Biochemical Actions of Hormones

VOLUBER VIE

GERALD LITWACK

Biochemical Actions of Hormones

Edited by GERALD LITWACK

Fels Research Institute and Department of Biochemistry Temple University, School of Medicine Philadelphia, Pennsylvania

VOLUME VII



ACADEMIC PRESS 1980

A Subsidiary of Harcourt Brace Jovanovich, Publishers

New York London Toronto Sydney San Francisco

Copyright © 1980, by Academic Press, Inc. all rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without permission in writing from the publisher.

ACADEMIC PRESS, INC.
111 Fifth Avenue, New York, New York 10003

United Kingdom Edition published by ACADEMIC PRESS, INC. (LONDON) LTD. 24/28 Oval Road, London NWI 7DX

Library of Congress Cataloging in Publication Data Main entry under title:

Biochemical actions of hormones.

Includes bibliographies.

1. Hormones—Collected works. I. Litwack, Gerald, ed. II. Axelrod, Julius, Date [DNLM: 1. Hormones. 2. Physiology. WK102 B615]

QP571.B56 574.19'27 70-107567

ISBN 0-12-452807-4 (v. 7)

PRINTED IN THE UNITED STATES OF AMERICA

80 81 82 83 9 8 7 6 5 4 3 2 1

Biochemical Actions of Hormones

VOLUME VII

Contributors

JAMES W. APRILETTI

F. JOHN BALLARD

JOHN D. BAXTER

NORMAN L. EBERHARDT

PETER ENEROTH

John N. Fain

ULRICH GEHRING

Jan-Åke Gustafsson

STEPHEN J. HIGGINS

Tomas Hökfelt

S. M. McCann

LORRAINE K. MILLER

AGNETA MODE

A. Negro-Vilar

GUNNAR NORSTEDT

S. R. OJEDA

MALCOLM G. PARKER

PAUL SKETT

CARLOS SONNENSCHEIN

ABRAHAM WHITE

List of Contributors

Numbers in parentheses refer to the pages on which authors' contributions begin.

- James W. Apriletti (311), Howard Hughes Medical Institute Laboratories and the Endocrine Research Division of the Department of Medicine, the Metabolic Research Unit, University of California, San Francisco, California 94143
- F. John Ballard (91), C.S.I.R.O. Division of Human Nutrition, Adelaide, S. A. 5000, Australia
- John D. Baxter (311), Howard Hughes Medical Institute Laboratories, Endocrine Research Division, Departments of Medicine and Biochemistry and Biophysics, University of California, San Francisco, California 94143
- Norman L. Eberhardt (311), Howard Hughes Medical Institute Laboratories and the Endocrine Research Division of the Department of Medicine, the Metabolic Research Unit and the Department of Biochemistry and Biophysics, University of California, San Francisco, California 94143
- Peter Eneroth (47), Hormonlaboratoriet, Karolinska Hospital, 104 01 Stockholm, Sweden
- John N. Fain (119), Section of Physiological Chemistry, Division of Biology and Medicine, Brown University, Providence, Rhode Island 02912
- Ulrich Gehring (205), Institut für Biologische Chemie, Universität Heidelberg, Im Neuenheimer Feld 501, 69 Heidelberg, Germany

- Jan-Åke Gustafsson (47), Department of Medical Nutrition, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
- Stephen J. Higgins (287), Department of Biochemistry, University of Leeds, Leeds LS2 9LS, England
- Tomas Hökfelt (47), Department of Histology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
- S. M. McCann (245), Department of Physiology, University of Texas Health Science Center at Dallas, Dallas, Texas 75235
- Lorraine K. Miller (233), Institute for Steroid Research, Montefiore Hospital and Medical Center, Bronx, New York
- Agneta Mode (47), Department of Medical Nutrition, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
- A. Negro-Vilar (245), Department of Physiology, University of Texas Health Science Center at Dallas, Dallas, Texas 75235
- Gunnar Norstedt (47), Department of Medical Nutrition, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
- S. R. Ojeda (245), Department of Physiology, University of Texas Health Science Center at Dallas, Dallas, Texas 75235
- Malcolm G. Parker (287), ARC Institute of Animal Physiology, Cambridge CB3 OJQ, England
- Paul Skett (47), Department of Pharmacology, The University, Glasgow G12 8QQ, Scotland
- Carlos Sonnenschein (47), Department of Anatomy, Tufts University Medical School, Boston, Massachusetts 02111
- Abraham White* (1), Institute of Biological Sciences, Syntex Research, Palo Alto, California 94304 and Department of Biochemistry, Stanford University School of Medicine, Stanford, California 94305

^{*} Deceased.

