Tumor Necrosis Factor:
Structure-Function Relationship and Clinical Application

3rd International Conference on Tumor Necrosis Factor and Related Cytokines,
Makuhari, Chiba, November 21-25, 1990

Tumor Necrosis Factor:
Structure-Function Relationship
and Clinical Application

Editors
Toshiaki Osawa, Tokyo
Benjamin Bonavida, Los Angeles, Calif.

83 figures, 1 color plate and 39 tables, 1992

KARGER

Basel • München • Paris • London • New York • New Delhi • Bangkok • Singapore .Tokyo. Sydney

Library of Congress Cataloging-in-Publication Data
International Conference on Tumor Necrosis Factor and Related Cytokines
(3rd: 1990: Chiba-shi, Japan)
Tumor necrosis factor: structure-function relationship and clinical application/
editors, Toshiaki Osawa, Benjamin Bonavida.
"3rd International Conference on Tumor Necrosis Factor and Related Cytokines, Makuhari,
Chiba, November 21-25, 1990."
Includes bibliographical references and index. (alk. paper)
I. Tumor necrosis factor — Congresses. 2. Cytokines — Congresses.
   I. Osawa, T. (Toshiaki) II. Bonavida, Benjamin. III. Title.
   [DNLM: I. Cytokines — physiology — congresses. 2. Tumor Necrosis Factor — physiology —
   congresses. 3. Tumor Necrosis Factor — therapeutic use — congresses. QW 630 I595t 1990]
   QB 185.8.784I57 1990a
   616.079—dc20
   ISBN 3-8055-5458-3

Drug Dosage
The authors and the publisher have exerted every effort to ensure that drug selection and dosage
set forth in this text are in accord with current recommendations and practice at the time of
publication. However, in view of ongoing research, changes in government regulations, and the
constant flow of information relating to drug therapy and drug reactions, the reader is urged to
check the package insert for each drug for any change in indications and dosage and for added
warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

All rights reserved.

No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher.

Copyright 1992 by S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland)

Printed on acid-free paper.

ISBN 3-8055-5458-3

Contents

Acknowledgements.VIII
Preface.IX

Key Note Addresses

Mizuno, D. (Kawasaki): Significance of Endogenous Production of TNF 1


Biochemical and Molecular Characterization of TNF Receptors/
TNF-Like Receptors

Loetscher, H.; Brockhaus, M.; Dembic, Z.; Gallati, H.; Gentz, R. (Basel); Gubler, U. (Nutley, N.J.); Lahm, H.-W.; Lustig, A. (Basel); Pan, Y.-C.E. (Nutley, N.J.); Schlaeger, E.-J. (Basel); Tabuchi, H. (Kamakura); Zulauf, M.; Lesslauer, W. (Basel): Two Distinct Human TNF Receptors: Purification, Molecular Cloning and Expression.34

Wallach, D. (Rehovot); Aderka, D. (Tel Aviv); Engelmann, H.; Iophar, Y.; Kemper, O. (Rehovot); Holtmann, H.; Brakebusch, C. (Hannover); Villa, S.; Grossi Gondi, F.; Bucciarelli, U. (Ardea): Cell Surface and Soluble TNF Receptors.47

Yonehara, S.; Ishii, A.; Yonehara, M. (Tokyo): Receptor System of Tumor Necrosis Factor: Cell Surface Fas Antigen Appears to Mediate Only the Cytolytic Activity of TNF.58

TNF-Mediated Cytotoxicity: Mechanism and Regulation
Contents VI

X.; Van Roy, F. (Gent): Tumor Necrosis Factor: Mechanism of Action at the Molecular, Cellular and in vivo Level.66
Leung, W.-C.; Leung, M.F.K.L. (Little Rock, Ark.): Carbohydrate Tagging of Human Tumor Necrosis Factor a.74
Lehmann, V.; Kinzer, D. (Heidelberg): Tumor Necrosis Factor-Induced Lysis of L929 Cells Is Modulated by Extracellular ATP.94

Role of TNF in Maturation and Differentiation

Schwartz, M.; Lavie, V. (Rehovot); Solomon, A.; Belkin, M. (Tel Hashomer); Cohen, A.; Sivron, T. (Rehovot); Ben-Bassat, S. (Tel Hashomer); Lotan, M. (Rehovot): Tumor Necrosis Factor and TNF-Like Factors in Central Nervous System Regeneration 135

Lebow, L.T.; Gan, X.-H.; Jewett, A.; Bonavida, B. (Los Angeles, Calif.): Induction and Secretion of TNF-a during the Maturation and Differentiation of Human Natural Killer Cells 144
Mahé, Y. (Kanazawa); Mukaida, N. (Tochigi); Matsushima, K. (Kanazawa): Mechanisms of Interleukin-8 Gene Regulation by Tumor Necrosis Factor and Interleukin-1 152

