Joint News Release

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MIT, SMART and NTU Singapore scientists have discovered a potential treatment for severe malaria

Scientists from **Massachusetts Institute of Technology (MIT)**, **Singapore-MIT Alliance for Research and Technology (SMART)** and **Nanyang Technological University, Singapore (NTU Singapore)** have discovered a potential treatment that could be effective against severe malaria and even drug-resistant malaria.

The joint research team discovered a new molecular pathway (a new series of interactions among molecules in a cell) and various compounds that could boost human immune cells' ability to identify and attack malaria-infected red blood cells (iRBCs). This could improve an infected patient's chances of recovery and lower the risk that they develop a more serious infection, which could lead to organ failure.

Malaria is a mosquito-borne parasite which affects over 216 million people worldwide and could be fatal in serious cases. It is still a huge problem in developing countries because there is no vaccine for malaria while antimalarial drugs are losing their efficacy with drug resistance on the rise, especially in Africa and South-east Asia. In 2017 alone, there are 445,000 malaria-induced deaths globally.

For decades, doctors and scientists have been baffled why some people are more vulnerable to malaria than others. This latest discovery by the joint research team which was published in the peer-reviewed academic journal *PLOS Pathogens* last week has shed light into this mystery.

Boosting the body's Natural Killer cells to fight malaria infection

During the initial phase of an infection by the malaria parasite, the first-line-of-defence cells known as Natural Killer (NK) cells will destroy the infected red blood cells if they detect them. Due to human genetic variation, some people have more responsive NK cells, while others do not.

By analysing responsive and non-responsive NK cells, the joint research team has discovered through their lab experiments the pathway used by NK cells to detect infected red blood cells.

Firstly, infected red blood cells secrete small microvesicles from their surface, which are extremely tiny sacs containing biomolecules such as ribonucleic acid (RNA) which are genetic instructions needed to produce proteins.

These microvesicles are then detected by the pathogen recognition receptor MDA5 located inside NK cells. The role of these receptors is to identify bacteria and viruses, thus triggering the NK cells into attacking and killing infected red blood cells.

Having established that NK cells with higher levels of MDA5 respond better to a malaria infection, the scientists were able to improve non-responding NK cells by activating MDA5 artificially with a synthetic drug compound in their lab tests.

Dr Ye Weijian, the lead author of the study said understanding this pathway that primes the NK cells to attack is important for developing novel strategies in boosting people's own immune system to fight malaria.

"Our discovery underpins future studies in immunotherapy and may hold the key to addressing multi-drug resistant diseases," said Dr Ye who is an NTU graduate under the SMART Graduate Fellowship.

SMART PhD candidate, Marvin Chew who is the co-first author, said, "Our four-year research findings bring a new level of insight into NK cell and disease severity. The identified drug target and synthetic compounds could form the basis for an effective treatment for malaria."

Professor Peter Preiser, Chair of NTU's School of Biological Sciences, a senior scientist in the research team with extensive experience in malaria biology, said this breakthrough could only have been achieved through interdisciplinary research.

"Moving forward, the possibility of applying the same concept for other infectious diseases is boundless. We know that MDA5 is a sensor for infected red blood cells, so we can use synthetic drugs to improve MDA5 and improve NK cell function against other infectious diseases such as dengue, TB or even cancer."

Leader of the research group, **Professor Chen Jianzhu**, **Professor of Biology at MIT and SMART Lead Investigator of the Infectious Diseases Interdisciplinary Research Group (ID IRG)** said, "With no viable vaccine for malaria in sight, coupled with increasing loss of efficacy in antimalarial drugs and prophylaxis as anti-malarial drug resistance, making this breakthrough discovery will open up new avenues for targeted approaches in our fight against malaria."

This research is reported in the *PLOS Pathogens* paper titled “Microvesicles from Malaria-infected Red Blood Cells Activate Natural Killer Cells via MDA5 Pathway”.

The research was funded by the **National Research Foundation Singapore (NRF)** through SMART at the **Campus for Research Excellence and Technological Enterprise (CREATE)**.

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About Singapore-MIT Alliance for Research and Technology (SMART) [新加坡-麻省理工学院科研中心]

Singapore-MIT Alliance for Research and Technology (SMART) is a major research enterprise established by the Massachusetts Institute of Technology (MIT) in partnership with the National Research Foundation of Singapore (NRF) since 2007. SMART is the first entity in the Campus for Research Excellence and Technological Enterprise (CREATE) developed by NRF. SMART serves as an intellectual hub for research interactions between MIT and Singapore. Cutting-edge research projects in areas of interest to both Singapore and MIT are undertaken at SMART. SMART comprises an Innovation Centre, the Infectious Diseases Interdisciplinary Research Group (ID IRG) and five other IRGs: Antimicrobial Resistance (AMR), BioSystems and Micromechanics (BioSyM), Disruptive Technology for Agricultural Precision (DiSTAP), Future Urban Mobility (FM) and Low Energy Electronic Systems (LEES).

SMART research is funded by the National Research Foundation Singapore under the CREATE programme. For more information, please visit - http://smart.mit.edu

About SMART Infectious Diseases Interdisciplinary Research Group

SMART Infectious Diseases IRG (ID IRG) seeks fundamental understanding of host-pathogen interactions as well as direct impact on human heath through translational research. The ID IRG focuses on infectious diseases that have major impact on human health, including influenza, dengue fever, malaria and tuberculosis. The strategy of the IRG is to develop enabling technologies, including humanised mouse model, high resolution proteomics, glycomics, metabolomics and cellular mechanics platforms, to study infectious diseases using novel approaches and from new angles. The ID IRG has developed an integrated, cutting-edge research program with participation of both MIT faculty and investigators from Singapore universities and research institutes.

About Campus for Research Excellence and Technological Enterprise

The Campus for Research Excellence and Technological Enterprise (CREATE) was set up by the National Research Foundation Singapore in 2007 as an international campus to forge partnerships between Singapore's universities/research institutions and leading overseas research institutions. CREATE provides a platform to attract top-notch talent from all over the world to conduct their research in Singapore.

Research at CREATE is highly interdisciplinary, and addresses large and important problems, especially those that are best conducted in or from Singapore.

Today, researchers from eight overseas partner universities – Massachusetts Institute of Technology (MIT), Swiss Federal Institute of Technology Zurich (ETH Zurich), University of California Berkeley (UC Berkeley), Cambridge University, Technical University of Munich (TUM), Hebrew University of Jerusalem (HUJ), Shanghai Jiao Tong University, and the University of Illinois at Urbana-Champaign – are co-located in CREATE, where they work with researchers from the National University of Singapore (NUS), Nanyang Technological University (NTU), Singapore Management University (SMU) and Singapore University of Technology and Design (SUTD) on several interdisciplinary research programmes.

About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 33,000 undergraduate and postgraduate students in the Engineering, Business, Science, Humanities, Arts, & Social Sciences, and Graduate colleges. It also has a medical school, the Lee Kong Chian School of Medicine, set up jointly with Imperial College London.

NTU is also home to world-class autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies, Earth Observatory of

Singapore, and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Nanyang Environment & Water Research Institute (NEWRI) and Energy Research Institute @ NTU (ERI@N).

Ranked 12th in the world, NTU has also been placed the world's top young university for the past five years. The University's main campus is frequently listed among the Top 15 most beautiful university campuses in the world and it has 57 Green Mark-certified (equivalent to LEED-certified) building projects comprising more than 230 buildings, of which 95% are certified Green Mark Platinum. Apart from its main campus, NTU also has a campus in Singapore's healthcare district.

For more information, visit www.ntu.edu.sg