

ANNUAL REPORT



Pharmaceutical Manufacturers Association Foundation Inc.

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# Report of the Chairman



IRWIN LERNER Chairman of the Board PMA Foundation President and Chief Executive Officer Hoffmann-La Roche Inc. Nutley, New Jersey

Pharmaceutical industry support for medical science and therapeutics is extolled in a recently released publication recounting the 20-year history of the Pharmaceutical Manufacturers Association Foundation.

The "Pharmaceutical Industry in Support of Medical Science" is dedicated to the pharmaceutical industry and to the 850 recipients of grants who have burnished the world of bioscience and extended its promises into the future.

Nowhere has so much been achieved in so short a time with so little. In its two decades, the Foundation has distributed some \$18 million, much of it for the education and training of today's younger generation of scientists so essential to pharmacology and its related disciplines—and thence of surpassing importance to the future of therapeutics.

A very large number of awardees have gone on to key professorships in medical schools, with a large majority still engaged in research. Virtually all can be said to have immensely strengthened the world of medical academe. A recent survey indicated that only 7% of the Foundation's awardees are employed fulltime in industry

or government. The overwhelming majority continue to combine teaching with research in positions seminal to the long-term development of their disciplines.

In attempting to put into perspective the Foundation's support of medical science, the publication describes progress that has evolved from the initial work of the Commission on Drug Safety under the guidance of Lowell T. Coggeshall, M.D. This august Commission issued, after 18 months of effort, a balanced, judicious and common-sense report. On its recommendation, the PMA Board of Directors, on May 31, 1965, formally established the PMA Foundation with E. Gifford Upjohn, M.D., as its first Chairman.

The publication delineates progress from the original faculty development awards to the present nine programs and from the initial contribution of \$136,500 to the current annual giving which exceeds \$1,600,000.

The Foundation's success is attributed to four factors: steady and growing support from the PMA Board of Directors, the use of advisory committees of acknowledged scientific experts, the calibre and quality of awardees, and the clear purposes and integrity of the programs without any commercial overtones. In addition to the chronological account of the two decades, the publication lauds PMA Board members, 34 of whom have served on the Foundation Board. One section, "Service at the Core," recognizes the work of the 128 Advisory Committee members, about half of them from industry and about half from academe, most of whom have served for many years. Without them, the publication states, "the Foundation would be a skeletal operation, rattling aimlessly down the corridors of science. With them, it has built practical programs, inexhaustible credentials and scientific relevance."

A major section entitled "A Cornucopia of Talent," contains unsolicited comments from awardees on the value of PMAF grants to their careers, and a random sampling of research and publication achievements. In the disciplines they pursue, they have clearly embellished medical science.

A final section, "Gatherings of the Clan," depicts the conferences given over to dialogue among awardees, advisory committee members and industry representatives. Keynote speeches at these affairs surely rank among classic scientific papers.

Over the coming years, there will be no scarcity of viewpoints on how the Foundation can best spend its money, regardless of how fruitfully the amounts may grow. Given the story to date, contributors can be sure that their outlays will flow through the bioscience community with frugality, care and wisdom.

The publication also pays special tribute to the late Thomas E. Hanrahan, who guided the Foundation for twenty years. The Foundation will be forever indebted to his dedicated and selfless leadership and energy.

The publication has an extensive appendix with the listing of contributors, past and present Board members, Advisory Committee members, and all awardees and their associations.

I commend the publication as a source of insight at a time when government is seeking to contain the cost of today's medicines, while making sure that tomorrow's will be here when we need them.

I know I speak for the entire PMA Foundation Board of Directors in expressing thanks to our PMA member contributing corporations and in welcoming the opportunity to serve such a worthwhile effort.

> Irwin Lerner Chairman

# 1985 Foundation Meetings

The annual awardees meeting of the Foundation was held in New York City on December 3-4. The format for the scientific sessions again included a very successful poster session held from 8:30 to 10:30 a.m. Even though the easels never arrived, the session was extremely well received with a large number of attendees and participants commenting that they were able to attend most of the presentations in their specific area of interest. Immediately following the poster sessions, Mr. William R. Miller, PMA Foundation Board member, Chairman-Elect of the PMA Board of Directors and Vice Chairman of the Board of Bristol-Myers Company, opened the plenary session with welcoming remarks expressing the Board's appreciation of the Foundation's programs.

