

**MOLECULAR BIOLOGY  
OF HEMOPOIESIS**

# ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Editorial Board:

NATHAN BACK, *State University of New York at Buffalo*

IRUN R. COHEN, *The Weizmann Institute of Science*

DAVID KRITCHEVSKY, *Wistar Institute*

ABEL LAJTHA, *N. S. Kline Institute for Psychiatric Research*

RODOLFO PAOLETTI, *University of Milan*

---

## Recent Volumes in this Series

Volume 234

**BIOLOGY OF GROWTH FACTORS: Molecular Biology, Oncogenes,  
Signal Transduction, and Clinical Implications**

Edited by Jeffrey E. Kudlow, David H. MacLennan, Alan Bernstein,  
and Avrum I. Gotlieb

Volume 235

**CENTRAL D<sub>1</sub> DOPAMINE RECEPTORS**

Edited by Menek Goldstein, Kjell Fuxe, and Irving Tabachnick

Volume 236

**NEURORECEPTORS AND SIGNAL TRANSDUCTION**

Edited by Shozo Kito, Tomio Segawa, Kinya Kuriyama,  
Masaya Tohyama, and Richard W. Olsen

Volume 237

**HISTOPHYSIOLOGY OF THE IMMUNE SYSTEM: The Life History,  
Organization, and Interactions of Its Cell Populations**

Edited by Sigbjørn Fossum and Bent Rolstad

Volume 238

**BIOTECHNOLOGICAL APPLICATIONS OF LIPID MICROSTRUCTURES**

Edited by Bruce Paul Gaber, Joel M. Schnur, and Dennis Chapman

Volume 239

**HOST DEFENSES AND IMMUNOMODULATION TO  
INTRACELLULAR PATHOGENS**

Edited by Toby K. Eisenstein, Ward E. Bullock, and Nabil Hanna

Volume 240

**PROTEASES: Potential Role in Health and Disease II**

Edited by Walter H. Hörl and August Heidland

Volume 241

**MOLECULAR BIOLOGY OF HEMOPOIESIS**

Edited by Mehdi Tavassoli, Esmail D. Zanjani, Joao L. Ascensao,  
Nader G. Abraham, and Alan S. Levine

---

A Continuation Order Plan is available for this series. A continuation order will bring delivery of each new volume immediately upon publication. Volumes are billed only upon actual shipment. For further information please contact the publisher.

# MOLECULAR BIOLOGY OF HEMOPOIESIS

Edited by

**Mehdi Tavassoli**

Veterans Administration Medical Center  
University of Mississippi  
Jackson, Mississippi

**Esmail D. Zanjani**

Veterans Administration Medical Center  
University of Nevada  
Reno, Nevada

**Joao L. Ascensao and**

**Nader G. Abraham**

New York Medical College  
Valhalla, New York

and

**Alan S. Levine**

National Heart, Lung, and Blood Institute  
Division of Blood Diseases and Resources  
Bethesda, Maryland

PLENUM PRESS • NEW YORK AND LONDON

---

Library of Congress Cataloging in Publication Data

Symposium on Molecular Biology of Hemopoiesis (3rd: 1987: Rye Brook, N.Y.)

Molecular biology of hemopoiesis / edited by Mehdi Tavassoli . . . [et al.].

p. cm. — (Advances in experimental medicine and biology; v. 241)

“Proceedings of the Third Annual Symposium on Molecular Biology of Hemopoiesis, held November 6–7, 1987, in Rye Brook, New York” — T.p. verso.

Dedicated to the centennial of the National Institutes of Health.

Includes bibliographies and index.

ISBN 978-1-4684-5573-1

ISBN 978-1-4684-5571-7 (eBook)

DOI 10.1007/978-1-4684-5571-7

1. Hematopoiesis—Congresses. 2. Molecular biology—Congresses. 3. National Institutes of Health (U.S.)—Congresses. I. Title. II. Series.

