

Activation of Hormone and Growth Factor Receptors

Molecular Mechanisms
and Consequences



Activation of Hormone and Growth Factor Receptors

Molecular Mechanisms and Consequences

edited by

Michael N. Alexis

and

Constantin E. Sekeris

**The National Hellenic Research Foundation,
Biological Research Center,
Athens, Greece**

Dordrecht / Boston / London

Published in cooperation with NATO Scientific Affairs Division

Proceedings of the NATO Advanced Research Workshop on
Molecular Mechanisms and Consequences of Activation of Hormone and Growth
Factor Receptors
Nafplion, Greece
September 25-30, 1988

ISBN 0-7923-0573-6

Published by Kluwer Academic Publishers,
P.O. Box 17, 3300 AA Dordrecht, The Netherlands.

Kluwer Academic Publishers incorporates the publishing programmes of
D. Reidel, Martinus Nijhoff, Dr W. Junk and MTP Press.

Sold and distributed in the U.S.A. and Canada
by Kluwer Academic Publishers,
101 Philip Drive, Norwell, MA 02061, U.S.A.

In all other countries, sold and distributed
by Kluwer Academic Publishers Group,
P.O. Box 322, 3300 AH Dordrecht, The Netherlands.

Printed on acid free paper

All Rights Reserved

© 1990 by Kluwer Academic Publishers

No part of the material protected by this copyright notice may be reproduced or
utilized in any form or by any means, electronic or mechanical, including photo-
copying, recording or by any information storage and retrieval system, without written
permission from the copyright owner.

Printed in The Netherlands

This book contains the proceedings of a NATO Advanced Research Workshop held within the programme of activities of the NATO Special Programme on Selective Activation of Molecules running from 1983 to 1988 as part of the activities of the NATO Science Committee.

Other books previously published as a result of the activities of the Special Programme are:

BOSNICH, B. (Ed.) - *Asymmetric Catalysis* (E103), 1986

PELIZETTI, E. and SERPONE, N. (Eds.) - *Homogeneous and Heterogeneous Photocatalysis* (C174) 1986

SCHNEIDER, M. P. (Ed.) - *Enzymes as Catalysts in Organic Synthesis* (C178) 1986

SETTON, R. (Ed.) - *Chemical Reactions in Organic and Inorganic Constrained Systems* (C165) 1986

VIEHE, H. G., JANOUSEK, Z. and MERENYI, R. (Eds.) - *Substituent Effects in Radical Chemistry* (C189) 1986

BALZANI, V. (Ed.) - *Supramolecular Photochemistry* (C214) 1987

FONTANILLE, M. and GUYOT, A. (Eds.) - *Recent Advances in Mechanistic and Synthetic Aspects of Polymerization* (C215) 1987

LAINE, R. M. (Ed.) - *Transformation of Organometallics into Common and Exotic Materials: Design and Activation* (E141) 1988

BASSET, J. M., et al. (Eds.) - *Surface Organometallic Chemistry: Molecular Approaches to Surface Catalysis* (C231) 1988

WHITEHEAD, J. C. (Ed.) - *Selectivity in Chemical Reactions* (C245) 1988

CHANON, M., JULLIARD, M. and POITE, J. C. (Eds.) - *Paramagnetic Organometallic Species in Activation/Selectivity, Catalysis* (C257) 1988

MINISCI, F. (Ed.) - *Free Radicals in Synthesis and Biology* (C260) 1989

SCHUBERT, U. (Ed.) - *Advances in Metal Carbene Chemistry* (C269) 1989

SCHINZER, D. (Ed.) - *Selectivities in Lewis Acid Promoted Reactions* (C289) 1989

FOREWORD

This volume contains the papers presented in the NATO Advanced Research Workshop "Activation of Hormone and Growth Factor Receptors: Molecular Mechanisms and Consequences" held in Nafplion, Greece on September 25-30, 1988.

The objective of NATO ARW is to assess the state-of-the-art in a given scientific area and to formulate recommendations for future research in emerging areas of science by promoting international scientific contacts. In the Nafplion meeting this objective was reached by an international group of speakers, senior Greek scientists and graduates involved in relevant research areas.