Role of TNF-a in Tumor Cell Destruction
Männel, D.N. (Heidelberg); Jänicke, R. (Singapore); Westenfelder, U.; Orosz, P.G.; Echtenacher, B.; Kist, A.; Falk, W. (Heidelberg): Tumor Cell-Induced TNF Production 166

Smith, D.M.; Epstein, L.B. (San Francisco, Calif.): Molecular Mechanisms Associated with the Synergistic Antiproliferative Action of Tumor Necrosis Factor and Interferon-γ on Human Melanoma Cells: Characterization of Proteins Induced or Suppressed by Cytokine Treatment 173

Matthews, I.; Neale, M.L.; Fiera, R.A.; Taylor, K.M. (Cardiff): Functional Differences between TNF-Susceptible and Resistant Variants of the Same Tumor Cell Line 183

Aggarwal, B.B.; Totpal, K. (Houston, Tex.): Synergistic Antiproliferative Effects of TNF and IL-4 against Various Tumor Cell Lines 191

Contents VII

Role of TNF in the Pathogenesis of Diseases


Roederer, M.; Staal, F.J.T.; Raju, P.A.; Herzenberg, L.A.; Herzenberg, L.A (Stanford, Calif.): The Interrelationship of Tumor Necrosis Factor, Glutathione, and AIDS 215

Satoh, M.; Yamazaki, M. (Kanagawa); Soma, G.; Mizuno, D. (Kawasaki): TNF-Driven Inflammation during Mouse Liver Regeneration and Its Role in Hepatic Growth Regulation 230


Clinical Applications


Scheringa, M.; de Bruin, R.W.F.; Heineman, E.; Jeekel, H.; Marquet, R.L. (Rotterdam): Anti-Tumor Necrosis Factor Alpha Antibodies Prolong Allograft Survival in Rats 262

Taguchi, T. (Osaka); Ikeda, S. (Saitama); Ishihara, K. (Tokyo): Recent Clinical Studies of Recombinant Human Tumor Necrosis Factor in Japan 269

Spriggs, D.R.; Yates, S.W. (Madison, Wisc.): Clinical Studies of Tumor Necrosis
Acknowledgements

The Organizing Committee of the Third International Conference on Tumor Necrosis Factor and Related Cytokines acknowledges, with sincere thanks, the generous contributions given by:

Asahí Chemical Industry Co., Ltd.
Asai Germanium Research-Institute
Banyu Pharmaceutical Co., Ltd.
Cancer Research Institute, New York
Chiba Flour Milling Co.
Chugai Pharmaceutical Co., Ltd.
Daiichi Pharmaceutical Co., Ltd.
Dainippon Pharmaceutical Co., Ltd.
Eisai Co., Ltd.
Fujisawa Pharmaceutical Co., Ltd.
Green Cross Corporation
Hayashibara Biochemical Laboratories, Inc.
Hoechst Japan Limited
Japan Tabacco Inc.
Kureha Chemical Industry Co., Ltd.
Kyowa Hakko Kogyo Co., Ltd.
Mect Corporation
Minophagen Pharmaceutical Co., Ltd.
Mitsui Pharmaceuticals Inc.
Mochida Pharmaceutical Co., Ltd.

Nippon Roche K.K.
Nippon Roussel K.K.
Nippon Shinyaku Co., Ltd.
Nippon Syntex K.K.
Ono Pharmaceutical Co., Ltd.
Otsuka Pharmaceutical Co., Ltd.
Sankyo Co., Ltd.
Sapporo Cancer Seminar
Shionogi & Co., Ltd.
SRL, Inc.
Preface

This volume contains the proceedings of the Third International Conference on Tumor Necrosis Factor and Related Cytokines. This conference was organized under the leadership of Professor Toshiaki Osawa and the local organizing committee. The conference was held in Makuhari, Chiba, November 21-25, 1990, and was dedicated to the most recent advances in the field of TNF and related cytokines. The main topics covered areas that related to structure-function relationship, advances in the molecular characterization of TNF receptors, the role of TNF in various infectious and noninfectious diseases, the role of TNF in the development and differentiation of various tissues, and clinical application of TNF in diagnosis and therapy and the role of TNF and inhibitors in infectious diseases, autoimmune diseases, and cancer. The conference attracted several hundred participants from all over the world. Representatives from various research institutions and universities as well as pharmaceutical houses participated in the formal presentations and in the discussions of various topics at several workshops. The open discussion and participation of scientists of different background and expertise resulted in continued exchange of information and knowledge in the rapidly expanding field of cytokines as represented in this book by TNF.

The editors trust that the volume will serve as a useful resource both for established investigators and novices in the field and will provide selected highlights of the most recent advances made in the field as well as new directions. The editors also acknowledge the participation and effort of the International Organizing Committee and the local organizing committee. Also, the editors wish to acknowledge the various institutions that provided financial support. The excellent and professional assistance of Karger publishers is greatly appreciated.