at this time it is known that studies are in progress aimed at ascertaining if this or other histones could serve as potential antigens in the MEM test for lymphocytes from patients with cancer. Such a hypothesis is strengthened by the observation that the addition of nuclei or DNA to cancer basic protein extracts renders them ineffective in the test. Furthermore, histones are basic proteins whose properties enable them to interact with the known types of negatively charged groups on cell surfaces. It may be that those tumour cells which have an increased surface negative charge could bind histones to a greater extent than normal cells and in this way account for the location in excess of the activity in relation to the plasma membrane and thus possibly initiate an autoimmunization process.

In view of these doubts about the nature of the "antigens" used in the MEM test, it is prudent to interpret cautiously the significance of detecting scrapie-like antigens in ageing tissues as reported on page 174 of this issue of *Nature* and with such preliminary experimental data the conclusions regarding the role of the thymus in influencing changes in antigenic determinants on cells which may occur with age.

Finally, although there is some doubt about the nature of the antigen, this need not detract from the apparent clinical value of the MEM test. After all, the widely used Wassermann reaction does not employ the appropriate antigen. It is difficult, however, to envisage the present MEM test or the Cardiff modifications of it being used on a wide scale as only a few samples can be analysed each day. One way which might result in some improvement without loss of the anticipatory element might be attained if the nature of the factor produced and/or released by the lymphocytes to act on the macrophage was identified. It might then be possible to develop a radioimmunoassay for this "lymphocyte mediator" measuring its level *in vitro* after interaction of the "sensitized" lymphocytes and "tumour antigen".

If future work confirms the concept of an antigen common to or released by all human tumours and the ability to detect its presence at the pre-clinical stage of development, then this will almost certainly represent the genesis of a new era of oncological investigation. A. M. N.

PROTEIN STRUCTURE

Elusive Electrons

from our Molecular Biology Correspondent

So insatiable nowadays is the clamour for novelty in the trade at large that a new structure determination of a hydrolytic enzyme, an apocalyptic event not so long ago, would probably already stand an outsider's chance for the Yawn of the Year award. An area in which the crystallographers' efforts are, on the other hand, beginning to compel biochemists' attention is electron transfer. As Kraut and his colleagues now show (Salemme *et al.*, *J. biol. Chem.*, **248**, 3910 ; 1973), there is enough information in their new high-resolution structure of a bacterial *c*-type cytochrome to let the curly arrows fly. Ferricytochrome c_2 from the photosynthetic bacterium, *Rhodospirillum rubrum*, has a chain of 112 residues, with a close affinity, in terms of sequence and structure, to horse heart cytochrome *c*. The haem group, which is covalently linked to the protein, lies in a deep crevice, one edge only projecting into the surrounding solvent. The walls of the crevice are made up mainly of hydrophobic side chains. Two thiol groups form covalent thioether bonds with the vinyl side chains of the haem, and one of the two external iron ligands is a histidine, the plane of its ring perpendicular to that of the haem, as expected. The ligand on the opposite side is, as in the eukaryotic cytochromes *c*, the sulphur of a methionine. Around the edges of the haem plane there are also the side chains of a serine, two tyrosines and a tryptophan, all so placed as to make hydrogen bonds with the haem propionyl groups.

Now a number of interesting inferences follow from the details of this structure. In the first place it seems to admit of little doubt about the site of its interaction with the membrane-bound bacteriochlorophyll, to which, when it is in the reduced state, it gives up an electron. Not only is a good part of the hydrophobic rim of the haem group exposed to the aqueous medium, with the polar propionyl side chains tucked into the essentially non-polar crevice, but the

Temperature Sensitive Elongation Factor Ts

BACTERIAL mutants with temperature sensitive enzymes have proved valuable tools in unravelling biological processes. Not least in studies of the mechanism of protein synthesis are such mutants playing an increasing role. Several mutants are now available to facilitate work on the function of tRNA in protein synthesis. The relevant proteins in this case are the elongation factors (EF) "G" and "T", the latter of which is composed of two components known as EFTu and EFTs. Temperature sensitive mutants of tRNA itself have been isolated before. Moreover, some time ago, temperature sensitive mutants of EFG were isolated in two different laboratories. A report from a member of one of these two laboratories, Kuwano, and his coworkers, in next week's issue of *Nature New Biology* suggests the availability of a temperature sensitive mutant of EFTs.

The *E. coli* mutant in question (HAK88) grows at elevated temperatures (42° C) only in the presence of added tRNA, similar in this requirement to the temperature sensitive tRNA containing mutants. The lesion, however, does not seem to be in the tRNA, for S100 from which tRNA has been removed exhibits the original temperature dependence, whereas both the extracted tRNA and the aminoacyl synthetases appear to be normal. S100 extracts from another mutant, containing a temperature sensitive EFG, complement the defective system, eliminating EFG as the responsible agent.

Restoration of protein synthesis *in vivo* by tRNA might be more likely if EFTs rather than EFTu were the defective factor. Whereas EFTu forms a stable complex with tRNA, Ts seems mainly to enhance the interaction of tRNA with EFTu.

First, at 0°, EFTs, whether from HAK88 or the parent strain HAK8, promotes the binding of GDP to EFTu and a strong EFTs concentration dependence of this binding is observed. EFtu, though itself readily inactivated by heating in the absence of GDP, is not more so when isolated from HAK88 instead of HAK8. The stimulation of GDP binding to EFTu, however, is significantly more temperature sensitive in the critical range, 36–42° C, when EFTs is taken from the mutant strain than when it is taken from the parent. Elegant confirmation of the identity of the defective protein in mutant HAK88 comes from work with the replicase of Qβ-infected cells. It is known that two of the four polypeptide chains of Qβ replicase are identical to EFTu and EFTs. When Qβ replicase is isolated from HAK88, unlike the parent strain, RNA synthesis *in vitro* exhibits the temperature dependency one would predict if it contained the sensitive EFT factor.

E. coli HAK88 grown at 42° C does not synthesize RNA. Kuwano *et al.* suggest that there may be a common function of EFTs in its interactions with tRNA and in the hypothetical control of RNA synthesis both in normal and in virus-infected cells.

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