Press Release
25 July 2024 No. 387

BioRegio STERN

Cellendes hydrogels avoid animal testing and will be a game-changer in research

An idea that benefits mice and men

(Stuttgart/Tübingen) – Cellendes GmbH, based in Kusterdingen, near Tübingen, develops and sells hydrogels. These are used to produce all kinds of three-dimensional cell cultures – often created using human cells – that can map the complex functions of organs such as skin, and also abnormal tissue such as that found in tumours. As a result, they offer great potential when it comes to drug development and the testing of toxic substances. Given the growing scepticism about applying research results from animal trials to humans, these cell culture systems offer numerous benefits – and not just as a replacement for animal testing. Company founders Dr. Brigitte Angres and Dr. Helmut Wurst are continuously enhancing their hydrogels, and are involved in international research projects. Besides collaborating with the NMI Natural and Medical Sciences Institute at the University of Tübingen on the FoBioGel project, Cellendes is also part of the EU-financed B-BRIGHTER bioprinting project.

To obtain the three-dimensional culture from differentiated primary cells and cell lines, a specific extracellular matrix is often used in the lab. An extract from mouse tumours is required for this purpose. This is obtained by implanting sarcoma tumours, which can be up to 20 percent of the mouse's total body weight by the time the animal is killed to remove the tissue and prepare it for three-dimensional cell cultivation. This has been regarded as the standard method for years, partly because the extract hugely accelerates the growth of any cells. Ethical considerations aside, one disadvantage is the culture's "unpredictability" due to the highly complex and partly unknown composition of the extracellular matrix, which can also vary from batch to batch. Furthermore, animal matrix components are not always suitable for a human cell culture.

Synthetic hydrogel offers a solution

Cellendes GmbH, which is based in the STERN BioRegion, set about resolving this problem 15 years ago. Biologists Dr. Brigitte Angres and Dr. Helmut Wurst developed

what was then a completely new kind of synthetic hydrogel that meets all research requirements for three-dimensional cell cultivation. It is fully synthetic, clearly defined and completely neutral – and it eliminates any ethical concerns, too. However, it also forces researchers to adopt a new mindset. They need to understand what the cells in their specific project require so as to create the relevant cultivation stimuli that will ensure these cells behave in the desired way. Biomimetic factors such as the gel's stiffness can be varied at will to achieve this. For this purpose, Cellendes offers a platform with a variety of modules and cell-attracting motifs, meaning any researcher can create their own "personal" cell culture.

The numerous international research projects Cellendes GmbH is participating in provide further proof that hydrogels are the future of cultivation. For example, the team is currently working on B-BRIGHTER with partners from Germany, Sweden, Spain and Israel. By 2025, this EU-financed project aims to optimise tissue cultivation using bioprinting, which is deemed a promising method for producing functional tissues with physiological properties. This additive production process makes it possible to "print" living cells along with scaffold agents to create larger tissue structures. The existing approach of bottom-up, layer-by-layer printing is associated with significant challenges when it comes to cell viability and is also subject to technical limitations in terms of printing speed and spatial resolution. As part of B-BRIGHTER, a top-down lithography approach is being developed whereby, with the help of digitally controlled high-speed illumination, three-dimensional areas are selectively crosslinked to form the hydrogel. This approach enables functional 3D geometries with a high spatial resolution to be produced quickly.

Many issues faced by researchers resolved

The new Cellendes hydrogels are playing a key role, because – unlike conventional hydrogels that "gel" as soon as the ingredients are mixed – they only form when exposed to a special light. These photoinducible hydrogels could therefore become a game-changer for the research group when preparing sophisticated tissue models of the cornea or intestinal wall. Reproducing gut tissue cells in a model that simulates ingestion has a particular reputation for being highly complex. However, the new gels

make it possible to print intestinal tracts and generate the gut's typical microvilli structures.

No less exciting is the FoBioGel project, in which Cellendes is collaborating with the NMI Natural and Medical Sciences Institute at the University of Tübingen. In this joint undertaking, too, the company is developing photostructurable, biochemically functionisable hydrogels. In this case, however, the principle works the other way round – the gels first form spontaneously and are then illuminated to break them down again. "These hydrogels are not just three-dimensional, but also offer a 4D aspect. We can determine different strengths at various points in the cultivation process, depending on when the light is applied," explains Dr. Angres. "The gels resolve many issues facing researchers, but this potential is still largely unknown and, as yet, there is no commercial product of this kind on the market, either," she adds. Cellendes is looking to plug this gap.

The gels are to be used as a biomimetic extracellular matrix in 3D bioprinting and in innovative, complex in vitro models (organ-on-chip) for drug development and personalised medicine. For instance, very fine structures are to be produced to form special barriers on the chips. The NMI will evaluate these properties, the application potential of the newly developed hydrogels and their use as bioinks for 3D bioprinting. In this project, too, the ultimate objective is to create tissue models that meet the 3R goals – replacement, reduction and refinement. Alternative or complementary methods are to be used as a substitute for animal testing wherever possible (replacement), experiments and the number of laboratory animals used in these are to be strictly minimised (reduction), and the suffering, pain and stress experienced by the animals involved in such testing must be kept to an absolute minimum (refinement).

"Bureaucracy is a killer for small companies"

Cellendes hydrogels are therefore extremely significant in terms of medical progress and take increased ethical requirements into account. Although the biotech company is receiving enquiries from all over the world, customers are not queuing up just yet. In 2022, Cellendes relocated to new premises at the Tübingen-Reutlingen Technology Park (TTR) and now has its own laboratory, with all the expense that involves. "Bureaucracy is a killer for small companies," complains Dr. Wurst. And Cellendes

isn't even working in the medical sector yet, but still exclusively in research. "Turning research products into pharmaceutical products is extremely costly," explains Dr. Wurst. Nonetheless, medical applications based on Cellendes hydrogel technology do already exist. TETEC AG in Reutlingen is combining the hydrogels with autologous chondrocytes to regenerate damaged cartilage in joints such as knees.

Dr. Angres and Dr. Wurst have achieved a great deal over the past 15 years. They have launched a unique product that has the potential to transform basic research as well as pharmaceutical and medical research and development work. It can naturally do a lot more than spare countless mice a great deal of suffering. Unfortunately, however, the two biologists have also been forced to acknowledge that a paradigm shift of this kind takes time. It is necessary to prove over and over again that the process is suitable for replacing conventional solutions. The trial results obtained using extracts from mouse tumours and those based on the new hydrogels also need to be comparable. Despite the bureaucratic challenges and financial constraints, the Cellendes founders have never regretted setting up their own business. "We enjoy being our own boss," emphasises Dr. Wurst.

https://www.cellendes.com/
https://b-brighter.eu/
https://www.nmi.de/en/projects/projektdetail/fobiogel-1

About BioRegio STERN Management GmbH:
BioRegio STERN Management GmbH promotes economic development in the life sciences industry, helping to strengthen the region as a business location by supporting innovations and start-up companies in the public interest. It is the main point of contact for company founders and entrepreneurs in the Stuttgart and Neckar-Alb regions, including the cities of Tübingen and Reutlingen.
The STERN BioRegion is one of the largest and most successful bioregions in Germany. Its unique selling points include a mix of biotech and medtech companies that is outstanding in Germany and regional clusters in the fields of automation technology and mechanical and plant engineering.

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