Guard plate for the *thyroid*

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The biotechnologist Dr Kostja Renko and his team are using animal-free methods to study the effect of chemicals on the thyroid and its regulation in the body.

It all starts in the depths of the primordial ocean. Billions of years ago, single-cell organisms were already using a trace element from their oceanic environment: iodine. This, at least, is the assumption regarding the trace element's evolutionary significance. It helps cells detoxify aggressive compounds containing oxygen. Iodine and compounds containing iodine are the cells' "primordial vitamin". And iodine can do even more. Bound to the amino acid tyrosine it functions as a messenger substance or "primordial hormone". In addition, the binding of tyrosine and iodine forms the foundation of thyroid hormones. As far back as 800 million years ago, these appeared in simple sea creatures such as sponges and corals and have been part of the biological "inventory" ever since, particularly in the animal kingdom.

DISRUPTORS IN THE SYSTEM

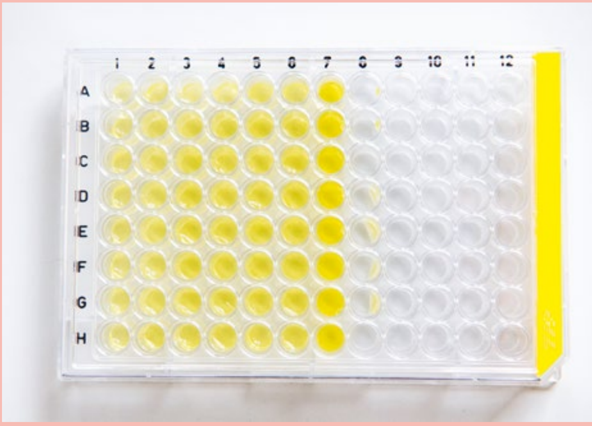
Returning to the present: in a laboratory at the German Centre for the Protection of Laboratory Animals (Bf3R) in Berlin-Marienfelde, the biotechnologist Dr Kostja Renko is using microtiter plates – small rectangular plates made of transparent plastic with tiny "cavities" – to examine how chemicals in various doses impact thyroid cells and the thyroid hormone system. This system is made up of more than just the hormone-secreting thyroid from which the system derives its name. Very important transport and transformation processes for these hormones take place in almost every cell of the body. "We are working on new methods that allow potential endocrine disruptors to be detected," Kostja Renko says. "We are talking about chemical compounds that can disrupt the normal functioning of the hormone system and thus harm health."

Situated below the larynx, the thyroid's shape, with its two symmetrical lobes, is vaguely reminiscent of a butterfly. This suits its role, as it "gives wings" to metabolism. Thyroid hormones regulate energy metabolism, body temperature, and heart function.

Too much, and it can lead to a dangerously rapid heart rate and weight loss. On the other hand, lower thyroid function causes metabolism to slow greatly, a drop in heart rate, and tiredness and lethargy.

DRIVING FORCE OF METABOLISM

Thyroid hormones function not only as a driving force of metabolism. They are also important for the development of foetuses in the womb, in particular when it comes to brain development. If pregnant women are deficient in iodine, it may also lead to a hormone deficiency. In extreme cases this may result in the child suffering from congenital iodine deficiency syndrome (CIDS). This massive variant in innate hypothyroidism and the associated hormone deficiency is linked to stunted growth, abnormalities of the skeleton, a greatly enlarged thyroid, and reduced mental capacity. In recent decades, better nutrition including iodised salt has largely eradicated CIDS. However, innate thyroid abnormalities still occur that have no connection to iodine deficiency. "In order to identify it early on, you can take a small blood sample from newborn babies," Renko explains. "By administering thyroid hormones a deficiency can then be reliably compensated for and harm prevented." However, it is not yet clear to what degree minor changes in the thyroid hormone system,



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Double dose: microtiter plates allow for the parallel testing of chemicals in varying concentrations.

for example due to unintended effects from chemicals, impact key phases in brain development. Endocrine disruptors can unbalance the thyroid at several levels. For example, they may disrupt the formation and secretion of the hormones T4 (thyroxine) and T3 (triiodothyronine), their distribution in the body, their metabolism, or the overarching regulation. The aim is to now develop and gain international recognition for reliable and animal-free methods for chemical tests relating to all these “sites of attack”. Only in this way can they replace or at least reduce animal experiments in the long term. In any case, this is Kostja Renko’s stated aim. Developing alternative methods is also a key task of the German Centre for the Protection of Laboratory Animals.

