Decoy Viruses Could Lead to Vaccines

The ploy works in duck hunting. A wooden decoy, artfully painted, can fool real ducks into thinking it is a fellow feathered friend.

Within our own bodies, vaccines work along similar lines. Take a virus, disarm its infectious machinery while preserving its immunity-stimulating surface proteins, and one can use it to prevent disease. Primed by the detoxified virus, the vaccinated body's immune system gears up to fight an infectious agent. When the real virus shows up, the body stands prepared to fell the invader.

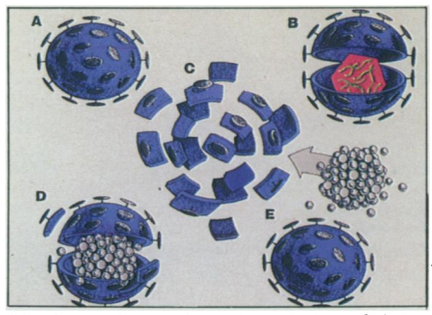
But using a whole virus for a vaccine presents problems. The deactivated virus might not prove harmless, or the body might not recognize the coreless, collapsed virus. Instead, why not hook the key proteins needed for an immune response to something else?

In essence, Nir Kossovsky, a pathologist at the University of California, Los Angeles, and his colleagues have done just that. Making decoy viruses from ceramic materials, coating them with sugars, then attaching key viral proteins to their outer shells, he has fashioned a phony virus that may some day lead to vaccines for a wide variety of illnesses.

At a meeting of the American Chemical Society in San Diego last week, Kossovsky said that "a vaccine agent works best when it looks like the organism it aims to cause an immunity against. . . . We take the virus' surface proteins, remove the infectious core, and replace that genetic core with a ceramic core. The proteins then reassemble themselves on the ceramic." The decoy virus has the same shape as the real virus, he adds, so "the decoy acts as an effective immunizing agent."

In general, a virus' core contains a matrix of proteins and genetic materials that keeps it intact, he says. That matrix supports an outer shell, which holds the proteins that trip an immune response. The catch, Kossovsky says, lies in removing the infectious core without collapsing the virus. Once collapsed, the virus no longer triggers an immune reaction.

Kossovsky's laboratory, in tandem with Structured Biologicals, a biotech firm in Toronto, is testing various ways to apply this concept. For vaccines, they take tiny carbon cores — diamond dust — and coat them with a bioactive sugar, which secures the proteins and keeps them from dehydrating. Kossovsky borrowed the sugar idea from desert fungal spores, which remain biologically active after baking for months in the sun. When moistened, the spores' major molecules, preserved by the sugar, return to life.



Kossovsky *et al.*

Making a decoy virus: A real virus (A) is stripped of its genetic core (B). The virus' surface proteins (C) then reassemble around an artificial granular core (D), yielding a decoy virus (E).

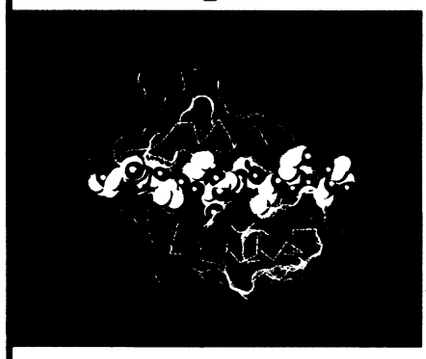
Tests under way involve proteins from the Epstein-Barr virus, HIV (the AIDS virus), and SIV — the monkey version of HIV. Kossovsky says early results show that the decoys do prompt immune responses in lab tests and in animals.

"In three animal groups tested over a year, the decoy viruses elicited immune responses comparable to those caused by live viruses." Also, data show that "the decoy virus' surface acts much like the real virus' surface. So the decoy virus has potential as a vaccine candidate."

Clinical trials remain years away. Yet other, related projects spur optimism. Kossovsky has made molecular transport agents for insulin and hemoglobin using tiny granules of a degradable bone-like material, calcium phosphate dihydrate, as cores. Measuring 50 to 80 nanometers wide — about one-thousandth the size of red blood cells — the ceramic nodules can carry either insulin or hemoglobin. In rabbit tests, nodule-bound insulin in blood remained active twice as long as unbound insulin, while still altering glucose concentrations, Kossovsky says. Tests of hemoglobin ferrying "artificial blood," he adds, show that the bound hemoglobin retains its full ability to transport oxygen.

Though a novel idea with a long way to go, this method could some day deliver many different drugs and antigens, Kossovsky says. It could even spawn a new class of vaccines made from agents with, literally, "a heart of stone." — *R. Lipkin*

Immune presentation: In the groove II



Stern *et al.*/NATURE

The body depends on a few types of large proteins to determine whether substances are friend or foe. These proteins get their names from the genes that code for them — the major histocompatibility complex (MHC).

Last year, several research groups figured out how one class of these molecules, known as MHC-I proteins, binds to small pieces of protein and presents those pieces, called peptides, to the body's immune system (SN: 1/30/93, p.72).

On the basis of X-ray crystallographic data, researchers have now created this computer graphic. It shows that another type of MHC molecule, MHC-II, does a similar job but in a different way, says Lawrence J. Stern of the Howard Hughes Medical Institute (HHMI) at Harvard University. Stern, HHMI's Don C. Wiley, and their colleagues used genetically altered insect cells grown in the laboratory to make the MHC-II proteins and then added peptides copied from a flu virus protein to get a pure, easy-to-study protein-peptide complex.

Like an MHC-I protein, this MHC-II protein (in blue) binds to the peptide's backbone and contains pockets that can hold the side chains of the peptide's amino-acid building blocks. (Its carbon, nitrogen, and oxygen atoms are yellow, blue, and red, respectively.) But this MHC groove contains specific amino acids (found in many organisms' MHC-II proteins) that make weak connections called hydrogen bonds along the length of the peptide rather than just grabbing the peptide at its ends, as MHC-I does. Thus, it can accommodate longer peptides than an MHC-I protein and even allow the ends to hang out of the binding site. This MHC-II molecule also has at least two more pockets for the peptide's side chains.

There's a reason for these differences, the researchers suggest in the March 17 NATURE. MHC-II molecules tend to attach to proteins coming from outside the cell and work alongside the cell's machinery for processing this extracellular material. In contrast, MHC-I handles peptides created internally by the cell, Stern says.

— E. Pennisi