[DNLM: 1. Hematopoiesis—congresses. 2. Hematopoietic Stem Cells—congresses. 3. Molecular biology—congresses. W1 AD559 v. 241 / WH 140 S9894m 1987]

QP92.S95 1987

612'.41—dc19

DNLM/DLC

88-28836

for Library of Congress

CIP

---

Proceedings of the Third Annual Symposium on Molecular Biology of Hemopoiesis, held November 6–7, 1987, in Rye Brook, New York

© 1988 Plenum Press, New York

Softcover reprint of the hardcover 1st edition 1988

A Division of Plenum Publishing Corporation

233 Spring Street, New York, N.Y. 10013

All rights reserved

No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise, without written permission from the Publisher

## PREFACE

Perhaps no scientific field in recent years has gained in techniques and applications as much as molecular biology, and it is certainly no exaggeration to say that among all the applications of molecular biology, hematology in general, and hemopoiesis in particular, have benefited most. Owing to the applications of molecular biology, we now live in a golden era of hemopoiesis. Our understanding of the intricate regulatory system in hemopoiesis has vastly expanded. The potential for future exploration is ever expanding, and finally, the possibility of gene manipulation, has provided the promise of fundamental treatment and "cure" of many genetic disorders involving hemopoietic cells.

In the ambiance of this rapidly moving scientific era, the necessity for review of what is being accomplished and where the technical potential is taking us needs no argument. This volume presents the proceedings of the third annual symposium on the Molecular Biology of Hemopoiesis, held in the Rye Town Hilton, New York, November 6 and 7, 1987, under the auspices of New York Medical College, Valhalla, New York. The fact that this was the third regular symposium covering this area in itself testifies to a need for exchange of the rapidly developing knowledge in this area. But this third symposium also coincided with the centennial of the National Institutes of Health and consequently the symposium was dedicated to this festive occasion. Biomedical scientists are an argumentative lot; but no one can argue that without generous help and direction from NIH, the impressive advances of the past century would not have been possible in biomedical sciences. Hence, it is only appropriate that in the present volume Dr. David Badman of NIH provides us with a historical role of NIH in biomedical research and Dr. Alan Levine of NIH concludes the conference with some remarks on the future perspective of biomedical research and the role of NIH.

The organizing committee are particularly indebted to Dr. Richard Levere, Chairman of the Department of Medicine at New York Medical College, without whose support this meeting would have not been possible. The organizers are also grateful to Leukemia Society of America (Westchester Chapter); Toyobo Co., Ltd.; Merck, Sharp and Dohme; Coulter Electronics; and Upjohn Laboratories for their financial support.

The Editors

CONTENTS

OPENING REMARKS

Historical Role of the National Institutes of Health in Biomedical Research.....	1
David Badman	
A Tribute to the National Institutes of Health.....	7
William Curry Moloney	

GENETIC CONSIDERATIONS

Retroviral Transfer of Genes into Canine Hematopoietic Progenitor Cells.....	9
F. Schuening, R. Storb, R. Nash, R.B. Stead, W.W. Kwok and A. D. Miller	
Retroviral-Mediated Gene Transfer into Hemopoietic Cells.....	19
M.A. Eglitis, P.W. Kantoff, D.B. Kohn, E. Karson, R.C. Moen, C.D. Lothrop, Jr., R.M. Blaese and F. Anderson	
Retroviral Gene Transfer: Applications to Human Therapy.....	29
E. Gilboa	
Construction of a Safe and Efficient Retrovirus Packaging Cell Line.....	35
D. Markowitz, S. Goff and A. Bank	
Lineage Specific Expression of a Human B-Globin Gene in Murine Bone Marrow Transplant Recipient.....	41
E.A. Dzierzak and R.C. Mulligan	
A Comparison of Methods for Analysis of mRNA in Hematopoietic Cells: Conventional and Clonal Northern Analysis and in Situ Hybridization.....	45
C. L. Castiglia	
Haemopoietic Regulation and the Role of the Macrophage in Erythropoietic Gene Expression.....	55
I.N. Rich	
Molecular Implications of Ph (+) Myelodysplastic Syndrome.....	67
T. Keisuke, O. Kasuma and O.H. Junko	

