Building antimicrobial viruses from breast milk

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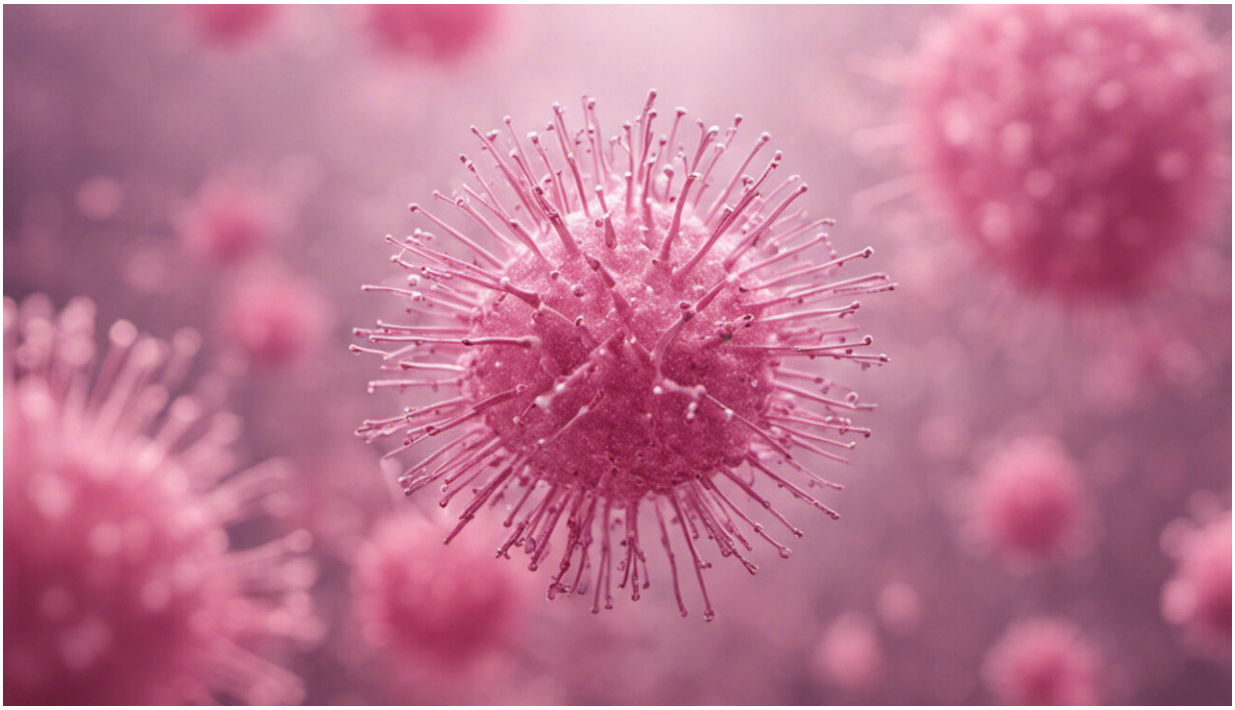


Credit: AI-generated image (disclaimer)

