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New tool for synthetic biology: DNA nanorobots that can alter artificial cells

Scientists at the University of Stuttgart have succeeded in controlling the structure and function of biological membranes with the help of "DNA origami". The system they developed may facilitate the transportation of large therapeutic loads into cells. This opens up a new way for the targeted administration of medication and other therapeutic interventions. Thus, a very valuable instrument can be added to the toolbox of synthetic biology. Prof. Laura Na Liu and her team published their findings in the journal "Nature Materials" (DOI: 10.1038/s41563-024-02075-9).

The shape and morphology of a cell play a key role in the biological function. This corresponds to the principle of "form follows function", which is common in modern fields of design and architecture. The transfer of this principle to artificial cells is a challenge in synthetic biology. Advances in DNA nanotechnology now offer promising solutions. They allow the creation of novel transport channels that are large enough to facilitate the passage of therapeutic proteins across cell membranes. In this emerging field, scientists such as Prof. Laura Na Liu, Director of the 2nd Physics Institute at the University of Stuttgart and Fellow at the Max Planck Institute for Solid State Research (MPI-FKF), have developed an innovative tool for controlling the shape and permeability of lipid membranes in synthetic cells. These membranes are made up of lipid bilayers that enclose an aqueous compartment and serve as simplified models of biological membranes. They are useful for studying membrane dynamics, protein interactions, and lipid behavior.

A milestone in the application of DNA nanotechnology

This new tool may pave the way for the creation of functional synthetic cells. The scientific work of Laura Na Liu aims to significantly influence the research and development of new therapies. Liu and her team have succeeded in using signal-dependent DNA nanorobots to enable programmable interactions with synthetic cells. "This work is a milestone in the application of DNA nanotechnology to regulate cell behavior," Liu says. The team works with giant unilamellar vesicles (GUVs), which are simple, cell-sized structures that mimic living cells. Using DNA nanorobots, the researchers were able to influence the shape and functionality of these synthetic cells.

New transport channels for proteins and enzymes

DNA nanotechnology is one of Laura Na Liu's main research areas. She is an expert in DNA origami structures — DNA strands that are folded by means of specifically designed shorter DNA sequences, so-called staples. The team of Liu used DNA origami structures as reconfigurable nanorobots that can reversibly change their shape and thereby influence their immediate environment in the micrometer range. The researchers found that the transformation of these DNA nanorobots can be coupled with the deformation of the GUVs and the formation of synthetic channels in the model GUV membranes. These channels allowed large molecules to pass through the membrane and can be resealed if necessary.

Fully artificial DNA structures for biological environments

"This means that we can use DNA nanorobots to design the shape and configuration of GUVs to enable the formation of transport channels in the membrane," says Prof. Stephan Nussberger, who is a co-author of this work. "It is extremely exciting that the functional mechanism of the DNA nanorobots on GUVs has no direct biological equivalent in living cells," adds Nussberger.

The new work raises new questions: Could synthetic platforms - such as DNA nanorobots - be designed with less complexity than their biological counterparts, which would nevertheless function in a biological environment?

Understanding disease mechanisms and improving therapies

The new study is an important step in this direction. The system of cross-membrane channels, created by DNA nanorobots, allows an efficient passage of certain molecules and substances into the cells. Most importantly, these channels are large and can be programmed to close when needed. When applied to living cells, this system can facilitate the transportation of therapeutic proteins or enzymes to their targets in the cell. It thus offers new possibilities for the administration of drugs and other therapeutic interventions. "Our approach opens up new possibilities to mimic the behavior of living cells. This progress could be crucial for future therapeutic strategies," says Prof. Hao Yan, one of the co-authors of this work.

About Prof. Laura Na Liu, her team, and the authors of the study

Laura Na Liu is the Director of the 2nd Physics Institute at the University of Stuttgart, Fellow at the Max Planck Institute for Solid State Research (MPI-FKF), and one of the main authors of the study. The interdisciplinary research team includes members of several institutes of the University of Stuttgart: the 2nd Physics Institute, the Department of Biophysics at the Institute of Biomaterials and Biomolecular Systems and the Institute of Theoretical Physics IV. Also involved in the study is Prof. Hao Yan, a recipient of the Alexander von Humboldt Research Award. He is hosted by Liu's group and is doing research at the Biodesign Center for Molecular Design and Biomimetics at Arizona State University.