Irwin C. Winter, M.D., Ph.D., the session's moderator, then introduced the keynote speaker, Edward A. Carr, Jr., M.D., Professor and Chairman, Department of Pharmacology and Therapeutics, University at Buffalo, State University of New York, who presented an address entitled, "An Image of Our Future: Scintigraphy and Magnetic Resonance in Non-invasive Studies of Drugs." Dr. Carr's address was followed by a spirited question-and-answer period.

After Dr. Carr's address, a joint reception and luncheon was held with the PMA Board of Directors and the awardees. Mr. Irwin Lerner, Chairman of the Board of the Foundation and President and Chief Executive Officer of Hoffmann-La Roche Inc., presented welcoming remarks commenting on the great strides the Foundation has made since its beginning in 1965.

Three subgroups of awardees met separately in the afternoon. The Clinical Pharmacology Subgroup Session centered around a presentation by Dr. Marcus Reidenberg, Professor of Pharmacology and Medicine and Head of the Division of Clinical Pharmacology at Cornell University Medical College, titled, "The Broad Discipline of Clinical Pharmacology." Dr. Reidenberg emphasized the differences in clinical pharmacology research when compared with research conducted by subspecialists, such as cardiologists.



PMA Foundation Awardee Meeting

Broad training in pharmacology and clinical investigation makes it possible for clinical pharmacology investigations to transcend usual subspecialty lines. Dr. Reidenberg emphasized another aspect of clinical pharmacology research—the development of new drugs. He cited important contributions academic investigators have made in collaboration with the pharmaceutical industry in developing new drugs and pointed out ways in which these efforts could be expanded. He also discussed other responsibilities of the academic clinical pharmacologist, including education and clinical service. A very spirited discussion with the awardees followed the session which led to consideration of other topics, including clinical pharmacology boards.



Foundation Advisory Committee Meeting

The Basic Pharmacology Subgroup attended a lecture by Dr. James R. Gillette, Chief, Laboratory of Clinical Pharmacology at the National Heart, Lung, and Blood Institute on "Perspectives on the Future Development of Drug Metabolism." In addition, a segment of the afternoon was devoted to presentations by awardees: Dr. Nancy Zahniser discussed her work on presynaptic dopamine receptors; Dr. Gregory Weiland presented data on the effects of substance-P on agonist-induced loss of nicotinic acid receptor activity and Dr. James Halpert spoke on selective inhibitors of cytochromes P-450.

At the subsection meeting of the Pharmacology-Morphology group, Dr. Michael D. Gershon presented a talk on the enteric nervous system (ENS) of the gut. Dr. Gershon at first stressed the unique features of this nervous system, which are generally little known by most physiologists and pharmacologists. These features, despite their relative obscurity, are of great importance in (1) leading to morbidity that is potentially treatable with drugs; and (2) causing a great many of the untoward "side effects" of drugs. Characteristics of the ENS that are found nowhere else in the peripheral nervous system include an ultrastructure that resembles the brain, many neurotransmitters, the presence of glia, and an ability to function independently of control by the brain or spinal cord.

After discussing what makes the ENS special, Dr. Gershon concentrated on factors that shape its development as well as on his recent discovery of a novel enteric neural receptor for serotonin. The origin of enteric neural and glia precursors was traced from the neural crest. They were shown to migrate along defined pathways to the bowel where migration finally ceased in response to contact with specific extracellular matrix proteins. Subsequent development was found to depend on an interaction with the enteric microenvironment. New advances in this area are expected to be of great use in drug design.



Showing the "20-Year History" are Maurice Q. Bectel, President, Donna Dieppa, Administrative Assistant, Irwin C. Winter, M.D., Ph.D., Consultant



Edward A. Carr, Jr., M.D.

# 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 \$18 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 \$12 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 1985 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 1985, 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 20 years of existence, helped over 900 individuals through its research and educational support program. A twenty-year historical perspective outlining Foundation activities has just been completed.

