1991 ANNUAL REPORT

Pharmaceutical Manufacturers Association Foundation





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Report of the Chairman



Sheldon G. Gilgore, M.D. Chairman, PMA Foundation

his Annual Report of the Pharmaceutical

Manufacturers Association Foundation represents my first opportunity to comment on Foundation activities through this medium. I am both pleased and proud to offer this Report as Chairman of the Foundation's Board of Directors.

Allow me to first thank the Foundation chairmen who precede me in this capacity. Special credit goes to my immediate predecessor as Chairman, Harvey S. Sadow, Ph.D., who led the Foundation to new growth records and made the transition to my chairmanship a pleasant task.

I have asked Secretary-Treasurer Joseph A. Mollica, Ph.D., to report on the 1990 financial affairs of the Foundation, and President Maurice Q. Bectel to report on the internal administrative workings of the organization and its staff. In both cases, these responsibilities have been capably executed, and for their ongoing support and dedication I extend my thanks for jobs well done.

I would like to devote my report to a matter which I am making the theme of my tenure as Chairman of the PMA Foundation—namely, affirming with new vigor the Foundation's commitment to encourage talented young scientists to pursue careers in biomedical research.

Do not misinterpret this as disappointment in the Foundation's past efforts; the fact that the Foundation has expended over \$30 million in support of more than 1,500 young scientists is a source of great industry and personal pride. And it is not merely a matter of the PMA Foundation doing more of what it already does, although clearly, that is a goal I hope to successfully address.

It is more a communications challenge to alert decision-makers and the public to the nature and scope of the emerging shortage of biomedical researchers. For without public support and that of the policy makers that represent them, no meaningful gains will be made against this problem. Certainly, the Foundation cannot by itself remedy the problem of maintaining an adequate supply of American biomedical research scientists to meet the exploding opportunities before us as we turn into the 21st century. U.S. leadership is at stake unless the steady stream of some of our nation's best and brightest students can be wooed into research careers—not only by the inherent challenge of scientific research, but also competitive compensation and job security.

It was toward that objective that the Foundation mounted a communications program that began with a Washington, D.C. press conference on February 13, 1991. Issueadvertisements in *The Washington Post, Wall Street Journal, The New York Times,* the *New England Journal of Medicine, Science,* and the *Journal of the American Medical Association* posed the question: "Can America afford to lose its lead in science and technology?"

The Foundation retained the Gallup Organization to conduct a survey of three research sectors: academic research leaders; NIH grant holders; and industry R&D leaders. The results revealed pervasive concern that America's pipeline of career scientist is in jeop-ardy. Several specific concerns included:

- Reduced math and science skills in high school students, leaving fewer qualified candidates;
- Researchers spending time hunting funds instead of engaging in research;
- Young investigators abandoning research for better paying, more secure jobs;
- The "graying" of the senior U.S. scientific community and consequent attrition;
- A shrinking college-age population.

Joining the Foundation and George Gallup at the February 13 press conference: William F. Raub, Ph.D., then-Acting Director of the National Institutes of Health; Donald N. Langenberg, Ph.D., President of the American Association for the Advancement of Science; Thomas E. Malone, Ph.D., Vice President for Biomedical Research, American Association of Medical Colleges; and John F. Beary III, M.D., Sr. Vice President for Science and Technology of the Pharmaceutical Manufacturers Association. The broad base of concern for this issue demonstrates the level of support for the Foundation's initiative: More must be done in career recruitment and retention of biomedical researchers!

The evening following the press conference, I addressed the awardees, Board members, and committee members stating that "We are dependent on the very awardees who sit here tonight for our future in biomedical science." I believe in that statement and urge others to give their encouragement—financial and otherwise—to young scientists to pursue a research career. I offer my own sincere appreciation and congratulations to the PMAF award recipients who are listed in the Foundation's Scholars publication.

My appreciation is also extended to the Board of Directors, and especially to those PMA members—the more than 100 research-intensive pharmaceutical companies—who enable the Foundation to pursue its objectives through their contributions.

