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KERALA NIPAH VIRUS OUTBREAK: WHAT ARE MONOCLONAL ANTIBODIES?

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A health worker coming out from the Isolation ward where patients under observation for Nipah are accommodated at the Government Medical College Hospital in Kozhikode on Tuesday. | Photo Credit: The Hindu/K Ragesh

The story so far: Last week, India reached out to Australia to procure monoclonal antibody doses to combat the Nipah virus outbreak in Kerala. India is expecting 20 more doses soon, Indian Council of Medical Research (ICMR) head Dr. Rajiv Bahl said on Friday.

The virus has killed two people so far and has infected at least five others in the Kozhikode district. The current Nipah outbreak is Kerala's fourth since 2018.

India currently has the antibody doses available for ten persons only. Addressing the press, Dr. Bahl said that no one in the country has been administered the dosage so far since it needs to be given at an early stage of infection.

Monoclonal antibodies are laboratory-made proteins that mimic the behaviour of antibodies produced by the immune system to protect against diseases and foreign substances.

An antibody attaches itself to an antigen – a foreign substance, usually a disease-causing molecule – and helps the immune system eliminate it from the body.

Monoclonal antibodies are specifically designed to target certain antigens.

Niels K. Jerne, Georges J.F. Köhler and César Milstein were awarded the medicine Nobel Prize in 1984 for their work on the "the principle for production of monoclonal antibodies".

According to research published in The Lancet journal of Infectious Diseases, m102.4 is a "potent, fully human" monoclonal antibody that neutralises Hendra and Nipah viruses, both outside and inside of living organisms. The antibody has passed phase-one clinical trials — which means that researchers tested it with a relatively small number of people to estimate the right dose of treatment that also doesn't cause side effects.

As of now, the drug is used on a 'compassionate use' basis — a treatment option that allows the use of an unauthorised medicine under strict conditions among people where no other

alternative and/or satisfactory authorised treatment is known to be possible and where patients cannot enter clinical trials for various reasons.

The m102.4 monoclonal antibody was first developed by Dr. Christopher Broder and his team at the Uniformed Services University of the Health Sciences (USU) in Bethesda, Maryland, with help from the U.S. National Institutes of Health (NIH).

Monoclonal antibodies are specifically engineered and generated to target a disease. They are meant to attach themselves to the specific disease-causing antigen. An antigen is most likely to be a protein.

For instance, most successful monoclonal antibodies during the pandemic were engineered to bind to the spike protein of the SARS-CoV-2 virus. The binding prevented the protein from exercising its regular functions, including its ability to infect other cells.

Dr. Köhler and Dr. Milstein, who established a generation of monoclonal antibodies for use in humans in 1975, used this principle to describe the hybridoma – a fusion cell made up of B cells (white blood cells that produce antibodies) and myeloma cells (abnormal plasma cells). These hybrid cells allowed the researchers to produce a single antibody clone, which came to be known as a monoclonal antibody.

The initial technology of producing hybridoma in mice was unsustainable. Today, these antibodies are made using recombinant DNA technology. Here, the gene that codes for the monoclonal antibody's binding region — also known as the variable region — is isolated from a B cell or synthesised in the laboratory. This antibody is then introduced into a host cell, often a bacterium or a mammalian cell, using recombinant DNA technology (which involves manipulating DNA material outside an organism to obtain specific traits or characteristics). The host cells, called bioreactors, produce large quantities of the monoclonal antibodies which are extracted, purified, and readied for use as desired.

Glycoproteins are one of the major components of viruses that cause diseases in humans. According to a research paper published in October 2020, the m102.4 monoclonal antibody binds itself to the immunodominant receptor-binding glycoprotein of the Nipah virus, potentially neutralising it.

The results of a successful clinical safety trial conducted with 40 volunteers between March 2015 and June 2016, for monoclonal antibody m102.4, were published in 2020. Led by Geoffery Playford of Princess Alexandra Hospital in Brisbane, Australia, it was the first in-human, randomised, controlled phase-one study of the safety, tolerability, and immunogenicity of m102.4.

The study was double blind, which means neither the participants nor the researchers knew who received the antibody and who received the placebo. The researchers created eight cohorts of five participants each. In each cohort, six people were randomly administered m102.4 of varying doses, while the remaining two received the placebo.

The most common treatment-related side-effect was headache, reported by 12 of 30 participants in the combined m102.4 group, and three from the pooled placebo group. No deaths or severe effects, which could have caused the study to be discontinued, were noted.

The results of the trial showed that single and repeated doses of m102.4 were well-tolerated and safe, and invoked no adverse responses from the immune systems of participants.

The monoclonal antibody m102.4 for Dr. Playford's clinical trial was manufactured by the Australian Institute for Bioengineering and Nanotechnology (AIBN) at the University of Queensland.

In his press conference, ICMR chief Dr. Bahl mentioned that "no opportunity presented itself to take the research forward" after the first phase of trial.

According to the Queensland Health Department, the antibody has been available in Queensland State since 2010 to treat Hendra virus infections, and has been shared by USU and the Henry M. Jackson Foundation for the Advancement of Military Medicine.

As of 2020, it had been administered to 13 people on compassionate grounds in Queensland. Hendra virus is on the World Health Organisation's list of priority diseases requiring urgent attention for research and development of therapeutics — as is the Nipah virus.

Both Hendra and Nipah viruses are bat-borne Paramyxoviridae – a family of viruses that contain a single-strand RNA of negative-sense genome, similar to the ones that cause diseases like measles, influenza etc., and replicate within infected cells.