Meetings

Cellular Dynamics: Hormones

Cellular mechanisms within or between chemical groups of hormones may be very similar or differ widely. Such similarities and differences were discussed at the fourth Conference on Cellular Dynamics, held in Princeton, New Jersey, 6–9 February 1966. Similar to other conferences in the series, the emphasis was on informal discussion of the present state of our knowledge and possible future directions of investigation rather than on formal presentation of recent research results.

Howard Rasmussen (Pennsylvania) opened the discussions on peptide hormones by posing two questions concerning the role of the conversion of adenosine triphosphate (ATP) to 3′,5′ cyclic adenosine monophosphate (cyclic-AMP) in the action of several hormones: (i) Is the conversion of ATP to cyclic-AMP the only route of action of these hormones? (ii) If the answer to the question is yes, then how can one explain multiple actions of a single hormone and different effects of different hormones if these agents all act through the ATP-to-cyclic-AMP conversion?

In reply to Rasmussen's questions, Earl W. Sutherland (Vanderbilt) first reviewed the evidence for a role of adenyl cyclase (the enzyme that converts ATP to cyclic-AMP) in hormone actions. He emphasized the wide distribution of this enzyme in animal tissues, and the observation of hormone-like responses of several tissues to externally applied cyclic-AMP. Sutherland was not, however, willing to rule out the possibility of other mechanisms acting as well. In other words, Sutherland answered Rasmussen's first question with a qualified "yes."

In answering the second question posed by Rasmussen, Sutherland pointed out several possibilities for multiplicity of responses: (i) different affinities of one receptor site for different hormones; (ii) different sites on the same receptor molecule; (iii) different cell types having separate responses following activation of their adenyl cyclases; and (iv) a population of cyclases with different properties (cofactor requirement, affinity, and others), perhaps dependent on such factors as cell age. G. P. Talwar (New Delhi, India) later presented the possibility of cyclases located in different compartments of a cell producing different physiological responses as a result of their localization.

Following a discussion by John R. Williamson (Pennsylvania) about experiments using epinephrine in perfused hearts of rats, the discussion centered on temporal and causative sequences in hormone mechanisms involving cyclic-AMP. Some participants felt that the effect on adenyl cyclase might not be the first step in the hormone action, but that some intermediate step, such as calcium release, might be possible. Sutherland emphasized the rapidity of the cyclase effects as supporting a primary position for these effects in the overall sequence. J. R. Tata (London, England) questioned the validity of using timing of events as conclusive evidence for cause and effect relationships, and Sutherland replied that timing considerations can be of some use in that in order to be causative, one event must necessarily precede the event it causes.

The discussion then turned to the biochemical reactions in which cyclic-AMP participates. There seemed to be little new information in this area.

Macromolecular synthesis was implicated in the mechanism of action of several peptide hormones. In the case of insulin, there is an apparent increase in protein synthesis without any apparent increase in messenger RNA or ribosome synthesis (Ira G. Wool, Chicago), while the increased protein synthesis induced by some peptide hormones that produce growth of organisms or alteration of development (thyroxine, growth hormone) seems to be preceded by increased synthesis of ribosomal RNA (Tata, Talwar). A possibility of specificity of effects of different hormones being determined by specificity of newly-synthesized ribosomes for certain messenger RNA's was suggested.

Jack Lucy (Strangeways, Cambridge, England) emphasized the possibility that steroids could fit into cellular membranes and mentioned that specificity of effects could be the result either of selectivity of various types of membranes for various steroids or of differences in cellular functions of various membranes. He illustrated his remarks with electron micrographs of artificial lipid systems treated with steroids. E. N. Willmer (Cambridge, England) discussed evolution of amoeboid and flagellate cell types from a similar point of view. A possibility of direct action of hormones on cellular membranes was also apparent from other discussions, in particular in the discussion by Rasmussen of effects of vitamin D and parathyroid hormone on calcium release from and magnesium uptake into mitochondria in vitro. In an extension of this idea, Hector DeLuca (Wisconsin) discussed the possibility that hormone-induced protein synthesis might be a consequence of hormone-induced alterations in the permeability of membranes to ions.

Lysosomes were implicated in steroid hormone actions in some experiments discussed by Gerald Weissmann (New York University). In particular, the anti-inflammatory action of cortisol in man is mimicked by a protection by cortisol of lysosomes in vitro against damage from certain labilizers, such as streptolysins and polyenes.

Again, macromolecular synthesis was implicated by the discussants in steroid actions. Charles D. Kochakian (Alabama) suggested that RNA synthesis may play a central role in the action of testosterone on the kidney, and Tata discussed increases in attached ribosomes in livers stimulated by triiodothyronine. Lucy reported an apparently opposite effect in which vitamin A induced in the epidermal cells of rats in culture a decrease in protein synthesis and a concomitant detachment of ribosomes from membranes. Gorbman (Washington) mentioned that in developing thyroid glands in a variety of animals, free ribosomes become attached ribosomes just at the time that colloid synthesis starts. Each of these examples relates ribosome attachment to synthesis.