“ The Workshop was made possible by the generous support of the Scientific Council of NATO. We thank Drs. G. Sinclair and L.V. daCunha, Directors of the NATO ARW's and ASI's (Advanced Study Institutes) respectively, for their wholehearted support and advice. The International Union of Biochemistry awarded additional travel grants leading to increased international participation. Furthermore, the Secretariat of Science and Technology, the Ministry of Culture and Sciences and the National Hellenic Research Foundation contributed financially and by supporting personnel. We sincerely thank all these organizations for their support. Our heartfelt thanks are also extended to the Mayor of the Municipality of Nafplion, Mr. G. Tsournos, who kindly put to our disposal the lecture hall of the Cultural Center of the City and hosted the participants. Thanks are also due to Mrs. M. Hatzistili who efficiently performed the secretarial work with unending patience.

LIST OF PARTICIPANTS

Organizing Committee

Dr. M.N. Alexis
National Hellenic Research Foundation
Athens

Prof. C.E. Sekeris (Director)
National Hellenic Research Foundation
Athens

Dr. G. Sotiropoulou
University of Athens
Athens

Dr. T. Sotiroudis
National Hellenic Research Foundation
Athens

Prof. F. Stylianopoulou
University of Athens
Athens

Prof. O. Tsolas
University of Ioannina
Ioannina

Prof. T. Valcana
University of Patras
Patras

Invited speakers

Prof. P. Aranyi
Institute for Drug Research
Szabadsagharcosok U 47-49
U-1325 Budapest, POB 72
HUNGARY

Prof. F. Auricchio
Istituto di Patologia Generale
II Cattedra
Facolta di Medicina
Universita di Napoli
80138 Napoli
ITALIA

Dr. G. Chalepakis
Institute of Molecular and Tumor Biology
University of Marburg
3500 Marburg/Lahn
W. GERMANY

Dr. M.G. Catelli
Unite 33
Universite Paris-Sud
Dept. of Biological Chemistry
78 Rue General Leclerc
94270 Bicetre
FRANCE

Prof. G. Chroussos
N.I.H.
Bldg. 10, Room 10N-244
Bethesda, Maryland 20892
U.S.A.

Prof. M. Dahmus
Dept. of Biochemistry
University of California at Davis
Davis, California
U.S.A.

Prof. R. Djordjevic-Markovic
Dept. of Biochemical and
Molecular Biology
University of Belgrade
Studentski TRG 16 P FAK 550
11000 Belgrade
YUGOSLAVIA

Prof. W. Engstrom
AVD for Tumorpatologi
Karolinska Sjukhuset
104 01 Stockholm
SWEDEN

Prof. D. Gallwitz
M.P.I.f. Biophysikalische Chemie
Abtl. Mol. Genetik
34 Gottingen - Nikolausberg
W. GERMANY

Prof. H. Gronemeyer
INSERM
U 184 Inst. of Biological
Chem. - Facul. Medecine
University of Strasbourg
11 Rue Humann
67085 Strasbourg
FRANCE

Prof. B. Groner
Ludwig Institute for Cancer
Research, Inselspital
Bern CH 3010
SWITZERLAND

Prof. J.A. Gustafsson
Dept. of Medical Nutrition
Karolinska Institute
Huddinge Univ. Hospital F 69
141 86 Huddinge
SWEDEN

Prof. P. Herrlich
Institut F. Genetik
Kernforschungszentrum
Karlsruhe
W. GERMANY

Prof. Michael Jaye
King of Prussia
Philadelphia, PA
U.S.A.

Prof. D. Kanazir
Serbian Academy of Sciences
and Art
Belgrade
YUGOSLAVIA

Prof. P. Karlson
Institute of Molecular
and Tumor Biology
University of Marburg
3500 Marburg/Lahn
W. GERMANY

Prof. J.T. Knowler
Dept. of Biochemistry
The University of Glasgow
Glasgow G12 800
UNITED KINGDOM

Prof. Chun-Yen Lai
Bldg. 86, Room 906
Dept. of Protein Biochemistry
Hoffmann - La Roche, Inc.
340 Kingsland Street
Nutley, NJ 07110-1199
U.S.A.

Prof. W.H. Moolenaar
Int. Embryol. Institute
Humbrecht Lab.
Uppsalalaan 8
3584 Utrecht
THE NETHERLANDS

Prof. G. Ringold
Dept. of Pharmacology
Stanford University
School of Medicine
Stanford, California 94305
U.S.A.

