NanoViricides, Inc.
www.nanoviricides.com

The virus catchers

By mimicking the way viruses bind to host cells, NanoViricides is developing unique nanomedicines that are able to trick, trap and destroy these pathogens.

Viral diseases pose a major public health threat worldwide, particularly in developing nations. With the emergence of new epidemics such as the Ebola and Zika viruses, for which there are no current treatment options, innovative technologies to target viruses are of high interest.

The first step in the life cycle of a virus is entry into the target host cell, which happens when a virus protein binds to a receptor on the host cell. After entry, viruses use the internal host cell machinery to replicate and are then released into the organism to infect other cells.

The immune system can inhibit viruses from spreading by various mechanisms, including the production of antibodies to viral proteins. Vaccines against viruses such as influenza induce the production of protective antibodies specific for the virus. However, viruses can escape recognition by such antibodies through natural variations or mutations in their surface proteins, which creates challenges for vaccine developers. Nanomedicine company NanoViricides believes it has found a way to overcome the problem of mutation and effectively target and destroy a wide range of viruses.

What is a nanoviricide?

A nanoviricide is a specially designed micelle that has multiple chemically attached ligands that mimic the host cell receptors preferred by the target virus. By fooling viruses into thinking it is a host cell, the nanoviricide binds to the virus particle; it can then encapsulate the virus by integrating into its lipids and dismantle it (**Fig. 1**). "Each micelle may carry 600–1,200 ligands, with each polymer chain carrying as many as 60 ligands depending upon the design," said Anil Diwan, chairman and president of NanoViricides. "The force of being pulled by the nanoviricide would act like a Venus fly trap, encapsulating the virus." Importantly, nanoviricides can contain multiple ligands, so that even if a virus mutated the nanoviricide would still be able to target and destroy it through another receptor—in contrast to antibodies induced by vaccines, which viruses may evade through mutation.

Nanoviricides also offer several advantages over existing antiviral drugs, many of which cause side effects owing to interactions with intracellular host cell proteins. "Instead of blocking multiplication in cells, our technology targets the viruses directly, and consequently has low toxicity," Diwan said. "Once the nanoviricide has dismantled the virus, the remaining complex is biodegradable in the body." They also work independently of the patient's immune system, which is important because viral infections can disrupt the patient's immune system in different ways.

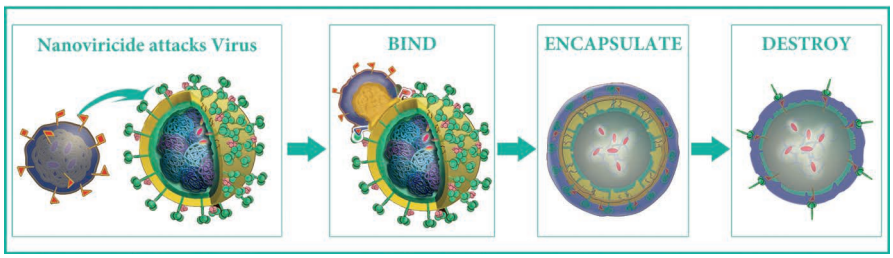

Figure 1: The mechanism by which a nanoviricide binds, encapsulates and destroys a virus.

Pioneers in the field

NanoViricides was founded in 2005 by two virus pioneers—Anil Diwan and Eugene Seymour, the CEO. Diwan sowed the seeds of the company back in 1991 after his research led to the invention of polymeric micelle-based nanomedicine technologies. In 2004, having secured both investor interest and a patent for his technology, Diwan teamed up with Seymour, a human immunodeficiency virus (HIV) specialist working in Los Angeles and specifically overseeing the development of the Hema-Strip blood test.

Diwan and Seymour created NanoViricides to commercialize Diwan's research. Over the next ten years, supported by funding such as $10 million from private angel investors, $25 million from several shelf offerings from Seaside 88 and $20 million in registered direct offerings, the company developed a portfolio of candidates and built its own state-of-the-art multi-kilogram-scale current good manufacturing practice (cGMP) manufacturing facility—a key asset enabling it to develop its candidates from the clinic to market.

Influenza and herpes lead programs

NanoViricides is using its unique technology to develop preclinical candidates that address prominent viral diseases, including influenza, herpes simplex virus (HSV), HIV, hepatitis C, dengue, rabies and Ebola.

The most advanced candidate is the injectable FluCide, a broad-spectrum injectable anti-influenza drug that is intended for hospital patients. Given that one of the main challenges in producing effective seasonal influenza vaccines is the high degree of natural variation in the hemagglutinin (H) and neuraminidase (N) proteins on the surface of the virus, the ability of nanoviricides to target many such proteins is a particular advantage. FluCide has recently demonstrated positive results in animal models against both H1N1 and H3N2 strains, reducing viral load and showing safety even at the maximum feasible dose. An oral version of FluCide that uses the same ligands as the injectable therapy is also being developed for outpatients; similar efficacy has been seen in animal models.

Alongside its lead influenza candidate, NanoViricides is also working on therapies that target the herpes virus family. A number of topical medications are under development that use the same broad-spectrum drug, HerpeCide, against infections caused by HSV-1 (orolabial sores), HSV-2 (genital lesions) and varicella zoster virus (shingles). Herpes keratitis, or ocular herpes infection, is also being addressed within this program with medicated eye drops. Additionally, the company is developing HIVCide, an injectable HIV therapy that has been shown to be over ten times more effective than standard antiretroviral therapy in a mouse model. NanoViricides is developing further candidates targeting the dengue virus, rabies and Ebola.

Partnering for the future

NanoViricides' emerging technology is widely recognized in the field of antivirals, and a number of collaborations have been established with organizations such as the Baylor College Medicine, the University of Pittsburgh, and the University of Wisconsin, among others. "A successful antiviral treatment must affect the viral life cycle at multiple points," said Diwan. "Most developments in the field have involved blocking intracellular virus replication. However, initial viral infection and further reinfection in the body also must be prevented to achieve cure. Nanoviricides are designed to do just that; further, they are designed to tackle the important problem of emerging drug resistance in the field."

The company is now seeking new partners to take its preclinical candidates through to marketing, in particular for its lead influenza and herpes candidates.

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