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**ADVANCES IN  
NEUROBLASTOMA  
RESEARCH 2**

**EDITORS: Audrey E. Evans  
Giulio J. D'Angio  
Alfred G. Knudson  
Robert C. Seeger**

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# ADVANCES IN NEUROBLASTOMA RESEARCH 2

Proceedings of the Fourth Symposium on Advances in Neuroblastoma  
Research Held in Philadelphia, Pennsylvania, May 14-16, 1987

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71 / QZ 380 S989 1987a]  
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## Contents

Contributors . . . . .	xiii
Preface	
Audrey E. Evans . . . . .	xxiii
Acknowledgments . . . . .	xxvii
<b>ONCOGENES</b>	
<b>Molecular Analysis and Clinical Significance of <i>N-myc</i> Amplification and Chromosome 1P Monosomy in Human Neuroblastomas</b> Garrett M. Brodeur, Chin-to Fong, Michon Morita, Rogers Griffith, F. Ann Hayes, and Robert C. Seeger . . . . .	3
<b>Human Neuroblastoma Metastases in a Nude Mouse Model: Tumor Progression and Onc Gene Amplification</b> Fred Gilbert, Kwei-Lan Tsao, Faustina LaLatta, Ling Xu, V.R. Potluri, and Gundula LaBadie . . . . .	17
<b>Biological Characteristics of <i>N-myc</i> Amplified Neuroblastoma in Patients Over One Year of Age</b> Akira Nakagawara, Keiichi Ikeda, Tohru Tsuda, and Ken Higashi . . . . .	31
<b>Expression of <i>N-myc</i> by Neuroblastomas With One or Multiple Copies of the Oncogene</b> Robert C. Seeger, Randal Wada, Garrett M. Brodeur, Thomas J. Slamon, Robert L. Bjork, Lawrence Sousa, and Dennis J. Slamon . . . . .	41
<b>Discussion: Oncogenes . . . . .</b>	51
<b>Characterization of Human Neuroblastoma Cell Lines That Lack <i>N-myc</i> Gene Amplification</b> Randal K. Wada, Robert C. Seeger, Garrett M. Brodeur, Dennis J. Slamon, Sylvia A. Rayner, Mary M. Tomayko, and C. Patrick Reynolds . . . . .	57
<b>Analysis of a Novel Locus Frequently Co-Amplified With <i>N-myc</i> in Human Neuroblastoma</b> Kate T. Montgomery and Peter W. Melera . . . . .	71
<b>Discussion: Oncogenes . . . . .</b>	89
<b><i>N-myc</i> Protein Expression by Neuroblastoma Cells That Have Metastasized to Bone Marrow</b> Thomas J. Moss, Yuk M. Law, Dennis J. Slamon, Garrett M. Brodeur, and Robert C. Seeger . . . . .	91

Prog  
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 ADV  
 RES  
 Proc  
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 chil  
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 cal  
 tion  
 stu  
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 tic  
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 in  
 cel  
 nic  
 tor  
 IS

viii / Contents

**Modulation of N-myc Expression, but Not Tumorigenicity, Accompanies Phenotypic Conversion of Neuroblastoma Cells in Prolonged Culture**  
 Richard W. Michitsch, June L. Biedler, and Peter W. Mclera . . . . . 103

**Rearrangement Dynamics Involved in Gene Amplification in Human Neuroblastoma Cells**  
 Hiroyuki Shimatake, Takanobu Kikuchi, Chizuru Abe-Nakagawa, Naotoshi Kanda, and Yoshiaki Tsuchida . . . . . 121

**Expression and Localization of the N-myc Protein in Human Neuroblastoma Cells: Analysis of the Effect of Gamma Interferon Treatment and Distribution of the N-myc Protein in the Nucleus**  
 Naohiko Ikegaki, Katarina Polakova, Laura Prince, and Roger H. Kennett . . . . . 133

