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Researchers Identify New Steps in Spread of Malaria Parasite Through Bloodstream

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(PhysOrg.com) -- Researchers at the National Institutes of Health have observed two previously unknown steps in the spread of the malaria parasite through the bloodstream. And in laboratory cultures, the researchers interfered with one of these steps, raising the possibility that new drug treatments could be developed to combat the disease.

In 2008, malaria is estimated to have caused as many as a million deaths worldwide.

Malaria is caused by a single-celled parasite from the genus Plasmodium, which is transmitted to humans through the bite of an infected mosquito. The parasite infects red blood cells and reproduces inside them. When the infected cell bursts, the new parasites spread, infecting more red blood cells.

In their study, the researchers focused on how the new parasites escape infected cells. They also discovered they could, in effect, seal the membrane of an infected blood cell with a surface-acting compound, halting the release of the parasites.

The study was published online in Current Biology.

The study's authors were Svetlana Glushakova, Glen Humphrey, Evgenia Leikina, Amanda Balaban and Joshua Zimmerberg, all of the NICHD, and Jeffrey Miller, an investigator from the National Institute of Diabetes and Digestive and Kidney Diseases.

To conduct the study, the researchers examined red blood cells from volunteers with sickle cell anemia, an inherited disease in which these cells have a curved, or sickle shaped, appearance. The misshapen cells can clog blood vessels and hinder blood flow. The mutation that causes sickle cell anemia is prevalent in parts of the world where malaria is common. Although having two copies of the mutated gene causes sickle cell anemia, having only one copy confers a resistance to malaria.

In normal red blood cells, the rupture of cells and subsequent release of the parasites proceeds almost instantaneously, and is very difficult to observe. However, the researchers found that in sickle cells, this process occurs at a much slower rate — slowly enough, in fact, to allow the researchers to observe it. By following the progression of the disease in infected sickle cells, the researchers were able to document stages in the process that had not been observed before.

Dr. Zimmerberg explained that, typically, a malaria parasite reproduces inside a sac within a red blood cell. In two days, the parasite multiplies, filling the sac until the new parasites burst out of their host cell. Many researchers believed that the pressure of the growing parasites inside the sac increased until the cell burst.

But in their observations of infected sickle cells, the researchers uncovered a more complex process. Several minutes before rupturing, the parasite-filled sac inside the cell swells and the remainder of the cell shrinks. Moreover, seconds before the infected cell bursts, the cell membrane turns porous, like a leaky plastic bag.

"It is not the simple explosion people thought it was," said Dr. Zimmerberg, senior author and director of the Program in Physical Biology at the NICHD. "It appears to be more like a ballet — an elegantly choreographed, regulated process."

Dr. Zimmerberg and his colleagues discovered that a sealing agent known as poloxamine prevented cells from rupturing and releasing the parasites. The researchers plan to study the effects of poloxamine and similar compounds on the bursting process in hopes of developing a new malaria treatment.

"Every step in this process is an opportunity to intervene and stop the disease from advancing. Identifying new stages in the release of parasites provides new leads in the search for anti-malaria drugs," said Dr. Zimmerberg.

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