Interferon
Properties, Mode of Action, Production, Clinical Application

Beiträge zur Onkologie
Contributions to Oncology

Vol. 11

Series Editors
S. Eckhardt, Budapest; J. H. Holzner, Wien; G. A. Nagel, Göttingen

S. Karger • Basel • München • Paris • London • New York • Sydney


Interferon
Properties, Mode of Action, Production, Clinical Application

Volume Editors
K. Munk and H. Kirchner, Heidelberg

50 figures and 70 tables, 1982

S. Karger Basel • München • Paris • London New York Sydney

Beiträge zur Onkologie
Contributions to Oncology

Herausgeber: D. Füllenbach, Freiburg i. Br.; G. A. Nagel, Göttingen; S. Seeber, Essen

Editors: J. H. Beyer, Göttingen; H. Borberg, Köln; Ch. Fuchs, G. A. Nagel, Göttingen
Drug Dosage
The author and 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 1982 by S. Karger AG, P. O. Box, CH-4009 Basel (Switzerland)
Printed in Germany
ISBN 3-8055-3482-5

Contents

Preface VII

Friedman, R. M.; Czarniecki, C. W.; Epstein, D. A. (Bethesda, Maryland); Jay, F. T. (Winnipeg, Manitoba); Maheshwari, R. K.; Sreevalsan, T. (Washington, D. C.), and Panet, A. (Jerusalem): Mechanisms of Interferon Action on Cell Growth and on Murine Leukemia, Vesicular Stomatitis, and
Encephalomyocarditis Viruses 1
Jungwirth, C.; Strube, W.; Strube, M.; Kroath, H. (Würzburg), and Graf, T. (Heidelberg): Interferon Inhibits the Establishment of Fibroblast Infection by Avian Retroviruses 11
Lucero, M. A.; Magdelenat, H.; Fridman, W. H.; Pouillart, P.; Billardon, C. (Paris); Billiau, A. (Leuven); Cantell, K. (Helsinki), and Falcoff E. (Paris): Pharmacological Properties of Human Alpha and Beta Interferons 17
Fleischmann, W. R., Jr. (Galveston, Texas): Interferon Potentiation: Antiviral and Antitumor Studies 53
De Maeyer-Guignard, J.; Dandoy, F., and De Maeyer, E. (Orsay): Host Genotype Influences Interferon Action in the Mouse 73
Burke, D. C. (Coventry, Warwickshire): A Monoclonal Antibody against Interferon-Alpha 83
Hochkeppel, H. K.; Menge, U., and Collins, J. (Braunschweig): Monoclonal Antibodies against Human Fibroblast Interferon 94
Sulkowski, E. (Buffalo, New York) and Goeddel, D. V. (South San Francisco, California): Hydrophobicity of Human Interferons 106

Contents VI
Berg, K.; Hokland, M., and Heron, I. (Aarhus): Biological Activities of Pure HuIFN-a Species 118
Knight, E., Jr.; Blomstrom, D. C. (Wilmington, Delaware), and Hunkapiller, M. W. (Pasadena, California): Characterization of Human (β) Fibroblast Interferon 127
Krammer, P. H.; Kees, U.; Marcucci, F., and Kirchner, H. (Heidelberg): Immune Interferon Production by T-Cell Clones 144
Vilek, J.; Yip, Y. K. (New York), and Pang, R. H. L. (Rockville, Maryland): Induction and Characterization of Human Immune (Gamma) Interferon 150
Oettgen, H. F. and Krown, S. E. (New York): Clinical Trials of Human Leukocyte Interferon at the Memorial Sloan-Kettering Cancer Center 159
Preface

The Deutsche Krebshilfe was founded by Dr. Mildred Scheel as a private foundation. The reaction and response of the German people to this foundation, which is dedicated to finding solutions for this urgent medical problem, has been very great. The Deutsche Krebshilfe received, throughout the years, money from individual private donors, legacies, and many other sources. The enthusiastic donations by the population have never ceased since the start of the foundation and continue in a way which gives reason to admire the goodwill of the people.

