(Gurdon & Woodland, 1968), so one must consider the possibility that a similar situation exists in the uterus. If so, one can ask if the cytoplasmic binding serves a function in addition to that of hormone transportation. Also, although oestradiol-17 β binding is related to biological action, is the converse true that, in order to get oestrogen action, one must have tight binding as in the uterus? No convincing evidence exists for this, but one observation raises the possibility that it might be so. The carcinogenic effect of oestrogen on the hamster kidney is accompanied neither by measurable nuclear binding of the hormone nor its marked retention by the kidney.

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Metabolism of Testosterone and Activity of Metabolites in Prostate Organ Culture

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Organ cultures of prostates of normal young adult rats (Lasnitzki, 1965) were incubated with [³H]-testosterone. After a 24 hr. incubation, radioactivity was somewhat concentrated in the tissue. At least two-thirds of the testosterone was metabolized and among the identified metabolites of the medium and of the tissue the main compound was 17 β -hydroxy-5 α -androstane-3-one (androstanolone), especially in the nuclear fraction of the homogenate. There were also androstane-3 β ,17 β -diol and -3 α ,17 β -diols (the former predominantly), and some of the corresponding 17-oxo steroids, but neither 5 β -derivatives nor oestrogens were observed. Unknown non-polar compounds (under study) were also found.

Testosterone and the main metabolites were

tested for their activity at various concentrations in 6-day experiments (two or three changes of medium containing 3.5-70 μ M). Testosterone maintained the epithelium cell height and secretory activity and kept the stroma at minimum. Androstanolone was somewhat more active than testosterone but provoked essentially a hyperplasia (heaping of cells between the basement membrane and the intact superficial secretory cells), which was seen only with very high doses of testosterone. The 5 α -androstane-3 α ,17 β -diol was not very potent, but the 3 β ,17 β -diol was very active, and in a different manner: there was no hyperplasia at all, but a single layer of tall epithelial cells, with considerable secretory activity and much repression of stroma. The corresponding 17-oxo steroids showed a relatively small activity, and the 5 β -metabolites were inactive.

These results suggest that testosterone action may be related to its metabolism in the prostate through the formation of metabolites of different activity.

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The Hormonal Control of Protein Synthesis

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Most hormones can influence protein synthesis in their target organs, but the mechanism by which they do so is not yet understood. At the present time several hypotheses are tenable once it is accepted that not all hormones act in the same way even to produce the same effect and that any one hormone might act by different mechanisms on different aspects of metabolism.

There is an impressive body of evidence implicating 3',5'-cyclic AMP involvement in the response of many metabolic events to hormones (Sutherland, Øye & Butcher, 1965). In a few instances, for example the action of adrenocorticotrophic hormone on the adrenal gland, indirect evidence suggests that cyclic AMP might promote protein synthesis. In most other cases, for example insulin and growth hormone, the evidence suggests that cyclic AMP is not involved in the protein anabolic action of the hormones, although it is involved in the hormonally induced changes in, for example, lipid metabolism (Goodman, 1968).

Some hormones stimulate the synthesis of proteins not previously synthesized by the organism: the most clear-cut examples occur during development. It is possible that, in these cases, de-repression of a portion of the genome has occurred so that new messenger RNA types are synthesized (Karlson, 1963). It seems unlikely, in

view of the evidence from experiments with bacteria, that the hormone could act directly to de-repress the genes and more likely that the hormone interacts with a protein that is itself the genetic repressor. No unequivocal evidence for the existence of such a repressor is yet available in eukaryotic cells, but the protein receptors for steroid hormones and the histones are among the possibilities that have been suggested.

Many hormones stimulate the production of proteins already synthesized by the organism. In some instances, for example insulin and growth hormone, the evidence shows that the anabolic response is not dependent on prior RNA synthesis, but that control of the translational processes is involved (Wool *et al.* 1968; Korner, 1968). It is known that diabetes results in a defect of the large ribosomal subunit of muscle, whereas hypophysectomy results in a defect in small ribosomal subunit of liver.

Corticosteroids can induce the synthesis of enzymes by an actinomycin-sensitive process, and this has been interpreted by several workers as indicating an action, direct or indirect, of the hormone on the genome (Kidson & Kirby, 1964), but this view is opposed by others (for review see Korner, 1967). The abolition of a response to a hormone by actinomycin is not, however, unequivocal evidence of the need for RNA synthesis, since the antibiotic has actions other than abolition of DNA-directed RNA synthesis. Tomkins *et al.* (1966) have argued, on the basis of the phenomenon of superinduction of enzymes by actinomycin, that regulator genes exist producing substances that inactivate the messengers for the enzymes, but this view has been challenged (Reel & Kenney, 1968). Corticosteroids, insulin and glucagon all induce

tyrosine transaminase in rat liver and in cells in tissue culture, but each hormone uses a different mechanism to achieve this.

Many of the hormones stimulate RNA synthesis and the activity of the RNA polymerase enzyme. In some cases (e.g. oestrogens and androgens) the evidence (Nicolette, Lemahieu & Mueller, 1968) suggests that this is a necessary prerequisite for the protein anabolic responses to these hormones, but in other cases (e.g. insulin and growth hormone) it appears to be secondary to the stimulation of protein synthesis.

There is no doubt that the long-term application of many hormones results in the synthesis of more ribosomes and endoplasmic reticulum. Tata (1968) is among those who have argued that this change in the cytoskeleton is of importance in the protein anabolic action of thyroid and other hormones.

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COLLOQUIUM ON 'LYSOSOMES AND DISEASE'

Lysosomes, Chromosomes and Cancer

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It is widely, although not universally, believed that the basic defect in cancer is a chromosomal mutation in somatic cells. This could allow deletion of genetic information (for instance that controlling growth) without affecting the capacity of cells to divide. Alternatively the chromosomal mutation could allow acquisition of new genetic information, e.g. by incorporation of a viral genome or by somatic recombination with gene conversion. The new information could be expressed as antigens not present in parental cells or in other ways. Examples of suggestive relationships between chromosomal

aberrations and cancer include the presence of the Ph¹ chromosome (with a partial deletion of the small chromosome 21) in chronic myeloid leukaemia. Children with Bloom's syndrome, Fanconi's anaemia and ataxia telangiectasia have a greatly increased tendency to develop malignancy. When their skin cells or blood leucocytes are cultured *in vitro* numerous chromosome aberrations are found (see German, 1969). Individuals homozygous for the recessive gene giving rise to xeroderma pigmentosum have a much increased risk of developing malignant changes where they are exposed to ultraviolet light. Evidence has been presented that the cells of these patients lack a mechanism that can repair damage produced by ultraviolet radiation (Cleaver, 1968). Hence further study of the mechanisms of chromosome breakage and repair