

Hope for 1st vaccine against virus driving 'mono,' cancers and maybe MS

May 8 2022, by Dennis Thompson



Two experimental vaccines show promise in protecting against infection



with the "mono" virus, which also causes cancer and has been implicated as a potential trigger of multiple sclerosis, a new paper reports.

Tested only in animals so far, the vaccines block two pathways by which the Epstein-Barr virus (EBV) takes root inside the body, said senior researcher Dr. Gary Nabel, president and CEO of ModeX Therapeutics, a small biotech startup in Natick, Mass.

Epstein-Barr is tricky to prevent because it takes up residence in two types of cells, Nabel said—B <u>immune cells</u> that produce antibodies, and <u>epithelial cells</u> that line the internal and external surfaces of the body.

These new vaccines are genetically engineered to induce an <u>immune</u> response that would block infection of both cell types, Nabel said.

"That gives us an opportunity to really damp down any foothold the virus may be able to take in establishing itself in the body," Nabel said. "That's why we think that this is a worthwhile approach, because we've essentially isolated two critical entry proteins for the virus, and can block its ability to enter cells and cause infection."

Currently, there's no approved vaccine that protects against Epstein-Barr virus, which has infected more than 95% of adults worldwide, researchers said in background notes.

Epstein-Barr is primarily known as the cause of mononucleosis.

"It infects B cells in the body, your antibody-producing cells, and it causes those cells to proliferate abnormally," Nabel said. "You get a lot of inflammation, and you get a lot of immune dysregulation. And that's why people feel lousy. That's why it takes several months to get over. That's why you get super infection with these <u>sore throats</u> and upper respiratory symptoms, and these systemic symptoms that give rise to



infectious mono."

But EBV also was the first human virus associated with cancers, primarily lymphomas and gastric cancers, Nabel said. The virus causes more than 200,000 cases of cancer every year.

More recently, researchers also have learned that a person's risk of multiple sclerosis (MS) skyrockets 32-fold if they've been infected with Epstein-Barr, according to a study published in *Science* in January.

It's believed that EBV triggers MS in some people by tricking the <u>immune system</u> into attacking the body's own nerve cells, according to another January study published in *Nature*.

The <u>experimental vaccines</u> work by genetically fusing two different attachment proteins—the keys that allow EBV to enter B cells and epithelial cells—onto a common particle called ferritin, Nabel said.

Ferritin's regular job is to carry iron in the bloodstream, but the <u>genetic</u> <u>engineering</u> gives it an extra purpose, Nabel said.

"It serves as a carrier, where we can essentially decorate the outside of the particle with the <u>viral proteins</u>," Nabel said. The immune system sees the viral infection proteins and mounts a response that theoretically would protect against future infection by the real virus.

The vaccines prompted strong antibody responses in mice, ferrets and monkeys, according to a new report published May 4 in *Science Translational Medicine*.

The vaccines also appeared to block development of lymphomas in "humanized" mice—rodents grafted with human stem cells.



The researchers hope to start <u>human clinical trials</u> for the vaccines within a year, Nabel said. However, it's important to note that results obtained from animal studies aren't always replicated in humans.

Effective EBV vaccines will be the key to ultimately proving the link between the virus and MS, said Bruce Bebo, executive vice president of research programs for the National MS Society.

"In order to prove causation, there's one experiment left to do. That experiment is to have a vaccine and deploy the vaccine, and then observe over a period of time whether it can prevent MS," Bebo said. "We have everything we need to know now to justify an investment in that type of experiment, once we have a safe and effective vaccine."

This study was funded by Sanofi, one of the <u>pharmaceutical companies</u> developing the vaccine.

More information: The U.S. National Institutes of Health has more about <u>Epstein-Barr virus and multiple sclerosis</u>.

Chih-Jen Wei et al, A bivalent Epstein-Barr virus vaccine induces neutralizing antibodies that block infection and confer immunity in humanized mice, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abf3685

Kjetil Bjornevik et al, Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis, *Science* (2022). DOI: 10.1126/science.abj8222

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Citation: Hope for 1st vaccine against virus driving 'mono,' cancers and maybe MS (2022, May



8) retrieved 18 June 2024 from https://medicalxpress.com/news/2022-05-1st-vaccine-virus-mono-cancers.html

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