**Discussion: Oncogenes** . . . . . 145

**N-myc: Studies on Gene Amplification/Expression and the Development of a Non-Isotopic Technique for Gene Mapping**  
 J.A. Garson, J. van den Berghe, P. Sheppard, and J.T. Kemshead . . . . . 151

**The neu Gene in 4 Human Neuroblastoma Cell Lines**  
 Henry C. Maguire, Jr., Erica Sibinga, David Weiner, and Mark Greene . . . . . 165

**Chromogranin A Expression in Childhood Peripheral Neuroectodermal Tumors**  
 Mark J. Cooper, Lee J. Helman, Audrey E. Evans, Sudha Swamy, Daniel T. O'Connor, Lawrence Helson, and Mark A. Israel . . . . . 175

**Developmentally Regulated Genes in Neuroblastoma**  
 Carol J. Thiele, Lorraine Cazenave, Joseph B. Bolen, and Mark A. Israel . . . . . 185

**Discussion: Oncogenes** . . . . . 195

**BONE MARROW TRANSPLANTATION**

**Bone Marrow Transplantation for Poor Prognosis Neuroblastoma**  
 Robert C. Seeger, Thomas J. Moss, Stephen A. Feig, Carl Lenarsky, Michael Selch, Norma Ramsay, Richard Harris, John Wells, Harland Sather, and C. Patrick Reynolds . . . . . 203

**Bone Marrow Transplantation (BMT) for Advanced Neuroblastoma (NBL): A Multicenter POG Pilot Study**  
 J. Graham-Pole, A.P. Gee, S. Gross, J. Casper, M. Graham, W. Harvey, N. Kapoor, P. Koch, N. Mendenhall, D. Norris, T. Pick, and P. Thomas . . . . . 215

**Very Long Delay to Engraftment After ABMT in Neuroblastoma Patients and Effect of CD8 Monoclonal Antibody In Vivo Therapy**  
 M.C. Favrot, T. Philip, V. Combaret, P. Biron, J. Morisset, and A. Bernard . . . . . 225

**In Vitro Treatment of Autologous Bone Marrow for Neuroblastoma Patients With Anti G<sub>D2</sub> Monoclonal Antibody and Human Complement: A Pilot Study**  
 Jerry Stein, Sarah Strandjord, Ulla Saarinen, Phyllis Warkentin, Stanley Gerson, Hillard Lazarus, Daniel Von Hoff, Peter Coccia, and Nai-Kong Cheung . . . . . 237

**Sensitive Detection of Rare Metastatic Human Neuroblastoma Cells in Bone Marrow by Two-Color Immunofluorescence and Cell Sorting**  
 Christopher N. Frantz, Daniel H. Ryan, Nai-kong V. Cheung, Reggie E. Duerst, and David C. Wilbur . . . . . 249

origenicity, Accompanies in Prolonged Culture V. Melera . . . . .	103
differentiation in Human Nishibe-Nakagawa, Yoshitaka . . . . .	121
role in Human Neuroblastoma in Treatment and Prognosis and Roger H. Kennett . . . . .	133
in the Development of a Neuroblastoma John T. Kemshead . . . . .	151
Genes John T. Kemshead, John T. Kemshead, and Mark Greene . . . . .	165
Central Neuroectodermal Neuroblastoma Sudha Swamy, Mark A. Israel . . . . .	175
Neuroblastoma in Culture Sudha Swamy, Mark A. Israel . . . . .	185
Neuroblastoma in Culture Sudha Swamy, Mark A. Israel . . . . .	195
Neuroblastoma in Culture Sudha Swamy, Mark A. Israel . . . . .	203
Neuroblastoma (NBL): Clinical Features Graham W. Harvey, John T. Kemshead, and P. Thomas . . . . .	215
Neuroblastoma Patients in Culture John T. Kemshead, and A. Bernard . . . . .	225
Neuroblastoma Patients in Culture John T. Kemshead, and A. Bernard . . . . .	237
Neuroblastoma Cells in Bone Marrow John T. Kemshead, and Reggie E. Duerst . . . . .	249

