found in the deer on which the ticks also feed (Piersman *et al. J. Med. Ent.* **15**, 573; 1979) and the fact that isolates of *Babesia* from wild mice and voles resemble the human isolates using immunological criteria (Benach *et al. Amer. J. Trop. Med. Hyg.* **28**, 643; 1979) confirms that these rodents are the sources of the human infections. In Mexico, an unidentified babesia that infects hamsters has been isolated from three asymptomatic individuals (Osorno *et al. Vet. Parasit.* **2**, 111; 1976).

In Europe, the human cases now total 6; 2 from Yugoslavia, 2 from France and one from each of Ireland, Scotland and the USSR. In all cases the infected individuals had been splenectonised and all but the two from France died. The parasites implicated are *B. bovis* and *B. divergens* in Yugoslavia, *B. divergens* in Ireland and Scotland and one of the French cases, *B. bovis* in the USSR and the identity of the parasite in the remaining French case is unknown (Garnham *Trans. R. Soc. Trop. Med. Hyg.* **74**, 153; 1980). In the Scottish case the parasite has been returned to cattle and also passaged into gerbils, the first time

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

a rodent has been successfully infected with a cattle piroplasm. (Lewis & Williams *Nature* **278**, 170; 1979). The vector of human babesiosis in Europe has not yet been identified but *Ixodes ricinis* must be a possibility (Donnelly *Trans. R. Soc. Trop Med. Hyg.* **74**, 158; 1980). It is unlikely that *B. microti* will infect man in Britain where the vector is *I. trianguliceps* which seldom, if ever, feeds on man.

Human babesiosis, then, occurs in two distinct forms. The American form, which is relatively avirulent, occurs in intact individuals and is caused by *B. microti* from rodents and the European form, which is usually fatal, occurs in splenectomised individuals and is caused by *B. divergens* or *B. bovis* from cattle. All these cases can be regarded as accidental infections of man acquired by farmers, campers and others likely to be bitten by ticks. The infection is characterised by fevers and anaemia with small rings resembling malaria parasites in the blood but the parasites are not killed by chloroquine.

This is a rare but interesting disease and is the latest addition to the growing list of zoonoses, those parasites transmissible from wild or domesticated animals to man. □

at least some recognition of the eukaryote signal sequence by the appropriate bacterial membrane receptors and possibly, processing enzymes.

A comparison of the gene and amino acid sequences of F-IF and Le-IF (T. Taniguchi *et al.* Nature, this issue, p547) reveals a number of interesting features. First, although there is an average homology of about 45% between the nucleotide sequences coding for amino acids, the longest common stretch is only 13 nucleotides indicating that the interferons are the products of two closely related genes and not the result of a differential splicing process on the pre-mRNA product of one common gene. Second, three (or four) main domains of homology can be discerned between the coding nucleotide sequences of the two interferons, a feature which is even more pronounced upon comparing the amino acid structures, having lined up the presumed initiator methionine codons. Clearly, it is possible to speculate that these domains are responsible for important common functions of the two proteins such as the binding to common cellular receptors (Wiranowska-Stewart *et al. J. Gen. Virol.* **37**, 629; 1977) and the anti-viral and anti-tumour activities. Third, the overall data clearly suggest that there was a common ancestral gene for these two interferons.

It is also revealing to compare the amino-terminal sequence and amino acid composition of a human lymphoblastoid interferon (Zoon *et al. Science* **207**, 527; 1980) with the corresponding Le-IF data. While the former is probably of the leukocyte type (see Paucker *The Interferon System. Texas Reports on Biology and Medicine* (eds. Baron & Dianzani) **35**, 23; 1977), it seems as if it is the product of a distinct, non-allelic gene. Indeed, a second Le-IF cDNA clone has been observed by Mantei *et al.* which appears different from the first in terms of its restriction enzyme map. However, its degree of relatedness to the latter and the human lymphoblastoid interferon remains to be seen.

Human interferon gene sequences

from Michael Houghton

THE excitement that has been generated recently by human interferon studies is continuing with the elucidation of the gene sequences (and hence polypeptide structures) of human fibroblast (F-IF) and Leukocyte (Le-IF) interferons. The two molecules are currently receiving much attention over their potential as *in vivo* anti-viral and antitumour agents (Stewart *The interferon system* Springer, Berlin, 1979).

Although both molecules seem to induce similar biological effects, the target cell specificities differ and antibodies raised against one type do not neutralise the other (Stewart *op cit.*). Also, there is some evidence that the two proteins are encoded by different mRNA molecules (Cavalieri *et al. Proc. natn. Acad. Sci. U.S.A.* **74**, 3287; 1977). The origins of these differences have become clearer now that sequences are available from both F-IF (Taniguchi *et al. Gene* **10**, 11; 1980; Houghton et al. *Nucl. Acids Res.* **8**, 1913; 1980; Derynck *et al. Nature* this issue, p542) and Le-IF (Mantei *et al. Gene* **10**, 1; 1980).

The F-IF mRNA contains 836 nucleotides (excluding the 3′ poly A tail and the possible 5′ cap structure) consisting of 72 and 203 nucleotides in the presumed 5′ and 3′ untranslated regions respectively, 63 nucleotides coding for a hydrophobic pre-peptide signal sequence that is responsible for protein secretion, and 498 nucleotides coding for a further 166 amino acids. If the latter are all present in the mature protein,

then a polypeptide molecular weight of 20,000 daltons can be predicted, a value which is significantly higher than the 16,500 dalton species that is thought to represent the cleaved, but unglycosylated protein observed in a reconstituted cell-free system (Derynck *et al.*). Also, the native glycosylated form of F-IF has itself been estimated to be 20,000 daltons (Havell *et al. J. Biol. Chem.* **252**, 4425; 1977) and so at this stage, one cannot completely rule out the possibility of additional processing of F-IF besides the cleavage of the N-terminal signal sequence.

Le-IF mRNA contains around 865 nucleotides (excluding the 3′ poly A tail and probably a small number of nucleotides at the 5′ terminus that have been removed during cDNA preparation) of which 242 are located in the presumed 3′ untranslated region. As in the case of F-IF mRNA, there seems to be a region coding for a pre-peptide signal sequence of either 15 or, more probably, 23 amino acids again followed by a coding sequence of 498 nucleotides corresponding to 166 amino acids in the mature protein, assuming no further processing. Interestingly, in view of the fact that the biologically active product of Le-IF genes cloned in bacteria seems to be sequestered into the periplasmic space (Mantei *et al.*), it would seem there is

Michael Houghton is in the Biochemistry Department, Searle Research and Development, G.D. Searle & Co. Ltd., High Wycombe, U.K.

We can now look forward to further results from cloning experiments (both cDNA and genomic cloning) to provide more valuable information on the number and arrangement of genes coding for a particular type of interferon and their relatedness to each other and other types of interferon genes. It may now also be possible to modify and re-arrange these genes using standard genetic engineering techniques and other methods (e.g. Muller *et al. J. Mol. Biol.* **124**, 343; 1978) to produce new interferons with some particular advantages in specificity and activity. Such studies could also help in the detailed assignation of structure to function. Clearly, the work discussed here signifies the start of an era from which the molecular mechanism of interferon action will hopefully be elucidated □