Nanoparticle vaccine candidate shows promise against emerging tick-borne virus in early studies

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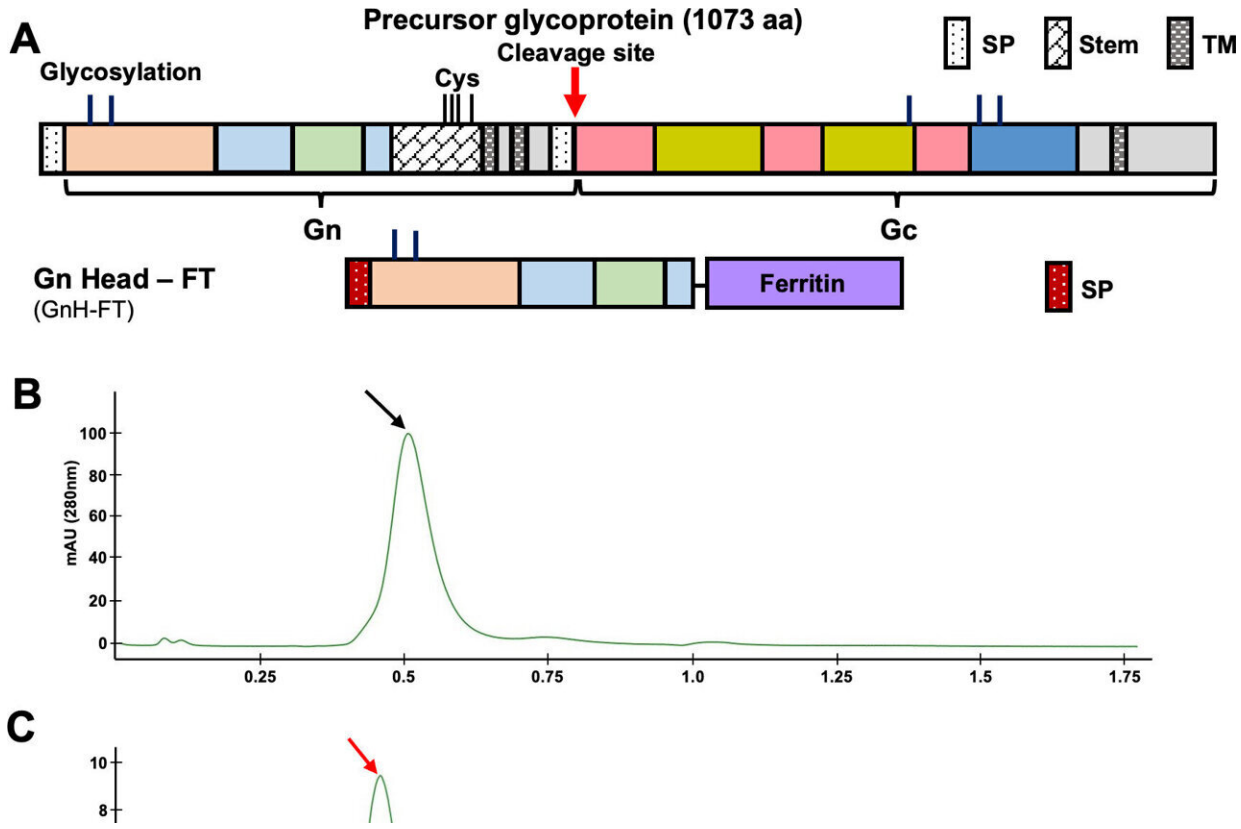

