

1984

ANNUAL
REPORT

PHARMACEUTICAL MANUFACTURERS
ASSOCIATION FOUNDATION, INC. 

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Dedicated to
THOMAS E. HANRAHAN
1932-1985

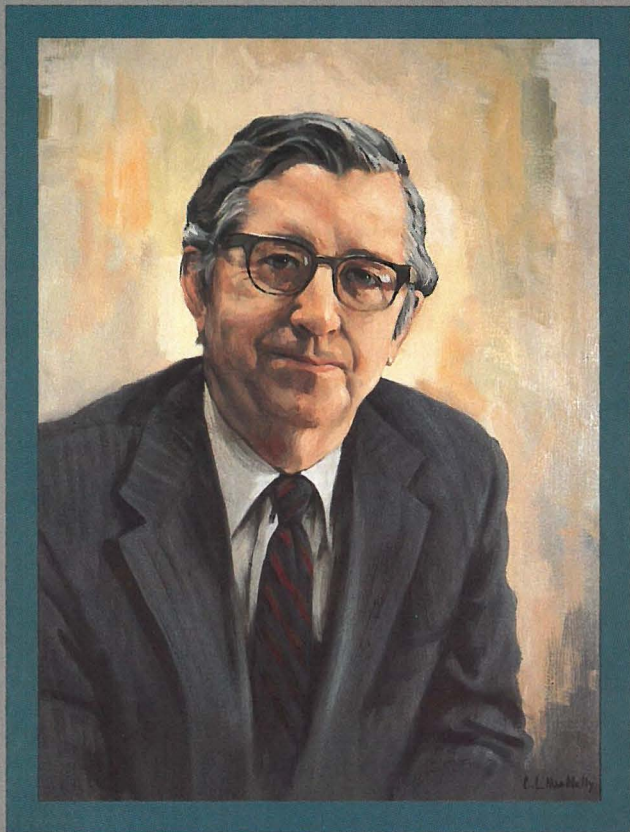
On January 13, 1985, Thomas E. Hanrahan died of cancer after many months of silent suffering and uninterrupted attention to his duties as President of the Pharmaceutical Manufacturers Association Foundation.

Tom will be missed by many—the members of the PMA Foundation Board of Directors, those who served on the Foundation’s several scientific advisory committees, his colleagues at PMA, his hundreds of friends and the many people who benefited from the programs he directed. It will be hard to think of the Foundation without Tom since over the years the two became synonymous.

The PMA Foundation was founded in 1965 and Tom became its Executive Director in 1966. After serving in that capacity for 13 years, he was appointed President in 1979. Thus, for 19 years—practically the entire existence of the Foundation—Tom guided its operations and provided the leadership that was responsible for its outstanding success.

Tom was a highly religious, civic-minded and dedicated family man, whose wife, Barbara, and five children generously supported him during his many years of dedicated service with the Foundation.

Tom was an educator by training and by nature, and all who met him learned from his quiet, good-natured approach to the work he loved. Those of us who knew him well benefited enormously from his friendship. Hundreds of others, currently, and in the future, will be assisted by the many Foundation programs that Tom Hanrahan helped to establish and perfect.



Thomas E. Hanrahan

The annual awardees meeting of the Foundation was held in New York City in December. The format for the scientific presentations was altered from last year at this meeting in order to promote greater scientific interchange among the attendees. Poster sessions were held from 8:30 a.m. to 10:30 a.m. These sessions were well received with many individuals commenting that they were able for the first time to attend most of the presentations in their areas of interest.

Following the poster sessions, Irwin Lerner, President and Chief Executive Officer, Hoffmann-La Roche Inc., and Chairman of the Board of the Foundation, opened the plenary session with welcoming remarks expressing the Board's appreciation of the Foundation's programs and accomplishments. David Winter, M.D., Director of Medical Research at Sandoz Research Institute, then presented the keynote address entitled, "Cyclosporine: Development Problems and Surprises." Dr. Winter gave a very interesting account of the development of cyclosporine—from its serendipitous discovery to its introduction for human use.

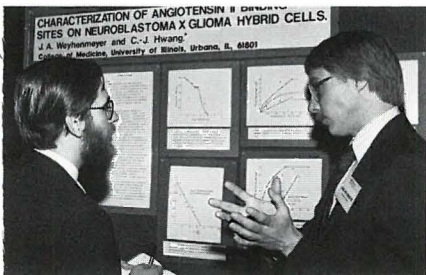


Three subgroups of awardees met separately in the afternoon. The Clinical Pharmacology Subgroup Session was devoted to the examination of the issues discussed and the conclusions developed at the Anglo-American Workshop in Clinical Pharmacology held in May, 1984, at the Airlie House, Warrenton, Virginia. Dr. Kenneth Melmon, Professor of Medicine, Stanford University, served as co-director of the workshop. Dr. Melmon discussed the findings of the workshop and, in particular, emphasized differences in the environment and in the opportunities for clinical pharmacologists in the United States and Great Britain. The formal lecture was followed by a spirited question-and-answer period.



1984

FOUNDATION MEETINGS



The Basic Pharmacology Subgroup attended a lecture by Dr. Robert E. Parks, Jr., M.D., Ph.D., Professor of Medicinal Sciences, Division of Biology and Medicine at Brown University on "Cancer Chemotherapy: Where Has It Been and Where Is It Going?" In addition, part of the afternoon was devoted to presentations by selected awardees.

The Pharmacology-Morphology Subgroup heard progress reports from three 1983 Pharmacology-Morphology Fellows, who were at that time 18 months into their postdoctoral research. This was followed by a ten-minute comment and question-and-answer period. Dr. Theresa Branchek discussed her work on localization of enteric receptors for serotonin; Dr. Christopher Lau described the status of his research on the influence of thyroid hormones on rat sympathoadrenomedullary development, and Dr. Dorie W. Schwertz reported on her studies of aminoglycoside nephrotoxic mechanisms in cultured pig kidney cells. The audience of approximately 30 people, mostly former P-M Fellows as well



as several members of the P-M Advisory Committee, provided lively discussion of the reports. Continuing the tradition of research presentations by members of the P-M Advisory Committee, Dr. William Riker concluded the afternoon session with a talk on his studies of synaptic function as modulated by Ca^{2+} entry facilitators and blockers.



