ininfrequently
employed drug.

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Contents

Acknowledgements VIII
Preface IX

Keynote Addresses
Haven, Conn.): TNF- (Cachectin) and TNF- (Lymphotoxin): 25 Years of
Progress 1
Kruys, V.; Thompson, P.; Beutler B. (Dallas, Tex.): Tumor Necrosis Factor Biosynthesis:
From Gene to Protein 10

Tumor Necrosis Factor and Lymphotoxin, Cell Bound and
Soluble Receptors

Nedospasov, S. (Moscow): Structure, Polymorphism and Regulation of Tumor
Necrosis Factor Genes at Genomic Loci 19
Goh, C.R.; Loh, Ch.S.; Ng, P.W.P. (Singapore); Hlodan, R.; Pain, R. (Newcastle
Upon Tyne); Porter, A.G. (Singapore): Localization of Receptor Binding Sites
and Functional Domains in Human Lymphotoxin (TNF-) 27
Angeharn, P.; Banner, D.; Braun, Th.; d'Arcy, A.; Gehr, G.; Gentz, R.; Mackay, F.;
Schlaeger, E.-J.; Schoenfeld, H.; Loetscher, H.; Lesslauer, W. (Basel): Two
Distinct Tumor Necrosis Factor Receptors in Health and Disease 33
Brakebusch, C.; Nophar, Y.; Kemper, O. (Rehovot); Aderka, D. (Tel Aviv); Engelmann,
H.; Wallach, D. (Rehovot): Diverse Functions of the Tumor Necrosis
Factor Receptors: Structure-Activity Considerations 40

Cellular Mechanism of Action
Scheurich, P.; Grell, M. (Stuttgart); Meager, A. (Potters Bar); Pfizenmaier, K. (Stuttgart): Agonistic and Antagonistic Antibodies as a Tool to Study the Functional Role of Human Tumor Necrosis Factor Receptors 52

Contents VI


Schütze, S.; Krönke, M. (München): Pathways of Tumor Necrosis Factor Signal Transduction 66

Aggarwal, B. B.; Totpal, K.; Pocsik, E.; Graff, K.; Liao, W.; Higuchi, M. (Houston, Tex.): Role of Protein Kinases and Phosphatases in Receptor Biosynthesis, Shedding and Mediation of Cellular Responses to Tumor Necrosis Factor 76

Guy, G.R.; Cairns, J.; Tan, Y.H. (Singapore): The Phosphorylation Pattern Induced by Tumor Necrosis Factor (and Interleukin-1) in Human Fibroblasts Is Mimicked by Okadaic Acid. Ligand-Induced Inactivation of a Phosphatase 81


Tumor Necrosis Factor and Antagonists in Pathophysiological Phenomena

Kunkel, S.L.; Rolfe, M.W.; Strieter, R.M. (Ann Arbor, Mich.): Expression of Tumor Necrosis Factor During Lung Allograft Revascularization and Rejection 96

Hervé, P.; Wijdenes, J.; Racadot, E.; Tiberghien, P.; Plouvier, E.; Flesch, M. (Besançon); Bordigoni, P. (Nancy); Holler, E. (München); Lioure, B. (Strasbourg); Bourdeau, H. (Paris): Kuentz, M. (Créteil); Wilmer, E.; Stephan, J.L. (Paris); Roche, C.; Cahn, J.Y. (Besançon): Monoclonal Anti-Tumor Necrosis Factor Alpha Antibody for the Treatment of Severe Acute Graft-versus-Host Disease. A Pilot Study 102

Memon, R.A.; Feingold, K.R.; Adi, S.; Grunfeld, C. (San Francisco, Calif.): Which Cytokines Mediate the Metabolic Effects of Endotoxin (Lipopolysaccharide)? 107

Ghezzi, P. (Milan); White, C.W. (Denver, Colo.); Salmona, M. (Milan): Reactive Oxygen Intermediates in Tumor Necrosis Factor Production and Endotoxin Shock 113

Wendel, A.; Tiegs, G. (Konstanz): Pharmacological Intervention Studies against Lipopolysaccharides or TNF Toxicity in Mice 120

Libert, C.; Everaerdt, B.; Takahashi, N., Cauwels, A.; Brouckaert, P.; Fiers, W.
Role of Tumor Necrosis Factor in Autoimmune Diseases

Nagata, S.; Watanabe-Fukunaga, R. (Osaka); Jenkins, N.A. (Frederick, Md.): The Fas Antigen Gene is the Structural Gene for Murine Lymphoproliferation Mutation (lpr) 132
Piguet, P.-F.; Grau, G.E. (Geneva): Tumor Necrosis Factor and Interleukin-1 Antagonists in Immunopathological Reactions 138

Contents VII


Tumor Necrosis Factor and Antagonists in Infectious Diseases

Grau, G.E.; Piguet, P.-F. (Geneva): Tumor Necrosis Factor in Cerebral and NonCerebral Malaria 162
Cohen, J. (London): Clinical Studies of Anti-Tumour Necrosis Factor in Sepsis 172
Zabel, P.; Greinert, U.; Entzian, P.; Schlaak, M. (Borstel): Effects of Pentoxifylline on Circulating Cytokines (TNF and IL-6) in Severe Pulmonary Tuberculosis 178
Waage, A.; Steinshammer, S.; Liabakk, N.; Sundan, A.; Espevik, T. (Trondheim): Tumor Necrosis Factor in Infection and Leukemia 182

