EC panel decisions surprise malaria community

Back in September, we reported on the anticipation of European malaria vaccine scientists that they would obtain a large chunk of fresh funding from the European Commission (EC) for clinical trial research, enabling them to compete with their American counterparts. However, these hopes have been dashed, as a panel appointed by the EC has backed only basic research programs. "We've defined so much on all stages of malaria infection, and we need clinical testing. These decisions have set European efforts back five years," one disappointed researcher told *Nature Medicine*.

Targeted at vaccine development in four areas—malaria, cancer, tuberculosis and HIV—the new funding, which is offered through two Fifth Framework Programmes called Key Action 2 (KA2) and INCODEV (*Nature Med.* **5**, 969; 1999), raised high expectations in the malaria field, which has traditionally been underfunded. The wording of the request for proposals, issued in March, led many to believe that projects close to clinical trials would be favored, and by the June deadline malaria researchers had assembled into four clusters to bid for money.

But learning which projects have been selected for KA2 funding has surprised all those contacted by *Nature Medicine*. For example, none of the pre-erythrocytic-stage vaccine projects, which are widely acknowledged to be closest to clinical trials, have been backed, and the only two clusters that recruited industrial partners were overlooked.

Pierre Druilhe of the Pasteur Institute headed one of the unsuccessful clusters. He voices the opinion of many when he says he finds it hard to reconcile the call for "development of improved or novel vaccines..." and "establishment of clinical trial networks for Phase I and Phase II trials" with the fact that his project, which is ready to start human testing, was rejected.

His cluster included scientists from 17 different laboratories across Europe, South America and Africa, representing 80% of European researchers working on pre-erythrocytic-stage vaccines. The work has been funded by INCO and the Wellcome Trust for the past decade. Yet, now that he has shown high protection rates in chimpanzees in centers as widespread as Holland, Gabon and Colombia, and had these results confirmed independently by laboratories in the US, Druilhe 's EC support has ended. By contrast, the two largest pharmaceutical vaccine manufacturers, Pasteur Merieux Connaught (PMC) and SmithKline Beecham, have already signed R&D agreements with Druilhe's team and are sufficiently convinced of its worth to take the project into clinical trials next year.

Druilhe received the news that his cluster was unsuccessful by telephone. He told *Nature Medicine* that he is unable to comment on the panel's decision because has not yet received its consensus report explaining the scientific rationale for the rejection. Such a lengthy delay in receiving a written report is unusual.

Malaria vaccine funding panel.

The second unfunded cluster, comprising scientists from 14 different laboratories, is headed by Michael Theisen at the Statens Seruminstitut, Denmark. Theisen's program, which had the industrial support of PMC, was focused on the development of a vaccine that raises antibodies against two *Plasmodium falciparum* merozoite surface proteins (MSP), MSP3 and GLURP, thus protecting against the blood stage of the disease. Again, Theisen has not received the panel's written report on his application five months after submission.

Transmission-blocking vaccines are a highly controversial strategy for malaria control, and are still in early stages of development. However, work on such a vaccine by University of Nijmegen researcher Robert Sauerwein's cluster has been funded. His team will receive ECU2.5 million (US$2.6 million) to develop a vaccine that relies on mosquitoes withdrawing blood from vaccinees that contains antibodies against the stages of parasite development within the mosquito. To be effective, community immunization with this type of vaccine must be 100%, because one person carrying infective parasites can trigger a chain reaction throughout those vaccinated with a transmission blocker, as they are not protected from infection.

Although the transmission-blocking concept is intellectually engaging—the US National Institutes of Health is to host a conference evaluating the potential of this strategy 3–5 December in Washington DC—the requirement for blanket immunization means that there is little industrial interest in this type of product, implying that its development will be problematic.

Finally, a 16-laboratory cluster headed by University of Edinburgh's David Arnot has also been funded, or at least in part. Arnot's cluster has a strong emphasis on basic research, illustrated by the inclusion of molecular biology expert Chris Newbold from the University of Oxford. The group will receive ECU3.5 million over three years. But not only was the cluster's most advanced project—an MSP-19 vaccine already formulated for clinical trials by Shirley Longacre's team at the Pasteur Institute—deferred for a year because it lacked industrial sponsorship, but also the closest clinical product behind that—a pre-erythrocytic stage vaccine developed by Mike Hollingdale at the University of Leeds, UK—was amputated from the cluster by the panel. Consequently, only the cluster's basic research is funded. Newbold has since withdrawn from the group.

This group has received its written evaluation, and the rationale for dropping Hollingdale's project has left him bewildered. "They made a surprising interpretation of the literature which is contrary to what is accepted across the broad field of malaria vaccinology," he told *Nature Medicine*.

In another blow to malaria research in

Europe, only one malaria project has been funded from the INCODEV budget. The funds will support a "concerted action" effort, which means that money must be used to facilitate meetings and travel of scientists, but not research. Thus, basic research to develop a vaccine against malaria has received ECU6 million in this, the first funding round of the Fifth Framework program. This is compared with ECU14.7 million and ECU6.1 million for HIV and tuberculosis vaccine research, respectively.