Shen D. Siegore

Sheldon G. Gilgore, M.D. *Chairman, PMA Foundation* Chairman, President and Chief Executive Officer G&D Searle & Co.



Report of the President



Maurice Q. Bectel President

ast year, we changed the format and the

reporting period of the PMA Foundation's "annual" report to reflect the fixed, calendar year of the Foundation's financial accounting, while allowing for the flexibility of the timing of the "annual" awardees meeting. The comments were favorable and we continue this report in a similar framework, which allows for the publication of more current information.

Nineteen-ninety was another year of record-setting and continuing high levels of activity, with 96 grants awarded in 1991 (for the 1990 grant review cycle). For the second year, total grants awarded exceeded \$2,000,000.

For the third year, the Foundation reported on the annual PMA Foundation Awards cycle via the separate publication, Scholars. A detailed listing of each award, the recipient, and the research project for which it was awarded are published, along with a description of all twelve Foundation Award Programs. This publication is used throughout the year to inform the public about the Foundation and its programs, and can be useful as a recruitment tool for careers in scientific research. Copies are even sent to members of the U.S. Congress to advise them of the industry's support of research through the Foundation's programs. Copies of the 1991 Scholars are available on request from the PMA Foundation office.

An additional report of current Foundation activities, aside from the Award Programs, can be found in the Foundation's newsletter, Tracking 24. Later in 1991, Tracking 25 will highlight the achievements of the Foundation during its first 25 years.

These three publication—the Annual Report, Scholars, and Tracking 24—provide documentation of the affairs and activities of the Foundation over the 1990-1991 period.

During 1990, the Chairmanship of the Foundation moved smoothly from 1989-90

Chairman Harvey S. Sadow, Ph.D., to 1990-91 Chairman Sheldon G. Gilgore, M.D., and the pace of activity continues to accelerate. Under Chairman Gilgore's leadership, the Foundation has added a most worthwhile "cause" to its activities—in addition to the continuing funding of the Awards Programs. The cause is a rededication of the Foundation to encouraging careers in biomedical research—the theme of this Annual Report and of Dr. Gilgore's activities as Chairman.

I welcome Dr. Gilgore's leadership, join with him in pursuing the "cause," and encourage others to lend their support to the encouragement of capable young people to pursue a career in biomedical research—the sine qua non of the advancement of health care.

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Maurice Q. Bectel President



Photograph courtesy of Searle



ACTIVITIES

1990-1991 Foundation Activities

The Pharmaceutical Manufacturers Association Foundation was established by the Pharmaceutical Manufacturers Association in 1965 for the purpose of promoting public health through encouraging scientific and medical research. We are celebrating the Foundation's Silver Anniversary of activity during 1991. Watch for a special issue of the PMAF newsletter, Tracking 25, to be published in late 1991, to commemorate this milestone.

The research-intensive pharmaceutical companies of the PMA are the original source of all Foundation funds, although earnings from reserves are also of significance. Since its funding, the Foundation has disbursed over \$30 million in grants. Some \$6 million (20%) has gone to support research, with the bulk of the balance going into educational awards. Over 1,500 scientists have been assisted through the Foundation's grant program.

Meetings and Other Activities

1990 ASPET Meeting

Ferid Murad, M.D., Ph.D., was the keynote speaker at the August 11, 1990 PMA Foundation Program, held for the 14th year in conjunction with the ASPET Annual Meeting. Since ASPET—the American Society for Pharmacology and Experimental Therapeutics—and the Foundation share areas of mutual interest the Foundation sponsors a scientific symposium and reception at the ASPET meeting.

Over 100 attended the meeting held in Milwaukee, Wisconsin.

Dr. Murad is Vice President, Pharmaceutical Products Research and Development for Abbott Laboratories. He spoke on "Relationships of Nitric Oxide Free Radical and Cyclic GMF as Second Messengers."



