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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

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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}I-meta-iodobenzylguanidine (^{131}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 polyprenoic 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}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}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}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