In August, 1984, a meeting was held with the Research Starter Grantees and the Advanced Predoctoral Fellows during the Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics. The speaker was Dr. August M. Watanabe, M.D., Professor of Medicine and Pharmacology, Indiana University School of Medicine, who illustrated the relationship between laboratory and clinical pharmacology with his own work on the calcium channel blockers.

Activities

The Pharmaceutical Manufacturers Association Foundation is a nonprofit organization, established in 1965 to promote public health through scientific and medical research. It provides funding for basic research on drugs and for educational training programs in basic and clinical pharmacology and toxicology. Since its formation, approximately \$16 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects, and educational programs. Of this amount, slightly more than \$5 million has been used to support research and approximately \$11 million has gone into educational awards. The Foundation continues to provide financial assistance for scientific meetings and small amounts for publications.

Virtually all of the 1984 grants and awards were made within programs sponsored by the Foundation. These include three faculty-level programs of salary and fringe benefit support, four fellowship programs, two postdoctoral—one at the advanced predoctoral level and one at the medical student level—plus a program of research starter grants for beginning investigators wishing to move into areas of independent research. An award to assist in expediting the research efforts of new clinical pharmacology units or those with new directors is also available.

Through these programs in 1984, the Foundation assisted an additional 58 individuals. All of these individuals were helped at a critical time in their professional development. The Foundation has, in its almost 20 years of existence, helped about 850 individuals through its research and educational support programs. A twenty-year historical perspective outlining Foundation activities is now in preparation.

Education and Training Programs

To further its objectives in the field of education, the PMA Foundation sponsors four programs in clinical pharmacology, one in the combined field of pharmacology-morphology, one in pharmacology or toxicology, one in basic pharmacology and one in toxicologic pathology.

Clinical Pharmacology **Faculty Awards in Clinical Pharmacology**

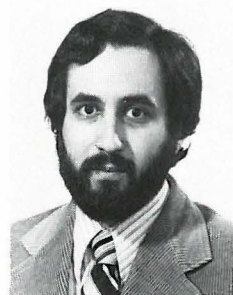
The four clinical pharmacology programs provide opportunities at the student, fellow and faculty levels. Through the Faculty Development Awards in Clinical Pharmacology program, the Foundation makes two-year awards to medical

schools for salary and fringe benefits support of full-time junior faculty members. The Foundation has set a ceiling of \$30,000 on the amount of its participation in total yearly salary and fringe benefits for any candidate.

With the awards scheduled to begin July 1, 1985, 71 individuals have been supported under this program since 1967.

Recipients of the four awards to begin July 1, 1985 are:

● Eric P. Brass, M.D., Ph.D., Assistant Professor, Medicine and Pharmacology, Division of Clinical Pharmacology and Toxicology, University of Colorado Health Sciences Center. Dr. Brass's research is concerned with the role of prostaglandins in the regulation of hepatic glucose metabolism. His preliminary work has shown that isolated rat hepatocytes rapidly metabolize PGE. By using frequent PGE additions (to compensate for catabolism) or synthetic PGE analogs, he has shown that PGE inhibits glucagon stimulated glycogenolysis. Based on this novel experimental approach, this proposal is designed to comprehensively define the role of prostaglandins in the regulation of hepatic glucose metabolism. Initial studies will define the kinetics and regulation of prostaglandin production and catabolism in the hepatocyte system. These studies will be expanded to examine the effect on glucose metabolism of pharmacologic agents which are known to affect prostaglandin synthesis.



Eric P. Brass, M.D.,
Ph.D.

● William Steven Dalton, M.D., Ph.D., Clinical Instructor, Section of Hematology/Oncology, Department of Internal Medicine, Health Sciences Center, The University of Arizona. Dr. Dalton's research is directed to the investigation of the mechanisms of multiple drug resistance in multiple myeloma. The mechanism of resistance to doxorubicin and its possible cross resistance with melphalan will be analyzed. Serial tumor specimens will be obtained via bone marrow aspirations and analyzed for specific plasma cell membrane glycoproteins as well as the ability to accumulate doxorubicin. In addition, human myeloma cell lines will be made individually resistant to doxorubicin and melphalan to determine if these variant cell lines are cross resistant and if there is an associated change in cell membrane glycoproteins as well as drug uptake.



William Steven Dalton,
M.D., Ph.D.

● Phyllis I. Gardner, M.D., Assistant Professor of Medicine, Stanford University Medical Center. Dr. Gardner's research will focus on single channel potassium currents in cultured chick ciliary ganglion neurones. Her interests lie in the general area of the molecular basis for membrane excitability. She has performed preliminary patch clamp experiments on cultured chick ciliary ganglion (CG) neurones and has identified at least



Phyllis I. Gardner, M.D.

three, operational distinct, voltage-sensitive potassium (K^+) conductances. The purpose of the proposed project is to continue single channel studies of the biophysical properties of these channels, including single channel conductance (ionic selectivity, susceptibility to channel blockade by Na^+ , Ca^{2+} , Ba^{2+}), gating kinetics, voltage sensitivity, and sensitivity to classical pharmacological K^+ channel blockers. The project will extend our knowledge of the electrophysiology of parasympathetic neurones and the role that neurotransmitters play in the system in complex chemical signalling.



Ruth Margrit Ruprecht,
M.D., Ph.D.

- Ruth Margrit Ruprecht, M.D., Ph.D., Assistant Professor, Dana-Farber Cancer Institute, Harvard Medical School. Dr. Ruprecht's research is directed to the expression of foreign drug resistance genes in hematopoietic cells as a function of viral enhancers. She proposes to insert genes capable of inducing resistance to cytotoxic agents into mouse bone marrow cells which will be transplanted into irradiated mice. The drug resistance genes will be coupled to various transcription enhancer signals derived from murine leukemia viruses, affecting different bone-marrow derived cell-lineages. She plans to test the hypothesis that the drug resistance genes will be active in the cell-lineage that was the target for the virus from which the transcription enhancer signal was derived.

