

# Biochemical Actions of Hormones

Edited by GERALD LITWACK

VOLUME XIII



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VOLUME XIII

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## Preface

"Biochemical Actions of Hormones" is a multi-volume treatise that was created to review a wide range of topics in the general field of hormones. Volume XIII carries on the tradition of previous volumes.

A number of contributions to this volume are of a more generalized nature and serve as introductory chapters. These particular articles are on the control of glucose transport by insulin by Ian Simpson and Samuel Cushman, participation of nuclear poly(ADP-ribosyl)ation in hormonal mechanisms by Ernest Kun's laboratory, and ovulation control by Nava Dekel.

Subsequently, there appear more specialized topics, first centered on polypeptide and insect hormones and concluding with steroid hormones. Robert Canfield and associates report on the immunochemistry of human chorionic gonadotropin, followed by two articles on ACTH. The first of these is by Robert Pedersen and Alexander Brownie on ACTH action on adrenal cholesterol metabolism, and the second is by J. Ramachandran on the interaction of ACTH with adrenal receptors. Victor Hruby reports on structure-activity relationships of neurohypophyseal hormones, and Manjusri Das and her associates review the interactions between different functional sites in the EGF receptor. John Koepppe and Gae Kovalick summarize the juvenile hormone-binding proteins.

Four chapters detail current considerations of steroid hormones. David Rowley and Donald Tindall describe recent work on the androgen receptor, Magnus Pfahl reviews interactions of the glucocorticoid receptor with specific DNA sequences, Vincent Cristofalo's laboratory reviews glucocorticoid actions on fibroblasts and, finally, M. Webb and C. Litwack discuss the potential role of RNA in the glucocorticoid receptor mechanism.

Although this publication has enjoyed wide usage by the scientific community, the publisher has determined that it cannot continue in its present format. This is partly the result of an upward spiral of the



cost of individual volumes which has forced the price above the purchasing ability of most individual users. Also, libraries have fallen victim to various budget crunches. These economic pressures, coupled with the increasing numbers of volumes on the market with, in some cases, overlapping subject matter, have impacted this treatise. Volume XIV will, consequently, appear as the last volume of "Biochemical Actions of Hormones." Production of that volume may entail some specific measures to reduce the cost, such as reproduction from camera-ready manuscripts.

Faithful readers of this publication can expect to receive future announcements of how we can continue this work following the appearance of Volume XIV, which will again be published by Academic Press.

Gerald Litwack

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# CHAPTER 1

## Mechanism of Insulin's Stimulatory Action on Glucose Transport in the Rat Adipose Cell

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Since the initial observations by Wertheimer and Shapiro (1948) that insulin stimulates glucose metabolism in a variety of peripheral tissues, rat adipose tissue has emerged as the tissue of choice for the study of insulin's action on carbohydrate metabolism. The reasons for this preference are (1) the ease with which homogeneous isolated cell preparations can be obtained (Rodbell, 1964) and (2) the extreme sensitivity and responsiveness of the rat adipose cell to insulin.

Crofford and Renold (1965a,b) recognized that the primary locus for insulin's stimulatory action on glucose metabolism in rat adipose tissue resides at the level of sugar transport into the cell and that the increase in sugar transport in response to insulin is the result of a change in the maximum transport velocity ( $V_{\max}$ ) and not a change in the apparent affinity ( $K_m$ ) of the transporter for glucose. These observations were confirmed by Vinten *et al.* (1976) in isolated rat adipose cells using the uptake of 3-O-methylglucose, a nonmetabolizable glucose analog, to accurately assess glucose transport activity (see Gliemann and Rees, 1983, for a review of methodologies).

## I. GLUCOSE TRANSPORT ACTIVITY IN THE INTACT CELL

Using the 3-O-methylglucose uptake technique, Figs. 1 and 2 indicate the rapidity and sensitivity, respectively, with which the isolated rat adipose cell responds to insulin. Figure 1 illustrates a typical time course for the stimulation of glucose transport activity. Insulin induces a 20- to 40-fold increase in the rate of transport within 15 minutes, with a half-time of 3-4 minutes. The stimulatory effect of insulin is also rapidly reversible, in this case by the addition of a 300-fold excess of anti-insulin antibody. However, under the conditions of the experiments depicted in Fig. 1, the rate of reversal of the transport response cannot be distinguished from the rate of dissociation of insulin from its receptor (similar experiments performed at lower incubation temperatures are discussed later).



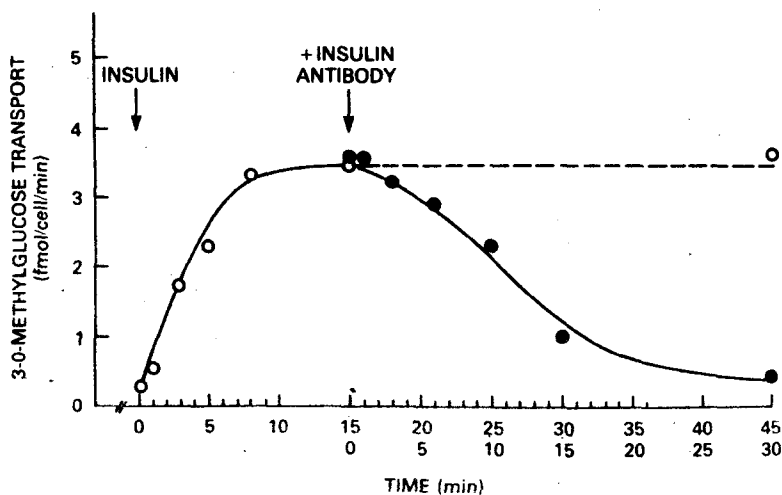


FIG. 1. Time courses of the stimulation of glucose transport activity by insulin (○) and its reversal by anti-insulin antiserum (●) (from Karnieli *et al.*, 1981b).

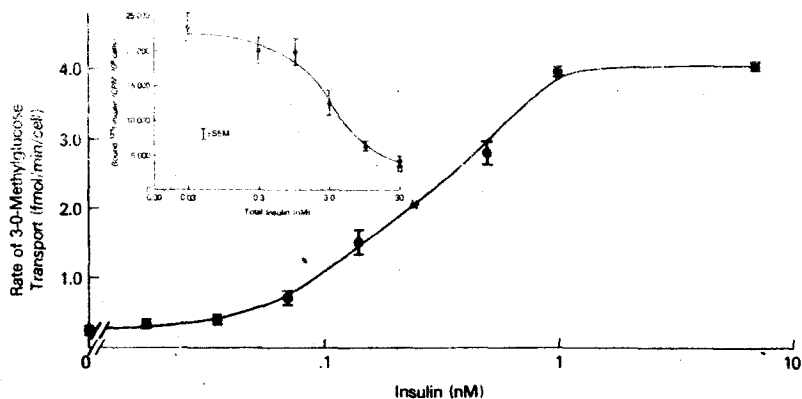


FIG. 2. Insulin concentration dependence of the stimulation of glucose transport activity (from Karnieli *et al.*, 1981b). Inset: insulin concentration dependence of insulin binding.