Mueller (Wisconsin) presented evidence for increased RNA and protein

synthesis and nuclear RNA polymerase activity in the uteri of rats stimulated by estrogen. He suggested that the hormone might act through increasing RNA polymerase activity by making available a "protecting protein" in the absence of which the enzyme is inactivated. According to this idea, the mechanism of action of estrogen is to activate RNA polymerase, but not, initially at least, to cause synthesis of new RNA polymerase.

Alexander Leaf (Harvard) showed how DNA-dependent RNA synthesis, followed by protein synthesis in the action of aldosterone, increases sodium transport across the toad's urinary bladder. Observations supporting this mechanism are a 60-minute delay in the effect, inhibition of the response by either $10^{-6}M$ actinomycin or $10^{-5}M$ puromycin, and a dependence on oxidative metabolism. This contrasts the aldosterone mechanism rather sharply with the similar effect of antidiuretic hormones on the same tissue, where macromolecular synthesis seems to have been ruled out.

Talwar then discussed the binding of estradiol to cell fraction from various tissues. In general, binding was greater to fractions from tissues that normally respond to estradiol (for example, uterus, hypothalamus) than to fractions of normally non-responsive tissues (for example, lung). H. G. Williams-Ashman (Johns Hopkins) recalled that estrogen does not accumulate significantly in mammary glands, where it is presumed to have an important function. Gorbman suggested an interpretation somewhat different from Talwar's, namely that estrogen might accumulate preferentially in tissue in which it is not metabolized.

A somewhat more detailed study of steroid incorporation into cell fractions was presented by J. D. Wilson (Texas). These results indicated incorporation of radioactive testosterone into the euchromatin portions of nuclei from the preen gland of the duck, and of 17-β-estradiol into chromosomal loops from ova of the newt.

Joseph Larner (Minnesota) discussed some studies of the action of insulin on glycogen synthesis in isolated diaphragms of the rat. Insulin increases base levels of transferase activities in the absence of added glucose-1-phosphate. It was suggested that insulin might act in the induction of glycogen breakdown in muscle by acting on the kinase system through a route which does not involve adenylate cyclase or

protein synthesis. This implies basic differences between insulin action on muscle and that on liver, where macromolecular synthesis has been implicated.

The conference was held under the auspices of the Interdisciplinary Communications Program of the New York Academy of Sciences, and was supported by the Office of Naval Research and the National Aeronautics and Space Administration. Murray D. Rosenberg (Minnesota) was chairman of the conference. The Academy was represented by Frank Fremont-Smith, director of the Conference Program.

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Forthcoming Events

January

25–27. American **Crystallographic** Assoc., mtg., Georgia Inst. of Technology, Atlanta. (W. L. Kehl, Gulf Research and Development Co., P.O. Drawer 2038, Pittsburgh, Pa. 15230)

25–27. American **Mathematical** Soc., 73rd annual mtg., Houston, Tex. (The Society, P.O. Box 6248, Providence, R.I.)

25–28. American **Group Psychotherapy** Assoc., New York, N.Y. (Mrs. M. Schiff, 1790 Broadway, New York 10019)

26–28. **Mathematical** Assoc. of America, 50th annual mtg., Houston, Tex. (H. L. Alder, Univ. of California, Davis)

28–30. **Radiology**, southern conf., Point Clear, Ala. (M. Eskridge, P.O. Box 4097, Mobile, Ala.)

28–1. American Acad. of **Allergy**, Phoenix, Ariz. (J. O. Kelley, 756 North Milwaukee St., Milwaukee, Wis. 53202)

29. **Mössbauer Effect Methodology**, 3rd annual symp., New York, N.Y. (P. A. McNulty, New England Nuclear Corp., 575 Albany St., Boston, Mass. 02118)

29–3. **Power**, mtg., Power Group, Inst. of Electrical and Electronics Engineers, New York, N.Y. (E. C. Day, IEEE, 345 E. 47 St., New York 10017)

30. American Soc. of **Heating, Refrigerating, and Air Conditioning Engineers**, semi-annual mtg., Detroit, Mich. (Miss J. I. Szabo, 345 E. 47 St., New York)

30–1. **Personnel Radiation Dosimetry**, symp., Chicago, Ill. (J. H. Pingel, Argonne Natl. Laboratory, Bldg. 301, 9700 S. Cass Ave., Argonne, Ill. 60439)

30–2. American **Physical** Soc., annual mtg., New York, N.Y. (The Society, Executive Secretary, Columbia Univ., New York 10027)

30–2. American Assoc. of **Physics Teachers**, New York, N.Y. (A. B. Arons, Physics Dept., Amherst College, Amherst, Mass.)

30–3. **Zodiacal Light and the Interplanetary Medium**, intern. symp., Honolulu, Hawaii. (F. E. Roach, Aeronomy Lab., Inst. for Telecommunication Sci-