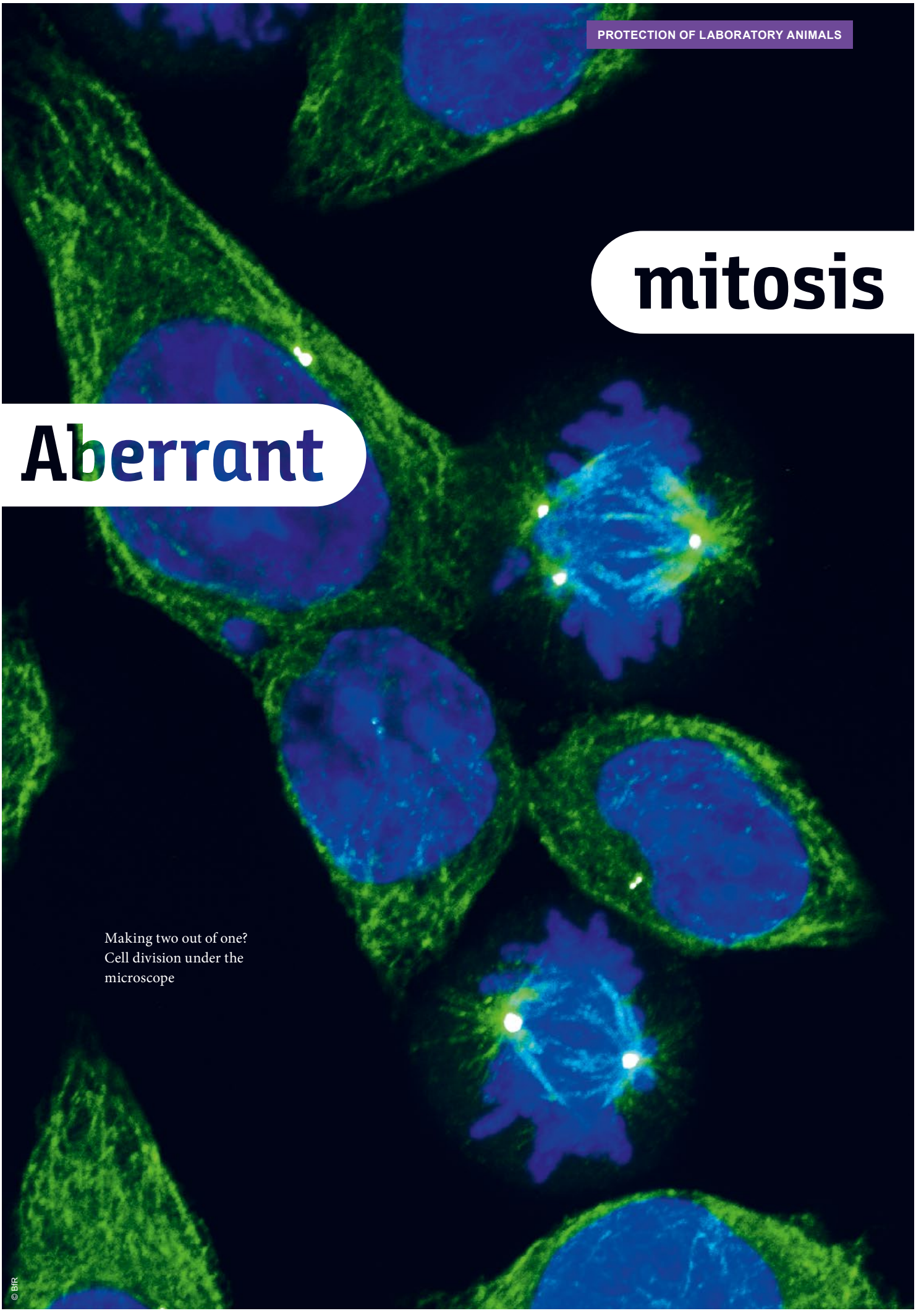
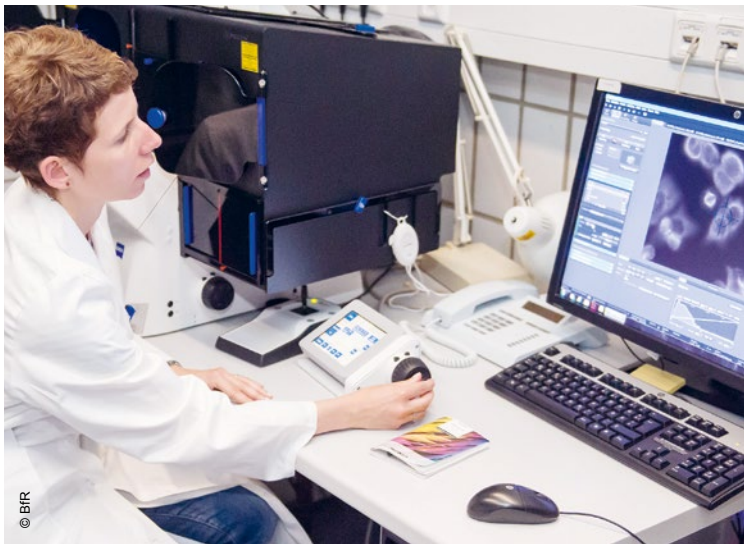
Aberrant mitosis



Making two out of one? Cell division under the microscope

Centrosomes direct cell division and ensure that each cell carries the same genetic material. Hormones or hormone-like substances can disrupt this process – thus promoting cancer.