Those individuals whose awards began July 1, 1984 are:

- Marc S. Ernstoff, M.D., Assistant Professor of Medicine, Department of Internal Medicine/Medical Oncology, Yale University School of Medicine.
- Marilyn C. Frederiksen, M.D., Assistant Professor, Department of Obstetrics and Gynecology, Northwestern University Medical School.
- Howard R. Knapp, Ph.D., M.D., Assistant Professor, Department of Pharmacology and Medicine, Vanderbilt University School of Medicine.
- Charles E. Riggs, Jr., M.D., Assistant Professor, Department of Internal Medicine, University of Iowa College of Medicine.

Those individuals who entered their second year of awards in July, 1984 are:

- Frank L. Douglas, M.D., Ph.D., Assistant Professor, Department of Medicine, Committee on Clinical Pharmacology, University of Chicago.
- Garret A. FitzGerald, M.Sc., M.D., Assistant Professor, Departments of Medicine and Pharmacology, Vanderbilt University School of Medicine.

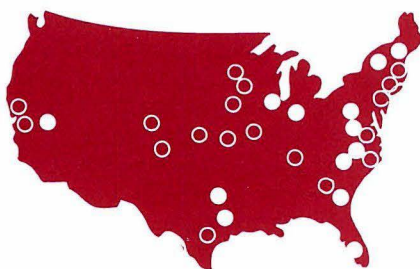
- David W. Nierenberg, M.D., Assistant Professor, Departments of Medicine and Pharmacology & Toxicology, Dartmouth Medical School.

Those individuals who concluded their awards in 1984 are:

- Brian B. Hoffman, M.D., Assistant Professor, Departments of Medicine and Pharmacology, & Toxicology, Dartmouth Medical School.

- Janice B. Schwartz, M.D., Instructor, Section of Cardiology and Section of Hypertension and Clinical Pharmacology, Baylor College of Medicine.

- Jack P. Uetrecht, M.D., Ph.D., Assistant Professor, Departments of Pharmacology and Medicine, Vanderbilt University School of Medicine.



Geographical distribution of Foundation awards under its "Faculty Development Awards in Clinical Pharmacology" program, 1967-1984.

● One
○ More than One

Fellowships for Careers in Clinical Pharmacology

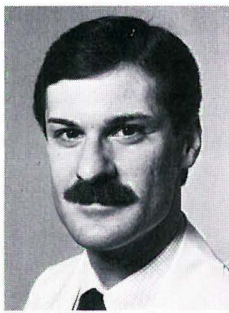
The second program provides Fellowships for Careers in Clinical Pharmacology. This award offers clinicians an opportunity for intensive study in any of the basic sciences that fall within the general field of pharmacology. The program is open to physicians, dentists and veterinarians who are well into their clinical training and wish to pursue careers in clinical pharmacology. With the year or two of support offered by this fellowship program, depending on the particulars of the undertaking, the individual can pursue full-time the basic pharmacologic sciences needed to complement his clinical skills.

The program was amended in 1982 to allow an individual to apply for a fellowship two years in advance of the activation date of the award. For example, those applying for a fellowship

in the Fall of 1985 may elect to ask that the fellowship be for July 1986 or July 1987.

The first awards under this program were made in 1973. Since that time, 35 fellowships have been awarded.

Recipients of the three fellowships beginning July 1, 1985 are:



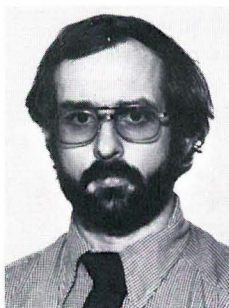
David Hayden S. Iansmith,
A.B., M.D., Ph.D.

- David Hayden S. Iansmith, A.B., M.D., Ph.D., Clinical and Research Fellow, Division of Cardiology and Clinical Pharmacology, Vanderbilt University. Dr. Iansmith's research project explores the stereospecific antiarrhythmic efficacy of propranolol. His initial observations led to the hypothesis that propranolol produced electrophysiologic effects *in vivo*. He has independently studied this same phenomenon in canine tissue and found that the dextro isomer of propranolol has electrophysiologic actions opposite to those of the levo isomer. He will expand these studies to evaluate the nature of these opposing actions in isolated canine Purkinje fibers.



Susan L. Kelley, M.D.

- Susan L. Kelley, M.D., Fellow in Medical Oncology, Dana-Faber Cancer Institute, Harvard Medical School. Dr. Kelley's research efforts will center on thiol compounds and the modulating effects on DNA damage, cytotoxicity and therapeutic efficacy of antineoplastic epoxias. She has investigated a number of epoxide compounds as potential antineoplastic agents. Dibromodulcitol (DBD) is felt to be a unique alkylating agent, with a clinical spectrum which justifies further investigations into its mechanism of action. Dianhydrogalactitol (DAG), the 1:2-5:6 diepoxide metabolite of DBD is also active against certain neoplasms. She will further be investigating the hypothesis that the mechanism of DNA alkylation by DBD includes adduct formation at guanine residues. Previous work suggests that thiol compounds may reverse the cytotoxicity of other alkylating agents such as cis-platinun and phenylalanine mustard. She will be studying the role of glutathione conjugation in the alteration of DNA-adducts formed, and in modulation of antineoplastic epoxide cytotoxicity.



Sidney Alexander
Scudder, M.D.

- Sidney Alexander Scudder, M.D., Fellow, Division of Oncology, Stanford University. Dr. Scudder's research efforts will center on mechanisms of resistance to vinca alkaloids and other heterocyclic compounds in the human tumor cell line, MES-SA. Investigations into the mechanisms of drug resistance and/or broad cross resistance in a human tumor cell line will be conducted using techniques already established in this laboratory. The established human tumor cell line will be exposed to vinca alkaloids; specifically vinblastine, to develop a drug resistant tumor cell line. Once established, the resistant line and the parent cell line will be used to study the possible mechanisms of resistance.