## **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, 1986, 75 individuals have been supported under this program since 1967.



William J. Elliott, M.D., Ph.D.



Desmond Fitzgerald, M.D.



Douglas G. Roberts, M.D.



Theodore Wang, M.D.

#### Recipients of the four awards to begin July 1, 1986 are:

William J. Elliott, M.D., Ph.D., Assistant Professor of Medicine, University of Chicago. Dr. Elliott's research involves the therapeutic potential of columbinic acid. Rather than isolating this material from vegetable sources, however, Dr. Elliott plans to chemically synthesize a large quantity of it in pure form and then investigate its effects in several animal models of human diseases, including psoriasis, high blood pressure, and elevated cholesterol levels in the bloodstream.

Desmond Fitzgerald, M.D., Instructor in Medicine and Pharmacology, Vanderbilt University. Dr. Fitzgerald's research will focus on the pathogenic role of prostacyclin and thromboxane  $A_2$  in two conditions: pregnancy-induced hypertension and unstable angina, where these eicosanoids may play a role in modulating platelet function and vascular reactivity. Biosynthesis of these metabolites will be determined by specific assay of their plasma and urinary metabolites and their functional importance evaluated using selective inhibitors both in models of these diseases and in clinical studies.

Douglas G. Roberts, M.D., Assistant Professor of Pediatrics and Pharmacology, Wayne State University School of Medicine. Dr. Roberts will pursue three aspects of non-steroidal anti-inflammatory drug (NSAID) pharmacology, involving therapeutics, drug interaction and basic pharmacology. Sulindac, which has been reported to have less renal toxicity in adults than other NSAIDS, will be evaluated in neonates with patent ductus arteriosus. His objective is to provide greater efficacy with less toxicity than currently available therapies.

Theodore Wang, M.D., Assistant Professor of Medicine, Tulane Medical Center Hospital and Clinic. Dr. Wang will be studying antiarrhythmic drug combinations primarily and secondly antiarrhythmic efficacy of NAPADE and PADE in animal models. With regard to his primary research, he proposes to compare the electrophysiologic effects of the combinations of quinidine and bretylium, and procainamide and bretylium in dogs. The antiarrhythmic efficacy and possible synergism of such combinations will also be tested in patients with ventricular arrhythmias treated with a combination of mexiletine and sotalol. With regard to his secondary study, he plans to test the antiarrhythmic efficacy of procainamide, desethyl-N-acetylprocainamide (NAPADE), and desethylprocainamide (PADE) metabolites in post-coronary artery occlusion conscious dogs and to determine the ventricular fibrillation threshold in anesthetized dogs as a means of further evaluating their antiarrhythmic efficacy.

#### Those individuals whose awards began 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.

 William Steven Dalton, M.D., Ph.D., Clinical Instructor, Section of Hematology/ Oncology, Department of Internal Medicine, Health Sciences Center, The University of Arizona.

• Phyllis I. Gardner, M.D., Assistant Professor of Medicine, Stanford University Medical Center.

• Ruth Margrit Ruprecht, M.D., Ph.D., Assistant Professor, Dana-Farber Cancer Institute, Harvard Medical School.

## Those individuals who entered their second year of awards in July, 1985 are:

• Marc S. Ernstoff, M.D., Assistant Professor of Medicine, Department of Internal Medicine/Medical Oncology, Yale University School of Medicine.

• Marilynn 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 who concluded their awards in 1985 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.



Geographical distribution of Foundation awards under the "Faculty Development Awards in Clinical Pharmacology" program, 1967-1985.

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 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 1986 may elect to ask that the fellowship begin July 1987 or July 1988.

The first awards under this program were made in 1973. Since that time, 39 fellowships have been awarded.

#### Recipients of the four fellowships beginning July 1, 1986 are:

Patrick Taylor Horn, M.D., Ph.D., Division of Clinical Pharmacology, University of Minnesota. Dr. Horn's experiments are designed to investigate the effects of the autonomic nervous system, biological maturation and nerve growth factor on growth and differentiation of murine neuroblastoma (MNB). Established models of MNB tumors will be used to extend previous findings that chemical

sympathectomy in the neonatal period but not in the adult period slows the growth of MNB. The areas to be addressed are the effects of chemical sympathectomy on: (1) MNB tumor growth and differentiation; and, (2) synthesis and release of nerve growth factor and the effect this has on MNB tumor growth and differentiation.

