Joint research team discovers potential new treatment for severe malaria

Reviewed by James Ives, MPsyCh  Oct 8 2018

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
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

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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."