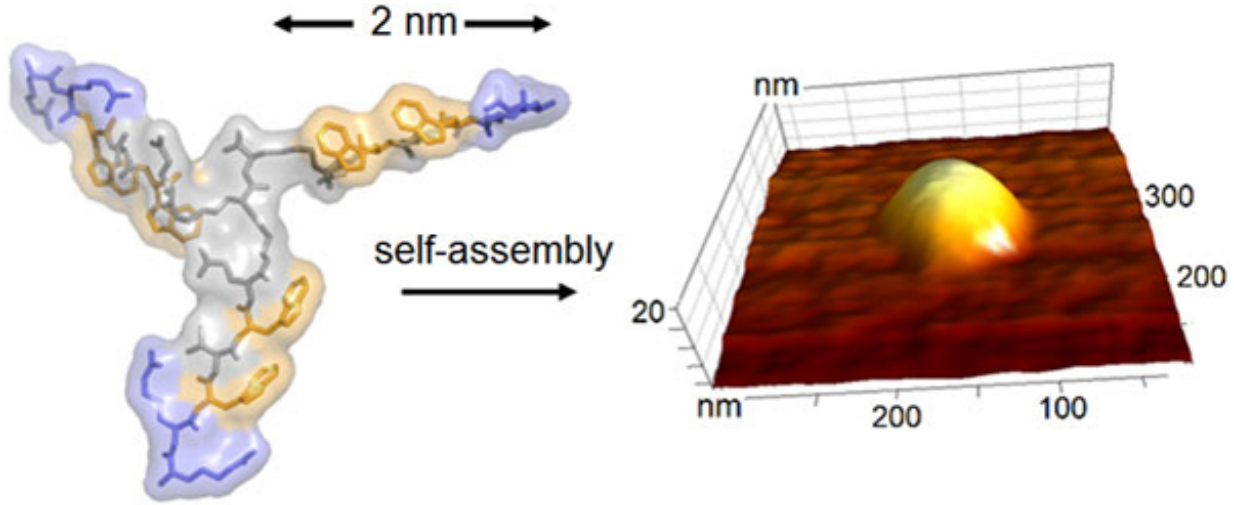
Scientists from the National Physical Laboratory (NPL) and UCL have converted a breast milk protein into an artificial virus that kills bacteria on contact.

As well as providing all the energy and nutrients that infants need for the

first months of life, breast milk protects against infectious diseases. Lactoferrin is a protein in milk which provides antimicrobial protection to infants, effectively killing bacteria, fungi and even viruses.

The antimicrobial activities of this protein are mainly due to a tiny fragment, less than a nanometre across, made up of six amino acids. Based on the metrology of antimicrobial mechanisms, the team predicted that copies of this fragment gather at the same time, and at the same point, to attack bacterial cells by targeting and disrupting microbial membranes.

Recognising the potential applications in the fight against antimicrobial resistance, the team re-engineered the fragment into a nanoscale building block which self-assembles into virus-like capsules, to effectively target bacteria (see figure below). Not only can these capsules recognise and bind to bacteria, but they also rapidly convert into membrane-damaging holes at precise landing positions.



The chemical structure of the nanoscale building block (left) and its assembly into a virus-like capsule (right, topographic AFM image)

Hasan Alkassem, a joint NPL/UCL EngD student who worked on the project, explains:

"To monitor the activity of the capsules in real time we developed a high-speed measurement platform using atomic force microscopy. The challenge was not just to see the capsules, but to follow their attack on bacterial membranes. The result was striking: the capsules acted as projectiles porating the membranes with bullet speed and efficiency."

Remarkably, however, these capsules do not affect surrounding human cells. Instead, they infected them like viruses do. When viruses are inside human cells they release their genes, which then use the body's cellular machinery to multiply and produce more viruses. But if viral genes are replaced with drugs or therapeutic genes, viruses become effective tools in the pursuit of gene therapy to cure many diseases, from cancer to cystic fibrosis.

The research team explored this possibility and inserted model genes into the capsules. These genes were designed to switch off, or silence, a target process in human cells. The capsules harmlessly delivered the genes into the cells and effectively promoted the desired silencing. With therapeutic genes, this capability could be used to treat disorders resulting from a single mutated gene. Sickle-cell disease, cystic fibrosis or Duchenne muscular dystrophy are incurable at present, but can be cured by correcting corresponding mutated genes. The capsules therefore can serve as delivery vehicles for cures.

The findings are reported in *Chemical Science* - a journal of the Royal Society of Chemistry which publishes findings of exceptional significance from across the chemical sciences - and effectively demonstrate how measurement science can offer innovative solutions to

healthcare, which build on and extend natural disease-fighting capabilities.

More information: Valeria Castelletto et al. Structurally plastic peptide capsules for synthetic antimicrobial viruses, *Chem. Sci.* (2016). DOI: 10.1039/C5SC03260A

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