Prof. G. Rousseau
Intern. Institute of Cellular
and Molecular Pathology
Box 7529
Av. Hippocrate 75
Bruxelles
BELGIUM

Prof. Sandro Rusconi
Institute of Molecular Biology II
University of Zurich
CH - 8093 Zurich
SWITZERLAND

Prof. W. Schmid
Institute of Cell Biology
D K F Z
6900 Heidelberg
W. GERMANY

Prof. K.H. Seifart
Inst. of Physiological Chemistry
University of Marburg
Marburg/Lahn
W. GERMANY

Prof. M. Sluysers
Division of Endocrinology
The Netherlands Cancer Institute
Amsterdam
THE NETHERLANDS

Prof. D. Spandidos
National Hellenic Research Foundation
Biological Research Center
48, Vas. Constantinou Avenue
Athens 116 35
GREECE

Prof. E. van Obberghen
INSERM
U 145 Faculte de Medecine
Nice, Cedex 06034
FRANCE

Prof. A. Venetianer
Biological Research Center
Szeged
HUNGARY

Prof. B. Vennstrom
E M BIL
Postfach 10209
6900 Heidelberg
W. GERMANY

Participants

Aidinis, V.
National Hellenic Research Foundation
Athens

Arzimanoglou, D.
National Hellenic Research Foundation
Athens

Baki, A.
National Hellenic Research Foundation
Athens

Baltas, L.
National Hellenic Research Foundation
Athens

Christou, E.I.
University of Thessaloniki
Thessaloniki

Dafgard, U., Dr.
Stockholm
Sweden

Dimou, K.
Aretaion Hospital
Athens

Dotsika, E.
Hellenic Pasteur Institute
Athens

Fragoulis, E.G., Prof.
University of Athens
Athens

Friligos, S.
University of Ioannina
Ioannina

Geledopoulos, T.
National Hellenic Research Foundation
Athens

Goula, I.
Papanicolaou Anticancer Center
Athens

Gounari, A., Dr.
Papanicolaou Anticancer Center
Athens

Hatzistili, M.
National Hellenic Research Foundation
Athens

Kakanas, Th.
National Hellenic Research Foundation
Athens

Kakari, S., Prof.
Agios Savas Hospital
Athens

Karagiorgou, M.
University of Ioannina
Ioannina

Karahaliou, L.
University of Thessaloniki
Thessaloniki

Karayianni, N.
National Hellenic Research Foundation
Athens

Kleanthous, M.
National Center of Marine Research
Athens

Kletsas, D.
Democritos Research Center
Athens

Kopsida, M.
National Hellenic Research Foundation
Athens

Korozi, V.
National Hellenic Research Foundation
Athens

Kourti, A., Dr.
Papanicolaou Anticancer Center
Athens

Kouretas, D.
Theageneio Research Institute
Thessaloniki

Kyriakidis, S.
National Hellenic Research Foundation
Athens

Lenas, P.
National Hellenic Research Foundation
Athens

Loukas, S., Dr.
Democritos Research Center
Athens

Maniatis, G., Prof.
University of Patras
Patras

Marselos, M., Prof.
University of Ioannina
Ioannina

Mavridou, I.
National Hellenic Research Foundation
Athens

Moraitou, M.
National Hellenic Research Foundation
Athens

Nicodimou, E.
National Hellenic Research Foundation
Athens

Pagoulatos, G., Prof.
University of Ioannina
Ioannina

Panotopoulou, E.
Papanicolaou Anticancer Center
Athens

Papadopoulos, G., Prof.
University of Ioannina
Ioannina

Papacharilaou, E., Dr.
National Hellenic Research Foundation
Athens

Pataryas, H., Prof.
University of Athens
Athens

Pintzas, A.
Hellenic Pasteur Institute
Athens

Psaras, S.
Democritos Research Center
Athens

Roussou, E.
University of Crete
Crete

Seferiadis, C., Prof.
University of Ioannina
Ioannina

Sitaras, N., Dr.
University of Athens
Athens

Stathakos, D., Dr.
Democritos Research Center
Athens

Troungos, C., Dr.
National Hellenic Research Foundation
Athens

Tsawdaroglou, N., Dr.
National Hellenic Research Foundation
Athens

Tsiftoglou, A., Prof.
University of Thessaloniki
Thessaloniki

Tsiriyotis, Ch.
National Hellenic Research Foundation
Athens

Vasiliou, V.
University of Ioannina
Ioannina

Venetsanou, K.
National Hellenic Research Foundation
Athens

Vorgias, C., Dr.
Göttingen
W. Germany

Yagnisi, M.
National Hellenic Research Foundation
Athens

Yioti, J.
Papanicolaou Anticancer Center
Athens

Zevgolis, V.
National Hellenic Research Foundation
Athens

CONTENTS

FOREWORD

xi

LIST OF PARTICIPANTS

xiii

Activation of Hormone and Growth Factor Receptors: Molecular Mechanisms and Consequences: A record of the Meeting.....	1
M.N. Alexis and C.E. Sekeris	

