Friederike J. Gruhl – biology is not always enough

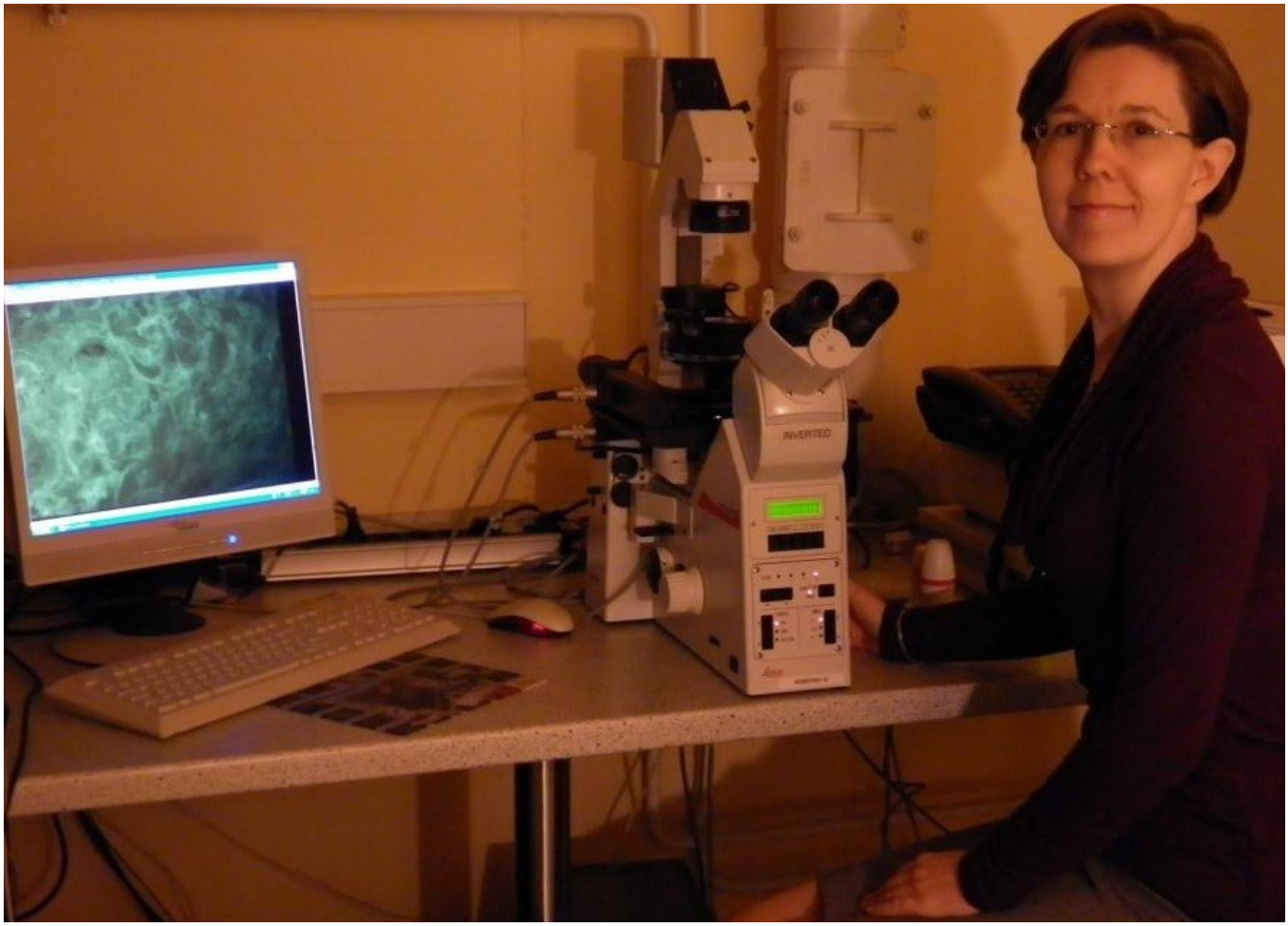
Researchers are usually only able to explore the development and growth of tumours with animal models. This is because many human cells lose their typical characteristics once outside the body. Friederike J. Gruhl from the Karlsruhe Institute of Technology (KIT) is working to create a biomimetic environment in Petri dishes in which prostate cells thrive and can be manipulated – to become tumours for example - if required. The three-dimensional prostate model will provide insights into the complexity of the prostate. Gruhl has expanded the horizons of biology during the course of her investigations.

