BIOMATERIALS

Trapping virus in a shell

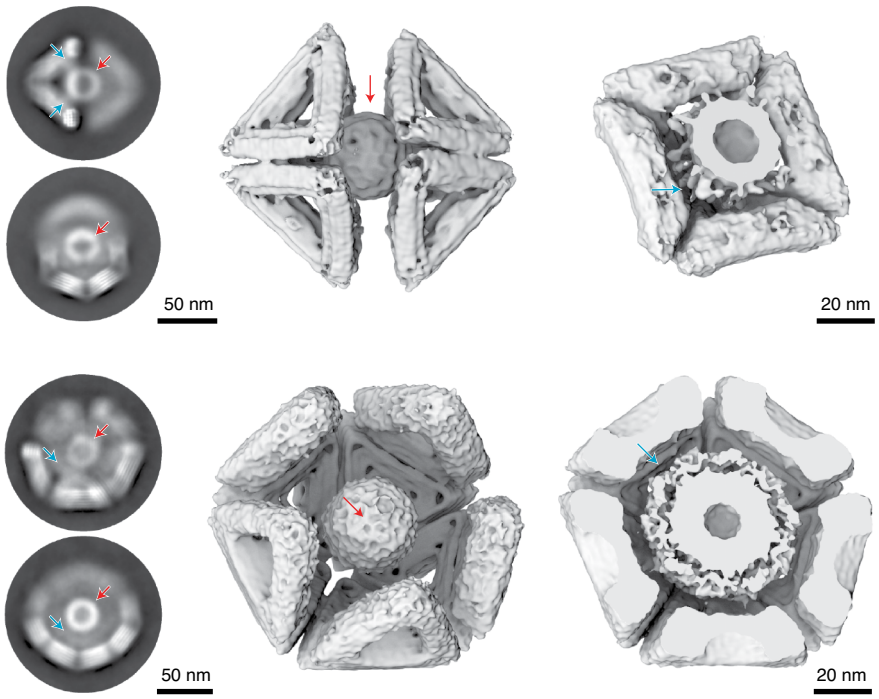
Researchers design DNA shells to trap virus particles and thus prevent interactions between viruses and host cells.

The inherent programmability in DNA molecules makes DNA an attractive material to create three-dimensional (3D) objects with predefined geometry, including virus-sized objects that can engulf and trap virus particles.

"In summer 2019, pre-COVID-19 actually, we had completed building first prototypes of icosahedral shells made from DNA, without any particular application in mind I must confess. This was purely an explorative design endeavor," says Hendrik Dietz from the Bionanotech & Molecular Robotics Lab at the Technical University of Munich, Germany. One day, he was staring at the models of these DNA icosahedral shells and wondered whether the DNA shells could be used to "quarantine" viruses.

The rules governing the structure of viral capsids were described by Casper and Klug in the 1960s: the triangulation number (T number), or the number of distinct quasi-equivalent triangular subunits, can be calculated by the arrangement of pentamers and hexamers within an icosahedral capsid. Dietz and colleagues implemented the same design principles to build synthetic icosahedral capsids from DNA building blocks, which offer advantages including "control over absolute dimensions, modularity, adaptability, multivalency," says Dietz. The triangular subunits, assembled from DNA molecules, provide the geometric instructions for the formation of the icosahedral canvas. Using cryo-electron microscopy, the team confirmed the formation of triangular subunits and assembled octahedral and icosahedral shell structures. They were able to construct shell structures from 180 DNA triangles with a diameter of 300 nm.

The programmable DNA triangles enable the design of different topographic features and thus offer the ability to cover a user-designed area on the icosahedral canvas. To confer specificity for trapping, virus binders such as oligo-labeled antibodies are hybridized to the interior shell for engulfing, for example, hepatitis B virus (HBV) core particles. The researchers demonstrated that octahedral half shells could effectively inhibit HBV interaction with surfaces in an in vitro blocking assay.



2D cryo-EM class averages (left), reconstruction (middle) and a cross-section through the cryo-EM map (right) of an octahedral half-shell with trapped HBV core particles. Credit: Reprinted with permission from C. Sigl et al. *Nat. Mater.* https://doi.org/10.1038/s41563-021-01020-4 (2021), Springer Nature

Changing the virus binders enables trapping of different types of virus. In a second example, the researchers trapped adeno-associated virus serotype 2 (AAV2) with anti-AAV2 antibody. The virus-engulfing half shells neutralized the virus better than free anti-AAV2 in cell culture.

In addition, multi-facet shells offer a way to display functionalization in a multivalent manner by employing a variety of binders such as antibodies, proteins and aptamers.

DNA shells do face some limitations. The native DNA structures become unstable at low ionic strength because of the expansion induced by internal electrostatic forces. To stabilize the shell structures, the researchers applied ultraviolet point welding to generate covalent bonds in the triangle subunits, and they protected the shells from nuclease degradation with an oligolysine–PEG copolymer coating.

Dietz's lab is working to construct shell variants that can engulf filamentous viruses, as well as larger half-shells that can be used to trap SARS-CoV-2 or Influenza. Dietz envisions the shells also being useful as carriers for multivalent display of antigens in vaccination. "You could put, for example, 180 copies of an influenza envelope protein on the outside, which is more than other existing platforms can currently accommodate and may help eliciting a potent antibody response."

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