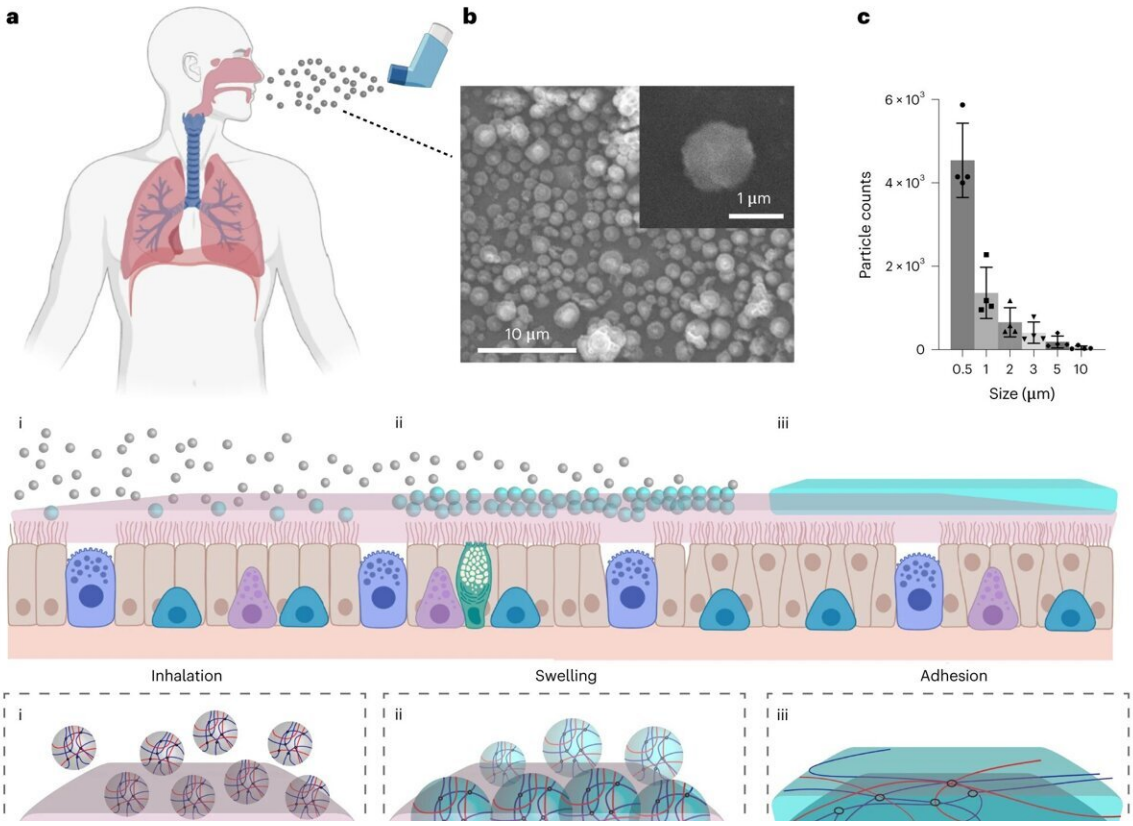
Inhalable powder could protect lungs against COVID-19, flu viruses

February 9 2023, by Tracey Peake



Fabrication and characterization of SHIELD. **a**, Schematic showing the concept of the SHIELD method. Dry SHIELD particles (gray spheres) are inhaled and they become swollen (blue spheres) once they are in contact with the mucus layer (pink layer). Finally, it forms a layer of hydrogel (blue layer) and adheres to the mucus layer. The process includes inhalation (i), swelling (ii) and adhesion (iii). **b**, A representative SEM image showing the morphology of SHIELD particles before swelling. The inset shows a zoomed-in view of one particle. **c**, Aerodynamic diameter of SHIELD particles. Data are mean ± s.d.; $n = 4$

independent experiments. **d–f**, Swelling behavior study. **d**, Representative optical microscopy images showing the morphological changes of SHIELD particles during a period of ten minutes in water. Scale, 50 μm. **e**, Volume change of spherical hydrogel in contact with water. The volume was calculated from the measured diameters during the swelling process. Data are mean ± s.d.; $n = 5$ independent experiments. **f**, A representative SEM image showing the hydrogel network after SHIELD particle swelling. **g**, Fourier-transform infrared spectrum showing the presence of PAAc-NHS ester within SHIELD particles. **h**, Mucoadhesive study using NH_2-labelled beads. Fluorescence images showing the interaction between microbeads (blue) and swollen SHIELD particles (red). In **b** and **h**, independent experiments were performed ($n = 5$) with similar results.

Researchers have developed an inhalable powder that could protect lungs and airways from viral invasion by reinforcing the body's own mucosal layer. The powder, called Spherical Hydrogel Inhalation for Enhanced Lung Defense, or SHIELD, reduced infection in both mouse and non-human primate models over a 24-hour period, and can be taken repeatedly without affecting normal lung function.

"The idea behind this work is simple—viruses have to penetrate the mucus in order to reach and infect the cells, so we've created an inhalable bioadhesive that combines with your own mucus to prevent viruses from getting to your lung cells," says Ke Cheng, corresponding author of the paper describing the work. "Mucus is the body's natural hydrogel barrier; we are just enhancing that barrier."

Cheng is the Randall B. Terry, Jr. Distinguished Professor in Regenerative Medicine at North Carolina State University's College of Veterinary Medicine and a professor in the NC State/UNC-Chapel Hill Joint Department of Biomedical Engineering.

The inhalable powder microparticles are composed of gelatin and

poly(acrylic acid) grafted with a non-toxic ester. When introduced to a moist environment—such as the respiratory tract and lungs—the microparticles swell and adhere to the mucosal layer, increasing the "stickiness" of the mucus.

The effects are most potent during the first eight hours after inhalation. SHIELD biodegrades over a 48-hour period, and is completely cleared from the body.

In a mouse model, SHIELD blocked SARS-CoV-2 pseudovirus particles with 75% efficiency four hours after inhalation, which fell to 18% after 24 hours. The researchers found similar results when testing against pneumonia and H1N1 viruses.

In a non-human primate model of both the original and delta SARS-CoV-2 variants, SHIELD-treated subjects had reduced viral loads—from 50 to 300-fold less than control subjects—and none of the symptoms commonly associated with infection in primates, such as lung inflammation or fibrosis. Since primates do not exhibit the same symptoms of infection as humans, viral load is the standard marker used to determine exposure.

The researchers also looked at potential toxicity both in vitro and in vivo: 95% of cell cultures exposed to a high concentration (10 mg ml-1) of SHIELD remained healthy, and mice who were given daily doses for two weeks retained normal lung and respiratory function.

"SHIELD is easier and safer to use than other physical barriers or anti-virus chemicals," Cheng says. "It works like an 'invisible mask' for people in situations where masking is difficult, for example during heavy exercise, while eating or drinking, or in close social interactions. People can also use SHIELD on top of physical masking to have better protection.

"But the beauty of SHIELD is that it isn't necessarily limited to protecting against COVID-19 or flu. We're looking at whether it could also be used to protect against things like allergens or even air pollution—anything that could potentially harm the lungs."

The study appears in *Nature Materials*.

More information: University of North Carolina at Chapel Hill and North Carolina State University, Chapel Hill & Raleigh, NC, USA, An inhaled bioadhesive hydrogel to shield non-human primates from SARS-CoV-2 infection, *Nature Materials* (2023). DOI: 10.1038/s41563-023-01475-7.
www.nature.com/articles/s41563-023-01475-7

Provided by North Carolina State University