Breakthroughs in Chikugunya research spell new hope for better treatment and protection

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Recent breakthroughs in Chikungunya research spearheaded by scientists at A*STAR's Singapore Immunology Network (SIgN) have made great strides in the battle against the infectious disease. Working in close collaborations with Singapore clinician-scientists and international researchers, Dr Lisa Ng, Principal Investigator of the Chikungunya research group at SIgN, led the team to discover a direct biomarker which serves as an early and accurate prognosis of patients who have a higher risk of the more severe form of Chikungunya fever (CHIKF). This means that doctors can now quickly and accurately identify patients at risk, facilitating a more targetted treatment and clinical care at the onset of the disease.

Chikungunya fever, caused by the Chikungunya virus (CHIKV), is a mosquito-borne, infectious disease endemic to Southeast Asia and Africa. Since its re-emergence in 2005, CHIKV infection has spread to nearly 20 countries to infect millions. Singapore, for instance, was hit twice by Chikungunya fever outbreaks in January and August 2008.

CHIKV infection is characterised by an abrupt onset of fever frequently accompanied by severe muscle and joint pains. Though most patients recover fully within a week, in severe cases, the joint pains may persist for months, or even years. For individuals with a weak immune system, the disease can result in death. With no clinically-approved vaccine or treatment for Chikungunya fever, it remains a worrying public health problem.

To devise strategies to stop CHIKV transmission, Dr Ng's team collaborated with Professor Leo Yee Sin and Dr Angela Chow, clinician-scientists from the Communicable Disease Centre (CDC) at Tan Tock Seng Hospital, to study how the human body responds to CHIKV infection. The team conducted a comprehensive study on the antibody response against CHIKV in patients. They discovered that patients who respond to the disease at the onset with high levels of Immunoglobulin G3 (IgG3), a naturally-acquired antibody, are protected from the more severe form of Chikungunya fever, characterised by persistent joint pains. On the other hand, patients with a delayed IgG3 response generally have less acute symptoms at the start, but are more susceptible to chronic debilitating joint pains at later stage of the disease. Hence, the IgG3 antibodies serve as a specific biomarker of patients with increased risk of the severe form of the disease.

Collaborating with computational experts from A*STAR's Institute for Infocomm Research (I2R), Dr Ng's team also uncovered that a very small defined segment of the Chikungunya viral protein, named "E2EP3", was able to induce the natural IgG3 protective response in preclinical models. They found that mice vaccinated with the E2EP3 peptides were protected against CHIKV with significant reduction in viral counts and joint inflammation. This finding raises hope for a new effective Chikungunya vaccine that can offer protection against Chikungunya virus in the event of an outbreak.

Dr Ng said, "Long-term treatment required for the chronic joint pain in Chikungunya-infected patients places social and economic burden for both patients and the public healthcare system. We are excited that the mechanistic insights gained through our collaborative research with the local hospitals and international research partners have led to discovery of 'new weapons' to tackle Chikungunya more effectively."

Scientific Director of SIgN, Professor Paola Castagnoli said, "With

increasing threat of Chikungunya virus infection, particularly in Asia and the Pacific region, this significant breakthrough is a step forward in enhancing our pandemic preparedness against the infectious disease. This is a testament to the successful collaborations between research scientists and clinicians in translating scientific discoveries into impactful healthcare solutions for the benefit of Singapore and beyond. ”

More information:

The Journal of Infectious Diseases

: Early Appearance of Neutralizing Immunoglobulin G3 Antibodies Is Associated With Chikungunya Virus Clearance and Long-term Clinical Protection by Yiu-Wing Kam et al. jid.oxfordjournals.org/content … jis033.full.pdf+html

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