About the study

Sisi Fan, Shuo Wang, Longjiang Ding, Thomas Speck, Hao Yan, Stephan Nussberger, Na Liu. Morphological transformation and formation of membrane channels in synthetic cells through reconfigurable DNA nanotubes. Nature Materials, DOI: 10.1038/s41563-024-02075-9

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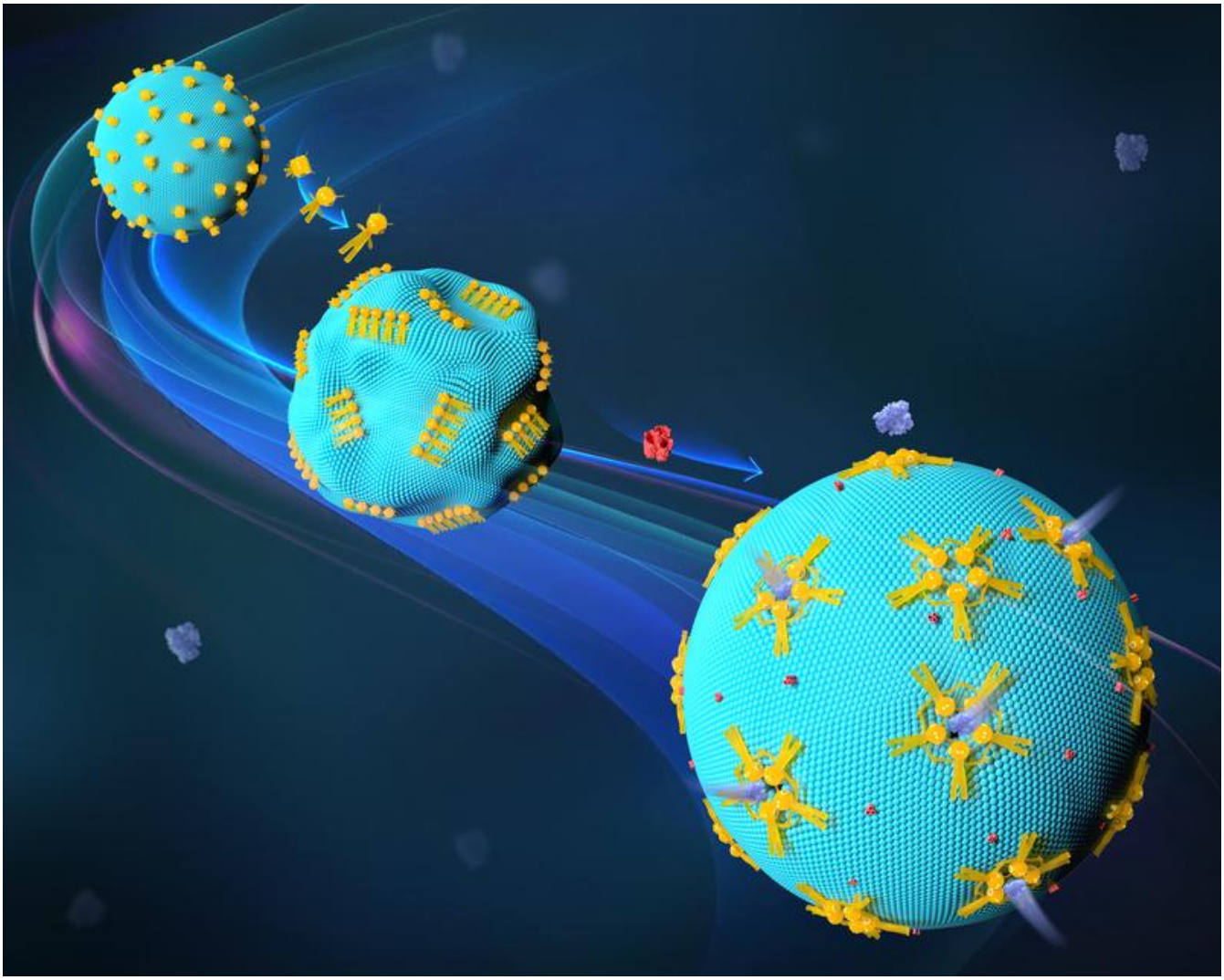

