Computer-Aided Influenza Virus Vaccine Method Could Lead To Effective And Safe Seasonal Vaccines

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(PhysOrg.com) -- A team of molecular biologists and computer scientists at Stony Brook University have used a novel method to weaken (attenuate) influenza virus by way of designing hundreds of mutations to its genetic code to create an effective vaccine.

A team of molecular biologists and computer scientists at Stony Brook University have used a novel method to weaken (attenuate) influenza virus by way of designing hundreds of mutations to its genetic code to create an effective vaccine. Reported online and in the July issue of Nature Biotechnology, the method may be a major step in developing more effective and safe vaccines against influenza, which claims 250,000 to 500,000 lives annually worldwide, partly because existing vaccines are not fully effective.

The research is an outgrowth of years of investigation by a team headed by Eckard Wimmer, Ph.D., Distinguished Professor, Department of Molecular Genetics and Microbiology at Stony Brook University. In 2002, Dr. Wimmer and colleagues synthesized and generated poliovirus, the first artificial synthesis of any virus. Two years ago, they designed and synthesized a new class of attenuated polio viruses. Viruses attenuated by traditional means often make effective vaccines but sometimes mutate to regain virulence. The creation of synthetic viruses nearly eliminates the possibility of the virus regaining virulence.

In their latest research, the same method that the team used to create weakened synthetic polio viruses was employed to design an influenza vaccine. They found this vaccine effective and safe against influenza in mice.

"Essentially, we have rewritten the virus' genetic instructions manual in a strange dialect of genetic code that is difficult for the host cell machinery to understand," says Steffen Mueller, Ph.D., Senior Author and Research Assistant Professor of Molecular Genetics and Microbiology. "This poor line of communication leads to inefficient translation of viral protein and, ultimately, to a very weak virus that proves to be ideal for immunization."

Dr. Mueller and colleagues made a synthetic influenza virus (strain A/PR/8/34) containing hundreds of changes in its genetic code. The changes they chose are commonly referred to as "silent" mutations because they do not alter the proteins that the virus produces. However, through computer algorithms developed by the researchers, mutations are arranged such that the resulting viral genome will produce less of those proteins, a process called "de-optimization," a weakening of the virus.

"We used our 'death by a thousand cuts' method to create the mutated synthetic virus," says Dr. Mueller. "Because the synthetic sequence contains hundreds of changes, the synthetic virus has essentially no possibility of regaining virulence."

The researchers call the process "Synthetic Attenuated Virus Engineering," or "SAVE." They believe the SAVE approach can be applied to any emerging influenza virus strain. If shown applicable to influenza in humans, the SAVE method could become an essential tool in developing vaccines that may be effective against seasonal and pandemic influenza threats.

The Stony Brook team discovered that very small amounts of the new synthetic influenza virus safely and effectively immunized mice against an otherwise lethal virus strain. The synthetic virus did not cause disease in the animals unless given at doses about 1000-fold higher than the dose needed for immunization.

Titled "Live attenuated influenza virus vaccines by computer-aided rational design," the journal piece summarizes the researchers' scientific approach to developing synthetic virus vaccines.

Provided by Stony Brook University

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