Ferid Murad, M.D., Ph.D., Keynote Speaker -PMA Foundation Program, August 11, 1990, ASPET Meeting



Foundation President Maurice Q. Bectel, Board Chairman Sheldon G. Gilgore, M.D., and former Award recipient Arthur Hull Hayes, Jr., M.D., visit during the Annual Awardee Meeting.

Advisory Committees Meet During AAPS Annual Meeting

Economy of time and costs influences yet another joint meeting to occur—this time the Foundation's Scientific Advisory Committee and several grant review committees met during the Las Vegas annual meeting of the American Association of Pharmaceutical Scientists (November 4-8, 1990).

In addition to the SAC, the following advisory committees met: Clinical Pharmacology, Basic Pharmacology, Toxicologic-Pathology, and Pharmaceutics. Committees meeting in February, 1991 included: Clinical Pharmacology and Pharmacology-Morphology.

During the AAPS meeting, President Bectel took the opportunity to address a gathering of pharmaceutics department chairmen on Foundation activities and the need for greater recruitment efforts for scientific manpower.

Press Conference, Annual Awardee Meeting Held in Washington

February 13, 1991, was a busy day for PMA Foundation Chairman Sheldon G. Gilgore, M.D., and President Maurice Q. Bectel. At the National Press Club, the Foundation held a morning news conference to dramatize concern over the impending shortage of qualified biomedical researchers. That theme has been repeated in several Foundation activities.

Approximately 40 representatives of the press and media attended the press conference. The results of a survey by The Gallup Organization were presented by George Gallup and Chairman Gilgore emphasized the need to recruit and retain talented young people in the field of scientific research.

Following the press conference, the Foundation held it's Annual Awardees Reception/Banquet and Meeting at the Capital Hilton in Washington.



Scientific Advisory Committee Chairman Frederick M. Radzialowski, Ph.D., addresses the Annual Awardee Meeting Luncheon on February 14,1991.



Jerry L. Spivak, M.D., Professor of Medicine, Director of the Division of Hematology and Professor of Oncology, Johns Hopkins Hospital spoke on "Erythropoietin: The Pharmacology of a Recombinant Growth Factor". Dr. Spivak delivered the "Thomas E. Hanrahan Memorial Lecture" at the Annual Awardee Meeting, February 14, 1991.

Frank Samuel, Jr., former executive officer of the Health Industry Manufacturers Association, was the banquet speaker. Mr. Samuel spoke as a Consultant to the Food and Drug Administration Advisory Committee regarding "Challenges Facing FDA." On February 14, the Thomas E. Hanrahan Memorial Lecture was delivered by Jerry L. Spivak, M.D., Professor of Medicine, Director of the Division of Hematology and Professor of Oncology, Johns Hopkins Hospital. In the afternoon, three break-out sessions were held in the areas of Basic Pharmacology, Clinical Pharmacology, and Pharmacology-Morphology.

Scientific Advisory Committee Meets with PMA R&D Section

The PMA Foundation's Scientific Advisory Committee met April 7 in conjunction with the PMA's Research and Development Section annual meeting. It was the fourth time the two groups had met jointly due to the crossover of memberships and mutual interest, making the joint meeting scientifically and economically advantageous.

The meeting was held in Carmel, California.



PMAF Board Chairman Sheldon G. Gilgore, M.D., discusses the busy day's events with Leo E. Hollister, M.D., a member of the Clinical Pharmacology Advisory Committee.

New Foundation Board Elected at PMA Annual Meeting

On April 29, 1991, the PMA Foundation Board of Directors held its meeting in Scottsdale, Arizona, in conjunction with the PMA Annual Meeting. Sheldon G. Gilgore, M.D., was elected to a second term as Chairman of the Foundation's Board. Newly elected Vice-Chairman is Charles A. Sanders, M.D., who serves as Chief Executive Officer of Glaxo, Inc. Dr. Sanders succeeds William F. Lalor, President, ICI Pharmaceutical Group, ICI Americas Inc., who has retired from the PMA Foundation Board.