Preface

This collection extends the pattern of previous volumes in this treatise. The intent is to cover a broad range of subjects representing research efforts at the cutting edge of hormone action. Sometimes there are noticeable gaps in the coverage by previous volumes and specific contributions are sought to fill these.

There are a variety of subjects included in this volume. A. White reviews recent developments on hormones of the thymus. J. A. Gustafsson and collaborators review new evidence on the regulation of liver steroid and drug metabolism by the hypothalamus and anterior pituitary. S. M. McCann and co-authors provide up-to-date information on the regulation by neurotransmitters in the hypothalamus of LHRH and somatostatin. F. J. Ballard presents a review of hormonal regulation of protein degradation in liver and in isolated cells which complements a contribution in a previous volume by H. E. Morgan and collaborators on the regulation of protein synthesis and degradation in heart and skeletal muscle. J. N. Fain presents a timely article on the hormonal regulation of lipid mobilization from adipose tissue. Steroid hormone mechanisms are represented in three contributions: U. Gehring reports on cell genetics of glucocorticoid responsiveness and L. K. Miller and S. J. Higgins review the mero-receptor and androgenic regulation in male accessory tissues, respectively. Finally, J. Baxter's group brings us up to date on current views of the molecular biology of thyroid hormone action.

It is hoped that this approach to timely critical reviews by experts in their respective fields will serve the advancement of the expanding subject of hormone action.

As this volume was near completion, Dr. Abraham White died suddenly on February 14, 1980. I decided that a fitting tribute would be the dedication of this volume to his memory. Dr. White's secretary, Edna Van der Vort, and Mrs. White generously made available the photograph which is reproduced in the early pages. I called on Dr. Maynard Makman, a long-time associate and friend of Dr. White, to prepare a brief tribute, which appears in the front matter.

GERALD LITWACK



Abraham White (1908-1980)

Abraham White (1908–1980)

The contributions of Abraham White to biochemistry, endocrinology, and medicine span a period of over 50 years. Abraham White was a scientist, educator, and author, as well as a founder and organizer of a school of medicine; in each of these capacities his accomplishments were distinguished and many. His career was rich and fulfilling and his energies undiminished to the end. He was widely recognized as an authority in biochemistry and as a leading medical educator. His numerous awards included the Eli Lilly prize, the Borden Award, and election to the National Academy of Sciences.

Abe White was born in Cleveland. He received a bachelor's degree from the University of Denver in 1927 and a Ph.D. from the University of Michigan in 1931. At the University of Michigan he studied with the great American biochemist Howard B. Lewis. The first publication of which Abe White was senior author concerned the metabolism of sulfurcontaining amino acids and was published in 1932 in the Journal of Biological Chemistry. His early work concerned primarily the chemistry and metabolism of amino acids, but as early as the 1930s his interests broadened to include insulin and the pituitary hormones. From 1931 until 1948, Dr. White was at the Yale University School of Medicine, and in 1948 he left to become Professor and Chairman of the Department of Physiological Chemistry at the University of California School of Medicine in Los Angeles. During the 1940s his research interests focused on the mechanism of action of adrenal corticosteroids. During the next several decades he made many important contributions to our understanding of the action of steriod hormones and the influence of steroids on xiv Dedication

lymphoid tissue. Abe White was one of the first investigators to recognize the importance of the thymus gland with respect to both immunological and endocrine functions. Some of these investigations were summarized in a review he co-authored with Allan Goldstein that appeared in the first volume of "Biochemical Actions of Hormones."

In the late 1940s, Abe White, together with Drs. Philip Handler, DeWitt Stetton, and Emil L. Smith, first became interested in writing a textbook of biochemistry. In 1954 "The Principles of Biochemistry," with Abraham White as first author, was published by McGraw-Hill. This book, now in its sixth edition, is one of the most widely recognized and used texts of biochemistry. Dr. White was intensely involved in the creation and further evolution of this work. His careful, thoughtful, and deep commitment to this endeavor clearly exemplifies his breadth and devotion as scientist and educator.

Abe White was the first faculty member of the Albert Einstein College of Medicine and the first chairman of the College's Department of Biochemistry. He was instrumental in the creation of the Medical School as well as in its further growth to become a leading medical institution. From 1952 to 1972 he was an Associate Dean and Professor and Chairman of Biochemistry at the Albert Einstein College of Medicine. After 1972, although he became a Professor Emeritus at Einstein, he and his wife, Edna, moved to Palo Alto where he continued to pursue an active research program at Syntex Laboratories, as well as to teach at Stanford University School of Medicine.