## DIFFERENTIATION AND CELL BIOLOGY

Transdifferentiation of Human Neuroblastoma Cells Results in Coordinate Loss of Neuronal and Malignant Properties June L. Biedler, Barbara A. Spengler, Tien-ding Chang, and Robert A. Ross . . . . .	265
Differential Expression of Intermediate Filaments and Fibronectin in Human Neuroblastoma Cells Robert A. Ross, Valentina Ciccarone, Marian B. Meyers, Barbara A. Spengler, and June L. Biedler . . . . .	277
Biological Classification of Cell Lines Derived From Human Extra-Cranial Neural Tumors C. Patrick Reynolds, Mary M. Tomayko, Ludvik Donner, Lawrence Helson, Robert C. Seeger, Timothy J. Triche, and Garrett M. Brodeur . . . . .	291
Induction of Catecholamine Fluorescence in Human Neuroblastoma Cell Lines Transplanted Into Nude Mice Mary M. Tomayko, Timothy J. Triche, Robert W. Newburgh, and C. Patrick Reynolds . . . . .	307
"In Situ" Modulation of Murine Neuroblastoma Growth and Biochemical Differentiation by the Adrenergic Nervous System and Nerve Growth Factor Bernard L. Mirkin, Donald W. Fink, Jr., and Robert F. O'Dea . . . . .	317
5-Bromo-2'-Deoxyuridine Induces S 100 Protein in Human Neuroblastoma Cells in Culture Kentaro Tsunamoto, Shinsaku Imashuku, Shigeyoshi Hibi, Noriko Esumi, and Kanefusa Kato . . . . .	327
Neuronal Differentiation of Human Neuroblastoma Cells by a Novel Synthetic Polyprenoic Acid Tohru Sugimoto, Tadashi Sawada, Takafumi Matsumura, Yoshihiro Horii, Tamaki Hino, John T. Kemshead, Yoshikazu Suzuki, Masaaki Okada, and Osamu Tagaya . . . . .	337
Removal of Polypeptides From Human Neuroblastoma Antigen Does Not Alter Recognition by Monoclonal Antibody PI 153/3 Jennifer P. Boyd and Mary Catherine Glick . . . . .	353
Discussion: Differentiation and Cell Biology . . . . .	359
Neuroblastoma Genes in <i>Drosophila</i> and Hereditary Suppression of Tumor Development by Gene Transfer Bernard M. Mechler . . . . .	377
Distinctive Membrane Phenotypes of Neuroblastoma Cells and Fetal Neuroblasts by a Panel of Monoclonal Antibodies Takafumi Matsumura, Tohru Sugimoto, Tadashi Sawada, Tohru Saida, and John T. Kemshead . . . . .	395
Biological Significance of HLA-A,B,C Expression in Neuroblastoma and Related Cell Lines Lois A. Lampson . . . . .	409
Monoclonal Antibodies as Probes for $\beta$ -D-N-Acetylglucosaminide $\alpha$ 1 $\rightarrow$ 3Fucosyltransferase in Human Neuroblastoma Christopher S. Foster and Mary Catherine Glick . . . . .	421

F  
V  
A  
F  
F  
A  
F  
C  
C  
C  
C  
C  
C  
C  
C

x / Contents

**Discussion: Differentiation and Cell Biology** . . . . . 433

**Effect of Cytosine Arabinoside on the Growth and Phenotypic Expression of GI-ME-N, a New Human Neuroblastoma Cell Line**  
M. Ponzoni, A. Melodia, C. Cirillo, A. Casalaro, and P. Cornaglia-Ferraris . . . . . 437

**Evidence for Reverse Transformation in Multidrug-Resistant Human Neuroblastoma Cells**  
Marian B. Meyers and June L. Biedler . . . . . 449