Re-elected Secretary-Treasurer was Joseph A. Mollica, Ph.D., President and Cheif Executive Office, The DuPont Merck Pharmaceutical Company. Also elected to the Board was Digby W. Barrios, President and Chief Executive Officer, Boehringer Ingelheim Corporation.



Meredith Mason-Garcia, Ph.D., a current Pharmacology-Morphology Awardee, explains her poster to one of the 130 annual meeting attendees.



PMA Foundation Chairman Sheldon G. Gilgore, M.D., addresses over 40 reporters and others at the Foundation's February 13 press conference, held at the National Press Club on the subject of manpower shortages in biomedical research.

Ten pharmaceutical company executives serve on the current Foundation Board of Directors along with Gerald J. Mossinghoff, President of the PMA, who is an ex-officio member. In addition to Gilgore, Sanders, Mollica and Barrios, Board members are: Theodore Cooper, M.D., Ph.D., Chairman and Chief Executive Officer, The Upjohn Company; Paul E. Freiman, Chairman and Chief Executive Officer, Syntex Corporation; Hubert E. Huckel, M.D., Chairman of the Board, Hoechst-Roussel Pharmaceutical Inc.; Irwin Lerner, President and Chief Executive Officer, Hoffmann-LaRoche Inc.; Klaus Heinz Risse, Ph.D., President and Chief Executive Officer. Miles Inc.: George J. Sella, Jr., Chairman and Chief Executive Officer, American Cyanamid Company.





Photograph courtesy of Searle



Photograph courtesy of Syntex Corporation

EDUCATION AND TRAINING PROGRAMS

he PMA Foundation, to accomplish its goals in education and research, sponsors twelve programs—four in clinical pharmacology, one in the combined field of pharmacology-morphology, one in pharmacology or toxicology, one in basic pharmacology, one in toxicologic-pathology and three in pharmaceutics. The Research Starter Grant provides starter funds in pharmacology, clinical pharmacology, drug toxicology and pharmaceutics. The Foundation also accepts applications in all program areas for research on drugs for rare diseases.

CLINICAL PHARMACOLOGY

Faculty Awards in Clinical Pharmacology

The four clinical pharmacology programs provide assistance at the student, fellow and faculty levels. Through the Faculty Development Awards in Clinical Pharmacology program, the Foundation makes three-year awards to medical schools for salary and fringe benefits support of fulltime junior faculty members. The Foundation has set a ceiling of \$40,000 on the amount of its participation in total yearly salary and fringe benefits for any candidate.

With the awards scheduled to begin July 1, 1991, 91 individuals have been supported under this program since 1967. Recipients of the three awards to begin July 1, 1991, are:



Daniel David Gretler, M.D., Instructor, University of Chicago School of Medicine—"Basic and Clinical Pharmacology of Dopamine Receptor Agonists." This research is aimed at elucidating the physiological and

pharmacological relevance of the dopamine receptor system. While considerable advances have been made in this regard for the central nervous system, other organ systems have not been extensively investigated. He plans to direct his lab's efforts particularly to the heart, the kidney and the eye. Experiments ranging from in vitro laboratory studies and intact animal models to clinical trials in man are designed to provide insight into such topics as dopaminergic control of coronary blood flow, renal physiology and intraocular pressure. Further studies are aimed at elucidating the role of vascular endothelium on the pharmacological actions of dopamine receptor agonists.



Michael J. Jamieson, MBChB, MRCP, Assistant Professor, University of Texas Health Science Center—"Studies in the Human Microvasculature." These studies will examine: (1) Differing effects of individual

antihypertensive drugs on resistance vessel morphology and function in hypertension; (2) The interactions of sulfhydryl compounds, including angiotensin converting enzyme inhibitors, with the resistance vascular endothelium, and (3) The integration of peripheral neural and vascular mechanisms in reflex cutaneous vasodilatation to whole body heat stress. The principal experimental models are (1 & 2) pressurized arteriography of isolated resistance vessel segments and (3) laser doppler flowmetry of the forearm cutaneous vasculature.