Richard D. Huhn, M.D., Fellow in Clinical Pharmacology, Department of Medicine, Brown University. Dr. Huhn's research involves molecular pathological and pharmacological studies on the Abelson tyrosine kinase in chronic myelogenous leukemia. Dr. Huhn aimes to characterize changes induced by exposure to pharmacologic maturational agent in the expression and activity of the altered cabl tyrosine kinase and its substrates in CML cell lines and patient isolates.

Therese M. Kitt, Fellow in Clinical Pharmacology, Department of Pharmacology, Internal Medicine, University of Iowa. The purpose of Dr. Kitt's research is to examine the effects of prolonged (28 days) protein restriction on renal clearance of oxipurinol. Oxipurinol, the major metabolite of allopurinol, is excreted primarily by the kidneys. Since the clearance of oxipurinol is dependent on dietary protein, the dosage of allopurinol in malnourished or elderly patients on a protein restricted diet may need to be decreased to avoid allopurinol toxicity. She also plans to study the transport of quinolinic acid in rabbit brain slices, choroid plexus and in vivo. In this research, she expects to find that, unlike monocarboxylic acids, the brain will not have an effective transport mechanism for quinolinic acid.





Richard D. Huhn, M.D.



Therese M. Kitt, M.D.



Thomas C. Shea, M.D.

Thomas C. Shea, M.D., Cancer Pharmacology Division, Harvard University, Dana-Farber Cancer Institute. Dr. Shea will investigate the pharmacokinetics, toxicity and efficacy of high doses of the alkylating agent dibromodulcitol. Also, he intends to become involved in similar studies of high dose thio-tepa and carboplatin to be used in combination with autologous bone marrow transplantation. In addition, his studies will focus on the role of the glutathione transferases in the metabolism of clinically active alkylating agents, with particular emphasis on the enzymes' possible role in the development of tumor cell resistance to these drugs.

#### Those individuals whose fellowships began July 1, 1985 are:

• David Hayden S. Iansmith, A.B., M.D., Ph.D., Clinical and Research Fellow, Division of Cardiology and Clinical Pharmacology, Vanderbilt University.

• Susan L. Kelley, M.D., Fellow in Medical Oncology, Department of Pharmacology, Yale University School of Medicine.

• Sidney Alexander Scudder, M.D., Fellow, Division of Oncology, Stanford University.

## Those individuals who entered the second year of their fellowships in 1985 are:

• Nancy Jo Braden, M.D., Fellow, Department of Pediatrics, the Ohio State University College of Medicine.

• Gregory G. Gaar, M.D., Fellow, Department 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 awards concluded in 1985 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, Department of Pediatrics and Pharmacology, University of Iowa College of Medicine.



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

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## 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. Sixty-eight awards have been made since 1974.

#### Those individuals who were awarded fellowships in 1985 were:

 Neri M. Cohen, University of Maryland, Baltimore, has a twelve-month fellowship. His principal advisor is W. J. Lederer, M.D., Ph.D., Associate Professor, Physiology.

• Kimberly Dunn, University of Texas, Houston, has a twelve-month fellowship. Her principal advisor is Dr. Alan Robison, Chairman, Department of Pharmacology.

• Barbara E. Erny, Stanford University, has a six-month fellowship. Her principal advisor is Terrence F. Blaschke, M.D., Associate Professor, Medicine.

• Tom Karnezis, University of Chicago Pritzker School of Medicine, has a fourmonth fellowship. His principal advisor is Dr. Leon Goldberg, Chairman of the Department of Clinical Pharmacology.

• Christine M. Kraras, The Medical College of Pennsylvania, has a three-month fellowship. His principal advisor is Claire M. Lathers, Ph.D., Associate Professor of Pharmacology.

