

Platelets as Defenders

ASPIRIN MAY THWART THE DEFENSIVE ROLE OF THESE BLOOD CELLS AGAINST MALARIA.

In the developing world, treating malaria usually involves anti-malarials to kill the parasite and aspirin to control the fever. But according to new research, aspirin may hamper the body's ability to fight malaria. The study found that blood platelets can kill malaria parasites—in the genus *Plasmodium*—but lose that ability if exposed to aspirin.

Plasmodium parasites infect red blood cells and have highly variable surfaces, making each infection a new challenge for the body, says HHMI international research scholar Simon Foote of the Menzies Research Institute at the University of Tasmania. “It takes quite a bit of time to develop a specific immune response to protect you from malaria. During that time, the body somehow has to stop you from dying.”

In the February 6, 2009, issue of *Science*, Foote and his colleagues report that blood platelets—involved in blood clotting—might be one of the body's interim defenses. The group discovered that mice genetically engineered to produce fewer platelets than normal were far more likely to die from a rodent version of malaria than other mice.

To determine whether low platelet levels directly caused this effect, the team gave aspirin, known to inhibit platelet function, to a group of mice lacking the mutation. Like the genetic mutants, the aspirin-fed subjects were more susceptible to the disease.

Foote and his team also exposed *Plasmodium*-infected human red blood cells to platelets. As they watched, the platelets bound to the cells and killed the parasites—an ability they lost when aspirin was added.

It's been known that platelets bind preferentially to malaria-infected red blood cells, says Foote. Researchers

had hypothesized, however, that these cell-bound platelets posed a danger to the infected body—they can build up in small blood vessels and cause clots in the brain. “They're essentially the glue between infected cells and vessels ... and they promote blockage,” he says. The new study suggests that platelets may do some good as well.

According to Foote, it's unclear how platelets' *Plasmodium*-killing ability functions, and the laboratory results don't necessarily translate to infected humans. “I think this needs a really good, closely monitored clinical trial,” he says. ■ —BENJAMIN LESTER



Platelets are one of the body's interim defenses against malaria.

IN BRIEF

FOUR BIRDS WITH ONE STONE

A new compound wipes out tuberculosis-causing bacteria in the test tube by disrupting four of their most vital processes. HHMI international research scholar Rajesh Gokhale thinks the compound, which mimics a fatty acid, is a step toward a single tuberculosis drug to replace the difficult four-drug regimen tuberculosis patients currently take to cure their disease.

Gokhale and coworkers at the National Institute of Immunology in New Delhi, India, had been studying how *Mycobacterium tuberculosis* infects human cells. The bacteria get much of their potency from complex lipids on their outer surfaces, so Gokhale's team focused on how to shut down an enzyme—in a class of fatty acyl-AMP ligases (FAALs)—that helps build these lipids from fatty acids. They designed a molecule that resembles a fatty acid but that the FAAL cannot process, stopping it from functioning.

The FAAL, they found, resembles other enzymes the bacteria need to survive at different stages of their infection cycles. The enzymes are similar enough that Gokhale's compound stops all four, delivering a powerful blow to the pathogen.

“The ‘one disease-one drug-one target’ paradigm that has dominated

thinking in the pharmaceutical industry is now being increasingly challenged by the discovery of compounds that bind to more than one target,” Gokhale says.

Gokhale's team published the results in the March 2009 issue of *Nature Chemical Biology*.

KILLER TRAINING

A type of immune cell previously thought to forget does have some memory, researchers have found.

Two kinds of cells dominate the immune system: innate immune cells respond early to infection; adaptive immune cells take longer. Adaptive cells, however, were thought to be the only immune cells to remember previous events. “Our findings essentially say: wait a minute, there is evidence for a memory in innate immune cells,” says HHMI investigator Wayne Yokoyama, who led the study.

Yokoyama's team found that natural killer cells—a type of innate immune cell—that have been exposed to a stimulus respond more robustly when they are exposed again. Although natural killer cells don't have the same molecular tools that adaptive immune cells use to remember all the specifics, they seem to have some kind of memory of past stimulation with cytokines—hormone-like

substances typically produced during infections. And they pass that memory to their progeny. Yokoyama and coworkers at Washington University School of Medicine reported their findings in the February 10, 2009, issue of *Proceedings of the National Academy of Sciences*.

Though the natural killer cells employ a previously unknown property to remember, the researchers hypothesize that other kinds of cells elsewhere in the body may also acquire new memories. And the study suggests that boosting innate immunity may boost a person's health, says Yokoyama.

RAIDING GIARDIA'S CLOSET

Giardia lamblia parasites are like microscopic bandits that evade the immune system for months. If recognized, they just change into another of their nearly 200 disguises. But scientists have now discovered how to see through *Giardia*'s many disguises.

Researchers knew that *Giardia* often goes undetected because it periodically changes the proteins on its surface; it has the genes to make about 200 such proteins, called antigens.

A new study, led by Hugo Luján, an HHMI international research scholar at the Catholic University of Córdoba in Argentina,