Protection of Laboratory Animals

Biorhythm of cells

GERMAN CENTRE
FOR THE PROTECTION OF
LABORATORY ANIMALS

BfR
Bundesinstitut für Risikobewertung

Rhythmic detoxification

For cells to function properly: the German Centre for the Protection of Laboratory Animals at the BfR is investigating how the internal clock can be used to replace animal experiments.

In the morning, daisies open up, humans awaken with new vigour and mice withdraw to their hideouts to go to sleep. In the evening when dusk falls and night approaches, flowers close, humans become tired and mice come to life. The same spectacle repeats itself day after day, night after night: from single-celled organisms to animals and plants, organisms have adapted to our planet's rotation, therefore increasing their chances of survival in one way or another.

Right down to each individual cell, the human metabolism has also adjusted to the rhythmic alternation of day and night. This even applies to detoxification – if you want to test health risks posed by chemicals on cells, there is no getting around setting the clock of the cells correctly. This is indicated by the research results obtained by biologist Dr. Michael Oelgeschläger and his team from the German Centre for the Protection of Laboratory Animals at the BfR.

Curious: a circadian rhythm in cells?

"In the beginning, everyone thought it was absurd – a circadian rhythm in cells!" recalls Oelgeschläger referring to the start of the research. However, it is now known that there is a whole molecular mechanism of hereditary factors (genes) that fulfil the tasks of an internal clock in human cells. As clocks, they control behaviour, hormone release, sleep, body temperature and metabolism. "It is estimated that up to 43 per cent of all genes are subject to the circadian rhythm," explains the scientist. In 2017, three pioneers researching the body clock received the Nobel Prize for Medicine. No more talk of absurdity.

Oelgeschläger wants to replace animal experiments with experiments on cells wherever possible. For example, those that investigated the effect of poisonous (toxic) substances. Therefore experiments "in the Petri dish" must come as close as possible to the conditions in humans. Of course, this also applies to the biorhythm. But while in the human organism all cells function properly thanks to a control centre in the brain, time chaos reigns in the Petri dish because every cell follows its own biorhythm.

As a consequence, laboratory results are distorted when compared to the real conditions in the body. Oelgeschläger and his team avoided these pitfalls. By bathing the human cells in dexamethasone – a substance related to the body's own hormone cortisol – they set their clocks to a single common time. Dexamethasone acted like a stopwatch that makes everything start over – with dramatic consequences, as it turned out.

Functioning together, reacting better to toxic substances

Oelgeschläger now confronted the cells with a toxic dioxin compound called TCDD. It turned out that the synchronously functioning cells showed an enhanced reaction to the substance compared to non-synchronised cells. Simply put: as in animals, the reaction to environmental toxins in cells is dependent on the time of day. However, to verify this, all cells must "go to sleep" or "wake up" at the same time.

Oelgeschläger and his team have broken new ground with their findings. "It was a feasibility study," says the scientist. "We showed that biorhythms are also signifi-

cant in cell culture." Now it is up to researchers to bring the cell tests even closer to the reality in humans. In the end, it could become apparent that even conventional experiments on animals need improving. Because a mouse that slips out of its hideout at night functions differently than a human being who crawls under their duvet at the same time.

More information:
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The German Centre for the Protection of Laboratory Animals at the BfR

The Centre combines the various areas of alternative method research on a national level in line with the 3R principle. The Centre coordinates activities all over Germany with the goals of restricting experiments with animals to a level which is absolutely necessary and affording laboratory animals the best possible protection. In addition, impetus is to be given to national and international research activities through the work of the Centre while encouraging scientific dialogue at the same time. The German Centre for the Protection of Laboratory Animals was established in 2015 in the course of the Animal Welfare Initiative of the Federal Ministry of Food and Agriculture. It is an integral component of the BfR which is subdivided into five areas of competence.

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