Molecular design and biochemical and antigenic characterization of ferritin nanoparticles (FT) and DBV Gn Head-ferritin (GnH-FT) nanoparticles. (A) Schematic representation of GnH-FT based on previously solved structures and domains of DBV Gn and Gc. The construct was transfected to HEK293T cells to collect the cell supernatant at 72 h after transfection for purification. SP, signal peptide; TM, transmembrane domain. (B and C) Size exclusion chromatograms

to purify FT (B) and GnH-FT (C) using Superdex 200 Increase 10/300 GL and Superose 6 Increase 10/300 GL columns, respectively, on Bio-Rad NGC chromatography system. Fractions corresponding to the colored arrows were separately collected for further analysis. (D and E) Fractions from size exclusion chromatograms of FT and GnH-FT were further analyzed by gradient (7%–20%) SDS-PAGE and Coomassie Brilliant blue staining. Fractions corresponding to the black and red arrows from FT and GnH-FT purifications were loaded to SDS-PAGE gel without boiling ("NB") and with boiling ("B") to characterize head-mediated disassembly of the 24-mer nanoparticle. Intact FT nanoparticle and GnH-FT nanoparticle each have expected molecular weight of approximately 432 kDa and 1,560 kDa. Dissembled FT and GnH-FT monomer each have expected molecular weight of 18 kDa and 65 kDa. (F) Western-blot analysis of different fractions collected from GnH-FT size exclusion chromatogram. In house-generated mouse monoclonal antibody recognizing DBV GnH region was used to detect GnH-FT subunit monomers. Credit: *mBio* (2023). DOI: 10.1128/mbio.01868-23

Cleveland Clinic researchers have used nanoparticles to develop a potential vaccine candidate against Dabie Bandavirus, formerly known as Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV), a tick-borne virus that currently has no prevention, treatment or cure.

The patent-pending vaccine uses nanoparticles to carry the antigens that contain instructions for fighting off a virus. Nanoparticle vaccines are designed to effectively deliver antigens at a lower dose with fewer side effects for at-risk groups—including adults over age 50, who are the most vulnerable to SFTSV and the most susceptible to vaccine side effects.

The pre-clinical research, published in mBio, was led by Jae Jung, Ph.D., Director of Cleveland Clinic's Sheikha Fatima bint Mubarak Global Center for Pathogen and Human Health Research.

"The Pathogen Center was founded to prepare for and protect against future global health crises before they start," says Dr. Jung, who also serves as Department Chair of Cancer Biology and Director of Infection Biology. "There is already a desperate need for a SFTSV vaccine in Asia. Our goal was to develop one before it's needed in America, too."

The World Health Organization had declared SFTSV as needing "urgent research attention" several years ago, and it is still listed as a threat by the National Institutes of Health in the US. The virus spreads through the Asian longhorn tick, a species already present in 19 U.S. states including Ohio. It can also sometimes spread from human to human, mainly in a hospital setting.

Currently, physicians can only address the virus's symptoms and keep infected patients hydrated and comfortable. While many people experience mild symptoms, adults over 50 years old can become severely ill and face a 30% mortality rate.

The benefits of nanoparticles

This same population unfortunately experiences certain vaccine side effects that typically don't affect younger people.

"We become more sensitive to certain vaccine side effects the older we get," says study first author Dokyun (Leo) Kim. "We wanted to develop a treatment that's age-dependent and can be given safely to the people who need it the most."

Nanoparticle vaccines are promising for treating these at-risk groups because the antigens are bundled together, instead of free-floating throughout our bodies. Because our immune cells can find "bundles" of antigens on a nanoparticle more easily, the vaccine can be effective using a lower dose. When the vaccine dosage is reduced, its potential

side effects are reduced as well, according to preliminary research conducted by Kim.

Dr. Jung's lab hopes to test the SFTSV vaccine in humans, next, and Kim says the possibilities don't end there.

"We're working to apply our nanoparticle technology to other viruses," he says. "We have already developed a candidate for COVID-19, and we're not stopping any time soon."

More information: Dokyun Kim et al, Self-assembling Gn head ferritin nanoparticle vaccine provides full protection from lethal challenge of Dabie bandavirus in aged ferrets, *mBio* (2023). DOI: 10.1128/mbio.01868-23

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