Those individuals whose fellowships began July 1, 1984 are:

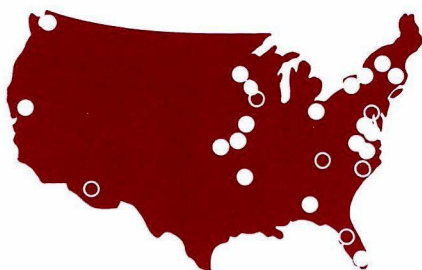
- Nancy Jo Braden, M.D., Fellow, Department of Pediatrics, the Ohio State University, College of Medicine.
- Gregory G. Gaar, M.D., Fellow, Departments of Pediatrics and Pharmacology, University of Arizona College of Medicine.
- Celine M. Stahl, M.D., Fellow, Department of Pharmacology and Medicine, Cornell University Medical College.

Those individuals whose fellowships entered the second year of the award on July 1, 1984 are:

- Bonnie S. Glisson, M.D., Fellow, Division of Medical Oncology, Department of Medicine, University of Florida College of Medicine.
- Andrew Guterman, M.D., Ph.D., Fellow, Department of Neurology, University of Miami School of Medicine.
- Jonathan R. Wispe, M.D., Fellow, Departments of Pediatrics and Pharmacology, University of Iowa College of Medicine.

Those individuals whose awards concluded in 1984 are:

- Howard R. Lee, M.D., Fellow, Department of Pharmacology, University of Arizona College of Medicine.
- Mark S. Smith, M.D., Fellow, Clinical Pharmacology Division, Duke University School of Medicine.



Geographical distribution of Foundation "Fellowships for Careers in Clinical Pharmacology" program, 1973-1985.

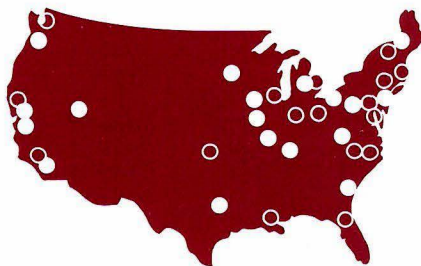
- One
- More than One

Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology

The third program is the Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology. This program, which began in 1974, provides students an opportunity to spend up to one year full-time conducting an investigative project in pharmacology-clinical pharmacology. The minimum period of the award is three months. It is hoped that by having students become involved in investigative projects at a point when career choices are still relatively flexible, they will opt for research careers in clinical pharmacology. Fifty-eight awards have been made since 1974.

The recipients of the fellowship beginning July 1, 1984 are:

- Jeanne E. Anderson, Stanford University, for one year.
- Robert E. Chase, Hahnemann University, for six months.
- Ted M. Dawson, University of Utah, for one year.
- W. Conrad Liles, Jr., University of Washington, for one year.
- Rosabel Garcia Ribares, University of California, for one year.



Geographical distribution of Foundation "Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology" program, 1974-1984.

- One
- More than One

Clinical Pharmacology Unit Support

This program is designed to assist directors of clinical pharmacology units established within the prior two years of the award and for units with a change in directorship during that period. The grant provides a total of \$50,000 which may be used at any time during a three year period. The program is aimed at providing some initial funds to enable the unit's research efforts to be maintained until other research grants are obtained. The first grants were made in 1978. The total number of awards made to date is eleven.

The awards beginning July 1, 1984 were made to:

- Division of Clinical Pharmacology, Department of Medicine, North Shore University Hospital. B. Robert Meyer, M.D. is Chief of the Division. The research interests of the unit are directed toward the pharmacology of pain control and using a "Cardiff Palliator." Another research interest of the unit involves investigation of nabilone and metoclopramide combination antiemetic therapy.
- Division of Clinical Pharmacology, The University of Texas. Alexander M. M. Shepherd, M.D., Ph.D. is Director of the Division. The research efforts of the Division will be directed toward cardiovascular clinical pharmacology-human studies, basic pharmacology, pharmacokinetic method development and development of new drugs.



Basic Pharmacology

Faculty Development Awards in Basic Pharmacology

The purpose of these Faculty Development Awards is to strengthen basic pharmacology by helping maintain existing academic capability and, ultimately, to expand it by enlarging the faculty base. To accomplish these goals, support is provided to full-time junior faculty members committed to careers in pharmacology who give promise of outstanding accomplishments.

The first awards, which are for a two-year period, were made in 1973. The program provides salary and fringe benefits. The Foundation has set a ceiling of \$25,000 on the amount of its participation in the total yearly salary and fringe benefits for any candidate beginning with the 1980 awards. The total number of awards made to date is 35.

Those who received awards beginning July 1, 1985 are:

- William Thomas Gerthoffer, Ph.D., Assistant Professor, Department of Pharmacology, University of Nevada School of Medicine. Dr. Gerthoffer's research involves the cellular mechanisms of smooth muscle relaxation. The specific aims are: (1) To determine the calcium-dependence of relaxation and myosin dephosphorylation in intact and chemically skinned canine tracheal smooth muscle; and (2) to determine whether the calcium-phospholipid-dependent protein kinase (C-kinase) can phosphorylate myosin in intact muscle cells, and whether this action has implications for measuring myosin phosphorylation in intact muscles.



Geographical distribution of Foundation "Faculty Development Awards in Pharmacology," 1973-1985.

- One
- More than One

Those who began their awards July 1, 1984 are:

- James R. Halpert, Ph.D., Assistant Professor, Department of Pharmacology & Toxicology, University of Arizona College of Pharmacy.

- Kevin M. Mullane, Ph.D., Assistant Professor, Department of Pharmacology, New York Medical College.
- Nancy Zahniser, Ph.D., Assistant Professor, Department of Pharmacology, University of Colorado School of Medicine.