Evaluation of C-SIS mRNA Expression by Human Megakaryocytic Cells in Normals and Patients with Myeloproliferative Disorders.....	73
L. Kanz, R. Mielke, A.A. Fauser and G.W. Lohr	
Expression of Specific Isoforms of Protein 4.1 in Erythroid and Non-Erythroid Tissues.....	81
T.K. Tank, T.L. Leto, V.T. Marchesi and E.J. Benz, Jr.	
Expression of Heme Oxygenase Gene in Hemopoiesis.....	97
N.G. Abraham, S.M. Mitrione, W.J.B. Hodgson, R. D. Levere and S. Shibahara	
Regulation of Fetal Globin Gene Expression in Human Erythroleukemia (K562) Cells.....	117
M. Donovan-Peluso, D. O'Neill, S. Acuto and A. Bank	
Human Gene Expression in Murine Hemopoietic Cells In Vivo.....	123
F.A. Fletcher, K.A. Moore, G.R. MacGregor, J.W. Belmont and C. T. Caskey	
CELLULAR CONSIDERATIONS	
Homing of Hemopoietic Stem Cells to Hemopoietic Stroma.....	129
C.L. Hardy and M. Tavassoli	
The Significance of Free Radicals and Free Radical Scavengers in L1210 Leukemia.....	135
A.C. Brown, and J.D. Lutton	
Exogenous and Endogenous Regulators of Human Megakaryocytopoiesis.....	149
A.M. Gewirtz	
Detection of a Human Hemopoietic Progenitor Cell Capable of Forming Blast Cell Containing Colonies In Vitro.....	165
J. Brandt, L. Lu, E.B. Walker and R. Hoffman	
Studies of Murine Megakaryocyte Colony Size and Ploidization.....	175
G.M. Segal	
Factors Regulatory Megakaryocytopoiesis and Platelet Formation.....	183
A. Tsutomu, J.P. Fuhrer, M.D. Bregman, A. Kuramoto and M. J. Murphy, Jr.	
Effect of Sustained Hypertransfusion of Rauscher Leukemia Virus-Variant A (RLV-A) Infection in BALB/c Mice.....	191
G.P. Leonardi, M. Manthos, J. LoBue, D. Orlic and J. Mitra	
Role of Immunocompetent Cells in the Regulation of Human Megakaryocytopoiesis In Vitro.....	199
R.A. Detrick, J.C. Schulman, S.W. Mamus, R.P. McEver and E. D. Zanjani	
The Effect of Prostaglandin E <sub>1</sub> on Megakaryocyte Proliferation In Vitro.....	217
G.W. Cooper and X.P. Hou	

Parabiotic Demonstration of a Substance Released from Burned Tissue Affecting Marrow Megakaryocyte Diameter and Number in Mice.....	225
G.D. Kalmaz, M.M. Guest and E.E. Kalmaz	

GROWTH FACTORS

Preclinical and Clinical Effects of the Hematopoietic Colony Stimulating Factors.....	233
H.E. Broxmeyer, S. Vadhan-Raj, Giao Hangoc, L. Lu, J.E. Gutterman and D.E. Williams	
Current Status of Thrombopoietin	
T.P. McDonald.....	243
Abnormalities of the Hematopoietic Regulatory Network.....	255
G.C. Bagby, Jr., B. Wilkinson, E. McCall and M. Lee	
Growth Factor-Related Mechanisms of Leukemogenesis.....	265
J.W. Schrader, K.B. Leslie, I. Clark-Lewis, H.J. Ziltener and S. Schrader	
Stimulation of Early and Late Erythropoietic Progenitor Cells by Insulin: Evidence for Different Mechanisms.....	273
G. Konwalinka, C.J. Wiedermann, A. Petzer, K. Grunewald, C. Breier, J. Patsch and D. Geissler	
Serine Proteases Promote Human CFU-GM in Methylcellulose Culture Systems.....	281
S. Gross, D.A. Worthington-White and C.M. Smith	
Molecularly Characterized Factors Governing the Growth of Murine Multipotent Stem Cells in Serum-Depleted Marrow Cultures.....	289
F.C. Monette and G. Sigounas	
Marrow Reticulo-Fibroblastoid Colonies (CFU-RF Derived) Spontaneously Release an Erythroid Colony (BFU-E) Enhancing Factor.....	303
C.A. Izaguirre, W.M. Ross and E.Y. Hsu	
Increased BPA Production Modulates EPO Sensitivity of Circulating BFU-E in Sickle Cell Anemia.....	311
H. Croizat and R.L. Nagel	
Production of Erythropoietin by an Established Human Renal Carcinoma Cell Line: In Vitro and In Vivo Studies.....	319
D. Shouval and J.B. Sherwood	

CLOSING REMARKS

Concluding Remarks and Future Directions	
A.S. Levine.....	329
Index.....	335





President Franklin D. Roosevelt is dedicating the present  
campus of NIH on October 31, 1940.