

## Grants will determine European malaria vaccine future

When Adrian Hill's team began Phase I clinical testing of its DNA malaria vaccine in Oxford last month, it became the first-ever academic group to study a malaria vaccine in clinical trials in the UK. "That tells you a lot about malaria vaccine research in Europe," says Hill, referring to the scarcity of human trials on such vaccines throughout Europe.

Funded by a £750,000 (US\$1.2 million) grant from the Wellcome Trust, Hill's group is testing the ability of a pre-erythrocytic antigen to immunize against the disease using a plasmid DNA injection followed by injection of a modified vaccinia virus Ankara expressing the same antigen (*Nature Med.* 4, 397; 1998).

Hill hopes to be part of another first next year when he joins partners, including Oxford University's Richard Moxon and Andrew McMichael, in opening the first academic center for vaccine testing in Oxford. "In the US there are seven NIH-funded vaccine evaluation units that do nothing but test vaccines. Comparable facilities don't exist in Europe," he says. The center, which will cost an estimated £5 million, is being paid for through a grant from the UK government and Wellcome Trust's Joint Infrastructure Fund and should open in October 2000. It will test vaccines for a range of diseases including malaria, melanoma and AIDS.

The lack of a suitable testing facility for vaccines discovered in academic laboratories has been a major drawback to malarial research in Europe, according to Hill. Another obstacle is the fact that, traditionally, malaria researchers tend to be parasitologists and vaccines require detailed knowledge of basic immunology and vaccinology. But perhaps the greatest problem is the lack of finances. Funding agencies have not been attuned to recognizing the value of vaccine development. "The academic system is set up to reward people who publish in top journals, and not to reward those who make a vaccine that's 40 rather than 10 percent effective," says Hill.

However, this situation looks set to change before the end of the year, because European researchers will hear this month whether they are to receive funding

from two complementary sources—the European Union (EU) and European Malaria Vaccine Initiative (EMVI).

Around ECU300 million (US\$321 million) are ear-marked for vaccine development over the next few years under "Key Action 2" and "INCO-DEV" of the EU's Fifth Framework Programme. ECU48 million are available at the moment, but in addition to supporting work on malaria, the money must also fund HIV, hepatitis C, tuberculosis and cancer vaccines research.

Scientists anticipate that EU funding for vaccine research could be between ECU9 and ECU15 million and many consider this a pivotal time for pan-European efforts to push candidates towards clinical trials. The money "is crucial for our consortium to pursue development of malaria vaccines as a cluster," says Thor Theander of the University of Copenhagen, "...the loss of this funding would be a blow to the European malarial research community."

Large teams of researchers from different EU countries have banded together to apply for the funding—one team combines 15 laboratories from multiple European countries—and are grouped largely according to the portion of the parasite's life-cycle that they are targeting for vaccine development.

MSP-1 is one example of a vaccine that targets the erythrocytic, or blood stage. Although MSP-1 was initially developed in the UK by Tony Holder's team at the Medical Research Council's National Institute for Medical Research, it is now undergoing Phase I trials in the US by the Walter Reed Army Institute for Research in Washington, DC. "This is in part because [they] have developed the infrastructure necessary to

produce clinical grade material and test it clinically," Holder told *Nature Medicine*. "In my opinion it would have been much more difficult to do this in Europe and I hope that the climate here changes to ensure that clinical trials of malaria vaccines can be carried out, but it's still unclear

whether or not the EU or EMVI initiatives will result in testing of appropriate vaccines," says Holder.

Mike Hollingdale of Leeds University, UK, agrees that this transatlantic agreement embodies the problem faced by European researchers: "More money is needed for the clinical trials. The bottleneck is manufacturing. It is hugely expensive, about half a million ECUs to make a small batch of vaccine."

EMVI, which was established last year with the aim of providing "a mechanism through which the development of experimental malaria vaccines can be accelerated within Europe and in developing countries," is also addressing the problem. EMVI will distribute ECU2 million over the next

three years to individual research teams, specifically to take candidate vaccines into early stage clinical trials. "Many of the major vaccine candidates have come from European labs, but the vast majority of trials have been in the US, European scientists have felt they can get only so far," says Hill.

"The money will be used to take three or four promising vaccine constructs into Phase I clinical trials. So ECU300,000 to 500,000 for each program will pay for the clinical grade material of the vaccine candidate produced to GMP specifications, plus quality control rubber stamping and then limited clinical testing," explains EMVI director, Søren Jepsen. Thereafter, it is hoped that research teams can interest industry in taking the vaccines through more advanced clinical trials.

Jepsen is convinced that the new funding makes Europe competitive with America in the field of malarial vaccine development. "This means that we have the chance of a European-based vaccine entering clinical trials in Africa as opposed to an American one," he says.

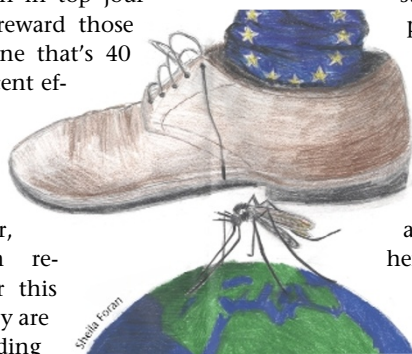
But he points out that ultimately the most important player is industry, which is not a nationalistic entity: "Industry will simply collaborate with the best scientists and this means that our competition is purely an academic one. Who are the smartest scientists developing malaria vaccines—American or European?"

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Anopheles mosquito

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