Those who entered the second year of their awards on July 1, 1984 are:

- Keith T. Demarest, Ph.D., Assistant Professor, Department of Pharmacology & Toxicology, Michigan State University.
- Edward Hawrot, Ph.D., Assistant Professor, Department of Pharmacology, Yale University School of Medicine.
- G. Allen Nickols, Ph.D., Assistant Professor, Department of Pharmacology, Southern Illinois University School of Medicine.

Those whose awards concluded in 1984 are:

- Walter R. Dixon, Ph.D., Assistant Professor, University of Kansas School of Pharmacy.
- Jerry A. Farley, Ph.D., Assistant Professor, Department of Pharmacology and Toxicology, University of Mississippi Medical Center.
- Gregory A. Weiland, Ph.D., Assistant Professor, Department of Pharmacology, New York State College of Veterinary Medicine.

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

The program, offered initially in 1977, is designed to assist those candidates who have one or two years remaining in their predoctoral training, the time during which they are engaged in their thesis research.

The fellowship program provides a stipend of \$5,040 a year, payment of tuition and \$500 a year for incidentals directly associated with the thesis research preparation. The program has been funded to provide eight fellowships each year. However, three extra fellowships were authorized for 1985. A total of 83 fellowships has been made since 1977.

Those who received fellowships which begin between January and August 1985 are:

- Adrienne L. Block, Northwestern University. Her advisor is Dr. Jerome Seldenfeld, Assistant Professor of Pharmacology.

Ms. Block's research concentrates on difluoromethylornithine-induced chemosensitization and blockade of cell cycle traverse in ME-180 and MCF-7 human carcinoma cells.

- Ughetta del Balzo Hachfeld, Cornell University Medical College. Her advisor is Dr. Robert Levi, Department of Pharmacology. Ms. Hachfeld's research is focused on cardiac effects of complement-derived anaphylatoxins.
- Michael De Vivo, Mount Sinai School of Medicine. His advisor is Saul Maayani, Ph.D., Associate Professor, Pharmacology. Mr. De Vivo's research is aimed at the characterization of the desensitization of 5-HT receptors linked to adenylate cyclase in guinea pig hippocampus.
- Patrice Ferriola, State University of New York at Buffalo. Her advisor is Margaret Acara, Ph.D., Associate Professor, Department of Pharmacology. Ms. Ferriola's research seeks to determine the mechanism of action of the thiazide diuretics.
- Leslie C. Griffith, Stanford University. Her advisor is Howard Schulman, Assistant Professor, Department of Pharmacology. Ms. Griffith's research studies the role of a Ca^{2+} / Calmodulin-dependent protein kinase in the regulation of catecholamine synthesis.
- Michael E. Hall, University of Colorado Health Sciences Center. His advisor is Barry J. Hoffer, Professor of Pharmacology. Mr. Hall's research is aimed at autonomic innervation of intraocular heart grafts.
- Ronald D. Johnson, Emory University. His advisor is Kenneth P. Mineman, Assistant Professor of Pharmacology. Mr. Johnson's research involves α_1 -adrenergic receptor binding and function in rat brain.
- Kevin A. Lee, Temple University. His advisor is Dr. Michael A. Sirover, Associate Professor, Pharmacology. Mr. Lee's research is aimed at the isolation and characterization of a base excision DNA repair multienzyme complex.
- Stephen Sorota, University of Connecticut. His advisor is Dr. Achilles Pappano, Professor of Pharmacology. Mr. Sorota's research involves chick heart muscarinic receptor and receptor-effector coupling.
- Elizabeth Ann VandeWaa, Michigan State University. Her advisor is James L. Bennett, Professor, Department of Pharmacology/Toxicology. Ms. VandeWaa's research deals with the effect of mevinolin on egg production in schistosoma mansoni.

- Jeffrey Martin Voigt, University of Iowa. His advisor is Dr. Jeffrey Baron, Ph.D., Professor of Pharmacology. Mr. Voigt's research focuses on the localization of xenobiotic-metabolizing enzymes within the respirator tract.



Fellowship Awards in Pharmacology-Morphology

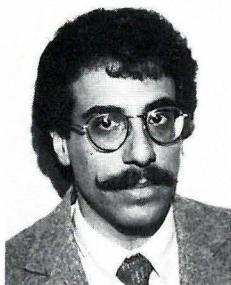
The aim of this program is to advance understanding of drug action through the discovery of specifically related cellular and tissue changes; and, concurrently, to uncover associations between normal and abnormal function in particular tissue and cellular structure.

The awards are two years each. The level of support varies and is aimed at keeping within the existing stipends for similarly trained individuals within the applicant university. Since 1968 when the first fellowships were offered, fifty-eight awards have been made.

The program requires that the candidate be qualified primarily either in a morphologic specialty or in pharmacology. However, training to be achieved under the fellowship in the complementary discipline need not be formal. The candidate's program should result in a familiarity with a new discipline approach by using his primary discipline as a medium for acquiring the second.

The recipients of the fellowships which began July, 1984 are:

- Robert S. Garofalo, Ph.D., Department of Anatomy and Cell Biology, College of Physicians & Surgeons of Columbia University. Dr. Garofalo's research is concentrated on early events triggered by growth factors in nerve growth cones. His proposed studies will examine the hypothesis that phospholipid methylation may be an early, key event in a growth-factor-activated cascade in neuronal plasma membranes, in particular, their growth cones. The overall objectives are: (1) to



Robert S. Garofalo,
Ph.D.

characterize the phospholipid methyltransferase system of growth cone membranes; (2) to isolate CNS growth factors which may be useful as novel pharmacologic agents; and (3) to examine the mechanism of action of these growth factors using pharmacological dissection.

- Michele S. Moss, Ph.D., Department of Obstetrics, Gynecology & Reproductive Sciences, University of California, San Francisco. The focus of Dr. Moss's research is directed toward understanding the neuroendocrine regulation of prolactin secretion from the anterior pituitary gland. The results will help determine whether the dopamine receptors in the pituitary are identical to dopamine receptors in the brain which could lead to new drugs to treat infertility associated with hyperprolactinemia and could also lead to a better understanding of the etiology of human prolactin secreting adenomas.

