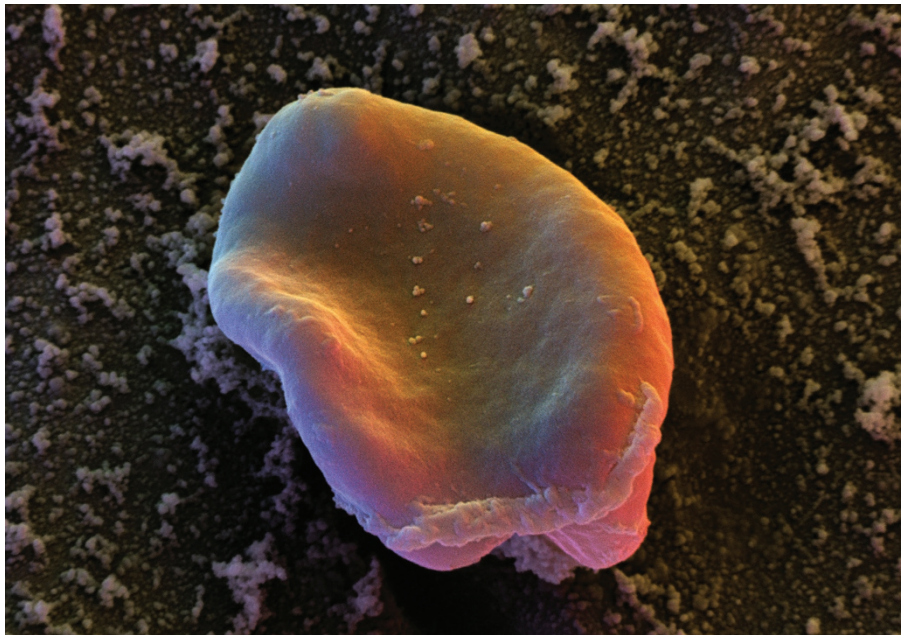
GSK plows ahead with EMA malaria vaccine submission

On October 8, GlaxoSmithKline and the PATH Malaria Vaccine Initiative (MVI) released 18-month data from a phase 3 trial of the RTS,S malaria vaccine. Although the vaccine has shown mediocre efficacy and its effect declines over time, it is still expected to become the first malaria vaccine to receive regulatory approval. Whether RTS,S will actually see widespread use will depend on recommendations by the World Health Organization (WHO) and deployment by the GAVI Alliance (formerly Global Alliance for Vaccines and Immunization). Their decisions will hinge on additional efficacy data of a booster dose expected next year. "Duration of protection is an important part of the vaccine," said Vasee Moorthy, technical officer at WHO's Department of Immunization, Vaccines & Biologicals in Geneva.

The most recent data taken from 11 African sites show that the vaccine does indeed protect against malaria, but the effect wanes over time. In children aged 5–17 months when vaccinated, it reduced the the number of clinical malaria by 46% at 18 months after vaccination, down from 56% reduction at 12 months after vaccination. Cases of severe malaria were reduced by 36% at 18 months, down from 47% at 12 months. The vaccine worked even less well in infants aged 6–12 weeks.

Although the data fall short of the goal of 50% efficacy against severe disease and death laid out by the Malaria Vaccine Funders Group in 2006 (*Nat. Biotechnol.* **29**, 1060–1062, 2011), even the slightest bit of efficacy is welcome, says Ashley Birkett, director of Washington, DC–based MVI. According to the WHO, there were about 219 million cases of malaria and 660,000 deaths in 2010, 86% of which were children younger than five years old. "Would we like a vaccine that has 80–90% efficacy and great immunogenicity? Of course we would, but we'll take something that works less [well]," says Birkett. "It is important to realize that RTS,S is going to have an important role in reducing the burden of malaria over the next several years because nothing else is on the near horizon," Birkett adds. GlaxoSmithKline plans to submit a regulatory application to the European Medicines Agency (EMA) in 2014 after full analysis of the 15,460-patient trial, including 32-month data and impact of the booster dose.



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Red blood cell infected with malaria.

RTS,S, which targets the sporozoite stage of *Plasmodium falciparum*, is a fusion protein comprising amino acids 207 to 395 of the circumsporozoite protein and hepatitis B surface antigen (RTS), co-expressed in *Saccharomyces cerevisiae* with unfused hepatitis B surface antigen (S). The resulting polypeptides spontaneously form viral-like particles, which are then added to the adjuvant AS01 from Agenus of Lexington, Massachusetts. Adrian Hill, director of the Jenner Institute in Oxford, UK, is leading development of ChAd63/MVA ME-TRAP, a prime-boost regimen using modified vaccinia virus Ankara (MVA) and chimpanzee adenovirus 63 (ChAd63) vectors encoding a liver-stage antigen. The vaccine candidate is currently in phase 2 testing in 40 healthy subjects in combination with RTS,S, with data expected by the end of the year. "We believe that our vaccine can be one of the components of a final vaccine. It's not great on its own, but it does show efficacy," says Hill, who predicts that an optimal vaccine will contain antigens from each of the parasite's four life-cycle stages: sporozoite, liver, blood and sexual.

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Another vaccine candidate being developed by the Rockville, Maryland–based Sanaria is using a live, attenuated vaccine, PfSPZ, of cryopreserved *P. falciparum* sporozoites. On August 8, the company announced that PfSPZ provided 100% protection in six volunteers who received the highest dosage in a phase 1 trial followed by malaria infection (*Science* **341**, 1359–1365, 2013).

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Corrections

In the May 2013 news analysis "Antimicrobials stage a comeback" (*Nat. Biotechnol.* **31**, 379–382, 2013), the Italian company researching the use of novel antibiotics was erroneously identified as NeED Pharmaceuticals. The company's name is NAICONS. The error has been corrected in the PDF and HTML versions of this article.

In the May 2013 news analysis "Footrace to clinic heats up for T-cell nuclear receptor inhibitors" (*Nat. Biotechnol.* **31**, 370, 2012) Gary Glick's affiliation was given incorrectly. He is at the University of Michigan, Ann Arbor, not at the University of Wisconsin, Madison. The error has been corrected in the PDF and HTML versions of this article.