news and views

Probing the insulin receptor

from P. H. Sönksen

THE German Wool Research Institute houses some of the foremost peptide chemists in the world who sharpen their teeth on insulin as a simple chemical model for the more complicated molecules that will be keeping us warm in the months to come. At the Institute two young students, Peter Thamm and Achim Schüttler have respectively synthesised a family of specifically photolabelled insulin analogues and made a variety of specific covalently-linked insulin dimers which together have led directly to major developments in our knowledge of the insulin receptor. The insulin receptor was perhaps the most popular subject at the International Insulin Conference* held at the Institute recently.

Remarkably concordant results on its composition were provided by three independent groups. M.H. Wisher and colleagues (St Thomas's Hospital Medical School, London) have specifically covalently labelled a membrane protein of approximately 300,000 molecular weight which can be resolved into a subunit of apparent molecular weight 130,000. This polypeptide runs atypically on polyacrylamide gels and may be a glycoprotein of true molecular weight nearer 90,000. Rather surprisingly this same membrane component was readily and specifically labelled with probes carrying the photoreactive group in the A_1, B_1 or B_{29} positions.

These observations were exactly in keeping with those of C. Yip (University of Toronto) working independently with similar but less specifically photolabelled probes. Yip reported two specifically labelled components (130,000 and 90,000 molecular weight) in membrane extracts from insulin-responsive cells but only the 130,000 molecular weight components in extracts of cells containing insulin binding sites but no insulin-responsiveness (such as brain) and went on to suggest that the 90,000 component may be an effector molecule. M.P. Czech (Brown University, Rhode Island) using a bifunctional cross-linking reagent was able to produce almost identical results by covalently linking radiolabelled insulin to the membrane receptor after the two had been allowed to react *in vitro*. He, like Wisher, had also isolated a 300,000 molecular weight component that could be dissociated into 125,000 molecular weight subunits after reduction of disulphide bonds. Early results from C. Diaconescu and D. Saunders (DWI) and A.R. Rees (University of Oxford) suggest that covalent linkage of insulin to its receptor in adipocytes may lead to prolonged activation of insulin-dependent processes.

Other remarkable observations on function of the receptor come from the synthetic dimers (Schüttler). They show considerable discrepancy between receptor-binding activity (100%) and biological activity (considerably impaired, 0–60% depending on assay). P. De Meyts (Institute of Cellular and Molecular Pathology, Brussels) and colleagues concluded, on the basis of their studies with these dimers, that each monomeric half of the dimers might bind to a component of the insulin receptor and in some way prevent activation (possibly by inhibiting subsequent conformational change). On the other hand K. Willey and colleagues (St Thomas's Hospital Medical School, London) felt that their own results were compatible with the simpler concept of dimer reaction through one component only.

Other examples of the important contribution made by the synthetic chemists include some very elegant experiments reported by A.S. Rosenthal (Merck Sharp and Dohme Research Laboratories, New Jersey).

In the presence of synthetic peptide fragments of insulin, ^{3}H-thymidine incorporation into lymphocyte DNA as a measure of T cell response, was used to delineate the specificity of the phenomenon. In one strain of guinea pigs

*The 2nd International Insulin Symposium was held at the Deutsches Wollforschungsinstitut, Aachen on 4-7 September, 1979, and organised by Professor H. Zahn and Dr Dietrich Brandenburg.

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More on anthropoid origins

from Peter Andrews

THE origin of the higher primates is a contentious issue at present. Traditional interpretations place the tarsier closest to the anthropoid primates but an alternative to this has been advocated for some years by P.D. Gingerich of the University of Michigan. Gingerich has demonstrated a nearly continuous series of fossil primates from the early Eocene to the Oligocene all belonging to the family Adapidae (for a review see *J. hum. Evol.* **6**, 483; 1977), and he has shown that these become adaptively similar with time to early anthropoids.

In this issue of *Nature* (page 65) a group of Burmese and American anthropologists have described a new specimen of fossil primate from the late Eocene of Burma. This is named *Pondaungia cotteri*, and it possesses a number of specialisations that suggest it had reached the anthropoid grade, specialisations such as the great depth of the lower jaw, and the cusp and wear patterns of the teeth. These specialisations are overlaid on a pre-anthropoid pattern that seems to be most similar to the generalised adapids of Europe and Asia that Gingerich advocates as the immediate precursors of the Anthropoidea, and if these conclusions are substantiated by further discoveries it might well be possible to locate the origin of the anthropoids in the late Eocene of Asia. Work is continuing in Burma, and it is to be hoped that Ba Maw and Russell Ciochon will find additional specimens.

By the middle of the succeeding period, the Oligocene, anthropoid primates are represented by a number of species in the Egyptian Fayum deposits, which are currently being excavated by Elwyn Simons of Duke University, and by the end of the Oligocene they are also known in tropical Africa. They diversified during the succeeding periods up to the present, giving rise to all the living species of monkeys and apes and man. The adapids on the other hand diminished in numbers after the end of the Eocene, with the latest known population occurring in 10 million year old deposits in India and Pakistan where they apparently existed as a relic population (described earlier this year by Gingerich in *Nature* **279**, 415; 1979).

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