinating world of cells. Students learn about the basics of cell theory and discover the origin of cells and how diverse they are. They acquire knowledge of the similarities and differences in cell structure, cell construction and how the cells function. In addition, questions are answered about, for example, the way in which cells produce energy, how they synthesize new molecules, how cells communicate and multiply, and how cells survive or die.

The microscope is one of the most important tools in cell biology. Microscopy is used to visualize cells in great detail, which then makes visible any biological processes at the cellular level. Cell biology research is an important prerequisite, for example, in the early detection of uncontrolled cell growth in instances of cancer, and for researching the development and treatment of cancer.

Introduction

Cell biology plays an important role in the study of medicine and biology. The aim is to acquire basic knowledge of cell biology and to learn about important organic molecules and their synthesis. Students learn about how cells and cell organelles are structured and how they function, how plant and animal cells are constructed and what the characteristics are that mark them, how cell division, cell growth and communication between cells takes place, and what leads to cells dying. Basic knowledge of cell biology is a prerequisite for work in biomedical research.

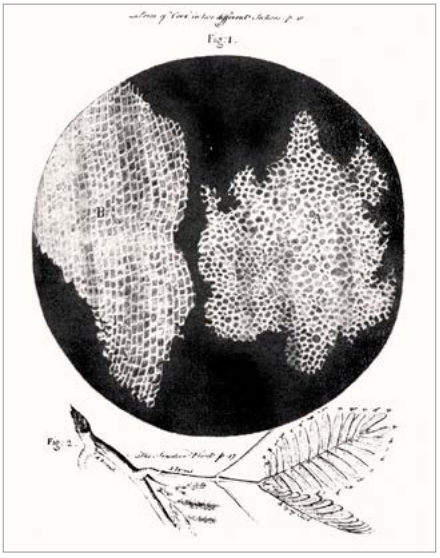

Image 1 *Suber cells and mimosa leaves Robert Hooke, Micrographia, 1665*

The history of cell biology

The English scholar Robert Hooke is credited with making the first drawings of cells in 1665. He drew a thin cage-like disc, the chambers of which he described as microscopic "pores" and "cells" [1].

Studies by Matthias Schleiden and Thomas Schwann further developed cell biology theories, which were finally concluded by Robert Virchow through his formulation *"Omnis cellula e cellula"*, or "Every cell derives from another cell", in 1850 [2].

The further development of cell theory was closely linked to the further development of microscopes, since the increasing resolving power of the equipment gradually made it possible to gain more detailed insights into the interior of the cell.

Microscopes are key tools in cell biology

Since most cells are tiny at less than 100 µm, it is not possible to have an insight into the cell interior with the naked eye. In addition, cells are usually colorless, making light microscopes into important tools.

Image 2 *The development of cells began approximately four billion years ago with prokaryotes; these were simply structured cells that did not have cell nuclei. They include bacteria and archaea. As time went on, cells with cell nuclei formed – the eukaryotes.*

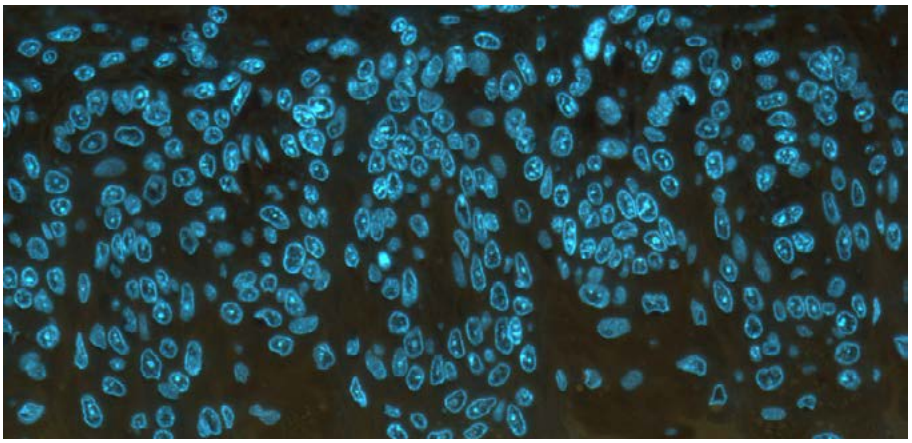

Figure 3 *In the fluorescence microscope, DAPI-labeled cell nuclei are illuminated blue against a dark background (rat's tongue, 40×)*

Light microscopes with phase contrast are ideal for thin, unstained cells where the human eye can barely perceive differences in brightness. Inside cells, there are different refractive indices between the cell nucleus and cytoplasm, thereby allowing light waves to be shifted by small degrees as they travel through the cell interior.