Tumor Necrosis Factor and Cancer

Gatanaga, T. (Irvine, Calif.); Granger, G.A. (Long Beach, Calif.): Basic and Clinical Studies of Soluble Tumor Necrosis Factor/Lymphotoxin Receptors 187
Aderka, D. (Tel Aviv); Engelmann, H.; Wallach, D. (Rehovot): Soluble Tumor Necrosis Factor Receptors in Health and Disease 191
Soma, G.-I; Mizuno, D.-I. (Kawasaki): Further Developments of the Therapy with Lipopolysaccharides of a Small Molecular Size on Various Intractable Diseases. A New Version of Coley’s Toxin 203
Fraker, D.L.; Norton, J.A. (Bethesda, Md.): The Role of Tumor Necrosis Factor in the Toxicity and the Antineoplastic Activity of Interleukin-2 Immunotherapy 221
Brouckaert, P.; Everaertd, B.; Libert, C.; Takahashi, N.; Cauwels, A.; Fiers, W. (Gent): Strategies to Broaden the Therapeutic Margin of Tumor Necrosis Factor 226

Liénard, D. (Lausanne); Eggermont, A.M.M. (Rotterdam); Schraffordt Koops, H. (Groningen); Lejeune, F.J. (Lausanne): High Dose of rTNF, rIFN and Melphalan in Isolation Perfusion Produce 90% Complete Response in Melanoma in Transit Metastases 233

Eggermont, A.M.M. (Rotterdam); Liénard, D. (Lausanne); Schraffordt Koops, H. (Groningen); Rosenkaimer, F. (Ingelheim); Lejeune, F.J. (Lausanne): Treatment of Irresectable Soft Tissue Sarcomas of the Limbs by Isolation Perfusion with High Dose TNF in Combination with Interferon- and Melphalan 239

Lejeune, F.; Liénard, D. (Lausanne); Eggermont, A.M.M. (Rotterdam); Renard, N.; Gérain, J. (Brussels): Evidence for Early Intratumoral Endothelium Activation, IL-6 Production and High Systemic TNF Levels after Isolation Perfusion with High Dose rTNF Associated with rIFN 244

Subject Index 249

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Preface

The 4th International Conference on Tumor Necrosis Factor and Related Cytokines was held from May 2 to 6, 1992, in Veldhoven, The Netherlands. In an amazingly brief time since its cloning in 1984, TNF has acquired a center stage role and has become recognized as perhaps the most important cytokine in health and disease. This is amply demonstrated by the plenary talks of the Conference, the text of which has been compiled in this volume, and also by the many abstracts presented at the Meeting [published in European Cytokine Network, Vol. 3, No. 2, 1992].

As before, the time interval between the previous TNF Conference at Chiba, Japan, and this one at Veldhoven was 18 months, and yet it is amazing how much progress has been achieved during this period. It would be futile and unfair to try to draw attention here to some highlights of the Meeting. The overwhelming impression is that the field of TNF research and related cytokines has now fully matured. In the past, occasional hints or preliminary evidence surfaced for a TNF involvement in one or other (patho) physiological phenomenon, but these and many more indications have now been fully ascertained and documented.

A number of contributions in this volume deal with the two soluble TNF receptors derived from the small TNF receptor (TNF-R55) and the large receptor (TNF-R75). Soluble TNF receptor release is becoming recognized as an important physiological response process and their concentration profoundly affects the pharmacokinetics and bioavailability of TNF present in circulation. The strong conservation of the TNF gene in the animal
kingdom is already an indication for its important role in various physiological phenomena, ranging from early embryogenesis to parturition, immune responses, antiviral, antibacterial and antiparasitic activities, neuron transmission, and finally programmed cell death. But overproduction is clearly the source of various pathophysiological phenomena and diseases, such as

Preface X

rheumatoid arthritis, ischemia-reperfusion damage, graft-versus-host disease, cerebral malaria, and many more disease states, as described in this volume.

The interest in TNF was originally based, to a large extent, on its potential as an antitumor agent. But it is fair to say that, because of toxicity, the clinical results obtained so far regarding the systemic use of TNF have been disappointing. However, the clinical approaches, described in this volume, involving the use of TNF in combination with IFN and a chemotherapeutic drug in isolated limb perfusion, have achieved a spectacular success rate.

This volume gives an up-to-date overview of the latest progress regarding all aspects of TNF, lymphotoxin, and their receptors, ranging from basic chemistry, gene structure, biochemical mechanism of action and cellular responses, to the involvement of TNF and its membrane-bound and soluble receptors in various infectious, autoimmune and malignant cell diseases. We hope that this volume will convey to the reader some of the pleasure and excitement which was evident at the Meeting, where so much excellent science and biomedical progress were witnessed.

W. Fiers
W.A. Buurman