The field of hormone research has benefited immensely from the research efforts of Dr. White. Those efforts span most of his professional career. Included are important contributions to hormone biochemistry, physiology, and pharmacology. Of particular significance is his early work on insulin, the crystallization of prolactin and studies of its properties, and studies of other pituitary hormones including the biochemistry and actions of adrenocorticotropin. Probably of even greater importance is his later work concerning the glucocorticoids and his studies of thymosin. He was involved actively and energetically in research concerning the purification and action of thymosin up to the time of his death. His latest studies and ideas concerning thymic hormones form the first chapter of this volume.

My association with Dr. White began 16 years ago when I became a member of his Department. Bernyce Dvorkin and I worked closely with him in studies of the influence of steroid hormones on lymphoid cells until he left Einstein. We all found this an exciting and challenging endeavor. In this as in other contexts Abe White had an amazing ability to communicate and share his wide range of knowledge as well as his enthusiasm for new ideas and findings. It seemed that there was nothing in the current literature of which he was not aware, and he had a unique

Dedication xv

perspective on past accomplishments. He was always interested in the ideas of others. He did not avoid controversy but carefully considered points of view considerably different from his own. Abe was a teacher, collaborator, and friend to me. The ambience of his department provided a marvelous atmosphere for work and for development of both students and faculty. He was always optimistic and could see the positive side of any situation or problem. Most important of all, he communicated a sense of the excitement and purposefulness of scientific work that left a lasting impression on all those with whom he came into contact. His legacy extends far beyond his work, as considerable as that is, to many individuals whose lives were permanently enriched by him.

MAYNARD H. MAKMAN Albert Einstein College of Medicine

Contents

3	Contributors .												ix xi
Abraha	am White (1908– 1 Maynard H. Ma	1980)											xiii
1.	Chemistry with Thyn								rodu	cts			
	Abrahan	n Wh	iite										
	I. Introduction												2
	II. Chemistry	-											6
	III. Thymic Ho												22
	IV. Biological I V. Mechanism	00											28
	Like Factor								nymu				39
	VI. Concluding												41
	References												42
2.	The Hypothalamo-Pituitary-Liver Axis: A New Hormonal System in Control of Hepatic Steroid and Drug Metabolism												
	Jan-Åke Norstedt Peter Er	, Toi	mas	Hö	kfelt	t, Co	arlos				ein,		
	I. Introductio	n .					.*:						48
	II. Androgenic	and E	stroge	enic (Contro	ol .					*		48
	III. Imprinting												51

vi Contents

	IV. The Role of the Pituitary Gland V. Model Systems for the Study of Pituitary Control of Hep	atic		5
	Metabolism			5
	VI. Production of Feminizing Factor by Nonpituitary Tumors			6
	VII. A Direct Effect of the Pituitary Gland on the Liver .			6
		7		6
	IX. A Proposed Model of the Hypothalamo-Pituitary-Liver Ax	is		7
	X. The Feminizing Factor			7
				7
	XII. Hepatoma Cell Cultures			7
	XIII. Correlation of in Vivo and in Vitro Results			7
	XIV. Effect of Female Pituitary Extract on Hepatocytes and HT	C Ce	lls	7
	XV. Effect of Standard Pituitary Hormones on HTC Cells .			7
	XVI. Study of the Mechanism of Action of Feminizing Factor			8
	XVII. Purification and Characterization of Feminizing Factor			8
	References			8
3.	Hormonal Control of Protein Degradation i	n L	iver	
	and Isolated Cells			
	F. John Ballard			
	I. Introduction			92
	II. Methods for the Measurement of Protein Degradation.			94
	III. Insulin			98
	IV. Serum Growth Factors			98
	V. Glucagon			10.
	VI. Steroids			104
	VII. Adrenergic Agonists			10
	VIII. Thyroxine			10
	IX. Protein Degradation during Growth and Differentiation		,	108
	X. Summary			113
	D (113
4.	Hormonal Regulation of Lipid Mobilization from Adipose Tissue John N. Fain			
	I. Introduction: Development of the Concept of Adipose Ti Metabolically Active Organ			120
	II. The Role of Lipid Mobilization from Adipose Tissue in Viv			122
	III. Adipose Tissue Preparations			124
	IV. Hormonal Regulation of Triglyceride Breakdown via cAM	D		128
	V. Role of cGMP in the Regulation of Lipolysis			135
	VI. Calcium in the Regulation of Lipolysis, Glycogen Phosph			100
	and Glycogen Synthase	orgia	oe,	137
	VIII. Catecholamine Effects on Phosphatidylcholine Turnover			144
	Time Careenoumine Lijeew on Phosphanayienoune Turnover			146

