Data on Novel Bi-specific Antibody to Treat Zika Virus Infection Published in "Cell"

Antibody shows strong therapeutic potential in vivo
Antibody neutralizes multiple strains of virus, prevents viral escape

Bellinzona, Switzerland and Singapore, September 21, 2017 – The journal Cell today published data with a bi-specific antibody against Zika virus infection. The article is entitled, "A Human Bi-specific Antibody against Zika Virus with High Therapeutic Potential." The study's co-senior authors are Luca Varani, PhD, Group Leader, Structural Biology, Institute for Research in Biomedicine (IRB); Shee Mei Lok, PhD, Associate Professor, Emerging Infectious Diseases Programme, Duke-NUS Medical School (Duke-NUS) and Davide Corti, PhD, Chief Scientific Officer of Humabs BioMed. The publication is accessible here: http://www.cell.com/cell/fulltext/S0092-8674(17)31051-6.

The bi-specific antibody, called FIT-1, which comprises the specificities of both human antibodies ZKA190 and ZKA185, was designed by Humabs BioMed using its proprietary CellClone technology. ZKA190 is a potent Zika virus-neutralizing antibody shown to bind to all surface E proteins on the virus particle and able to distort the quaternary viral structure, while ZKA185 binds to a distinctly different site on the virus and helps prevent viral escape. FIT-1 was shown to potently neutralize strains of the Zika virus isolated around the world and the virus was unable to escape from it.

The interaction between virus and antibody was elucidated by a combination of experimental and computational techniques to understand how FIT-1 blocks the infection cycle. The work took advantage of a recently acquired IRB NMR (nuclear magnetic resonance) machine, the IRB being one of the very few laboratories where high resolution magnetic resonance is used to characterize antibodies.

The laboratory of Associate Professor Shee-Mei Lok at Duke-NUS used electron microscopy imaging at liquid nitrogen temperature to examine the binding effect of the ZKA190 antibody to the Zika virus under high magnification. ZKA190 was observed to break the surface structure of the Zika virus particle, thus explaining its high potency in clearing the virus.

The therapeutic potential of FIT-1 was evaluated in vivo by administering three different doses (15, 5 and 1 mg/kg) at three different time points (one, two and three days post infection). While all doses provided protection against infection, the highest dose (15 mg/kg) had survival rates of 100% with no signs of morbidity, even when treatment was given three days post infection. No viral escape was detected at any of the dose levels at the measured time point of five days post infection.

Luca Varani, PhD, Group Leader, Structural Biology, Institute for Research in Biomedicine, said: “We have shown that Zika has a remarkable ability to change and evade the human immune response. We designed the FIT-1 bispecific antibody to overcome this problem. The strong collaboration of our research teams allowed us to characterize the interaction between Zika virus and the immune system, spanning from atomic interactions to the molecular level,
cells and finally the whole individual. The data we have reported support our design premise and provide a solid basis for bringing FIT-1 forward in development."

“Zika virus infection has turned into a public health threat, particularly due to its association with severe congenital birth defects. The development of an effective vaccine to prevent Zika virus infection poses some risks, and it is important to develop new and alternative approaches,” said Davide Corti, PhD, Chief Scientific Officer of Humabs BioMed, a subsidiary of Vir Biotechnology Inc. “The preclinical data published with FIT-1 bi-specific antibody show early signs of efficacy. We plan to conduct further experiments to determine FIT-1’s effectiveness in blocking fetal infection. We also hope to explore alternative delivery mechanisms for the antibody that could make it more cost effective and thus more accessible to the parts of the world most in need of cures for this disease.”

Associate Prof Shee-Mei Lok from Duke-NUS added: “The FIT-1 antibody has potential to be developed as a therapeutic for the treatment and prevention of Zika virus infection in adults and pregnant women. Hopefully, clinical trials can be accelerated so that the FIT-1 antibody may be used in future outbreaks, as well as to tackle emergency cases of Zika infection in pregnant women.”

About Zika virus
Zika virus belongs to the class of viruses called flaviviruses, which also includes the dengue and West Nile viruses. Zika virus is spread by mosquitoes and has reached large parts of the tropical and subtropical regions of the world, including parts of the United States. The World Health Organization (WHO) declared in early 2016 a state of Public Health Emergency of International Concern (PHEIC) and predicted that 3-4 million people would become infected annually, 1.5 million of these in Brazil alone. While the symptoms of Zika virus infection can be absent or generally mild, the virus appears to invade the neural tissue of the fetus, leading to microcephaly and other neural defects in offspring in up to 13% of cases. The virus can also be spread by bodily fluids, including semen, and so can also be sexually transmitted. While attempts have been made to reduce the spread of the virus by spraying with insecticides, there are currently no vaccines or treatments against Zika, and WHO has declared a need for a long-term approach to combatting this infection. Thus, there is an urgent need to develop therapies to treat this rapidly spreading disease.

About the study authors
Humabs BioMed, a subsidiary of Vir Biotechnology, Inc., San Francisco, California, is based in Switzerland and is focused on discovering and developing fully human monoclonal antibodies to treat serious infections.

The Duke-NUS Medical School (Duke-NUS, 杜克-新加坡国立大学医学院) was established in 2005 as a strategic collaboration between the Duke University School of Medicine, located in North Carolina, USA, and the National University of Singapore (NUS). Duke-NUS offers a graduate-entry, 4-year MD (Doctor of Medicine) training program based on the unique Duke model of education, with one year dedicated to independent study and research projects of a basic science or clinical nature. Duke-NUS also offers MD/PhD and PhD programmes. Duke-NUS has five Signature Research Programs: Cancer and Stem Cell Biology, Neuroscience and Behavioural Disorders, Emerging Infectious Diseases, Cardiovascular and Metabolic Disorders, and Health Services and Systems Research.
Duke-NUS and SingHealth have established a strategic partnership in academic medicine that will guide and promote the future of medicine, tapping on and combining the collective strengths of SingHealth's clinical expertise and Duke-NUS' biomedical sciences research and medical education capabilities.

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The Institute for Research in Biomedicine
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