Vaccine Watch

STRATEGIC VARIETY

Four new studies show the ever-increasing complexity of vaccine approaches that are being developed to increase immunogenicity, improve safety and decrease production costs.

Perhaps the 'simplest' approach to vaccination is to use the whole microorganism, which contains both the protective antigen or antigens and natural 'built-in' adjuvants. Reporting in *Cell Host & Microbe*, Coban *et al.* investigate the adjuvant in *Plasmodium falciparum* that potentiates the immune response to blood-stage malaria parasites. They show that the parasite product haemozoin specifically ligates Toll-like receptor 9 without any requirement for parasite DNA or for signalling through the inflammasome. Synthetic haemozoin is a potent adjuvant for *P. falciparum* antigens in mice and dust mite allergens in dogs, which indicates its potential for development as a vaccine adjuvant.

A contrasting approach to vaccination against malaria, using recombinant *P. falciparum* antigens, is described by Thera *et al.* in *PLoS ONE*. They report a Phase I randomized controlled trial of a malaria vaccine containing the recombinant protein FMP2.1 — part of the ectodomain of apical membrane antigen 1 from *P. falciparum* — in AS02A adjuvant. This is the first evaluation of FMP2.1 in malaria-experienced children; it has a good safety profile and induces high and sustained antibody levels. If further clinical trials are successful, FMP2.1 could become one component of a multistage, multi-antigen vaccine for malaria.

Virus-like particles (VLPs) combine the immunogenic advantages of a whole microorganism with the improved safety and standardization of recombinant proteins. Akahata *et al.* in *Nature Medicine* describe the production of VLPs for Chikungunya virus (CHIKV) using human 293T kidney cells transfected with eukaryotic expression vectors for CHIKV structural proteins. The VLPs mimic repetitive surface features of the virus that facilitate B cell stimulation, and they induce high-titre neutralizing antibodies that protect against high-dose virus challenge in mice and rhesus macaques.

Strategies for the induction of cytotoxic T lymphocytes (CTLs), as well as neutralizing antibodies, are also important for some diseases. Flatz *et al.* (*Nature Medicine*) report a method to replace the gene encoding lymphocytic choriomeningitis virus (LCMV) glycoprotein with a vaccine antigen to create a replication-defective LCMV vector. As LCMV targets and activates dendritic cells, this vector elicits both CTL-mediated immunity and antibodies specific for the vaccine antigen. No vector-specific antibodies are produced, which facilitates the use of the same vector for booster vaccination.

ORIGINAL RESEARCH PAPERS Coban, C. *et al.* Immunogenicity of whole-parasite vaccines against *Plasmodium falciparum* involves malarial hemozoin and host TLR9. *Cell Host Microbe* **7**, 50–61 (2010) | Thera, M. A. *et al.* Safety and immunogenicity of an AMA1 malaria vaccine in Malian children: results of a phase 1 randomized controlled trial. *PLoS ONE* **5**, e9041 (2010) | Akahata, W. *et al.* A virus-like particle vaccine for epidemic Chikungunya virus protects nonhuman primates against infection. *Nature Med.* 28 Jan 2010 (doi:10.1038/nm.2105) | Flatz, L. *et al.* Development of replication-defective lymphocytic choriomeningitis virus vectors for the induction of potent $CD8^+$ T cell immunity. *Nature Med.* 7 Feb 2010 (doi:10.1038/nm.2104)