- Jan Rosenbaum Sass, Ph.D., Stanford University. Dr. Rosenbaum's research involves the adverse consequences of excess catecholamines on the heart using a rat pheochromocytoma model. She intends to further elucidate the mechanism by which catecholamines damage the heart by treating animals with either phenoxybenzamine or timolol alone, or the calcium antagonist, verapamil. The extent of cardiac damage in the treated, untreated and age-matched controls will be evaluated pathologically. Also, the functional activity of the cardiomyopathic hearts will be investigated using an electrically driven isolated muscle preparation. The response of the hearts to isoproterenol and calcium will be evaluated in an attempt to explain whether the anticipated decreased performance of the cardiomyopathic hearts is due to events at the adrenergic receptor alone, or if events distal to the receptor are influenced as well.

Those who entered the second year of their fellowships in 1984 are:

- Theresa Brancheck, Ph.D., Postdoctoral Fellow, Department of Anatomy and Cell Biology, College of Physicians and Surgeons of Columbia University.

- Christopher Lau, Ph.D., Postdoctoral Fellow, Department of Anatomy, Medical College of Pennsylvania.

- Dorie W. Schwertz, Ph.D., Research Fellow, Department of Pathology and Department of Medicine, University of Texas Health Science Center, San Antonio.

Those individuals whose fellowship concluded in 1984 are:

- Mark G. Currie, Ph.D., Postdoctoral Fellow, Department of Pharmacology, Washington University School of Medicine.
- Linda M. Marshall-Carlson, Ph.D., Postdoctoral Fellow, Department of Biochemistry, University of Texas Health Science Center, San Antonio.



Faculty Awards in Toxicologic Pathology

This program was new in 1983 and was developed to attract scientists interested in analyzing, reviewing and questioning where appropriate, the present state of the art in the field of toxicology. To examine the degree of interest the academic community may have, a junior faculty program was authorized for a three-year period. The goal of the program was to attract veterinary and comparative pathologists who were interested in spending two years in drug toxicology research. In 1984 two awards were made, bringing the total number of awards during the pilot period to six. Now that the pilot period has been concluded, the program will operate on a permanent basis beginning in 1985.

Those individuals whose awards begin July 1, 1985 are:

- Kim Boekelheide, M.D., Ph.D., Assistant Professor, Department of Pathology and Laboratory Medicine, Brown University. Dr. Boekelheide's project concerns the pathogenesis of 2,5-Hexanedione induced testicular atrophy. 2,5-Hexanedione is the toxic metabolite of the environmental agent *n*-hexane and a prototypal agent for a class of compounds which includes β,β' -iminodipropionitrile and the important industrial toxins acrylamide and carbon disulfide. A combination of morphological and biochemical techniques will be utilized in localizing the microtubule injury to a particular



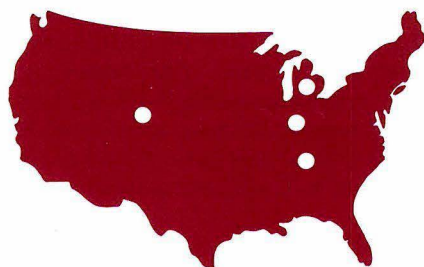
Kim Boekelheide, M.D.,
Ph.D.

cell type within the testis and defining the chemical nature of the tubulin abnormality. The significance of this project lies in the ability to generalize from the proposed mechanism to predict those agents which might act in a similar fashion. Also, during the course of the study, methods will be developed which readily allow early assessment of new compounds which may be testicular toxins.

- Kevin P. Keenan, D.V.M., Ph.D., Assistant Professor, Department of Pathology, University of Maryland at Baltimore. Dr. Keenan's research involves an extensive *in vivo* study of the interactions of cell injury and cell proliferation on the process of chemical carcinogenesis in the hamster respiratory tract. This study will investigate the promotional effects of intratracheal wounding, dosing with ferric oxide particles or saline on tumor genesis of hamsters previously treated with a carcinogen. The importance of proliferation during tumor development will be determined by morphological techniques.

Those who received awards beginning July 1, 1984 are:

- R. Gayman Helman, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Pathobiology, University of Tennessee College of Veterinary Medicine.
- Richard K. Jensen, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Michigan State University, College of Veterinary Medicine.



Geographical distribution of Foundation awards under the "Faculty Awards in Toxicologic Pathology" program, 1982-1985.

- One
- More than One

Research Grants

An important aspect of the PMA Foundation effort has been the support of fundamental research in drug toxicology. Between 1966 and 1971, 26 research awards of relatively large amounts for two to five years were awarded, principally to established investigators to either extend existing research or to provide “seed” monies to follow a promising lead. In 1971 a change in emphasis within the Foundation programs shifted the bulk of the funds into educational support programs and, therefore, less into research. It is understood however that these educational programs place high emphasis on the research programs of the applicants for each award. In this sense, these educational support programs are in fact also supporting research. The Foundation does, however, continue to accept requests for support and suggestions for pertinent research projects since it is important that the potential within the Foundation for helping that particularly promising effort be maintained.



Geographical distribution of Foundation general research grants, 1966-1984

- One
- More than One
- ★ Outside continental U.S.

Research Starter Grants

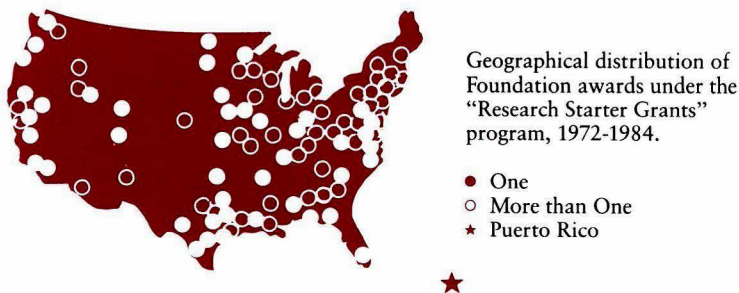
As part of the change of emphasis in 1971 which sought to direct monies more toward the development of the individual, a program of Research Starter Grants was initiated. These grants are intended to provide financial support for beginning investigators. The program allows for approximately 20 research starter grants each year. The first awards were made in 1972. A total of 331 research starter grants have been made, including the 20 awards beginning January 1, 1985.

