# Letters

## Malaria Vaccines

It was with great surprise that I read the description of our work in your correspondent Jeremy Cherfas' article "Malaria vaccines: The failed promise" (News & Comment, 26 Jan., p. 402). Our 1987 paper (*1*) reported the results of a malaria vaccine trial in monkeys, not humans, while our 1988 paper (*2*) reported the results of a malaria vaccine trial in humans. Both of our papers showed good protection against infection. The trial carried out last spring by Bill Collins and his associates in the Malaria Branch of the Centers for Disease Control in Atlanta, Georgia, was in monkeys, not humans.

Perhaps Cherfas was misinformed, but what Collins describes as "slight differences" between our monkey trial (repeated several times by our group with results similar to those we published in 1987) and his monkey trial were described in a report (*3*) to the World Health Organization's Lindsay Martinez as follows: "We feel that the most likely explanation for the different serologic responses in animals immunized with the peptide mixtures in Atlanta and Colombia was a problem with the peptide—BSA conjugation procedure. This probably also explains the lack of protection in the two groups of animals immunized with a mixture of 3 peptides in Atlanta."

Perhaps most disturbing is the statement by Cherfas that "Patarroyo has not given up. . . .[T]here is 'tremendous excitement' in Venezuela and Colombia. . . .[but] few scientists outside those countries share wholeheartedly in that enthusiasm." This implies that no one believes good science can be carried out in developing countries. In our view, science exists only in two forms—good or bad; and good science, like truth, is based on facts. Our clinical trials in humans are under way, and their results should settle the issue.

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Cherfas states that "In two trials of different vaccines only one of nine subjects was protected—and even that case is suspect." As the senior investigators who ran the trials, we can attest that one of three volunteers immunized with a synthetic peptide conjugate vaccine $(NANP)_3$-TT was protected against sporozoite challenge (*1*), and one of six immunized with a recombinant vaccine FSV1 was protected (*2*). Andy Waters, a molecular biologist who was not involved in either clinical trial, is cited as suggesting that an allergic reaction to the vaccine was responsible for the subsequent protection against malaria. We are unaware that persons can be protected from a sporozoite challenge by virtue of an allergic reaction stimulated 12 months previously and think it is far more likely that specif c vaccine-induced antisporozoite immunity was responsible. This interpretation of the results is supported by the fact that, in both clinical trials, the vaccinated individuals had signif cantly longer prepatent intervals than did unimmunized control subjects, which indicates that vaccination stimulated some degree of antisporozoite activity, albeit a level that was completely protective in only two of the nine vaccinees. We believe these results provide evidence that biologically relevant antisporozoite antibodies can be stimulated by subunit vaccines.

Furthermore, in contrast to what is stated in the article, there are no data demonstrating any signif cant variation in the central repeat region of the *Plasmodium falciparum* circumsporozoite protein. This apparently invariant region remains an excellent target for protective antibodies. A major challenge is to design vaccines that consistently induce higher concentrations of such antibodies.

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It is true that the promise of a malaria vaccine seems as distant in 1990 as it did in 1985, if not more so. However the same is also true of many areas of biotechnology. Attempts to find the elusive malaria vaccine should certainly be subjected to scrutiny and, where necessary, shortfalls highlighted and admitted. The public has a right to be kept thoroughly informed about the progress being made when its money is made available for such research. But to concentrate purely on the "failure" to find a vaccine is to overlook the huge contribution that the "search" has made to the understanding of the basic biology of the parasite and the nature of its interaction with the host immune system. For instance, selective pressure on the circumsporozoite (CS) protein results not in myriad sequence variation but instead in limited changes focused on small, distinct regions of the protein which have been shown to elicit immune responses. This, when allied with our increasing knowledge of host genetics and immune effectors, suggests that a CS-based vaccine holds more promise than it did 5 years ago.

Cherfas uses a fragmentary quote of mine to imply the complete failure of the CS protein vaccine trials. While I do not have perfect recall of our conversation, I remember also enthusing about progress in the field. An individual exhibiting an allergic response may clear a challenge of parasites for one of two reasons, either because of a specific antisporozoite response or a nonspecific reaction. I believe that I made these two options clear to Cherfas. If not, then I would like to take this opportunity to do so. It would have been quite simple to confirm the facts with one of the authors of the study.

The vaccination against malaria is one of the most complicated biological puzzles that man has attempted to solve. If it seems that the public has been misled into believing that it would be a simple process, then that is indeed unfortunate. It would be unfair to the scientists involved to ignore that the last 5 years have produced a much more detailed picture of the object of that challenge.

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## Light Bending: Prediction and Theory

Stephen Brush (Articles, 1 Dec., p. 1124) gives an interesting account of the shifting importance of light bending as evidence for relativity. He appears, however, to have mixed this up with the question of falsifiability, apparently because of Popper's report of being led to the notion by Einstein's prediction of light bending prior to observation of the effect.

The central historical facts seem to be two. First, in the early days of relativity, scientists were substantially more impressed