According to German Cancer Aid, around 67,000 men are diagnosed with prostate cancer in Germany every year. Around 12,000 of them die. The prostate, which is located just below the bladder, is an organ that produces part of the semen. Prostatic secretions are composed of at least three different cell types. Although the prostate is not as complex as the human brain, the cellular and molecular processes occurring between the different cell types and the extracellular space in the prostate tissue are not yet understood in detail. What makes healthy prostate cells become cancerous? How do metastases develop?

Microstructure and biosensor technology

"Experiments involving mice and rats have provided us with detailed insights into the healthy and diseased function of the prostate. However, the prostate of rodents is very different from that of humans," said Dr. Friederike J. Gruhl from the Institute of Microstructure Technology (IMT) at the Karlsruhe Institute of Technology (KIT). "Experiments with human tissue are essential, both in basic research as well as in the identification of new anti-cancer drugs." Gruhl is currently working on the development of a three-dimensional in vitro prostate model. She is using synthetic 3D carrier materials to create an environment in which prostate cells behave just like in the human body. "Traditional methods like those used in cell biology are not enough for our studies", the researcher said.

During her degree thesis at the University of Karlsruhe, Friederike Gruhl, who was born in Karlsruhe in 1980, studied the molecular mechanisms in cells of developing embryos in great detail. Biology was and still is the basis of her work. However, what characterises her current research is her interest in the technical aspects and their interfaces with classical biology. She did her doctorate in the field of biosensor technology at the Institute of Microstructure Technology between 2007 and 2010 where she came into contact with physicists, chemists and engineers. Her doctorate was focused on methods that enabled her to detect specific breast cancer markers in the blood or serum of patients. In order to do this, she used hydrogels (water-saturated polymer gels) whose surface



Dr. Friederike J. Gruhl
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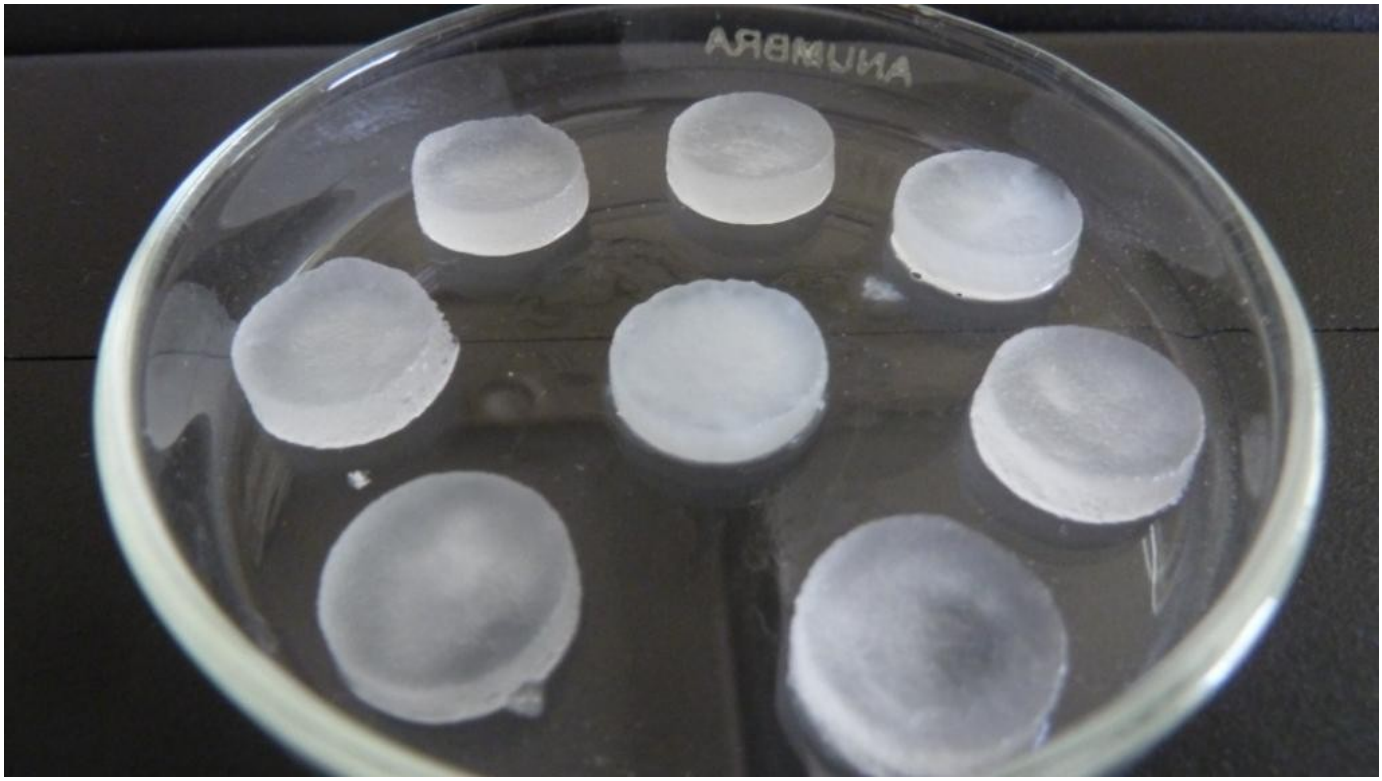
could be modified and coupled with antibodies. “This is a highly interdisciplinary field of research,” Gruhl said. “But it is exactly what I was looking for as I was especially interested in scrutinising and expanding traditional biological methods.” This approach makes Gruhl one of the many interdisciplinary scientists without whom cutting-edge research would be impossible.