**Olfactory Neuroblastoma Is Not a Neuroblastoma but Is Related to Primitive Neuroectodermal Tumor (PNET)**  
Andrea O. Cavazzana, Samuel Navarro, Rosa Noguera, C. Patrick Reynolds, and Timothy J. Triche . . . . . 463

**N-myc Protein Expression in Small Round Cell Tumors**  
Timothy J. Triche, A.O. Cavazzana, S. Navarro, C.P. Reynolds, D.J. Slamon, and R.E. Seeger . . . . . 475

**Ewing's Sarcoma Is an Undifferentiated Neuroectodermal Tumor**  
Andrea O. Cavazzana, John L. Magnani, Robert A. Ross, J. Miser, and Timothy J. Triche . . . . . 487

**Discussion: Differentiation and Cell Biology** . . . . . 499

**CLINICAL STUDIES AND INNOVATIVE THERAPIES**

**International Criteria for Diagnosis, Staging and Response to Treatment in Patients With Neuroblastoma**  
Garrett M. Brodeur, Robert C. Seeger, Ann Barrett, Robert P. Castleberry, Giulio D'Angio, Bruno De Bernardi, Audrey E. Evans, Marie Favrot, Arnold I. Freeman, Gerald Haase, Olivier Hartmann, F. Ann Hayes, Larry Helson, John Kemshead, Fritz Lampert, Jacques Ninane, Thierry Philip, Jon Pritchard, Stuart Siegel, Ide E. Smith, and P.A. Voute . . . . . 509

**Mass Screening for Neuroblastoma in Infancy**  
T. Sawada, T. Sugimoto, T. Matsumura, A. Tunoda, T. Takeda, K. Yamamoto, R. Koide, N. Nagahara, Y. Hanawa, K. Nishihira, N. Sasaki, Y. Ishiguro, N. Nakata, I. Okabe, M. Kaneko, T. Yazawa, and H. Ando . . . . . 525

**Monoclonal Antibodies to the Small Round Cell Tumours of Childhood: An International Workshop**  
J.T. Kemshead . . . . . 535

**Bone Marrow Metastases in Children's Neuroblastoma Studied by Magnetic Resonance Imaging**  
Dominique Couanet, Anne Geoffray, Olivier Hartmann, Jérôme G. Leclère, and Jean D. Lumbroso . . . . . 547

**Elevation of Lumbar Cerebrospinal Fluid Catecholamine Metabolites in Patients With Cranial and/or Intracranial Metastatic Neuroblastoma**  
Bruce Bostrom and Bernard L. Mirkin . . . . . 557

