scales for the unstable modes far exceed typical observed lifetimes (viz., days) of the loop structures in question; remarkably little low-temperature material is, in fact, required to quench the instability. Theory can thus now be fully reconciled with observation: if proper account is taken of the stabilizing influence of the boundary layer separating the solar corona from the underlying (visible) photosphere, analytical normal mode analysis does predict stability for time scales of the order of the observed coronal structure lifetime; the error of previous calculations — and the source of the apparent discrepancy with observations — was simply the neglect of this stabilizing factor.

From both the observational and the theoretical perspectives, it thus now appears that the gross properties of the confined solar corona can be understood by considering simple hydrostatic equilibrium models, although the reasons for this are quite complex and, in some cases, are still not well understood[9]. However, when one looks at the corona in some detail the simplicity disappears, and it is apparent that hydrostatic models are seriously inadequate. Observations of intensity fluctuations, of persistent up and down flows, of relatively cool matter residing at coronal heights, of apparent spatial mingling of hot plasmas at quite different temperatures, all call for more sophisticated modelling. Analytical methods seem inadequate for such modelling; the new plasma simulations have thus appeared at an opportune time. □

Hybridoma technology identifies protective malaria antigens

from F.E.G. Cox

VARIOUS partially successful attempts have been made to immunize experimental animals against malaria but preparations of the most easily obtained antigens, those derived from the forms of the parasite in the blood, have been relatively crude and poorly characterized. The use of monoclonal antibodies has now enabled scientists at the Wellcome Research laboratories to identify specific protective antigens and to use them to immunize mice against a virulent form of malaria[1].

A vaccine against malaria is one of the prime needs in tropical medicine and in a variety of models in laboratory animals vaccines have been prepared from sporozoites, the infective stages injected by the mosquito; schizonts, the dividing forms in the red blood cells; and merozoites, the products of this division that invade fresh cells. Monoclonal antibodies have been used to identify an antigen with a molecular weight of 44,000 that completely envelops the sporozoite and induces immunity to the rodent malaria parasite *Plasmodium berghei*[2]. This antigen is specific to the sporozoite and seems to be a differentiation antigen that appears while the sporozoites are in the salivary glands of the mosquito and disappears soon after they have been injected by the mosquito and have entered the liver cells where they undergo their first phase of multiplication[3].

Although a sporozoite vaccine is a logical and feasible possibility and would prevent the parasite from developing in the liver and thence the blood, a number of workers feel that should a single sporozoite escape the immune response, infection of the red blood cells would eventually ensue and therefore a vaccine should be based on the blood stages. The most promising candidate is the merozoite, and injections of merozoite antigens combined with adjuvants have been shown to protect monkeys against several species of malaria parasite[4].

F.E.G. Cox is Professor of Zoology at King's College, University of London.

A monoclonal antibody against merozoite antigens of the rodent malaria parasite, *Plasmodium yoelii*, is known to confer protection on passive transfer[5] and it has now been used to identify the antigen involved[1]. The latter has a molecular weight of 235,000, is associated with an internal organelle of the merozoite and is specific to the merozoite. When mice were immunized with this antigen in Freund's adjuvant, they responded with high levels of merozoite-specific antibody and were protected from death following challenge, although they experienced relatively high parasitaemias lasting about 16 days. A second monoclonal antibody known to react with schizonts, but which was not protective on passive transfer[5], was used to identify a second protective antigen. This is a surface antigen with a molecular weight of 230,000 which is present early in the maturation of the schizont and occurs on both schizonts and merozoites. Mice immunized with this antigen produced high titres of antibody against schizonts and were very resistant to challenge, experiencing only a mild infection lasting about 9 days. The significance of these results is that monoclonal antibodies can be used to identify protective antigens, but it is also interesting that the best protective immunity was produced in response to the antigen whose corresponding monoclonal antibody failed to provide passive protection.

What exactly is the nature of these antigens? Using similar virulent and avirulent forms of *P. yoelii*, Taylor *et al.*[6] also have produced a range of monoclonal antibodies to sporozoites, schizonts and merozoites. Their antibody to merozoites was specific to merozoites but cross-reacted with those of several species, was associated with an internal organelle possibly involved with penetration into the red blood cell but was not protective. Epstein *et al.*[7], using *Plasmodium knowlesi* in monkeys, have obtained three hybridoma lines that produce monoclonal antibodies against merozoites. All three agglutinate merozoites and two block red cell invasion. The antigen involved has a molecular weight of 250,000 (or 240,000 if saponin lysis of infected cells is used) and cross-reacts with various strains of *P. knowlesi*. A fourth group of workers (Perrin *et al.*[8]) have also raised monoclonal antibodies to various stages including merozoites, this time to the human parasite, *Plasmodium falciparum*, in the mouse, a non-susceptible host. The merozoite antigens involved were surface polypeptides with low molecular weights, 36,000 and 96,000, and antibodies against these inhibited the development of *P. falciparum in vitro*. Antigens with low molecular weights like these must be viewed with caution, because Holder and Freeman also detected low molecular weight polypeptides associated with schizonts and concluded that they were proteolytic fragments of the 230,000 molecular weight antigen[1].

Thus a number of potentially protective antigens on the merozoite have already been identified using monoclonal antibodies. Some are surface antigens and some are internal, some cross-react with other stages or the merozoites of other species and there is also variation in molecular weight. It is likely, therefore, that a number of antigens are involved in the immune response to the merozoite alone and these may operate sequentially, concurrently or alternatively. Antigens associated with schizonts[1] and sporozoites[2,3] have also been identified using monoclonal antibodies. It is going to be a long time before anyone identifies the most important protective antigens in a malaria parasite but in the meantime there will be a quantum jump from the use of crude homogenates as vaccines to cocktails of characterized polypeptides and these are much more likely to be acceptable in human medicine than anything in experimental use at the present time. □

1. Holder, A.A. & Freeman, R.R. *Nature* **294**, 361 (1981).
2. Yoshida, N. *et al. Science* **207**, 71 (1980).
3. Aikawa, M. *et al. J. Immun.* **126**, (1981).
4. Cohen, S. *Proc. R. Soc.* **203**, 323 (1979).
5. Freeman, R.R. *et al. Nature* **284**, 366 (1980).
6. Taylor, D.W. *et al. Infect. Immun.* **32**, 563 (1981).
7. Epstein, N. *et al. J. Immun.* **127**, 212 (1981).
8. Perrin, L.H. *et al. Nature* **289**, 301 (1981).

0028-0836/81/510612-01$01.00