Sponge-like substance that gives cells a feeling of comfort

The development of hydrogels and techniques that enable polymer surfaces to be modified still constitutes a major part of her work. A natural extracellular matrix consists of a network of proteins and long-chain hydrocarbons and forms a kind of sponge-like basic substance in any tissue of an organism where cells can position themselves, move around and communicate with each other. The combination of this matrix with an artificially created environment is the basis of any three-dimensional prostate cell culture. In chemical terms, the matrix is rather complex: it not only provides support and structure, but also contains molecular components that can serve as position signals for cells. “We have spent the last few months using artificial polymers to build different environments and will now study the conditions under which the individual prostate cell types feel most comfortable.”

The hydrogel layer is around 5 mm thick. Its sponge-like structure is clearly visible under the microscope, and can also be discerned with the naked eye. It might be an excellent tool for basic researchers and, as mentioned above, also an alternative to animal experiments. It is also extremely practical. Cells can be stained and investigated under a fluorescence microscope. Because they are so



Different hydrogels which human prostate cells can colonise in future.
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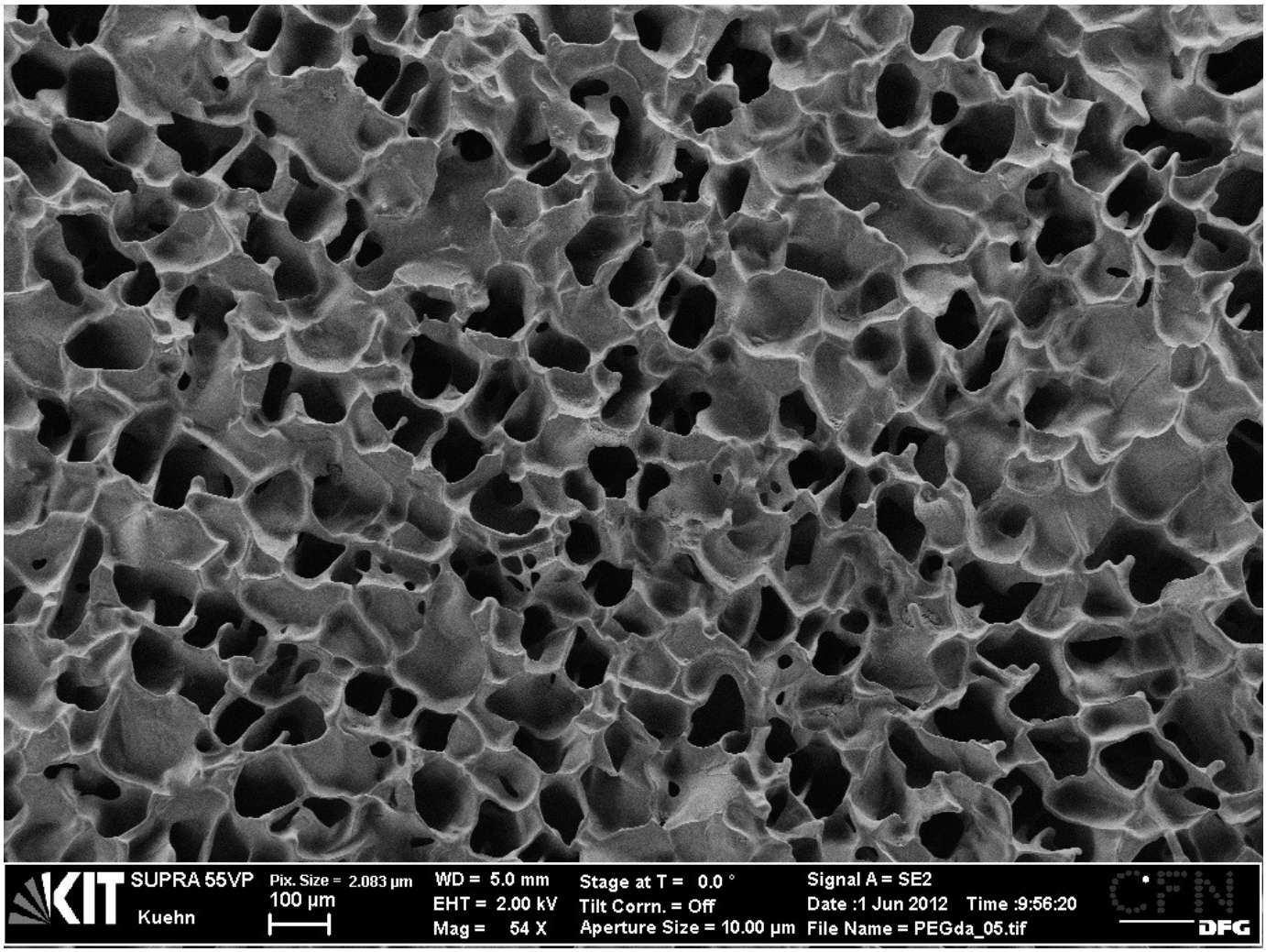

Porous, sponge-like structure of a hydrogel seen under a microscope
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small (1 to 2 cm in diameter), hydrogels also have the potential to be used for high-throughput experiments in the pharmaceutical industry.