.....	433	Discussion: Clinical Studies and Innovative Therapies .....	565
and Phenotypic Expression of ne		Phase II Studies of Combinations of Drugs with High Dose Carboplatin in Neuroblastoma (800 mg/m <sup>2</sup> to 1 g 250/m <sup>2</sup> ): A Report from the LMCE Group	
and P. Cornaglia-Ferraris ..	437	Thierry Philip, Jean-Claude Gentet, Christian Carrie, Anne Farge, Fathia Meziane, Eric Bouffet, Jean-Michel Zucker, Bernard Kremens, and Maud Brunat-Mentigny .....	573
ug-Resistant Human		Kinetics of Very High-Dose Cisplatin in Stage IV Neuroblastoma	
.....	449	J.C. Gentet, M. Charbit, J.L. Bernard, T. Philip, J.M. Zucker, V. Breant, C. Raybaud, and J.P. Cano .....	583
but Is Related to Primitive		Iodine 131 Labeled G <sub>D2</sub> Monoclonal Antibody in the Diagnosis and Therapy of Human Neuroblastoma	
iera, C. Patrick Reynolds,	463	Nai-Kong V. Cheung and Floro D. Miraldi .....	595
umors		Repeated Exposure of Non-Human Primates to Monoclonal Antibody and Fragments: Pharmacokinetic Studies and Their Implications for Targeted Therapy	
.P. Reynolds, D.J. Slamon,	475	L.S. Lashford, G. Elsom, J. Clarke, I. Gordon, and J.T. Kemshead .....	605
odermal Tumor		Immunotherapy With G <sub>D2</sub> Specific Monoclonal Antibodies	
Ross, J. Miser, and Timothy	487	Nai-Kong V. Cheung, M. Edward Medof, and David Munn .....	619
.....	499	Discussion: Clinical Studies and Innovative Therapies .....	633
.....			
<b>RAPIES</b>		<b><sup>131</sup>I-META-IODOBENZYLGUANIDINE THERAPY</b>	
Response to Treatment in		A Comparative Study of the Biodistribution of Meta-Iodobenzylguanidine (mIBG) and the Monoclonal Antibody UJ13A in Patients and Animal Models	
, Robert P. Castleberry,		L.S. Lashford, J. Clarke, I. Gordon, J. Pritchard, and J.T. Kemshead .....	643
ans, Marie Favrot,		The Therapeutic Use of I-131 Meta-Iodobenzylguanidine (mIBG) in Neuroblastoma: A Phase II Study in 12 Patients	
n, F. Ann Hayes,		Olivier Hartmann, Jean D. Lumbroso, Jean Lemerle, Martin Schlumberger, Marcel Ricard, Bernard Aubert, Sabine Coornaert, Louis Merlin, and Claude Parmentier .....	655
ues Ninane, Thierry Philip,		MIBG-Treatment in Neuroblastoma; Experiences of the Tübingen/Frankfurt Group	
Voute .....	509	J. Treuner, V. Gerein, Th. Klingebiel, D. Schwabe, U. Feine, J. Happ, D. Niethammer, F. Maul, R. Dopfer, B. Kornhuber, F. Berthold, H. Jürgens, and G. Hör .....	669
.....		Side Effects of Treatment with I-131-Meta-Iodobenzylguanidine (I-131- MIBG) in Neuroblastoma Patients	
....., T. Takeda, K. Yamamoto,		P.A. Vouïte, C.A. Hoefnagel, J. de Kraker, and M. Majoor .....	679
N. Sasaki, Y. Ishiguro,		Meta-Iodobenzylguanidine (mIBG) Scans in Neuroblastoma: Sensitivity and Specificity, A Review of 115 Scans	
I. Ando .....	525	Jean D. Lumbroso, Fadhel Guermazi, Olivier Hartmann, Sabine Coornaert, Yvon Rabarison, Jérôme G. Leclère, Dominique Couanet, Chantal Bayle, Jean M. Caillaud, Jean Lemerle, and Claude Parmentier .....	689
umours of Childhood: An			
.....	535		
stoma Studied by Magnetic			
ann, Jérôme G. Leclère, and	547		
.....			
olamine Metabolites in			
atic Neuroblastoma	557		
.....			

Proc  
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xii / Contents

**Pitfalls and Solutions in Neuroblastoma Diagnosis Using Radioiodine MIBG:  
Our Experience About 50 Cases**

J.F. Bouvier, T. Philip, P. Chauvot, M. Brunat Mentigny, F. Ducretet,  
N. Maïassi, and B.E. Lahneche . . . . . 707  
Discussion: <sup>131</sup>I-Meta-Iodobenzylguanidine Therapy . . . . . 721

Index . . . . . 727

ISBN 0



**: Using Radioiodine MIBG:**

tigny, F. Ducretet,	707
.....	721
py .....	727
.....	

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xiv / Contributors

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## Preface

This volume contains papers presented at the Fourth Symposium on Neuroblastoma Research held at The Children's Hospital of Philadelphia in May 1987. The preface to the previous volume noted an explosion in the basic research in human neuroblastoma starting at the beginning of this decade. At this fourth meeting, the number of people attending and the number of abstracts submitted (83) were similar to the 1984 meeting, but there was an increase in the depth of research, and larger numbers of papers reported results of molecular biological research.