Theresa A. Shapiro,

M.D., Ph.D., Assistant Professor of Medicine, Johns Hopkins University School of Medicine— "Development of New Antiparasitic Chemotherapy." Dr. Shapiro proposes to study

antiparasitic drugs at two levels, in the laboratory and in the clinic. The DNA topoisomerases are an attractive target for potential new antiparasitic therapy: her preliminary experiments suggest there is a basis for selective toxicity, and there are numerous antitumor and antibacterial topoisomerase inhibitors available for testing. In this project, she will continue to evaluate the molecular effects of topoisomerase inhibitors on trypanosomes. She will also determine whether these agents have antitrypanosomal activity in vitro and in mice. Type II topoisomerases will be purified from Trypanosoma equiperdum, and used to characterize inhibitor susceptibility. In a new series of experiments, the effects of topoisomerase inhibitors on the DNA of the malaria parasite, Plasmodium falciparum, will be examined and compared with antiparasitic activity in vitro.

Individuals whose awards began July 1, 1990, are:

Joseph J. Crowley, M.D., Assistant Professor, Division of Geriatric Medicine, University of Washington.

Paolo B. DePetrillo, M.D., Instructor, Department of Medicine, Brown University.

Charles W. Flexner, M.D., Assistant Professor, Department of Medicine and Department of Pharmacology, The Johns Hopkins University School of Medicine.

Joseph F. Foss, M.D., Assistant Professor, Department of Anesthesia and Critical Care, Committee on Clinical Pharmacology, University of Chicago.

Individuals who entered the second year of their awards in July 1990 are:

Patrick Taylor Horn, M.D., Ph.D., Assistant Professor, Committee on Clinical Pharmacology, University of Chicago.

Ralph A Kelly, M.D., Assistant Professor, Harvard Medical School.

Lawrence G. Miller, M.D., Assistant Professor, Tufts University School of Medicine. Individuals who entered the third year of their award in July 1990 are:

Thomas C. Shea, M.D., Assistant Professor, Department of Medicine and Oncology, and Director Bone Marrow Transplantation Program, University of California, San Diego.

John Tangney Sullivan, M.D., Assistant Professor, Francis Scott Key Medical Center, Johns Hopkins University.

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 study in 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 1991 may request that the fellowship begin July 1992 or July 1993.

The first awards under this program were made in 1973. Since that time, 55 fellowships have been awarded.

Recipients of the four awards beginning July 1, 1991:



Nabil S. Andrawis, M.D., Ph.D., Program in Clinical Pharmacology, Department of Medicine, Brown University School of Medicine—"Calcium Channel Blockers Block Angiotensin II-mediated

Vascular Responses.⁷⁷ Dr. Andrawis' research speculates that a significant part of the antihypertensive effect of calcium



Irwin M. Weiner, M.D., Chairman of the Basic Pharmacology Advisory Committee, Theodore Cooper, M.D., Ph.D., PMAF Director, and Paul Calabresi, M.D., Chairman of the Clinical Pharmacology Advisory Committee, pause during the Awardee Banquet reception.



Claire M. Lathers, Ph.D., relaxes, recalling her experience as a former awardee and poster presenter. She is now on loan from the Food and Drug Administration.

antagonists is directly related to their ability to block angiotensin II effect on vascular smooth muscle cells. Acutely this is the result of direct antagonism of AII effect resulting in vasodilation and during chronic treatment they prevent and/or reverse the effects of AII on vascular smooth muscle at the molecular level. The research suggests that the mechanism for the acute effect is blockade of AII signal transduction processes and the chronic effect due to blockade of AII-induced vascular smooth muscle hypertrophy. The specific aims: (1) Determination of in vivo peripheral vascular mechanism of response to calcium antagonists in the presence and absence of angiotensin II. (2) presence and absence of angiotensin II. (2) In vitro analysis of the cellular mechanisms causing the acute interaction between calcium of blockers and AII. (3) Characterization

of actin isotypes expression as an *in vivo* marker of vascular smooth muscle cell (VSMC) hypertrophy in chronic hypertension, and an in vitro marker of VSMC hypertrophy after chronic AII treatment. (4) Compare the effects of angiotensin converting enzyme inhibitors and calcium blockers on vascular actin isotype expression by in vivo and in vitro experiments.