However, in regard to this money donated to the Deutsche Krebshilfe, there are, of course, great demands placed upon these persons, particularly on Dr. Scheel and her scientific and organizational advisors, and suggestions on how to make the best use of these donations. The people expect, of course, this money to be given to the discovery of solutions to the most urgent problems in the medical care of cancer and to the most fruitful projects in cancer research. In regard to this challenge, the Deutsche Krebshilfe always followed one main goal, that is the idea that a private foundation should always be innovative. It should always start and support projects which are...
new, which cannot be started because of the lack of official initiative, or because of the lack of official financial support, or because there are administrative barriers which inhibit or retard the tackling of urgent projects. These goals, however, require the persistent efforts and the expertise of those who are asked to advise the Deutsche Krebshilfe. In addition, since the cancer problem is international and the fight against cancer needs a combined international effort, a comprehensive, world-wide group of experts is needed. The Deutsche Krebshilfe always sought the advice of international experts in order to help the foundation work best for the benefit of the cancer patients of today and tomorrow. The meetings of experts, of which this was the third one, are examples for the international and comprehensive discussions on the aims and tasks of the Deutsche Krebshilfe. The idea to devote this meeting to interferon is Dr. Scheel’s because she was frequently approached by patients to supply the financial means for individual interferon therapies. Since the interferon problem is, at present, extensively discussed within the community of scientists as well as the laypress, Dr. Scheel again sought the advice of internationally recognized experts in this field. She expects, from the results of this meeting, the best possible clarification and an expert evaluation of the significance of interferon therapy, particularly in comparison with other forms of cancer treatment. During the past year, the interferon field has exploded scientifically. Some of the dynamite workers involved were at this meeting. The reasons for the enormous progress in interferon research have been basically threefold; First, there have been breakthroughs in the protein chemistry and the molecular biology of interferon. Thus, it is now proven that interferons are a class of different proteins, and the amino acid sequence of some has been identified. We want to stress the following: Interferons are a group of defined proteins with exceedingly high biologic activities in different systems. Secondly, it has been possible to introduce and express the gene of human interferon in E.coli. This may be a promising way towards producing interferon in sufficient quantities. Most excitingly, the E. coli product seems to share many of the known properties of human
interferon.
Thirdly, there has been a tremendous clinical interest in interferon due to the possibility that interferon may be of some use in the treatment of neoplastic disease.
Please note that we have used the term may. It was obviously one of the purposes of this meeting to achieve a critical evaluation of the available clinical data.

When a research field explodes, as it has happened to interferon research, people working in the field may have a twofold reaction, and this applies to those who have worked in the field for ten or more years, particularly our distinguished guests.
On the one side, it is a good feeling to realize that the scientific community finally acknowledges the importance of something of which we have been convinced for quite a while.
On the other side, one is afraid when there is too much uncritical enthusiasm, particularly when something as serious as the treatment of cancer is involved and when the lay-press begins to be interested.
Now, in this situation, we feel that we owe the public clear-cut statements about the state of affairs. Dr. Scheel is very concerned about these matters.
As it has happened often in cancer medicine, so-called new forms of therapy have raised much optimism, then failed, and subsequently seriously blocked future developments. In such situations, short-cuts to practical medicine have turned out to be disasters.
All of us are convinced that interferons are of tremendous biologic significance. Interferons may turn out to be of clinical value but we are far from having a sound evaluation on this point. We want to stress, however, that most likely no progress will be made unless the way is paved by thorough research in the laboratories. Clinical application of interferons would probably have never occurred if scientists did not treat mice with interferons about ten years ago. Similarly, we believe that future therapeutic improvements will depend on the progress made in laboratories. Furthermore, in regard to clinical studies, the very least we have to postulate is that therapeutical trials are accompanied by thorough clinical investigations so that we may learn more about the pharmacokinetics of interferons and many other things. Otherwise, the therapeutic trials may turn out to be useless and extremely costly.
The editors acknowledge the competent assistance of Ms. Marion
Kasamasch.

Heidelberg, 1981

Klaus Munk

Holger Kirchner