The discussions, which occupied almost half of the total conference time, have been summarized by the chairperson of each session and are included after each group of papers dealing with a given topic.

The first day of the conference was devoted to studies of oncogenes, the second to cell biology and differentiation, and the third to innovative therapies. There were enough reports related to  $^{131}\text{I}$ -meta-iodobenzylguanidine ( $^{131}\text{I}$ -MIBG) to fill an entire afternoon. One evening during the conference was devoted to clinical studies of bone marrow transplantation for primary treatment of patients with neuroblastoma and for treatment of patients in relapse. Two international reports were presented during the clinical session, one devoted to a proposed international staging system for neuroblastoma (with response criteria) and another to a multi-center blind study on the reactivity of a panel of monoclonal antibodies on neuroblastoma and other small round-cell tumors of childhood.

The first six papers published here and two related discussion periods were devoted to amplification of *N-myc* and its biological characteristics. Two papers reported neuroblastoma cell lines that expressed only one copy of the *N-myc* oncogene. In a second session devoted to molecular genetics, *N-myc* protein expression was characterized, and one paper reported the immunologic characteristics of the *N-myc* protein as measured by monoclonal antibodies. The session included a paper on the *neu*-oncogene, originally discovered in rats and now studied in human neuroblastoma. Another participant reported alterations in gene expression during retinoic acid induced differentiation.

The papers in the second section of this volume are devoted to differentiation and various aspects of cell biology. Several papers address the changes in

various characteristics of the cells after differentiation, including expression of different proteins such as intermediate filament and fibronectin, S-100 protein induced by 5-bromo-2-deoxyuridine. One paper addresses neuronal differentiation by synthetic polyprenic acid and in situ modulation of murine neuroblastoma nerve growth factor.

In a major invited lecture, Dr. Bernard M. Mechler reported his and Elizabeth Gateff's extraordinary studies on the neuroblastoma genes in *Drosophila* and the hereditary expression of tumor development by gene transfer.

Monoclonal antibodies were used in several studies to determine various changes in the expression of the cell membrane. One presentation provided comparison of the membrane phenotypes of neuroblastoma cells with fetal neuroblasts, and another demonstrated the significance of the absence of HLA-A, B, and C expression in neuroblastoma cells and other related cell lines.

The clinical sessions involved both diagnostic and therapeutic studies. As mentioned earlier, a proposal for a new staging system, including the studies necessary to confirm response to treatment, was discussed at length. There was general agreement to try the new staging system, but conference participants disagreed about which studies would be necessary for confirmation. The European group feels that  $^{131}\text{I}$ -MIBG provides the most effective means of detecting small amounts of neuroblastoma, but it was pointed out that this nuclide study is not commonly available in the United States. The Japanese group presented data on mass screening of neuroblastoma in infancy, and this program was discussed with great interest. The session also included an interesting radiographic study of bone marrow metastasis detected by magnetic resonance imaging.

The papers that address recent advances in therapy fall mainly into two groups dealing with  $^{131}\text{I}$ -MIBG and bone marrow transplantation. It is striking that there are only two papers on chemotherapy—carboplatin and very-high-dose cisplatin—which points up the fact that there have not been many recent advances in chemotherapy regimens. The six papers on  $^{131}\text{I}$ -MIBG are all from Europe and report single institution or collaborative studies that show the effectiveness of this radiolabeled metabolic compound. However, the therapeutic response seems to be short-lived. Perhaps the next series of studies will be related to use of this compound earlier in the course of disease.

Papers reporting results of bone marrow transplantation had larger numbers and more uniform patients than the series reported at the previous meeting. It appears that the inclusion of superlethal chemotherapy and irradiation during first remission has led to larger numbers of long-term survivors. The improvement in results between transplantation after recurrence or in first remission of neuroblastoma are not as impressive as for acute myeloid leukemias, where long-term survival improved from 25% to 60%. Three papers