IN THE NEWS

West Nile virus

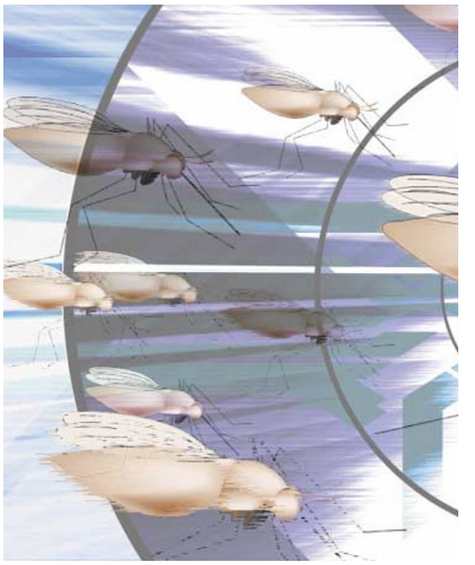
This month has seen reports of the sixth death this year in Colorado from the mosquito-borne disease West Nile virus, and it seems that cases will reach record levels in 2003. West Nile virus, which is common in Africa, arrived in New York in 1999, and has since spread across the continent. As Mark Loeb, Associate Professor of Clinical Epidemiology and Biostatistics at the University of McMaster, said, "There's more and more evidence telling us that West Nile is here to stay" (*The Globe and Mail*). Worryingly, although there have been no cases of the disease in the United Kingdom so far, a recent survey of British birds showed that "an unexpectedly high proportion" contained antibodies specific for the virus (*BBC News*).

So, the publication (in *Proceedings of the National Academy of Sciences*) of a successful vaccine study in mice is welcome news. The new DNA vaccine contains a replication-defective, harmless relative of West Nile virus known as Kunjin virus. The authors suggest that this "may provide ... an effective vaccination strategy against further outbreaks" (*New Scientist*). However, others have raised concerns that this weakened virus might be "more virulent than we believe it is at the moment" (*New Scientist*). The new vaccine joins two other candidates — a hybrid of yellow fever and West Nile virus, and a hybrid of dengue virus and West Nile virus. None of these vaccines has yet been tested in humans, so as Diane Griffin of Johns Hopkins School of Public Health points out, "it's good to have other candidates in the wings" (*Science Now*).

Kirsty Minton

VACCINES

New targets for malaria vaccines identified



More effective malaria vaccines could now be developed thanks to a new approach for mining the genomic sequence of *Plasmodium falciparum*, which has led to the identification of new antigens with enhanced immunogenicity.

It is possible to generate protection against malaria by immunization with sporozoites (the infectious form of *P. falciparum* injected by the mosquito) that have been attenuated by radiation, so justifying the search for a malaria vaccine. However, the antigens mediating this protective immunity induced by vaccination with the whole organism are unknown. It is unlikely that a vaccine directed against a single antigen will be protective, so multivalent vaccines that combine antigens expressed at different stages of the parasite life cycle have been developed.

The search for further parasite antigens has been aided by the availability of the genomic sequence of *P. falciparum*, as well as the elucidation of the *P. falciparum* proteome. Here, Doolan *et al.* combine bioinformatic epitope predictions and *in vitro* cellular assays to identify new malaria target antigens.

First, multidimensional protein identification technology was used to identify 27 open-reading frames that encode antigens that are potentially expressed by the sporozoite and intra-hepatic stages of the parasite life cycle. Of these, antigens with predicted HLA-binding capacities were tested, together with four previously

APOPTOSIS

Lifesaver

How the pro-apoptotic molecules BAK and BAX — which are potentially lethal — are maintained in an inactive, monomeric conformation in viable cells is poorly understood. However, recent structural insights into the monomeric BAX molecule have provided a possible mechanism for its inactive status. And now, reporting in *Science*, Stanley Korsmeyer and colleagues have identified a protein — voltage-dependent anion channel 2 (VDAC2) — that keeps BAK in check.

BAK and BAX are required for mitochondrial apoptosis — 'BH3-only' members of the BCL2 family respond to death signals and subsequently trigger the activation of BAK and BAX, which leads to mitochondrial membrane permeabilization and the release of cytochrome *c*. This then initiates the caspase cascade.

To investigate whether BAK interacts with another mitochondrial protein that regulates its activity, Korsmeyer and colleagues used protein crosslinkers to identify a candidate protein (X) that complexes with BAK in purified mitochondria or whole cells. This BAK–X complex was lost when mitochondria were treated with the BH3-only protein BID or when cells were treated with death stimuli. By testing various BH1- and BH3-domain mutants of both BID and BAK, the authors concluded that X interacts with the BAK pocket that is formed by the BH1, BH2 and BH3 domains and can be displaced, directly or indirectly, by BH3-only molecules.

Protein X was identified as VDAC2, a low-abundance isoform of the VDAC outer-mitochondrial-membrane porin. VDAC2 was further implicated when the authors found that VDAC2-deficient embryonic stem cells lacked the BAK–X complex, which