TRACING THE TRACE ELEMENT

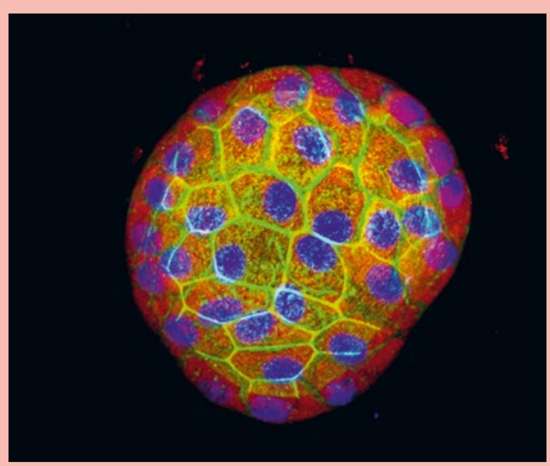
Renko’s scientific path begins at the Institute of Experimental Endocrinology at Berlin’s Charité Hospital. There his research involves, among other things, plant substances with possible side-effects on the thyroid hormone system. At this time, detection procedures are still often required that use radioactive iodine to trace disruptions to the formation, activation, or transport of the hormone.

“The tests make it necessary to work in an isotope laboratory,” Renko recalls. “To put it bluntly: it’s not much fun.”

Obviously, the fun factor is not the (only) thing of importance to the scientist. Working with radioactive isotopes is time-consuming and expensive, entails health risks, and limits the number of tests that can be performed simultaneously. “Against this backdrop, an almost one-hundred-year-old method from analytical chemistry came to our aid,” the researcher says. “We successfully used a ‘classic’ procedure for measuring iodine – the Sandell-Kolthoff reaction, first described in 1937 – in various tests to replace the radioactive iodine-containing tracer that we had been using up to that point.” To put it simply, researchers use the Sandell-Kolthoff reaction to measure the iodine concentration in a liquid. The faster the yellow solution turns pale, the higher the iodine content.

TEST FOR THE WHOLE WORLD

Renko wants to help establish internationally recognised alternatives to animal experiments. These are published as test guidelines by the Organisation for Economic Cooperation and Development (OECD) facilitate the use for legally required testing of chemicals. “The path to obtaining such international recognition is long,” the biotechnologist says. It requires formal proof that a method can be used globally in other laboratories with comparable results. “Together with our partners from academic research and industry, we are already making good progress with some of our methods.” Each new method enlarges the tool box for risk assessment.



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Living bioreactor: the thyroid consists of innumerable vesicles made up of follicles such as these.

“We are working on new methods that allow potential endocrine disruptors to be detected”

Dr Kostja Renko, biotechnologist

To finish, Kostja Renko allows the visitor to take a look through the microscope. Individual vesicles can be seen, transparent and surrounded by cells. These are thyroid follicles that make up the glandular tissue. The scientist and his doctoral student Lars Dahmen are working to make the follicles suitable for future use as “mini thyroids” in tests on endocrine disruptors. The material for this cell culture system are the thyroids of slaughtered pigs, normally a waste product of the meat industry.

“The fascinating thing about thyroid follicles is that they are microscopically small bioreactors,” Renko says. “The ‘final assembly’ of the hormones does not take place in the cells themselves, but rather in the follicle vesicles.” In other words, what nature does with the follicles “anticipates” a piece of biotechnology. Seen in this light, what actually is the primordial ocean but a huge bioreactor? With, of course, a decisive sprinkling of iodine. —

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Taking due care with chemicals and cells: the safety workbench serves to protect the thyroid follicles and the researchers.