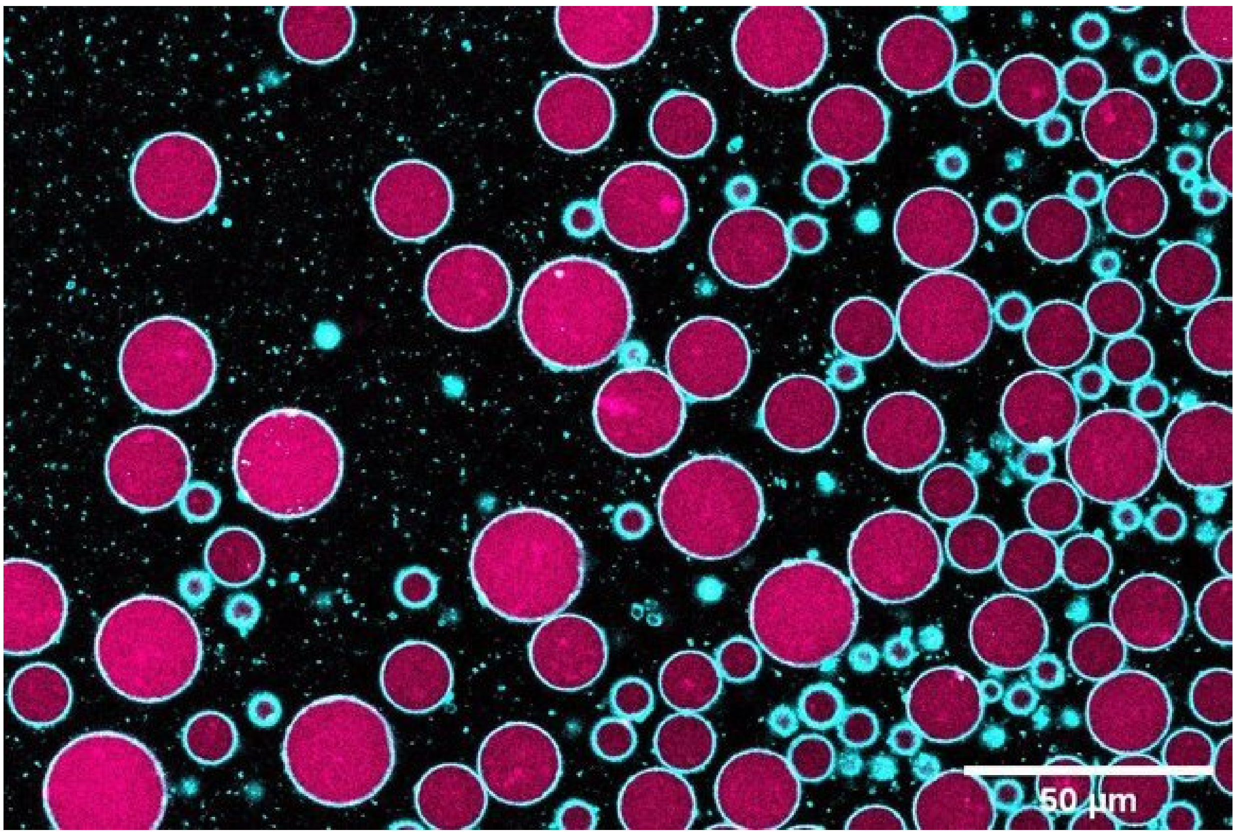
PHYS.ORG

Synthetic cells communicate with organic cells

October 12 2022, by Nicole van Overveld



Microscopic image of the synthetic cells. Pink is protein, cyan is membrane staining. Credit: Marleen van Stevendaal

Many things are already possible when it comes to mimicking organic cells. For example, Jan van Hest's group has developed a synthetic cell platform in which all kinds of cell aspects can be mimicked in order to better understand them. With her background in cell biology and biochemistry, Marleen van Stevendaal wanted to investigate whether it was possible for these synthetic cells to communicate with organic cells. In her thesis, she describes how she succeeded in this.

For decades, researchers have been fascinated by the question of what constitutes life. As a result, the definitions of living tissue and organisms are constantly improving. For instance, the smallest forms of life are cells, which are made up of different compartments. In addition, these are able to produce energy, multiply and communicate with the environment. To better understand these phenomena, researchers are trying to create living cells from the very smallest building blocks. This means putting individual building blocks together like Lego to mimic cellular characteristics.