SIGNAL TRANSDUCTION AND CONTROL OF CELL PROLIFERATION AND DIFFERENTIATION

Insulin Receptor and Insulin Action.....	9
E. van Obberghen and R. Ballotti	

Signal Transduction by Growth Factor Receptors.....	19
W.H. Moolenaar	

Cholera Toxin: Transport and Structural Basis of Action.....	27
C-Y. Lai	

Analysis and Transfection of Human Acidic Fibroblast Growth Factor (aFGF) cDNA Clones and Structural Analysis of the Human aFGF Gene reveals Features Shared within a Family of Homologous Proteins.....	41
M. Jaye, G. Crumley and J. Schlessinger	

Growth Factor Synthesis by a Human Teratocarcinoma cell line: Implications for Autocrine Growth in the Human Embryo?.....	49
P.N. Schofield, M. Tally and W. Engström	

THE ROLE OF ONCOGENE ACTIVATION

The Role of Ras P21 Product in Cell Transformation.....	63
D.A. Spandidos	

DNA Binding Properties of the Thyroid Hormone Receptor/c-erbA Protein and its Viral Homologue P75 gag-v-erbA	69
B. Vennström, J. Sap, J. Schmitt, D. Forrest, A. Muñoz, M. Zenke, H. Stunnenberg and H. Beug	

The Role of Fos in Gene Regulation.....	77
P. Herrlich, H. Ponta, B. Stein, S. Gebel, H. König, A. Schönthal, M. Büscher and H.J. Rahmsdorf	
6-Phosphofructo-2-Kinase links Glycolysis to Mitogenic Agents and has Sequence Similarity with Proteins encoded by Oncogenic DNA Viruses.....	93
G.G. Rousseau and L. Hue	

STEROID RECEPTORS AND TRANSCRIPTIONAL CONTROL

The Regulation of RNA Polymerase II Activity by Multisite Phosphorylation.....	105
M.E. Dahmus, B. Bartholomew D.L. Cadena, G.K. Dahmus W-Y. Kim, P.J. Laybourn and J. Payne	
Transcription Factors of RNA Polymerase III from Mammalian Cells.....	119
K. Seifart, R. Waldschmidt and H. Schneider	
Steroid response elements: Composite Structure and Definition of a Minimal Element.....	137
W. Schmid, U. Strähle, R. Mestril, W. Ankenbauer and G. Schütz	
Gene Regulation by Steroid Hormones.....	151
G. Chalepakis, M. Schauer, E.P. Slater and M. Beato	
Regulation of Liver Gene Expression in Dexamethasone Resistant Hepatoma Cells.....	173
A. Venetianer and D. David	
The Kinetics of Oestrogen-induced Gene Expression in the Immature Rat Uterus.....	195
J.T. Knowler, M.T. Travers and N.A. Brockdorff	

STRUCTURE AND FUNCTION OF STEROID RECEPTORS

Functional Domains of Steroid Hormone Receptors.....	203
H. Gronemeyer, V. Kumar, S. Green, M.T. Bocquel, L. Tora, M.E. Meyer, J. Eul and P. Chambon	
Genetic and Biochemical Analysis of a Steroid Receptor.....	215
S. Wieland, I. Galli, M. Schatt, Y. Severne and S. Rusconi	
Analysis of Subunit Interactions in Steroid Receptors using Chemical Cross-Linking.....	227
P. Arányi and E. Rusvai	
Possible Functional Interaction between Steroid Hormone Receptors and Heat Shock Protein Mr 90.000 (hsp 90).....	239
M.-G. Catelli, N. Binart, C. Vourc'h, J. Devin and E.E. Baulieu	
Mechanism of Action of Estrogens: Phosphorylation of Estradiol Receptor on Tyrosine.....	257
F. Auricchio, A. Migliaccio, G. Castoria, M. Di Domenico, M. Pagano, A. Rotondi and E. Nola	
Glucocorticoid Receptor and Hormonal Extragenomic Effects.....	269
D.T. Kanazir	
CLINICAL IMPLICATIONS OF STEROID RECEPTOR RESEARCH	
Estrogen Receptors in Mouse Mammary Tumors.....	289
M. Sluysen	
Structure of Glucocorticoid Receptor in Cancer Tissues.....	295
R. Djordjević-Marković	
Index.....	317