The recipients of the grants beginning January 1985 are:

Ann M. Blacker, Ph.D. University of Nebraska	Richard M. LoPachin, Ph.D. University of Houston
William D. Blaker, Ph.D. Virginia Polytechnic Institute	William R. Mancini, Ph.D. University of Michigan
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Paul R. Housley, Ph.D. University of South Carolina	Barbara L. Waszczak, Ph.D. Northeastern University
Victoria P. Knutson, Ph.D. University of Texas, Houston	Molly Weiler, Ph.D. University of Wisconsin, Madison
Iris Lindberg, Ph.D. Louisiana State University	Francis J. White, Ph.D. University of Illinois

Review of the need of the 21 research starter grantees whose awards began January 1, 1984 for a second year of the awards resulted in 16 of them having their awards continued. These are:

John R. Babson, Ph.D. University of Minnesota	Jonathan Maybaum, Ph.D. University of Michigan
James P. Bennett, Jr., M.D., Ph.D. University of Virginia	David C. Perry, Ph.D. George Washington University
Marc C. Browning, M.D. Bowman Gray School of Medicine	Robin W. Rockhold, Ph.D. University of Mississippi
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Other Support

A special fund was made available to the PMA Foundation to provide support for projects in postmarketing drug monitoring. The Foundation decided to focus on providing a methodological grant. The intent of the grant is to fund studies aimed at extending or developing imaginative, feasible methodologies to systematically generate information about prescription medications as they are customarily used in the non-hospitalized population, with particular application to the study of adverse reactions.

Entering the second year of support for a one-time grant is:

- Holly L. Mason, Ph.D., Assistant Professor of Pharmacy Administration, principal investigator, and Robert K. Chalmers, Ph.D., Professor of Pharmacy Practice, co-investigator, Purdue University School of Pharmacy and Pharmacal Sciences. This award will end April 30, 1986.

The methodology is designed to examine the possible role of community pharmacists in gathering information on prescription drugs from patients.

Another one-time awardee whose grant support ended May 1984 is:

- Ann Karen Henry, Pharm.D., Assistant Professor, Department of Pharmacy Practice, College of Pharmacy, and Adjunct Assistant Professor, Department of Family Community Medicine, College of Medicine, University of Arizona, as principal investigator.

The goals of the project were to evaluate direct-patient-to-data-center reporting of information and to develop the methodology for collecting the data.

Purpose

The PMA Foundation was established to promote the betterment of public health through scientific and medical research, with particular reference to the study and development of the science of therapeutics. In achieving this goal, the Foundation plans and initiates scientific and medical research activities, collects and disseminates the results of these activities, and provides financial support and aid to individuals or institutions whose purposes are scientific, educational or charitable.

Certain guidelines have been developed to promote the wise and proper use of the limited resources available. The areas of interest which govern the distribution of funds are support of fundamental research on drugs and programs for training personnel in basic and clinical pharmacology and toxicology.

Throughout the year, programs have been supported and developed which provide the means of achieving the goals of the Foundation. Many worthwhile proposals have been submitted. It has been necessary to limit support to those who hold the highest promise of advancing the purposes of the Foundation.

Those areas not supported within the existing guidelines are:

(1) Research on specific drugs. This exclusion is not meant to preclude support of projects which, of necessity, use a number of drugs to establish a methodology or screening program of potential general applicability. It does exclude those efforts primarily aimed at learning more about specific drugs or classes of drugs.

(2) Funds for construction. The Foundation is not unmindful of the needs and the tremendous pressures for private funds for construction projects. However, it is believed that the scientific community can be better served by channeling the Foundation's available resources into other areas.

(3) Funds for travel.

(4) Funds to cover entertainment costs.

In 1971, the Board of Directors authorized a major shift in program emphasis. While Foundation support of research continues, such support is to be primarily available in a redirected fashion, such as the Research Starter Grants program discussed on page 20.

In line with this change of emphasis, the Foundation is expanding support within its current educational programs as outlined in the Education and Training Programs Section on page 5.

While meetings have never received a large portion of the support dollar, only in very exceptional circumstances will meetings receive support in the future.

Foundation Finances

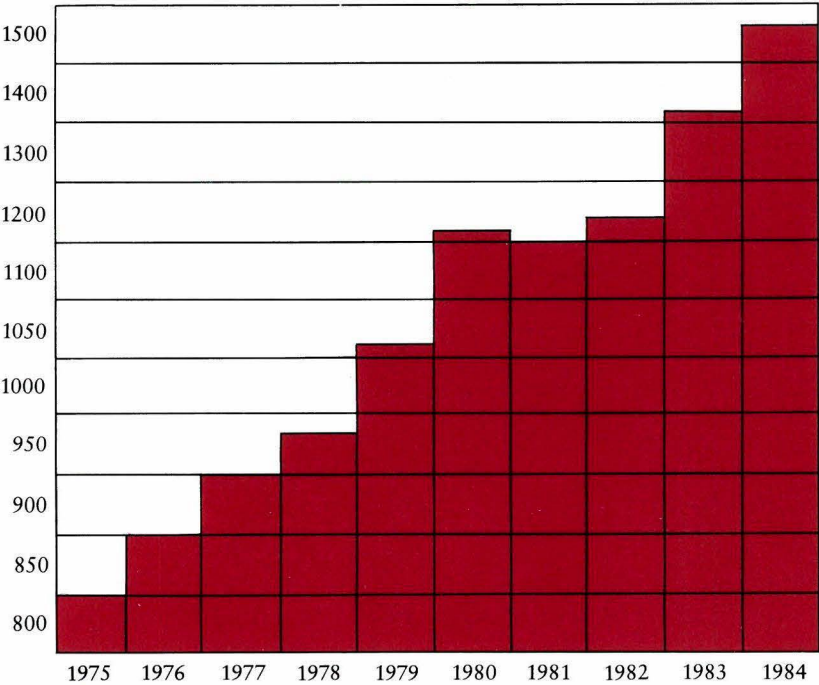
The total income of the Foundation in 1984 was \$1,713,082. Of this amount, \$1,476,700 came from contributions. The balance of \$236,382 came from investments, gain on sale of stock, and refunds of unexpended balances from grants.

