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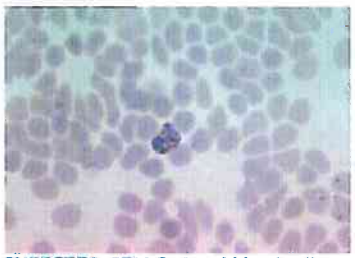
RESA, a culprit behind malaria

"This successful collaboration shows the power of multidisciplinary research to answer biological questions. There is no better time to do this as technologies have progressed so much over the last decade or so." -- Dr Kevin Tan, Department of Microbiology.

In their latest study, the team of NUS researchers working with the Massachusetts Institute of Technology (MIT) and the Institut Pasteur in Paris, has gained a firm foothold into the inner workings of red blood cells infected by the malaria parasite, *Plasmodium falciparum*. When the parasite infects red blood cells, the cells lose their elasticity, eventually clumping together and getting stuck in the capillaries. They found that by knocking out the gene for a parasite protein called RESA (ring-infected erythrocyte surface antigen), the red blood cells become less deformable.

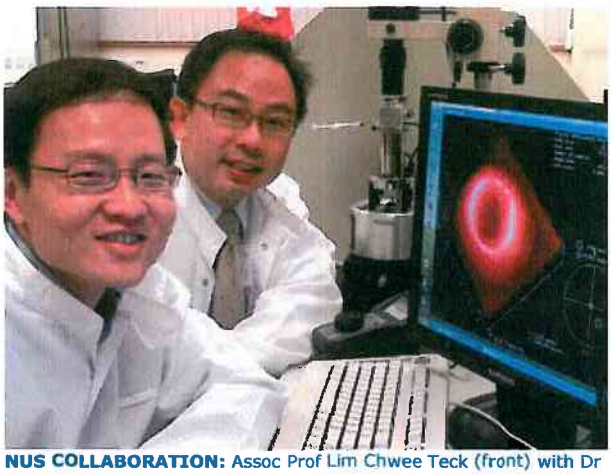


INFECTED CELLS: A red blood cell infected with the schizont stage of *Plasmodium falciparum*.

"This is the first time a particular protein has been shown to have such a large effect on red blood cell deformability," said a leader in the research team, Prof Subra Suresh, Ford Professor of Engineering, MIT and Tan Chin Tuan Centennial Professor, NUS.

The team found that red blood cells infected by parasites without RESA, remained normal during the first 24 hours of infection. But in other parasites where RESA was turned back on after being knocked out, their elasticity was affected. They also found that RESA affected deformability to a greater extent at fever temperature.

The team's paper, *Effect of plasmodial RESA protein on deformability of human red blood cells harboring Plasmodium falciparum*was published in the **Proceedings of the National Academy of Sciences** (online edition of May 21). The authors of the paper from **MIT** are Diez-Silva, John P Mills, David J Quinn, Ming Dao, Matthew Lang; Genevieve Milton, Peter H David, Odile Mercereau-Puijalon and Serge Bonnefoy from **Institut Pasteur**; and Kevin S W Tan and Lim Chwee Teck from **NUS**.



NUS COLLABORATION: Assoc Prof Lim Chwee Teck (front) with Dr Kevin Tan at their lab in NUS.

"This successful collaboration shows the power of multidisciplinary research to answer biological questions. There is no better time to do this as technologies have progressed so much over the last decade or so," said Dr Kevin Tan, one of the authors.

MALARIA CULTURE SAMPLE: Nuclei of individual *Plasmodium falciparum* cells are revealed in green.

"The novelty of this work is the coupling of the optical tweezers experiments, a biophysical technique that uses laser to stretch cells, with targeted gene disruption, a biological technique that prevents production of a specific protein. The combination of these methods from different fields allows us to address the question of the role of RESA protein on the deformability of the early stage infected red blood cells," explained collaborator, Assoc Prof Lim Chwee Teck, NUS Division of Bioengineering. He is also Deputy Director, NUS Office of Life Sciences.

The team plans to study the effects of proteins produced by the malaria parasite during later stages of infection, as well as by other species of malaria parasite such as *Plasmodium vivax*. Their work, could ultimately lead to the development of treatments that prevent such proteins from making cells rigid.

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