As a result of this, a light wave which has passed through a cell nucleus remains behind the light waves that pass through the cytoplasm. The level of "delay" is called a phase shift. Before entering the cell, the waves are still "in phase"; this is no longer the case once they have passed through the various cell components. It is not possible for the human eye to recognize these phase shifts. It can only distinguish between different intensities and colors. The phase contrast method therefore uses optical tricks to turn phase shifts into gray values.

A further possibility for visualizing colorless cells is fluorescence microscopy. The dyes selected for this purpose form selective bonds with different cell components. The special feature of fluorescent dyes is that their individual molecules are able to absorb light of a specific excitation wavelength for an extremely short time – usually billionths of a second – and then emit it again. The light that is emitted is specific to each fluorescent dye and is usually within the range of blue, green or red wavelengths. This effect is very useful in terms of microscopy because the illuminators become visible in the microscope image and precisely indicate which cell components are associated with the dye. The fluorescent dye DAPI, for example, binds to cell nuclei. In the fluorescence microscope, DAPI-labeled cell nuclei are illuminated blue against a dark background [3].

By using electron microscopes, it is possible to achieve an even more detailed resolution. The shorter-wavelength electron beams enable the resolution to be increased by 2000 times, meaning that the tiniest of cell structures become visible, right down to a size of 0.5 nm.

Microscopy with students

When undertaking microscopy courses at schools and universities, students usually work with light microscopes. Fresh preparations are made for this by preparing plant or animal material.

A popular starter preparation when using a microscope on plant cells is the membrane of a kitchen onion (*Allium cepa*). To prepare a fresh wet specimen, any dry outer onion skins are removed. Using a scalpel, a small square (approx. 0.5 cm edge length) is scratched into the epidermis of the onion skin, which is carefully removed with tweezers and positioned on a slide using distilled water. The thinner the onion skin, the easier it is to see the cell structure under the microscope.

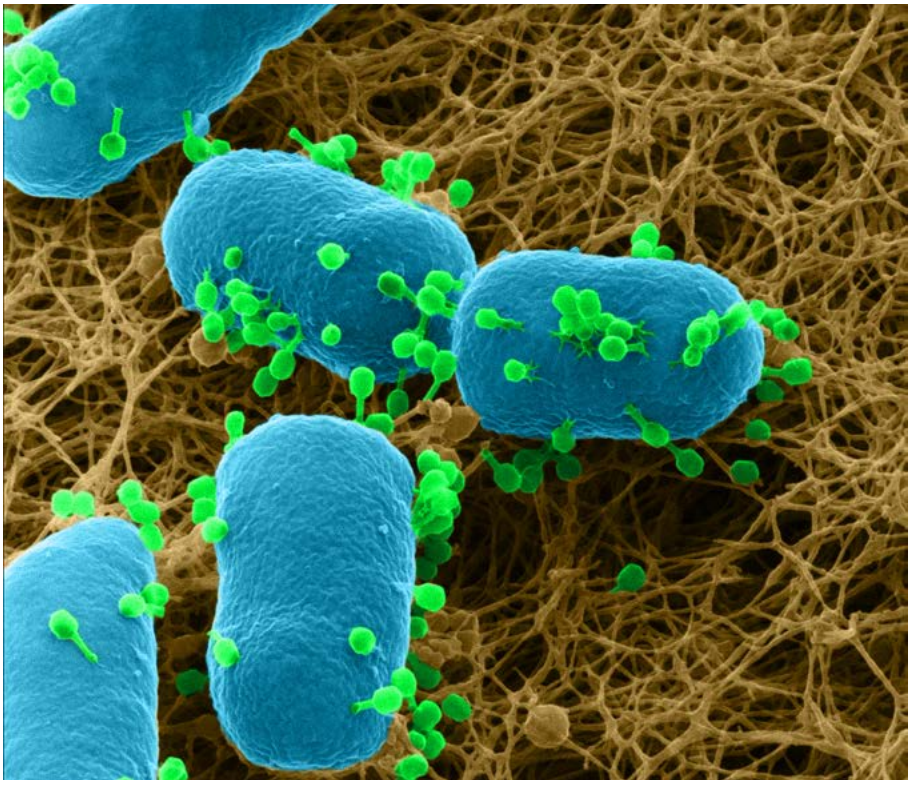

Figure 4 *E. coli bacterium under an electron microscope*
Courtesy of M. Leppänen, University of Jyväskylä, Finland

Figure 5 *Making wet preparations yourself*

Figure 6 *Epidermis cell of the onion skin under the microscope (phase contrast)*

A cover glass is then placed over the membrane. Since the epidermal cells of the onion are uncolored, methylene blue solution can be used for staining. Alternatively, red onions can be used for the preparation. Under the microscope, the structure of a plant cell becomes visible.