Contributions were received from approximately four out of every five PMA Member Firms. Contributions were also received during 1984 from other groups in the health field.

Grants, Foundation-sponsored programs, special meetings and other expenses for 1984 amounted to \$1,424,442. Of this total, \$1,124,829 represent expenditures for grants. The fund balance as of December 31, 1984 was \$2,104,321. This figure, however, does not reflect the tentatively authorized, undisbursed funds for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are disbursed. As of December 31, 1984, the contingency liability for 1985 was approximately \$1,177,378.

The Foundation's financial position as of December 31, 1984 has been audited by the Washington, D.C. accounting firm of Buchanan & Company.

PMA Foundation
Contribution Income
1975-1984 (Thousands)



Statement of Income and Expenditures For the Year Ended December 31, 1984

Income

Contributions—Note A	1,476,700
Income from Investments	164,259
Gain of Sale of Stock	62,060
Miscellaneous Income.....	<u>10,063</u>
 Total Income	 1,713,082

Expenditures

Grants—Note B	
Clinical Pharmacology Faculty Awards	225,000
Clinical Pharmacology Fellowships	102,596
Clinical Pharmacology Unit Support	76,968
Basic Pharmacology Faculty Awards	149,663
Medical Student Research Fellowships	27,000
Pharmacology-Morphology Fellowships.....	107,888
Research Starter Grants	234,250
Advanced Predoctoral Fellowships.....	126,464
Toxicologic Pathology Faculty Awards	<u>75,000</u>
	1,124,829
Administrative, December Awardee	
Meeting and Other Expenses.....	317,748
TOTAL EXPENDITURES.....	1,442,577
Excess of income over expenditures	270,505
Fund balance at January 1, 1984	1,833,816
Fund balance at December 31, 1984	2,104,321

Note A—The Foundation received contributions of \$272,500 prior to December 31, 1984 which was pledged for 1985 and, therefore, not recorded as income in 1984.

Note B—In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 31, 1984, the amounts still to be disbursed with respect to these grants amounted to approximately \$2,109,214 with approximately \$1,177,378 of this to be disbursed during 1985.

Organization And Administration

The PMA Foundation operates through its officers, Board of Directors and four advisory committees. In April, 1984, Irwin Lerner, President and Chief Executive Officer, Hoffmann-La Roche Inc., was re-elected Chairman of the Board, Albert Bowers, Ph.D., Chairman, President and Chief Executive Officer, Syntex Corporation, was re-elected Vice Chairman and William R. Miller, President, Pharmaceutical and Nutritional Group, Bristol-Myers Company, was re-elected Secretary-Treasurer. Thomas E. Hanrahan served as President with Irwin C. Winter, M.D., Ph.D. serving as staff consultant.

Following the death of Mr. Hanrahan in January, 1985, Mr. Maurice Q. Bectel, of Muskegon, Michigan, was named his successor by the PMA Foundation Board of Directors at its meeting on April 13, 1985 in Boca Raton, Florida. Mr. Bectel assumed his responsibilities as President of the PMA Foundation on June 17, 1985.

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William R. Miller, Secretary,
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Maurice Q. Bectel, President²
I. C. Winter, M.D., Ph.D.³



Irwin Lerner



Maurice Q. Bectel



Irwin C. Winter

¹Died January, 1985

²Assumed Presidency PMA
Foundation June, 1985

³Consultant, PMA Foundation

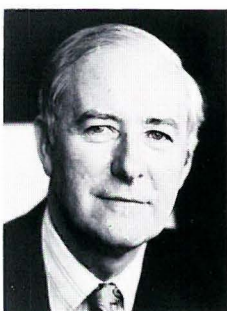
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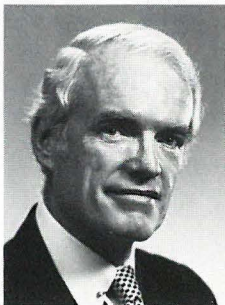


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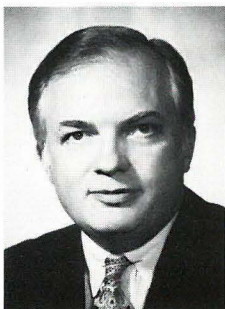


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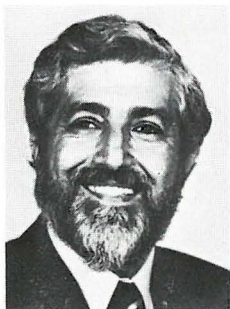
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Applications

The Foundation accepts requests for support and suggestions for pertinent research projects from qualified institutions and individuals. However, in 1971 the Foundation underwent a major shift in program direction, now emphasizing education and training support.

To expedite the handling of requests for research support, it is suggested that a brief one or two page letter be directed to the Foundation, outlining the intended project and an estimate of the funds involved. After review of this more informal request by members of the Scientific Advisory Committee to determine the degree of likelihood of the project falling within Foundation guidelines, a decision can be made as to whether a formal proposal is warranted.

Inquiries should be addressed to:

**Maurice Q. Bectel
President
Pharmaceutical Manufacturers
Association Foundation, Inc.
1100 15th Street, N.W.
Washington, D.C. 20005**

**Pharmaceutical Manufacturers
Association Foundation, Inc.
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