Cancer research at the BfR: cell biologist Dr Ailine Stolz-Ertych examines the distribution of chromosomes.

Sometimes life hangs by a thin thread. Or more precisely: on thin spindle threads. When a human cell divides, it's vital that the duplicated genetic material is distributed equally to the two newly emerging daughter cells. This is ensured by a "spindle apparatus" consisting of many filigree fibres. The chromosomes, which carry the genetic information, attach themselves to the spindle fibres and are then pulled to the two opposite poles of the spindle. This way, a completely identical set of genetic material assembles at each pole and cell division can begin – thanks to the spindle fibres.

Billions of cells divide in the human body every day. At the German Centre for the Protection of Laboratory Animals (Bf3R) of the German Federal Institute for Risk Assessment (BfR), cell biologist Dr Ailine Stolz-Ertych and her team are investigating how hormones and hormone-like substances affect cell division. "We have discovered that certain hormone-active substances can promote the uneven distribution of chromosomes to the daughter cells," says Stolz-Ertych. "This uneven distribution is a major feature of cancer cells."

Centrosomes: the poles of the spindle

The "central body" or centrosome is of great importance in cell division. It is a small cell organelle that is duplicated just like the genetic material. The two centrosomes form the two opposite poles of the spindle. From here, they guide the equal division of the chromosomes via the spindle fibres to the daughter cells that are to be formed – making two out of one.

In human cancer cells, this process is often disturbed. One major cause involves the fact that tumour cells often have more than two centrosomes. "If there are three centrosomes, for example, we can observe the temporary formation of three spindle poles under the microscope. This makes cell division impossible," says Stolz-Ertych. To avoid total chaos – and thus death – a cancer cell has the ability to turn three poles back into two. "This often results in erroneous attachment of the chromosomes to the spindle fibres. The distribution of chromosomes is a game of chance then, and one reason why tumour cells often have either too many or too few chromosomes," the scientist adds.

Bisphenol A under the microscope

Ailine Stolz-Ertych has been working at BfR since 2016 and is researching healthy cells of the intestinal mucosa as well as intestinal cancer cells. She is studying the effects of oestrogens (female sex hormones) or oestrogen-like substances such as bisphenol A (BPA) on cell division. BPA is a compound commonly found in plastic food contact materials and used as a starting substance for polycarbonate plastics and epoxy resins, for example in the manufacture of food cans. Due to

The substance bisphenol A is a starting material for the production of epoxy resins, which are often used to coat food cans.

> **We assume that the effects are minor, but they must nevertheless be taken seriously**

adverse effects arising from the hormone-like action of BPA, the substance has been classified as "of very high concern" by the European Chemicals Agency (ECHA) and its use in many plastic materials such as baby bottles or thermal papers (sales receipts, for example) has been banned throughout the EU. Stolz-Ertych discovered that oestrogens, like BPA, can promote the uneven distribution of chromosomes in intestinal mucosa and colon cancer cells. "We assume that this effect is caused by an increase in the number of centrosomes," says the scientist.

How does an excess of centrosomes occur? To understand this, you have to take a closer look at the centrosome. Inside it, there are two identical cylindrical tubes made of protein molecules that are linked together at right angles and, with a little imagination, resemble a bent drainage pipe. These tubes are called centrioles. They are effectively the heart of the centrosome and responsible for the outgrowth of the spindle fibres. Oestrogens or oestrogen-like substances can disrupt the regulated doubling of the centrioles, leading to a tripling, for example – and a corresponding increase in the number of centrosomes.

Ailine Stolz-Ertych wants to elucidate the mechanisms of this "disturbance" in the intestinal cells. This sounds easier than it actually is, as hormonal effects are sometimes difficult to grasp. Like all hormones, oestrogens are messenger substances. They act by attaching to suitable docking sites (receptors) on or in the cell. Stolz-Ertych is particularly interested in these hormone receptors.

Results provide important clues

"Results from cell experiments such as the ones we are conducting cannot be applied one-to-one to humans," says Stolz-Ertych, limiting the scope of her experiments when it comes to the question of how hazardous substances with oestrogenic activity such as BPA are. "We assume that the effects are small, but they must nevertheless be taken seriously because they can have a carcinogenic effect," adds doctoral student Miriam Bühler.

The basic research of Stolz-Ertych and her team not only aims to better understand the effect of hormones, but could also lay the foundation for new test methods for chemicals that do not involve animal experiments. For example, it could be tested whether a chemical compound leads to centrosome proliferation and unevenly distributed chromosomes. Stolz-Ertych and her team are relying on extremely high-resolution microscopy technology that can be used to detect even single molecules. After all, the aim is to find the thin thread on which life can hang. ◘

More information:
Bühler, M., A. Stolz. 2022. Estrogens – Origin of centrosome defects in human cancer? Cells 11: 432. DOI: 10.3390/cells11030432