HORMONE RECEPTOR ASSAY IN DIFFERENT MALIGNANT DISEASES

Essay

Submitted for Partial Fulfillment of Master Degree in Clinical Pathology



Presented By Manal Mohamed Fahim Salem M.B., B.Ch.

63089

Under Supervision of

Prof. Dr. Gihan Kamal Hassan Ali

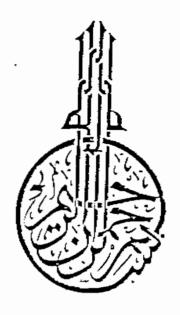
Assistant Professor of Clinical Pathology Ain Shams University



Lecturer of Clinical Pathology Ain Shams University



Ain Shams University 1993



المنافع المناف

إِنَّكَ أَنْ الْعَسَّالِيمُ لِلْحَكِسِيعُ

متقالسطيم



Acknowledgement

I would like to express my sincere gratitude to Prof. Dr. Gihan Kamal Hassan Ali, Assistant Professor of Clinical Pathology, Ain Shams University, for the great support and encouragement that she gave me throughout the whole work. It is a great honour to work under her guidance and supervision.

Also, I wish to express my grateful thanks to Dr. Dalia Helmy Farag, Lecturer of Clinical Pathology, Ain Shams University, for her careful guidance, valuable discussions and criticism and also for her patience.

It is a great honour for me that I take this opportunity to express my sincere appretiation and my deep respect to Prof. Dr. Sawsan Hossny Hamza, Professor of Clinical Pathology for her encouragement and sympathy.

Last, but not least, I would like to extend my sincere thanks to my husband and my parents.

CONTENTS

Page
List of Tables
List of Figures
Elst of Abbreviations
Infroduction 1
Chapter 1: Types And Variants of Hormone Receptors 4
Types of Hormones5
(A) Lipid Soluble Hormones
(B) Water Soluble Hormones 6
Classification of Hormone Receptors8
Hormone Receptor Variants
A. Polypeptide Hormone Receptors 9
B. Steroid Hormone Receptors
C. Thyroid Hormone Receptors
Chapter II: Value of Hormone Receptor Assay 26
A. Breast Cancer26
B. Prostatic Cancer43
C. Endometrial Carcinoma 52
D. Gastrointestinal Cancers58
E. Malignant Melanoma62
F. Skeletal Tumors
G. Leukaemia and Lymphomas

	Page
H. Testicular Tumors	69
I. Laryngeal Carcinoma	70
J. Renal Cell Carcinoma	71
Chapter III: Hormone Receptor Assay	72
A. Steroid Binding Assays	74
1. Biochemical Method	74
2. Histochemical Method	82
B. Immunological Assays	88
Immunocytochemical Staining Assay (ICA)	
2. Quantitative Enzyme Immunoassay (EIA)	
3. Immunoradiometric Method (IRMA)	
C. Polymerase Chain Reaction [PCR]	. 108
Summary	111
References	116
Arabic Summary	

List of Tables

		Page
Table 1	Comparaison between peptide hormones and steroid hormones	7
Table 2	Chemical characteristics of some poly-peptide membrane receptors	10
Table 3	Mediatros of polypeptide hormones	13
Table 4	Steroid hormone receptors in various tissues	19

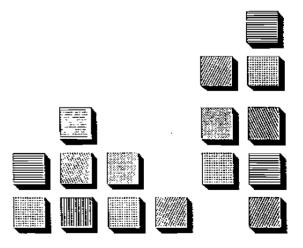
List of Figures

		Page
Figure 1	Mechanism of action of polypeptide hormones	14
Figure 2	Mechanism of action of steroid hormones	22
Figure 3	AR concentration and response to endocrinal therapy for adenocarcinoma of prostate	49
Figure 4	Relation between ER Status and disease free survival in cancer prostate	51
Figure 5	Relation between ER status and disease for survival in endometrial carcinoma	54
Figure 6	Relation between PR status and disease free survival in endometrial carcinoma	55
Figure 7	Relation between ER and PR status and disease free survival in endometrial carcinoma	56
Figure 8	Sucrose density-gradient separation of estrogen and progesterone receptors	79
Figu re 9	Immunocytochemical technic	90
Figure 10	Relation between immunocytochemical and DCC assays	97
Figure 11	Diagrammatic representation of EJA assay for dtermination of ER	101
Figure 12	Diagrammatic representation of IRMA	106
Figure 13	Diagrammatic representation of PCR	110