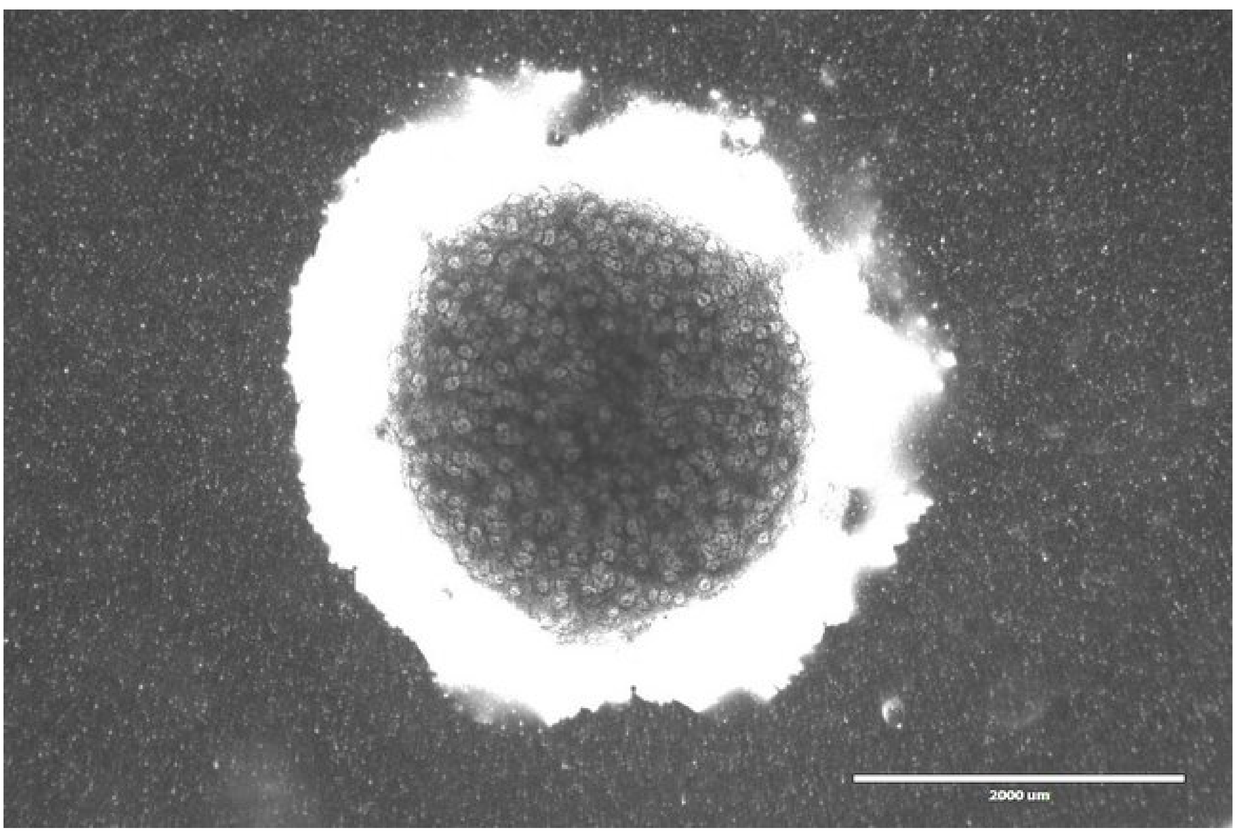
In her Ph.D. research in the Bio-Organic Chemistry group, Marleen van Stevendaal focused on developing synthetic cells that can cooperate well with living tissue. This cooperation could make it possible to eventually apply synthetic cells to the targeted delivery of signaling molecules, for example. In addition, this research enhances our understanding of how organic tissue communicates at a fundamental level.

First and foremost, good communication requires that the synthetic cells not be harmful to living cells. Furthermore, they must have a communication system through which living cells can respond and modify their behavior. Finally, it must be possible to incorporate the synthetic cells into the complex environment of living cells and tissues.

Cell platform

"I did several internships during my bachelor's and master's, including an internship with Jan van Hest (professor of Bio-Organic Chemistry and director of the institute ICMS). Some research was purely chemical, while in others I worked with living cells. During my Ph.D., I wanted to connect those worlds," says van Stevendaal. "I wanted to develop a synthetic cell platform that meets the criteria for cooperation with living cells. A cell platform means that we have a basic method with which we can mimic different types of cell aspects with exactly the properties we are looking for.

"The platform that we use for this is based on phase-separating polymers that form droplets called coacervates. First, we investigated how the use of structure and materials and the construction of these synthetic cells affect the viability of different cell types. We found that we had to remove the free polymers in the synthetic cells to prevent them from becoming toxic. But it was nice to find that the synthetic cells themselves did not harm the living cells."



Microscopic image of a kidney organoid. Credit: Dr. Jitske Jansen (Radboud UMC)

Communications

Cells communicate in different ways, but one of these is through proteins. The synthetic cells cannot yet regulate the protein release needed for this form of communication via the pores located on an organic cell's membrane—but van Stevendaal found a solution to this. "We developed a system that will be able to communicate with living cells in the future. This communication system is designed to transfer proteins between synthetic cells. In our research, the system has already worked in the presence of living cells, using proteins that also have the potential to start passing signals to living cells. Examples of such proteins include antibodies and cytokines. Chemokines are a special group of cytokines and we started working on those."

Chemokines are the proteins that cells use to guide one another. Under the influence of the right chemokines, tissues know, for example, where blood vessels should be created. Van Stevendaal used cultured organoids of kidney tissue. These are pieces of living kidney tissue that do not yet collectively form a functional kidney but do react in the same way that kidney tissue reacts. In other words, a simplified organic version of a piece of kidney.

"The synthetic cells we use are constructed from materials that do not occur at all in nature, although other researchers make synthetic cells solely with natural building blocks such as DNA," adds van Stevendaal.

"We started our communication system with a 'model' protein around our synthetic cells so that we could properly characterize our system with the microscope. However, living cells do not respond to this protein, which is why we switched to chemokines. We then had the system react to ultraviolet (UV) light. In doing so, we created a simple on/off system that could be used in complex environments. We were therefore able to make synthetic cells that secrete chemokines as soon as they are exposed to UV light."

Cooperation at the cellular level

The study of synthetic cells and communication with living cells offers all sorts of opportunities for follow-up research. Van Stevendaal says, "One day, we hope to learn more about how life originated and how certain cellular processes take place, such as DNA translation. Additionally, these synthetic cells hold great promise for use as smart micromachines to solve biomedical problems."

Van Stevendaal's research is an excellent step towards communication and cooperation between synthetic cells and living tissues, but more research is needed. A follow-up direction is making the organoids more complex so that they mimic organs even better, for example. Over the coming years, research will continue around chemokine signaling using other known chemokine constructs.

More information: Marleen Helena Martina Elisabeth van Stevendaal, Engineering interactions at the interface of living and synthetic cells. research.tue.nl/nl/publication … living-and-synthetic

Provided by Eindhoven University of Technology