 James Luketich, Medical College of Pennsylvania, has received a six-month fellowship. His principal advisor is Peter R. Kowey, M.D., Associate Professor of Medicine, Assistant Professor of Pharmacology.

• Eric Munoz, Stanford University, has received a six-month fellowship. His principal advisor is Brian B. Hoffman, M.D., Assistant Professor of Medicine and Pharmacology.

 James P. Rathmell, Wake Forest University, has received a three-month fellowship. His principal advisor is Robert L. Capizzi, M.D., Director, Oncology Research Center.

• Lisa G. Rider, Duke University, has received a twelve-month fellowship. Her principal advisor is James E. Niedel, M.D., Ph.D., Associate Professor, Department of Medicine; Assistant Professor, Department of Pharmacology; Chief, Division of Clinical Pharmacology.

• John D. Rockefeller, University of Kansas, has received a three-month fellowship. His principal advisor is Walter R. Dixon, Ph.D., Associate Professor, Department of Pharmacology and Toxicology.



Geographical distribution of Foundation "Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology" program, 1974-1985.

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## **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 thirteen.

#### The awards beginning July 1, 1985 were made to:

• Clinical Pharmacology-Toxicology Unit, University of Texas Medical School. Wayne R. Snodgrass, M.D., Ph.D., Associate Professor of Pediatrics and Pharmacology-Toxicology was made Head of the Unit. The Unit will be involved in a variety of research programs regarding diseases of children, ranging from efforts to prevent birth defects, metabolism in premature infants to the treatment of childhood leukemia.

• Division of Clinical Pharmacology, Department of Medicine, Brown University. Robert M. Swift, M.D., Ph.D., was appointed Director, Clinical Pharmacology Unit. The experimental protocols conducted through the Clinical Pharmacology Unit will investigate a variety of research questions in the areas of cardiac, pulmonary, neurologic and psychiatric pharmacology including: studies on adrenergic function in congestive heart failure; the central nervous system control of ventilation; non-adrenergic function in depression and drug and alcohol withdrawal states; and the comparative effects of anxiolytic drugs in anxious patients with respiratory disease.



Geographical distribution of Foundation "Clinical Pharmacology Unit" program, 1978-1985.

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## 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 38.

#### Those who will receive awards beginning July 1, 1986 are:

Kelvin W. Gee, Ph.D., Assistant Professor, Department of Pharmacology, University of Southern California. Dr. Gee's research involves benzodiazepine receptor heterogeneity: the molecular basis and functional significance. The specific aims are to determine: (1) the biochemical basis of apparent benzodiazepine (BZ) receptor heterogeneity; and (2) the physiological significance of putative BZ receptor subtypes.

Jonathan Maybaum, Ph.D., Assistant Professor, Department of Pharmacology, University of Michigan. Dr. Maybaum's research will concern the actions of antileukemic drugs which become incorporated into DNA in place of naturally occurring purines or pyrimidines. One major aim is to determine if the sequence into which these substitutions take place has any significance with respect to the biological consequences of analog incoporation. In order to perform this research, Dr. Maybaum will insert the antileukemic agent 6-thioguanine into specific regions of the DNA of a well-characterized virus (SV40), and then examine the effects of these substitutions on the ability of the viral DNA to become replicated and to bind specific proteins, among other effects.

Michael K. Skinner, Ph.D., Assistant Professor, Department of Pharmacology, Vanderbilt University. Dr. Skinner's project focuses on the cellular functions and interactions in the testis and ovary. The purpose of this research is three-fold: (1) to investigate the cellular interactions between testicular peritubular cells and Sertoli cells; (2) to investigate the cellular interactions between ovarian theca cells and granulosa cells; and (3) to investigate the mechanisms by which regulatory agents influence Sertoli cell and granulosa cell functions and cytodifferentiation along with an analysis of what protein factors and pharmacological agents influence these cells.



Kelvin W. Gee, Ph.D.



Jonathan Maybaum, Ph.D.



Michael K. Skinner, Ph.D.

#### Beginning his award July 1, 1985:

• William Thomas Gerthoffer, Ph.D., Assistant Professor, Department of Pharmacology, University of Nevada School of Medicine.