Figure 7 *Work on the ZEISS Primo Star microscope*

The epidermal cells of the onion display a structured cell compound. The cells are almost completely filled by the vacuole. The cell walls can be identified by a central lamella. Upon close observation, a seam on the cell wall – the cytoplasm – can be seen, in which the cell nucleus is located.

Hand drawings

Hand drawings of the microscopic image are created to make observations of the key structural elements more precise and to help internalize what is seen. The drawing must be clearly labeled. It should describe the slide and staining depicted, the magnification at which the analysis was carried out, and any particularly relevant details.

After students have placed plant and animal cells under the microscope, similarities and differences between the two cells become visible. The central element of both cell types is the cell nucleus, which is the control center of the cell and carries genetic information. Both cell types contain cytoplasm. Plant cells have a cell wall made of cellulose, while animal cells have an enclosing cell membrane. In addition, plant cells are characterized by vacuoles, tonoplasts and plastids.

Over the further course of the study, the structure and function of other cell components such as ribosomes, endoplasmic reticulum, mitochondria, lysosomes, Golgi apparatus and vesicles are discussed. In addition, relevant biomolecules are discussed as well as the role that the respective cell organelles play in their synthesis and / or secretion. Furthermore, the structure of the plasma membrane, membrane potential, signal recognition and transmission, as well as the basics of the cell division cycle including the processes of mitosis and meiosis, are learned.

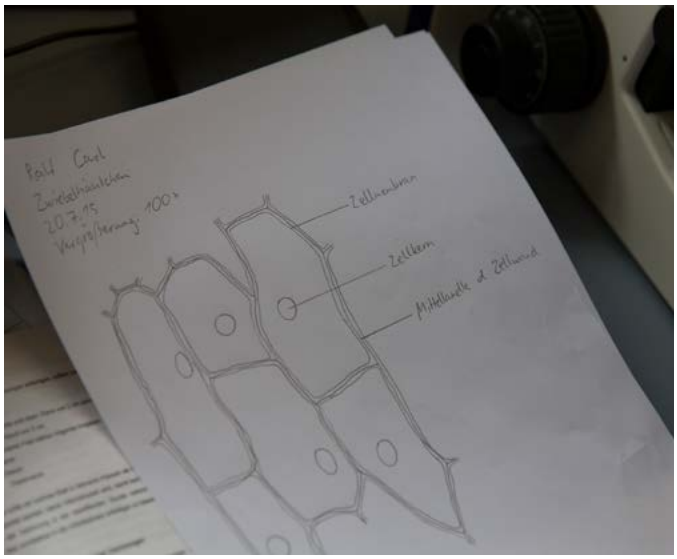

Figure 8 *Hand drawing*

Summary

Cell biology is an important module in the study of medicine and biology.

It teaches important basics about how animal and plant cells and their components are structured and how they function. This knowledge is the basis for further work in biomedical research and in the everyday professional life of doctors and biologists.

A range of ZEISS microscopes support successful learning and teaching of cell biology.

Recommended products

Teaching microscopes by ZEISS, especially those from the Primostar 3 range. Various packages are available, the Fixed-Köhler illumination types or Full-Köhler types where the Köhler illumination can be adjusted using phase contrast (515501-0021-000).

A digital course room is possible if WiFi-capable cameras are used, which can be adapted and integrated into the unit (415501-0071-000).

Equipment for LED-based fluorescence applications is also available (490980-0003-000).

Higher quality microscopes from the Axiolab or Axioscope series (490980-0002-000) are available for teachers.

References:

[1] https://en.wikipedia.org/wiki/Micrographia/04.05.2020

[2] https://en.wikipedia.org/wiki/Rudolf_Virchow#Medical_terms/04.05.2020

[3] Kapitza H.G.: Microscopy from the very beginning. 2nd edition, ZEISS, 1997

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