List of Abbreviations

AC Adenyl cylase
ALLAcute lymphblastic leukaemia
AR Androgen receptor
ATPAdenosine triphosphate
CaCalcium
cAMPCyclic adenosine monophosphate
DCC Dextran coated charcoal
DNA Deoxyribonucleic acid
E ₁ Esterone
E2 Estradiol
E ₃ Estriol
EIA Enzyme immunoassay
ER Estrogen receptor
FSHFollicular stimulating hormone
GDP Guanine diphosphate
GTP Guanine triphosphate
ICA Immunocytochemical assay
IRMA Immunoradiometric assay
K-ATPasePotassium adenosine triphosphatase
LH Lutenizing hormone
Mg Magnesium
Na-ATPase Sodium adenosine triphosphatase
PAP Peroxidase antiperoxidase
PR Progesterone receptor
T ₃ Tri-iodothyronine
T4 Tetra-iodothyronine
TSHThyroid stimulating hormone

INTRODUCTION AND AIM OF THE WORK



INTRODUCTION

Hormone receptors are macromolecules in or on cells that mediate physiological responses upon binding specific hormones. Receptors bind their hormones with remarkable selectivity and high affinity, permitting a given physiological response to be elicited in the target tissues. Some of these receptors are located inside the cell, nuclear or cytoplasmic in origin, others are on the cell membrane (Birnbaumer et al., 1974).

Hormones may be classified as lipid soluble and water soluble. The more lipid soluble hormones as steroid and thyroid hormones diffuse through the cell membrane and bind receptors in the cytoplasm and nucleus, respectively (Hughes, 1984; Oppenheimer, 1985). On the other hand peptide hormones bind receptors located in the cell membrane (Katt and Dufau, 1983).

The specific binding of hormones to receptors lead to generation of signals that modulate cellular functions. The signals may be expressed as an altered rate of enzyme activity or ion transport which then leads to the characteristic physiological respons. Hormone receptors may regulate cellular hormone response through modulation of their number, binding affinity or coupling to their effector system. Several hormone receptors have been purified and understanding of their function at the molecular level is now being realised (Bar and Roth, 1977).

In recent years, hormone receptor assay was found to be important in predicting the response to treatment and prognosis in some malignant diseases. In breast cancer, for example, the prognostic importance of cestrogen receptor (ER) content of the primary tumour has become apparent and hormone receptor status can help in predicting the risk of relapse, the overall survival and prognosis. Also, it was found that receptor status predicts which patient will benefit from hormonal treatment, involving ovariectomy and anti-cestrogen drugs as tamoxifin, as ER positive patients do better than ER negative patients (Merkel et al., 1989).

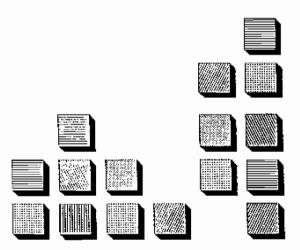
More recently, some studies postulated oestrogen sensitivity of tumours arising from melanoblasts as conjunctival malignant melanoma. It had been showed that this tumour have oestrogen receptor positivity (Paridaens et al., 1991).

Aim of the Work

The aim of the present work is to give a detailed account on the hormone receptor assay, their clinical significance in some malignant diseases and their implications on therapy and prognosis.

Different methods of hormone receptor assay will be discussed.

TYPES AND VARIANTS OF HORMONE AND HORMONE RECEPTORS



CHAPTER I TYPES AND VARIANTS OF HORMONE RECEPTORS

Hormone receptors are macromolecules in or on cells that mediate physiological responses upon binding specific hormones. Receptors bind their hormones with marked selectivity and high affinity, permitting a given physiological response to be elicited in the target tissue (Roth and Grunfeld, 1985).

Some investigators have suggested that the term "receptor" should be reserved for those conditions in which both binding and biological response are observed and that a hormone binding site detected in the absence of biological response is referred to as "acceptor" (Birnbaumer et al., 1974).