





Going viral

From SARS to the common cold,
Baric's research could lead to vaccines

An issue of *Carolina Public Health* on innovation would be incomplete without an article on Ralph Baric, PhD, and his work with viruses.

After all, he's the epidemiology professor who synthetically reproduced the variant of the SARS virus found in bats—probably the species from which the deadly human version emerged.

"Only three other teams of researchers have synthetically reconstructed a virus," he said when his research was published in the *Proceedings of the National Academy of Science*. "It will provide a model to understand the means and ease by which animal coronaviruses move from one species to another."

Baric and his team of researchers at UNC Gillings School of Global Public Health are world leaders in coronavirus research. This type of RNA virus is responsible not only for

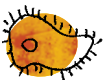
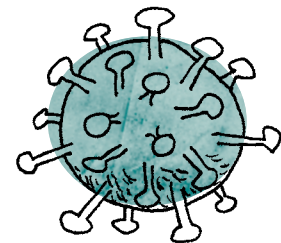
SARS but also for other types of childhood pneumonia and even the common cold.

"The lab has rewired the coronavirus genome—taking out the natural regulatory signals and rewiring them with synthetic signals," explains Eric Donaldson, PhD, research assistant professor of epidemiology.

"This prevents the rewired virus from recombining with natural strains of the virus and prevents reversion of vaccine strains into more dangerous strains. However, the rewired virus still causes a similar immune response in the body."

Baric and his team were awarded a Gillings Innovation Lab (GIL) to develop a low-cost, single-dose vaccine against respiratory illness in children living in developing countries. This vaccine would treat influenza, RSV and measles; be stable at room temperature; and inhaled, rather than given with a needle. If they are successful, their work could lead to a new approach for designing and administering other global health vaccines.

"No one has ever successfully delivered three antigens from three



different highly pathogenic respiratory viruses simultaneously in a highly portable platform that would be affordable and easy to use in the developing world," Baric said after receiving his GIL.

Any of these three projects—the synthetic reproduction of SARS, the genetic rewiring of coronavirus or the multivalent vaccine—could yield astounding stories about innovation. But Baric wanted to focus on yet another innovative project.

"Let's talk about norovirus," he suggested.

Noroviruses are those nasty little bugs that cause great misery—48 to 72 hours of vomiting and/or diarrhea in healthy adults. In infants and the elderly, the virus can be fatal.

"It only takes a few virus particles from respiratory droplets or fecal contamination to cause explosive transmission of the disease, especially in isolated communities," he said.

In communities such as retirement homes, college dormitories, military installations, cruise ships and even airplanes, the infection can have devastating results.

People can acquire norovirus infections more than once in a season.

"It's been thought that the body's immune response to norovirus infection is short-lived, and that's why people become reinfected," Baric said. "We don't believe that this represents the whole story. We think the virus is changing rapidly, so the body's immune



RAMONA DUBOSE

Lisa Lindesmith, an epidemiology research specialist at the School, studies norovirus immunity in Dr. Ralph Baric's laboratory.



Dr. Ralph Baric's innovative work with viruses may lead to a portable, single-dose vaccine to prevent respiratory illness in children in developing countries.

system doesn't recognize the new strain."

The change is known as "antigenic drift." Immunity a person might have built up to one variation of the virus is powerless against the next strain. But Baric hopes that by finding common elements of the viruses' genetic structure—and then causing the body to build immunity to those elements—he can create a vaccine effective against about 95 percent of the norovirus strains that infect humans.

"His work, although still with mice, has shown there is a way to develop effective vaccines against these viruses, even though you have to cover quite a few genetic types," said Jan Vinjé, PhD, norovirus team leader in the Gastroenteritis and Respiratory Viruses Laboratory Branch of the U.S. Centers for Disease Control and Prevention.

"[Baric] brings a fresh, new perspective to the field," Vinjé said.

Lisa Lindesmith, an epidemiology research specialist who's been working with Baric for 10 years, agrees.

"We are moving the field from the idea of short-term immunity. This is groundbreaking work, and so is the coronavirus work. It's very rare for a lab to be so good at two different things." ■

—Ramona DuBose