

APOPTOSIS

PEZCOLLER FOUNDATION SYMPOSIA

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Springer Science+Business Media, LLC

Library of Congress Cataloging-in-Publication Data

Apoptosis / edited by Enrico Mihich and Robert T. Schimke.
p. cm. -- (Pezcoller Foundation symposia ; 5)
Includes bibliographical references and index.

1. Apoptosis--Congresses. I. Mihich, Enrico. II. Schimke,
Robert T. III. Series.

QH671.A65 1994
574.87'65--dc20

94-12196
CIP

1098765432

Proceedings of the Fifth Pezcoller Symposium on Apoptosis, held June 9-11, 1993, in Trento, Italy

ISBN 978-1-4757-9219-5 ISBN 978-1-4757-9217-1 (eBook)

DOI 10.1007/978-1-4757-9217-1

©1994 Springer Science+Business Media New York

Softcover reprint of the hardcover 1st edition 1994

Originally published by Plenum Press, New York in 1994.

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Professor Alessio Pezcoller
(Photo by Dino Panato, Trento, Italy)

THE PEZCOLLER FOUNDATION

The Pezcoller Foundation was created in 1979 by Professor Alessio Pezcoller (1896-1993) who was the chief surgeon of the S. Chiara Hospital in Trento from 1937 to 1966 and who gave a substantial portion of his estate to support its activities; the Foundation also benefits from the cooperation of the Saving Bank Cassa di Risparmio di Trento e Rovereto.

The main goal of this non-profit foundation is to provide and recognize scientific progress on life-threatening diseases, currently focusing on cancer. Towards this goal, the Pezcoller Foundation awards, every two years, the Pezcoller Prize, recognizing highly

meritorious contributions to medical research; it also sponsors a series of annual symposia promoting interactions among scientists working at the cutting edge of basic oncological sciences.

The award selection process is managed by the European School of Oncology in Milan, Italy, with the aid of an international committee of experts chaired by Professor U. Veronesi.

The symposia are held in the Trentino Region of Northern Italy and their scientific focus is selected by Enrico Mihich with the collaboration of an international Standing Symposia Committee. A Program Committee determines the content of each symposium.

The first symposium focused on *Drug Resistance: Mechanisms and Reversal* (E. Mihich, Chairman, 1989); the second on *The Therapeutic Implications of the Molecular Biology of Breast Cancer* (M.E. Lippman and E. Mihich, Co-Chairmen, 1990); the third on *Tumor Suppressor Genes* (D.M. Livingston and E. Mihich, Co-Chairmen, 1991), and the fourth on *Cell Adhesion Molecules: Cellular Recognition Mechanisms* (M.E. Hemler and E. Mihich, Co-Chairmen, 1992). The sixth symposium (1994) will be focused on *Normal and Malignant Hematopoiesis: New Advances* (E. Mihich and D. Metcalf, Co-Chairmen).

PREFACE

The fifth Annual Pezcoller Symposium entitled, Apoptosis, was held in Trento, Italy, June 9-11, 1993 and was focused on the specific phenomena leading to Programmed Cell Death (PCD) or Apoptosis, and the mechanisms involved. With presentations at the cutting edge of progress and stimulating discussions, this Symposium addressed the genetics and molecular mechanisms determining PCD and the role of this suicidal process in cancer and the immune system. The functions of p53, c myc and bcl 2 in affecting apoptosis in different cell types and the role of ions and intracellular pH changes and that of intranuclear endonucleases are given particular emphasis as are the effects of anticancer agents, hormone imbalances and growth factors.

The role of p53, a tumor suppressor gene, in inducing PCD is discussed in detail as pertinent to hematological and non-hematological tumors. The requirement of p53 for the induction of apoptosis by ionizing radiation or adenovirus oncoproteins is outlined. Decision points during the cell cycle affecting the cascade of events leading to PCD are discussed as is their role as "switches" under the control of c-myc and bcl-2 proteins or the influence of cycle specific drugs. The concurrent requirement of multiple signals in determining apoptosis is emphasized. The examples of the role of PCD in the regulation of hematopoiesis, and in the generation of antigen-specific immune repertoire are illustrated. The role of calcium ions and ion signaling in determining apoptosis, in part through activation of endonuclease and increased DNA susceptibility to these enzymes consequent to changes in chromatin conformation, are outlined. In conclusion, the multiplicity of mechanisms determining PCD was extensively discussed. The role of genes like wt p53 or c-myc and of accessory factors in directing cells through "switch" decision points towards proliferation or PCD is demonstrated in various cellular systems. The inhibition of PCD, by growth factors or by products of genes like bcl-2 and the induction of PCD by hormones and by growth factors withdrawal, or by DNA damaging and anticancer drugs, are described. The function of PCD in hematopoiesis and in negative and positive selection during the development of the immune repertoire is discussed as is the cascade of events resulting in apoptotic death in each of the models examined and the factors regulating them.

We wish to thank the participants in the Symposium for their substantial contributions and their participation in the spirited discussions which followed. We would also like to thank Drs. J. Michael Bishop, Arnold Levine and David M. Livingston for their essential input as members of the Program Committee, and Ms. A. Toscani for her invaluable assistance. The aid of the Bank Cassa di Risparmio di Trento and Rovereto, and the Municipal, Provincial and Regional Administrations in supporting this Symposium through the Pezcoller Foundation are also acknowledged with deep appreciation.

Finally, we wish to thank the staff of Plenum Publishing Corporation for their efficient cooperation in the production of these Proceedings.

Enrico Mihich
Robert T. Schimke

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