Contents	vii

	IX.	Effects of Pl												7.40
	Y	Metabolism Structural C	hanges	in th	ne Pla	isma l	1emb	rane	of Fat	Cells	duri	ng		148
	70.		·											149
	XI.	Hormonal A												151
		Inhibitors of		,		0								173
		Mode of Inst												188
		Lipoprotein			,			•	-			ipose		
		Tissue .						,						190
	XV.	Summary												193
		References				٠								195
5.	C	ell Geneti			ıcoc	ortic	oid	Res	pons	iven	ess			
		Ulrich G	ehrin	g										
		Introduction												205
		Cell Systems												206
		Receptor Bir	_											210
		Variant Cell												211
		Analysis of C												217
		Chromosom												223
		cAMP and C												226
	VIII.	Summary ar											•	228
		References				34								230
6.	T	he Mero-I	Recep	tor										
		Lorraine	K. N	1ille	r									
	1	Introduction												233
		The Progeste	rone-F	Sindir	og Me	ro-Re	· rentor	of Cl	nick O		+			234
		Reported Me										•		235
		Possible Mer												237
		Biological Si		,										241
		Summary	0 0											242
		References												243
7.	Ro	ypothalan ole of Cen essengers	tral	Neu	rotr	ansn	nitte	ers a	nd I	ntra	cell	ular		
		A. Negro	-Vila	r, S	. R.	Oje	da,	and	S. I	М. Л	1cC	ann		
	I.	Introduction												246
		Hypothalam												246
		Control of L										imate	ed	210
		from LH Rel												249

viii Contents

IV.	Neurotransi	mitters	and i	LHRI	H Rele	ease							256
	Control of t												260
VI.	Neurotransi	nitters	and S	Soma	tostati	n Rel	ease						264
VII.	Involvemen	t of In	itrace	llular	Mess	enger	s in th	e Re	lease o	f LH	RH		
	and Somato	statin											266
VIII.	Concluding	Rema	rks										279
	References												279
R	ndrogenic esponses i ale Rat Stephen	n Ac	ccess	ory	Sexi	ual '	Tissu	ies (of the	е	eific	,	
II.	Introduction Seminal Ves Summary References	ricles a	nd Ve	entral	Prosto.	ate as	Andre	ogen-	Depen	dent	Tissue	es .	287 291 305 306
9. T	he Molect Norman and John	L. E	Eber	hard							etior	1	
I. II.	Introduction The Actions Structure-A				none		roid H	ormo	nes				312 314 318
IV.	Hormones S Plasma-Bine	ynthes	sized b	by the	r Thyr	oid G	land o	ind T	heir M	etabo	lites		321 324
V.	Cellular Up	take a	rotetti nd Pla	S.	Momb	rana	Rindia	ng of	Thuro	d Ho	rm on		326
	Cytoplasmi												327
	Possible Act												021
* 4441	Events .												328
IX.	Nuclear Rec												332
	Influences o		-									Ċ	355
	Actions of T												362
	Complexity									ılar L	evel		363
	Effects of T												365
	General Mo	0											367
	Thyroid Ho												369
	Cooperative										ith		
	Other Horn												381
XVII.	Regulation of	of Cell	ular S	ensiti	ivitu to	Thu	roid H	lorma	one				382
	Summary												383
	References												384
	,												
													395
Contents of I	Previous Volu	imes											419

CHAPTER 1

Chemistry and Biological Actions of Products with Thymic Hormone-Like Activity

Abraham White

I.	Introduction	4
	A. Historical Background	4
II.	Chemistry of Purified Thymic Factors Isolated from Thymic	
	Tissue	(
	A. Thymosin and Its Composite Polypeptides	(
	B. Thymic Humoral Factor (THF)	10
	C. Thymopoietins I and II; Ubiquitin	12
	D. Homeostatic Thymic Hormone (HTH)	14
	E. Thymic Factor (TFX)	13
	F. Lymphocytopoietic Factors (LSH $_h$ and LSH $_r$)	17
	G. Hypocalcemic and Lymphocytopoietic Substances	
	(**1 ***** ***/*************************	18
	H. Thymic Epithelial Supernatant (TES)	19
		20
	J. Nonpolar Extracts: Thymosterin	2
III.	Thymic Hormone-Like Factors Isolated from Blood	22
	A. Facteur Thymique Sérique (FTS) from Pig Serum	22
	B. Protein Fraction from Human Plasma	23
	C. Thymus-Dependent Human Serum Factor (SF)	27
IV.	Biological Effects of Isolated Products	28
	A. Experimental Animals	28
	B. Clinical Studies	37
V.	Mechanism of Action of Thymic Hormones and Thymic	
	Hormone-Like Factors	38
VI.	Concluding Comments	41
	References	42