Reconfigurable DNA nanorobots that are working on the surface of synthetic cells.
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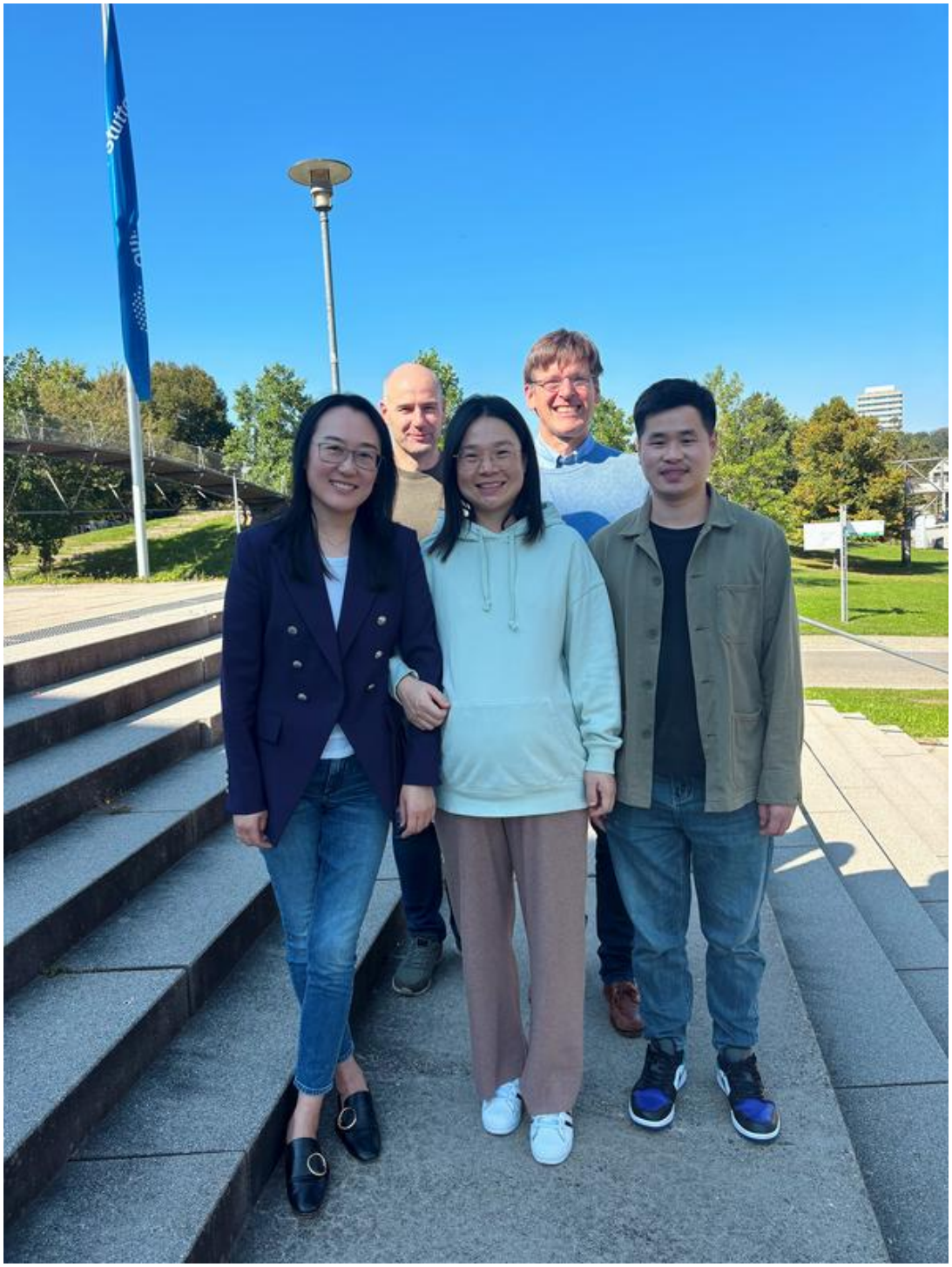

The Stuttgart team (from left to right): Prof. Laura Na Liu, Prof. Thomas Speck, Dr. Sisi Fan, Prof. Stephan Nussberger, Dr. Longjiang Ding.
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