Hopeful that they will be financed from next year's EC budget round, many researchers were reluctant to criticize the malaria vaccine panel. Those who offered an opinion off-the-record as to why the projects funded did not match the initial call for clinical stage work pointed to the fact that the panel members are not actively engaged in malaria vaccine research themselves, and seem to be "misguided" as to the value of projects such as pre-erythrocytic vaccines. In addition, researchers who spoke to *Nature Medicine* called for transparency of the vaccine panel, as unlike in the US, EC panel members are not named publicly.

Fortunately, a ECU1 million silver lining will be provided by a separate initiative, the European Malaria Vaccine Initiative (EMVI). According to its director, Soren Jepsen, this organization will announce support this month for four clinical trial projects—two of which involve pre-erythrocytic-stage vaccines, headed by Druilhe and Adrian Hill of the University of Oxford, and the other two, lead by Druhile and Theisen, will focus on asexual blood stage vaccines.

Meanwhile, the US is continuing to push ahead with clinical testing of malaria vaccines. On hearing that Hollingdale's project did not receive European funding, the Walter Reed Army Research Institute in Washington DC has contacted him with a proposal to take the project into human studies next year. In addition, the National Institutes of Allergy and Infectious Diseases has issued a call for bids on a multi-million dollar contract to develop five vaccines per year for the next seven years (http://www.niaid.nih.gov/contract/rfp's/rfp0018.htm). As one European researcher put it, "The Americans move fast. They see the opportunities weigh up the scientific evidence and go for it, whereas Europe is still messing about on the bench."

Karen Birmingham, London

Critics rain on MMV parade

After more than a year of pre-publicity, a major scheme to bring private and public sectors together in the search for new drugs against malaria was launched officially in Geneva last month. But even as the director-general of the World Health Organization (WHO), Gro Harlem Brundtland, shook hands with the cosponsors of the Medicines for Malaria Venture (MMV), critics of the venture were voicing their concerns.

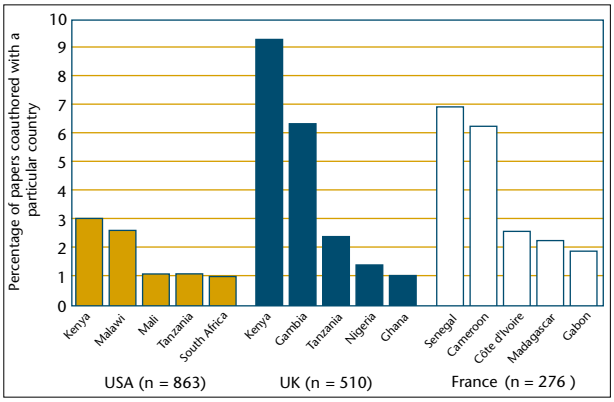
The MMV aims to reverse the pharmaceutical companies' near-abandonment of research into drugs for malaria, a disease that overwhelmingly affects developing countries. The venture aims to produce one new antimalarial drug every five years on average, raising US$30 million a year once it is fully fledged. In addition to the WHO, sponsors include the World Bank, the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), and several national governments and philanthropic foundations.

The MMV will take the form of a "public venture capital fund": promising drug discovery projects will be supported by the MMV and some will go on to be developed. The development stage will be financed and administered by the MMV but will be done by whoever wins the contract. If a compound proves successful in trials, the MMV will seek partners in industry to commercialize the product.

Lodewijk de Vink, president of the

Wellcome reports on malaria research in Africa

Malaria research is the richest seam in Africa's otherwise impoverished biomedical science output, according to a new report from the Wellcome Trust. But the first detailed assessment of the state of malaria research in the continent that is home to 90% of the world's malaria deaths holds few other comforts.



Seventeen percent of the malaria papers on the Science Citation Index and Medline databases have an African address—in stark contrast to biomedical papers overall, where only 1.2% come from Africa. Collaboration with industrialized countries is strong—almost four of five African malaria papers (79%) involve authors from Europe and the US, and 88% of grants listed by African laboratories between 1993 and 1998 were from outside Africa. However, there are few collaborations between African institutions.

The report from the Wellcome Trust is part of the Multilateral Initiative on Malaria (MIM; see main story). It was intended as a baseline assessment of research capacity in Africa so that potential links could be identified and efforts to improve research and training there—one of the MIM's goals—could be evaluated.

It points to "a number of areas of weakness in current international research training activities," which remain a poor relation in malaria programs. Training is provided largely outside Africa, is fragmented and inadequately monitored. The report calls for more investment in African training centers.

Carlos Morel, head of the Special Programme for Research and Training in Tropical Diseases, a United Nations-funded program based at the World Health Organization, which spends a quarter of its US$28 million annual budget on training, insists there have been improvements in the past two years. During the period of 1997–1998, the proportion of the budget spent on training rose to 34% with the establishment of a MIM task force for research capacity building in Africa. For all areas funded under the task force, "local or regional training has increased from 31% [before 1996] to 65%," he says. And research groups have been established in several of the poorest countries, including Uganda, Benin and Mali.

The report, "Strengthening Health Research in the Developing World: Malaria research capacity in Africa" is available at www.wellcome.ac.uk/publications

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