effect on glyceraldehyde 3-phosphate dehydrogenase and α-glycerophosphate dehydrogenase, but does not affect hexokinase, phosphofructokinase, aldolase, lactate dehydrogenase, glucose 6-phosphate dehydrogenase, alcohol dehydrogenase, malate dehydrogenase, isocitrate dehydrogenase, malic enzyme or aspartate aminotransferase.

The same group has also shown that preparations of growth hormone will also inhibit glyceraldehyde 3-phosphate dehydrogenase, but only if the hormone has been treated with acid and then returned to neutral solution (*Biochim. Biophys. Acta*, **156**, 38; 1968). They were able to separate two polypeptide fractions from this acid-treated growth hormone. The fraction called In-G inhibited glyceraldehyde 3-phosphate dehydrogenase and also decreased the incorporation of acetate into fatty acids in liver slices. The other fraction, Ac-G, was able to prevent the inhibition caused by In-G without itself having any effect on the enzyme activity. The two polypeptides appeared to be similar to, if not identical with, the two polypeptides extracted from the anterior pituitary. Ac-G seems to reverse the dehydrogenase inhibition produced by In-P. Because the action of these two peptides is in many ways antagonistic, growth hormone may have different effects on the metabolism of different tissues, depending on the tissue *p*H and possibly other factors.

In the same journal, Butcher and Serif (*Biochim. Biophys. Acta*, **156**, 59; 1968) present evidence that another pituitary hormone, thyroid stimulating hormone (TSH), affects the carbohydrate-degrading enzyme phosphorylase. Other workers have not been able to find phosphorylase in thyroid, but Butcher and Serif, using a new sensitive assay, have shown that thyroid does contain phosphorylase and that TSH changes the ratio of inactive phosphorylase *B* to the active phosphorylated form—phosphorylase *A*. Within one minute after the addition of TSH, the proportion of phosphorylase *A* had increased substantially. Since compounds related to cyclic adenosine 3′,5′-monophosphate produced the same effect, TSH may increase the cyclic adenosine 3′,5′-monophosphate and increase phosphorylase *A* indirectly. Phosphorylase is regarded as a key enzyme in the control of carbohydrate metabolism in other tissues, so that this effect of TSH may be important in thyroid stimulation. Pituitary hormones may alter the metabolism of target tissues by these effects of key enzymes.

Exchange of Ribosomal Sub-units

from our Cell Biology Correspondent

ARE the 30*S* and 50*S* sub-units of *Escherichia coli* ribosomes permanently associated *in vivo* in a 70*S* ribosome, or do they undergo exchange ? The elegant experiments which Kaempfer, Meselson and Raskas have just reported (*J. Mol. Biol.*, **31**, 277; 1968) firmly establish that there is sub-unit exchange in *E. coli* during protein synthesis. Last year (see *Nature*, **216**, 853; 1967) Mangiarotti and Schlessinger reached the same conclusion from somewhat less compelling evidence.

Kaempfer *et al.* have analysed, on sucrose and caesium chloride density gradients, the density distribution of ribosomes extracted from *E. coli* cells which had been uniformly labelled with heavy isotopes (deuterium and ^{15}N) and then transferred to a medium containing only light isotopes. Following the classic Meselson and Stahl experiment, they argued that if sub-unit exchange occurs, then, on transfer to a light medium, heavy ribosomes should be progressively replaced by two species of ribosomes with hybrid densities. One species of hybrid would have a heavy 50*S* sub-unit and a newly synthesized light 30*S* sub-unit and the other hybrid a light 50*S* and heavy 30*S* sub-unit. This interpretation is only valid, of course, if the ribosomal sub-units labelled with heavy isotopes are stable and remain heavy when the cells are grown in a light medium.

In fact, as predicted, both hybrid species are formed during growth in the light medium. Furthermore, virtually all the ribosomes undergo at least one cycle of sub-unit exchange during a cell generation. Kaempfer *et al.* have found no evidence for ribosomes which were incapable of dissociation nor for the accumulation of sub-units that were unable to cycle through ribosomes. Their experiments also show that ribosomal sub-units are stable; heavy 50*S* sub-units maintain their original density during growth in the light medium. Less than 3 per cent of their protein is exchanged in 1·3 generations (about 1 h).

Ribosomal proteins are apparently themselves also stable during cell growth. Schlief has recently reported (*Mol. Gen. Genetics*, **100**, 252; 1967) that the rate of degradation of ribosomal protein to free amino-acid cannot be greater than 0·7 per cent per hour.

The simplest explanation of sub-unit exchange in growing cells is that it is a necessary step in protein synthesis. The current interpretation is that a round of translation 30*S* and 50*S* sub-units from an intracellular pool join to form a ribosome and at the end of translation they dissociate and return to the pools (see *Nature*, **216**, 638; 1967, and **217**, 508; 1968). A search for evidence of sub-unit exchange in eucells is needed now.

Carboxypeptidase

from our Molecular Biology Correspondent

THE successful determination of a protein structure at high resolution is still an event to be celebrated. The structure of the proteolytic enzyme, carboxypeptidase *A*, at a resolution of 2·0 Å has been described by Lipscomb and his associates (Reeke *et al.*, *Proc. US Nat. Acad. Sci.*, **58**, 2220; 1967). In the absence of extensive data on the sequence, many of the side chains cannot be uniquely identified, but the course of the backbone is unambiguous.

The essential structural features include four α-helical regions making up some 30 per cent of the chain in all, and two sections of the distorted α-helix also seen in lysozyme are present. The model bears out once more the ubiquity of the β-structure, for 20 per cent of the backbone has the form of a pleated sheet containing four pairs of parallel and three of antiparallel chains. The active site, as elsewhere, is located in a cavity, and includes the zinc atom, which is present in the native enzyme and is required for activity. Three side chains are thought to function as ligands for the zinc, but only one—a histidine residue—has been identified.

The most interesting feature of this work concerns the introduction of a substrate, glycyltyrosine. The electron density map of the complex at 2·8 Å reveals

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