#### Entering the second year of their awards in 1985 are:

• James R. Halpert, Ph.D., Assistant Professor, Department of Pharmacology and 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 whose awards concluded in 1985 are:

• Keith T. Demarest, Ph.D., Assistant Professor, Department of Pharmacology and 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.



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

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 More than One

## 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 \$6,552 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 additional fellowships were authorized for 1986. A total of 94 fellowships has been made since 1977.

#### Those whose fellowships will begin between January and August 1986 are:

• Lisa A. Bero, Duke University. Her advisor is Cynthia Kuhn, Ph.D., Department of Pharmacology. Ms. Bero will research the role of opiates in the development of central nervous system regulation of prolactin secretion.

• John D. Bell, University of California, San Diego. His advisor is Dr. Laurence L. Brunton, Assistant Professor of Medicine. Mr. Bell's research is directed toward the effects of phorbol esters on hormonally sensitive adenylate cyclase in S49 lymphoma cells.

 Janet L. Christiansen, Cornell University Medical College. Her advisor is Dr. Robert F. Oswald, Assistant Professor, Department of Pharmacology. Ms. Christiansen's research will involve the interactions of channel antagonists with voltage-sensitive calcium channels.

• Mary E. Dogramajian, Cornell University Medical College. Her advisor is Hazel H. Szeto, M.D., Ph.D., Associate Professor, Department of Pharmacology. Ms. Dogramajian's research is focused on the effects of central histamine depletion and specific agonist replacement on developing sleep-wake behavior and cardiorespiratory function.

• Donald W. Fink, Jr., University of Minnesota. His advisor is Bernard L. Mirkin, M.D., Ph.D., Professor and Head, Department of Pharmacology. Mr. Fink's research is aimed at epigenetic regulation of neuroblastoma growth and differentiation.

• Gifford L. Hoyer, University of Arizona. His advisor is Thomas P. Davis, Ph.D., Department of Pharmacology. Mr. Hoyer's research deals with peptide E processing and motility effects in the small intestine.

• Lori L. Isom, Vanderbilt University. Her advisor is Lee E. Limbird, Ph.D., Professor, Department of Pharmacology. Ms. Isom's research intends to answer the question, "Are Alpha<sub>2</sub>-Adrenergic Receptors Linked to Effector Systems Other than the Inhibition of Adenylate Cyclase?"

• Rosemary Kraemer, New York Medical College. Her advisor is Kevin Mullane, Ph.D., Associate Professor, Department of Pharmacology. Her research will focus on modulation of leukocyte function and inflammation by two novel metabolites of arachidonic acid formed by neutrophils.

• Clay W. Scott, University of Texas Health Sci. Center, Dallas. His advisor is Marc Mumby, Ph.D., Assistant Professor, Department of Pharmacology. Mr. Scott's research involves dual regulation of type II cAMP-dependent protein kinase in intact tissue.

• Thomas G. Steffens, State University of New York. His advisor is Oliver M. Brown, Ph.D. Mr. Steffen's research is directed toward neural regulation of heart rate: Influence of adrenergic presynaptic receptors on parasympathetic nerve fibers.

• Roseann L. Vorce, Michigan State University. Her advisor is Jay I. Goodman, Professor and Chairman, Department of Pharmacology/Toxicology. Her research looks toward the potential for oncogene activity in B6C3F1 mouse liver.



Geographical distribution of Foundation awards under the "Fellowships for Advanced Predoctoral Training in Pharmacology/Toxicology" program, 1972-1985.

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## 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, 60 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 1, 1985 are:

Paul J. Millard, Ph.D., Department of Pharmacology, Cornell University. Dr. Millard's research is concentrated on the role of calcium in stimulus-secretion coupling in normal mast cells and cultured rat basophilic leukemia cells (RBL). Fluorometric measurements of intracellular Ca<sup>+2</sup> will be made using suspensions of cells which have been loaded with the new fluorescent indicator of calcium, quin2, under varying conditions of stimulation. Generalized or localized changes in quin2 fluorescence due to changes in cytoplasmic Ca<sup>+2</sup> in individual stimulated mast cells will be observed using the powerful new technique of computer-assisted video fluorescence microscopy.

