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Joint News Release

Scientists in Singapore develop new type of mice with human immune system and red blood cells for malaria research

Singapore – Scientists in Singapore have developed a new type of mice which not only has human immune system, but also human red blood cells, and is expected to accelerate malaria research.

The researchers, comprising scientists from Singapore-MIT Alliance for Research and Technology (SMART) [新加坡-麻省理工学院科研中心], Nanyang Technological University (NTU), and SingHealth KK Women's & Children's Hospital, said having mice which can react specifically to malaria will speed up the search for vaccines and treatments for malaria. This is the first animal model with human immune system which scientists can infect with using human strains of the malaria parasite.

Malaria is a mosquito-borne parasite which affects over 60 million people worldwide and in serious cases, could be fatal. There is currently no viable vaccine for malaria and antimalarial drugs and prophylaxis are losing its efficacy as anti-malarial drug resistance is on the rise.

The ground-breaking findings, published last week in the prestigious academic journal Proceedings of the National Academy of Sciences USA (PNAS), showed that researchers have successfully identified a key host defence mechanism which revealed for the first time how malaria begins its infection. This has led to key insights into two important molecules which help the human body fight the parasite infection during the early stages.

During the initial phase of an infection by the malaria parasite, the first-line-of-defence cells known as natural killer (NK) cells will kill malaria-infected red blood cells if they detect them through the two discovered molecules. Such containment will help the body have more time to produce anti-bodies that will eventually kill all the malaria parasites in the second phase and defeat the infection.

SMART lead scientist for the project, Professor Chen Jianzhu (陈建柱), the Ivan R. Cottrell Professor of Immunology at MIT and SMART Lead Investigator of the Infectious Diseases Interdisciplinary Research Group (ID IRG) said, “Building on our success for the humanised mouse for dengue

research, we have developed a humanised mouse for the study of malaria. This animal model, with both the human immune system and injected human red blood cells, is important as human malaria studies have been hampered by a lack of animal models. This will pave the way to discovering how the host human immune system interacts with the pathogen."

Professor Peter Preiser, Chair of NTU's School of Biological Sciences, one of the key scientists in this research team said this breakthrough could only have been achieved through interdisciplinary research.

"Now that we have a platform for malaria which we can manipulate, we can study what happens during the infection process from start to end. Armed with this knowledge, scientists will be able to better develop treatment and vaccines that are effective at combating the malaria parasite," said the parasitic diseases expert, who had just published a paper on malaria in Nature Communications, another top academic journal, two months ago.

"Considering that malaria is a very complex disease, with scientists trying to develop a vaccine over the past 40 years, I think humanised mice for malaria is a great step forward, as it will allow us to rapidly test promising vaccines for malaria without going through highly expensive human trials. This will make it more cost-efficient as well as faster to develop a vaccine that works well in humans, and not just in animals."

Moving forward, the research team aims to further improve on the humanised mice model for malaria, to study in-depth the different proteins found in the human immune system and its interaction with the malaria parasite and to test antibodies, which would pave the way for malaria vaccines.

This research is based on the paper "Human natural killer cells control *Plasmodium falciparum* infection by eliminating infected red blood cells". The research was funded by the Singapore National Research Foundation (NRF) through SMART at the Campus for Research Excellence And Technological Enterprise (CREATE).

This project took the team three years to achieve the significant breakthrough, as they had faced numerous challenges in making the mice affected by the human malaria strain, due to the complexity and multiple strains of the malaria parasite.

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