"Over the last few months, we have been able to show that our biomimetic gels are excellent environments for fibroblasts, which can also be cultivated easily in other cell culture systems," said Gruhl. "We still need to find out whether prostate cells can also be cultivated in hydrodels. But they are a lot more demanding than fibroblasts, so we will see." Gruhl and her co-workers will start off with a single prostate cell type and vary different parameters, including the number of cells grown simultaneously, duration and the composition of the liquid medium used to cultivate the cells. Once the conditions are right, several cell types will be added.

A diagnostic device and channels for the tiniest amounts of liquid

Besides the development of the prostate model, which is now being funded by the Baden-Württemberg government for a period of three years, Friederike Gruhl also focuses on biosensors. Working in cooperation with a partner from industry, she is currently developing a diagnostic device for use in hospitals that enables disease markers to be measured in the blood or serum of patients in the concentration range of a few nano- and even picogrammes per millilitre. Gruhl is also extremely interested in microfluidics. "Handling the tiniest amounts of liquids will eventually also be what we do in the biosensor and the prostate model projects," said Gruhl, "because these projects will also have to deal with issues such as how to bring a sample to a sensor or how to provide cells in the culture dish with nutrient medium and soluble signalling substances. The development and use of microfluidic channels is feasible for both projects."

The interdisciplinary area in which Gruhl is working has huge potential for the future. "At first, I was sometimes faced with a sceptical frown when talking with colleagues who worked in different scientific fields," the researcher recalled. "But nowadays, interdisciplinary cooperation has become an integral part of our work at the IMT."

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