Gary M. Mawe, Ph.D., Department of Anatomy and Cell Biology, College of Physicians and Surgeons of Columbia University. Recent studies in Dr. Mawe's laboratory have partially characterized the enteric neural 5-HT ("M") receptor. He intends to pursue initial results which indicate that an azido derivative of 5-HT, "ANPA-5-HT," can be used as a specific photoaffinity ligand for labeling these receptors. The interaction of the photoaffinity probe with the receptor will be characterized, its specificity determined, and the effects of the probe on 5-HT binding will be assessed.



Paul J. Millard, Ph.D.



Gary M. Mawe, Ph.D.

#### Those who entered the second year of their fellowship in 1985 are:

• Robert S. Garofalo, Ph.D., Department of Anatomy and Cell Biology, College of Physicians & Surgeons of Columbia University.

• Michele S. Moss, Ph.D., Department of Obstetrics, Gynecology & Reproductive Sciences, University of California, San Francisco.

#### Those individuals whose fellowship concluded in 1985 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.



Geographical distribution of Foundation "Fellowship Awards in Pharmacology-Morphology" program, 1968-1985.

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 More than One

## Faculty Awards in Toxicologic Pathology

This award began as a pilot program in 1983 and was made permanent in 1985. It was developed to attract scientists interested in analyzing, reviewing and questioning, where appropriate, the present state of the art in the field of toxicology. The goal of the program is to attract veterinary and comparative pathologists who are interested in spending two years in drug toxicology research. In 1985 two awards were made, bringing the total number of awards to eight.



#### Merl F. Raisbeck, D.V.M., Ph.D.

#### Those who will receive awards beginning July 1, 1986 are:

Merl F. Raisbeck, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Pathology, University of Missouri. Dr. Raisbeck's research is designed to discover if the interaction between 2-hexanone and haloalkane 1,2-dibromo, 3-chloroethane extends to the combination of 2-hexanone with other gonadotoxic agents (specifically chlordecone, para tert butyl benzoic acid and cadimium); if ketones other than 2-hexanone potentiate the gonadotoxic effects of DBCP. This information will be useful in predicting the potential hazard of certain solvent combinations to workers. The second phase of the project examines the underlying mechanism of the interaction.



Dennis W. Wilson, D.V.M., Ph.D.

Dennis W. Wilson, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Pathology, University of California, Davis. Dr. Wilson's research involves an evaluation of the effects of inhalation of synthetic "smog" mixture on the lungs of rats. A comparison will be made of the responses of normal rats with rats made emphysematous by an intratracheal injection of elastase. Detailed morphometric measurements of inflammation, fibrosis and pulmonary structure will be correlated with physiologic and biochemical measurements done by collators. A second project of Dr. Wilson's will be to examine the mechanism of short chain alkenal toxicity.

#### Those who received awards beginning July 1, 1985 are:

• Kim Boekelheide, M.D., Ph.D., Assistant Professor, Department of Pathology and Laboratory Medicine, Brown University.

• Kevin P. Keenan, D.V.M., Ph.D., Assistant Professor, Department of Pathology, University of Maryland at Baltimore.

#### Those who entered the second year of their award July 1, 1985 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.

#### Those individuals whose awards concluded in 1985 are:

• Gerald G. Long, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Microbiology, Pathology and Public Health, Purdue University School of Veterinary Medicine.

• Glen K. Miller, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Colorado State University College of Medicine and Biomedical Sciences.



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, 1966-1985.

- One
- More than One
- \* Outside continental U.S.

## Use and Care of Laboratory Animals

The Project Review Committees of the PMA Foundation are sensitive to the appropriate use of experimental subjects, animals and human, in research. In their deliberations, they consider all aspects of a proposal and may deny support for many reasons. These include the assessment of humane use and care of the animal subject, qualifications of an investigator, originality and creativity, suitable use of experimental subjects, and likelihood of successful outcome. The committees have acted and will continue to act to assure that research supported by the Foundation will be based upon the appropriate use of experimental subjects.

