This led to a considerable yield of 186,000 copies of radioimmunoassayable hGH activity per *E. coli* cell (2.4 $\mu g\ ml^{-1}$). Furthermore, and as planned, the product was of about the correct molecular size, not being fused to a plasmid-determined protein as has been the case in most previous approaches to the bacterial production of hormones (see for example Martial *et al. Science* **205**, 602; 1979).

Given Genentech's efforts and their plans to market hGH in collaboration with Kabi, it was surprising to hear doubts expressed that more hGH is really needed. In the USA at least, said S. Raiti (National Pituitary Agency), although there were theoretical grounds for believing that several thousand untreated patients existed, in practice the medical demand for hGH was readily met by hGH isolated from cadaveric pituitaries. On the other hand he conceded that lashings of the hormone would allow proper trials of its mooted efficacy on burns, non-healing fractures, ulcers and haemopoiesis.

As yet, however, not even the biological activity of the presumed hGH has been tested. Indeed it remains to be shown that any bacterially-produced hormone has proper biological activity although Lydia Villa-Komaroff (University of Massachusetts, Worcester) reported that the substance released by trypsin treatment of fused β-lactamase–insulin produced by bacteria was somewhat active in a rat fat pad bioassay.

Another polypeptide (?hormone) that is attracting the attention of genetic manipulators is interferon. One only has to read *Omni* these days to discover that interferon is the great white hope of cancer therapy. The problem with both *Omni* and interferon is to separate science fiction from fact. For interferon that problem will only be overcome when it is available in sufficient quantities and in pure enough form for proper trials to be carried out. As yet the few, if encouraging, results that have emerged from clinical tests have relied on interferon that is less than 10% pure.

Greater purity is one of the main aims of both S. Pestka (Roche Institute of Molecular Biology, New Jersey) who is purifying interferon from chronic myeloid leukaemia serum and of C.B. Anfinsen (National Institutes of Health) who will soon be growing 1,000 litres of human lymphoblastoid cells as his source. Purity is important not only for clinical trials but for the determination of interferons's structure. So far it is thought to be a polypeptide of about 154 amino acids. The polypeptide is associated with carbohydrate components which, however, are not essential for activity. It is said (by others) that both at NIH and at Dupont the N-terminal amino acid sequence of interferon has been determined. If true that may give the genetic manipulators their entrée. For with a synthetic polynucleotide complementary to the N-terminal amino acid sequence it may be possible to fish out pure messenger RNA for interferon to make cDNA for subsequent cloning.

Does the bacterial approach leave anything for the synthetic peptide chemist to do? Certainly! In the first place chemical synthesis still makes much sense for the smaller peptides, 'smaller' being less than 20 to 75 amino acids, depending on whose opinion one takes. It should however be noted that even for such a small peptide as the 14-amino acid somatostatin the bacterial route of production may be commercially viable; otherwise why will it become Genentech's first marketed chemical (for research purposes only) by the end of this year? Second, chemical synthesis is inherently 'cleaner' and has been considerably improved by the advent of continuous flow techniques with the prospect of real time monitoring of the products (B. W. Erickson, Rockefeller University). Third, chemical synthesis is well suited to the production of labelled peptides and peptide analogues. That is particularly the case when the analogues contain either modified or D-amino acids.

The synthetic peptide chemists have had, for example, considerable success in producing potent agonists and antagonists of the 10-amino acid peptide, luteinising-hormone-releasing-hormone (LHRH). Chiefly by the substitution of a D-amino acid at the sixth of the ten positions and by N-terminal changes, it has been possible to produce 'super LHRHs' with more than a hundredfold the potency of the natural hormone but also with paradoxical antifertility effects (see for example Ying & Guillemin, *Nature* **280**, 593; 1979). Considerable progress has also been made in producing analogues that are LHRH antagonists. The most active antagonists described by D. H. Coy (Tulane University, New Orleans) have para-halogenated D-phenylalanine at position 2 and acylated D-phenylalanine at position 1. Those substitutions together with a D-tryptophan at position 6 result in an antagonist that blocks ovulation at 0.03 mg per rat. Three years ago the best antagonists were 30-fold less potent.

The peptide chemists have had less success so far in improving on those thymic hormones whose structure has been determined, thymopoietin and FTS ('facteur thymique serique'). Thymopoietin is 49 amino acids long but a constituent pentapeptide has the biological activities of the full molecule (G. Goldstein, Ortho Pharmaceutical Co.). FTS is a nonapeptide first isolated from pig serum, now from human serum, and shown also to be present in thymic epithelium (J. F. Bach, Hôpital Necker, Paris).

Another serum peptide with effects on T cells is likely to be a tetrapeptide, possibly with a methylated amino acid at the N-terminus (A. Astaldi, Netherlands Red Cross Blood Transfusion Service). Ironically the only clinical trials that were reported involved either the relatively crude 'thymosin fraction V' of A. W. Goldstein (George Washington University, Washington) or the unsequenced 'THF' polypeptide of N. Trainin (Weizmann Institute). Thymosin fraction V has recently proved effective in prolonging the survival of patients with oat cell carcinoma. And THF has induced a remarkable recovery in immunosuppressed children with lymphoproliferative diseases who had developed infections. The basis of these clinical successes, the cellular or molecular effects of thymic hormones and the relationship of the various contenders for that title remain mysterious.

The testing and production of polypeptide hormones is clearly a very competitive business. It will not be unprecedented if the clinical optimism evident at this stage has to be moderated when larger scale trials can be completed. Meanwhile amongst the genetic manipulators the perceived returns have led them to adopt Madison Avenue tactics. A sobering-up period will doubtless follow when the products have to be shown to be suited to clinical use. Meanwhile many claims are made to the effect that bacterial production is both cheaper and easier than present techniques. It will be interesting to see whether the eventual price as well as the availability of the hormones reflects current optimism. □

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A hundred years ago

But there is, perhaps, nothing which shows more strikingly the identity of the protoplasm in plants and animals, and the absence of any deep-pervading difference between the life of the animal and that of the plant, than the fact that plants may be placed, just like animals, under the influence of anaesthetics.

We owe to Claude Bernard a series of interesting and most instructive experiments on the action of ether and chloroform on plants. He exposed to the vapour of ether a healthy and vigorous sensitive plant, by confining it under a bell-glass into which he introduced a sponge filled with ether. At the end of half an hour the plant was in a state of anaesthesia, all its leaflets remained fully extended, but they showed no tendency to shrink when touched. It was then withdrawn from the influence of the ether, when it gradually recovered its irritability, and finally responded, as before, to the touch.

It is obvious that the irritability of the protoplasm was here arrested by the anaesthetic, so that the plant became unable to give a response to the action of an external stimulus.

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