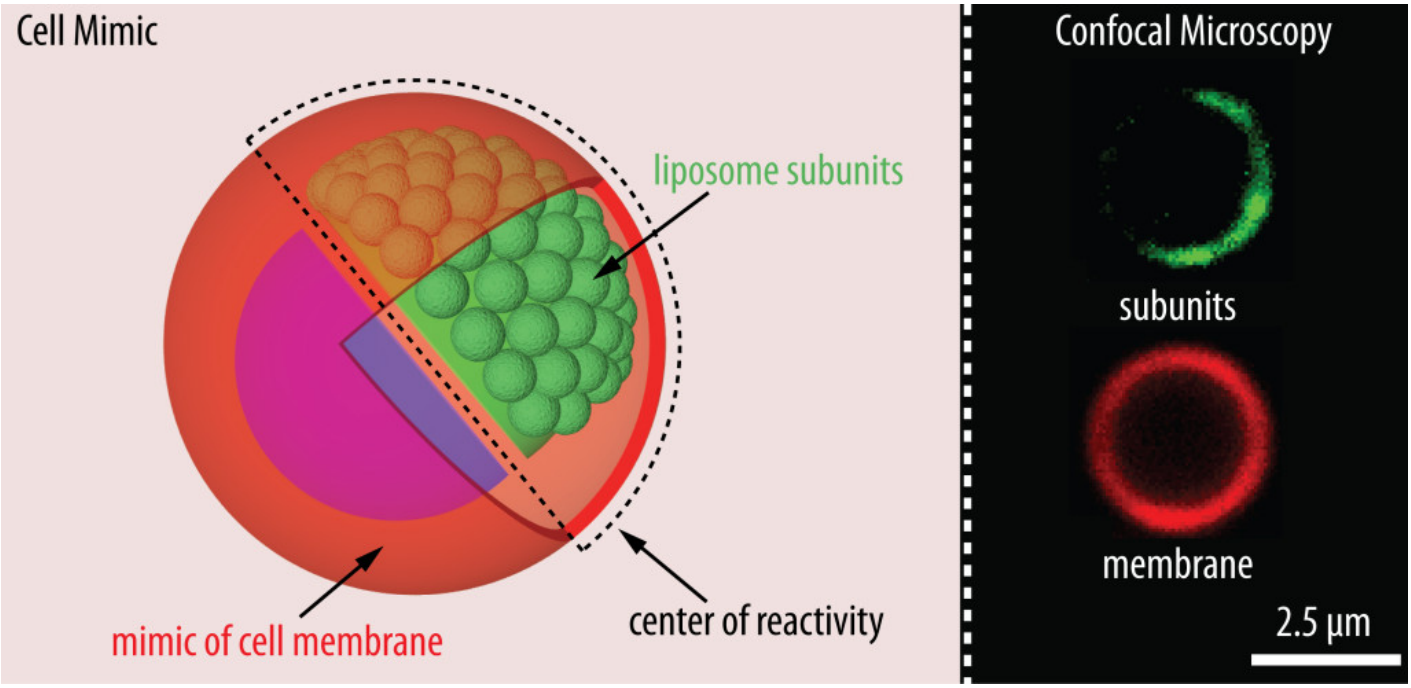
Janus subcompartmentalized microreactors

When we are sick and have to take medicine, the first thing we do, is reading the package leaflet. We want to know the potential side effects of the drug. Sometimes the side effect of one drug is even that serious, that our doctor prescribes another medication, just to relieve the side effect. In this context it would be highly desirable to invent a novel drug system, which considerably decreases the risks of side effects. Imagine a drug which gets activated as soon as it arrives at the side of infection, which can be administered at minimal concentrations, and which can be easily degraded by our body. The emerging field of cell mimicry addresses this drug delivery issue exactly from this perspective and takes the eukaryotic cell as a prototype: surrounded by a lipid bilayer membrane, a plethora of cell organelles simultaneously perform their designated tasks. In order to protect the cell interior from the chemistry of each individual subunit, each organelle is confined by its own membrane.



At Aarhus University (Denmark), the group of Dr. Brigitte Städler focuses on the question how synthetic cells can be realized. During their research they found, that the cell membrane can be mimicked by the utilization of polymers, rather than using lipids. Polymers can be imagined as a chain of single molecules bound together. The utilization of polymers offers several advantages over small molecules: the permeability of the artificial cell membrane can easily be modified, the polymer can be equipped with different functionalities, and polymer membranes are multiple times more stable than lipid bilayers. The spherical shape of the cell membrane is achieved by using a silica sphere template. This glass bead interacts with the polymer and allows for the polymer to be arranged around the template. By dissolving the silica template a well-defined polymer capsule is obtained.

On the other hand lipids are well-suited as artificial cell subunits. As a consequence of their molecular structure, they self-organize into spherical assemblies when exposed to water. These structures are called liposomes and consist of a lipid bilayer. During the assembly step, cargo, like drugs or enzymes, can be easily entrapped within the liposomes. Once confined in the liposome the cargo is protected from its environment. However, the permeability of the lipid bilayer allows for a steady exchange of small molecules to be maintained.

The combination of both the artificial cell membrane, made by polymers, and the liposomes as subunits, enables to fabricate simple artificial cells.

In a recent report, the Städler group took one further step and addressed the question, if the liposomal subunits can be positioned at a well-defined location within the artificial cell. Since almost all cell types have a kind of cell polarity, i.e. the asymmetric organization of cellular components, the answer to this question will considerably enhance the progress in the field of cell mimicry. In their approach they encapsulated trypsin, a digestive enzyme, within the liposome subunits and deposited them in a controlled-fashion in one half of the synthetic cell. The activity of trypsin was monitored by adding a fluorescent protein to the cell mimics. Using microscopic characterization techniques the group was able to localize a center of reactivity in the artificial cell and thus confirmed the successful asymmetric organization of the subunits.

These fundamental findings will help to improve the discipline of cell mimicry. By addressing the aspect of the controlled positioning of subunits, synthetic cells can be fabricated with enhanced enzymatic activity, which in turn will allow for a decreased concentration of drugs to be used and substantially decrease the risks of potential side effects.

Publication

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