## **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 351 research starter grants have been made, including the 20 awards beginning January 1, 1986.

Michael J. Meldrum, Ph.D.

#### The recipients of the grants beginning January 1986 are:

Alan P. Agins, Ph.D. Brown University Richard H. Alper, Ph.D., The University of Kansas Matthew P. Galloway, Ph.D. Wayne State University Kelvin W. Gee, Ph.D., University of Southern California Steven S. Gross, Ph.D., Cornell University Calvin C. Hale, Ph.D., University of Missouri, Columbia Robert P. Hartshorne, Ph.D. Oregon Health Sciences University Cecilia J. Hillard, Ph.D. Medical College of Wisconsin David S. Loose, Ph.D. University of Texas Health Science Center. Houston

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Kathryn K. McMahone, Ph.D. University of South Carolina

Based on need for funds, a review of the 20 research starter grantees whose awards began January 1, 1985 for a second year of the awards resulted in 14 of them having their awards continued. These are:

William D. Blaker, Ph.D. Virginia Polytechnic Institute Albert Chan, Ph.D. University of Mississippi Charles Chavkin, Ph.D. University of Washington Carl W. Christensen, Ph.D. University of Wisconsin Randall L. Commissaris, Ph.D. Wayne State University Jerry J. Hjelle, Ph.D. University of Wisconsin, Madison Paul R. Housley, Ph.D. University of South Carolina

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Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1972-1985.

- 🛛 One
- More than One
- \* Puerto Rico

## 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 methological grant. The intent of the grant was 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 third year of support in 1985 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 August 31, 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 final report was made in 1985 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.

This direct reporting project evaluated the ability and willingness of patients to report drug adverse effects directly to a data center. The project was judged a success in determining that, if used selectively in situations requiring one-time participation, the method will be successful in evaluating adverse drug effects and drug induced disease.

# 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 6.

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 1985 was \$1,837,029. Of this amount, \$1,607,593 came from contributions. The balance of \$229,436 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 Members Firms. Contributions were also received during 1985 from other groups in the health field.

Grants, Foundation-sponsored programs, special meetings and other expenses for 1985 amounted to \$1,595,374. Of this total, \$1,223,676 represent expenditures for grants. The fund balance as of December 31, 1985 was \$2,345,976. 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, 1985, the contingency liability for 1986 was approximately \$1,318,943.

The Foundation's financial position as of December 31, 1985 has been audited by the Washington D. C. accounting firm of Buchanan & Company.

#### PMA Foundation Contribution Income





## Statement of Income and Expenditures For the Year Ended December 31, 1985

#### Income

Contributions	1,607,593
Income from investments	. 144,555
Gain of Sale of Stock	16,454
Miscellaneous Income	68,427
Total Income	1,837,029

#### **Expenditures**

Grants – Note A	
Clinical Pharmacology Faculty Awards	224,750
Clinical Pharmacology Fellowships 1	119,108
Clinical Pharmacology Unit Support 1	104,999
Basic Pharmacology Faculty Awards 1	124,326
Medical Student Research Fellowships	33,500
Pharmacology-Morphology Fellowships 1	103,126
Research Starter Grants 2	274,588
Advanced Predoctoral Fellowships 1	145,529
Toxicologic Pathology Faculty Awards	93,750
1,2	223,676
Administrative, December Awardee	
Meeting and Other Expenses	371,698
TOTAL EXPENDITURES 1,5	595,374
Excess of income over expenditures	241,655
Fund balance at January 1, 1985 2,1	104,321
Fund balance at December 31, 1985 2,3	345,976

Note A — In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 31, 1985, the amounts still to be disbursed with respect to these grants amounted to approximately \$2,228,472 with approximately \$1,318,943 of this to be disbursed during 1986.

# Organization and Administration

The PMA Foundation operates through its officers, Board of Directors and five advisory committees. In April, 1985, 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 M. Sullivan, Chairman of the Board and President of Burroughs Wellcome Co., was elected Secretary-Treasurer. From June, 1985, Mr. Maurice Q. Bectel, served as the Foundation's President with Irwin C. Winter, M.D., Ph.D. serving as staff consultant for the year.

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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:

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