Halina S. Darling, M.D., Loyola University of Chicago School of Medicine—"Cytochrome P450III Family Enzymes During Human Development." This research will explore the Cytochrome P450 family III in

the human newborn, infant, child and adolescent. Cytochrome P450III enzymes are the predominant P450 enzyme family in the human fetus (30-40% of total P450) but only a minor component of total P450 in the human adult (<5%). This family of enzymes is markedly induced during pregnancy and lactation in the mouse model by the induction of a new P450III family enzyme. Therefore, P450III appears to play an important role in development. The changes in family III enzyme activities and enzyme profile of P450III subfamilies in the human during postnatal development have never been explored. This study will characterize the human P450III family during postpartum development using in vivo and in vitro techniques. P450III will be characterized in vivo by using the [13C] erythromycin breath test in children beginning with sexually mature adolescents, then Tanner III adolescents, Tanner I children, 2-5-year olds, and 6 to 12-month old children. The enzyme family will also be characterized in vitro using DNA probes and monitoring enzyme function with immunoperceptation in hepatic tissues obtained at autopsy. The long-term research goals are to explore and identify the role of this

enzyme family in development, in chemical induced birth defects and altered drug metabolism in the human.



Andre Terzic, M.D., Ph.D., Thomas Jefferson University, Jefferson Medical College— "Mechanism of the Positive Inotropic Effect of alpha-Adrenoceptor Agonists." Despite standard pharmaco-

therapy, cardiac insufficiency and blood clot formation remain to be two major causes of mortality among cardiovascular diseases. The general purpose of this investigation is two fold: (1) to uncover the positive inotropic mechanism of aadrenoceptor agonists, a new inotropic class of drugs, and (2) to gain more insight into the pharmacological regulation of the synthesis of plasminogen activators, which are essential for the activation of fibrinolysis. Towards the first goal, the following hypothesis will be assessed: a-adrenoceptor occupation stimulate Na/H exchange to produce an intracellular alkalinization which in turn leads to a positive inotropic effect. The second aim will focus on the elucidation of mechanisms underlying pharmacological modulation of tissue plasminogen activator (tPA) expression by sulfonylureas.

Individuals who began their awards in July 1990 are:

David Michael Kerins, M.R.C.P.I., Division of Clinical Pharmacology, Vanderbilt University.

Therese K. Schmalbach, M.D., Ph.D., Department of Biology, Chemistry and Molecular Pharmacology, Harvard Medical School.

Individuals who entered the second year of their fellowships in July 1990 are:

David W. Rudy, M.D., Indiana University.

Daniel Ward, D.V.M., University of Georgia.

Ending their awards in 1990 are:

Li Wang, M.D., Department of Pharmacology/Toxicology, Children's Hospital (Ohio State University).

Daniel David Gretler,

M.D., Departments of Medicine and Pharmacology, University of Chicago.

William B. Abrams, M.D., member of the Clinical Pharmacology Advisory Committee, and a PMAF Awardee discuss the findings of one of the exhibits at the Poster Session of the Annual Awardee Meeting.



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, offers students an opportunity to spend up to two years fulltime conducting an investigative project in pharmacology-clinical pharmacology. The minimum period of the award is three months and maximum is two years. It is hoped that by having students become involved in investigative projects at a point when career choices are still relatively flexible, they will eventually choose research careers in clinical pharmacology. One-hundred awards have been made since 1974.

Individuals whose awards will begin in July, 1991, are:

Marlys R. Crane, Thomas Jefferson University, Jefferson Medical College (one year). Ms. Crane's research is entitled "Characterization of E. coli Heat-Stable Enterotoxin Receptors and her principal advisor is Scott A. Waldman, M.D., Ph.D., Assistant Professor of Pharmacology.

Douglas L. Gillott, Tulane University Medical School (one year). Mr. Gillott will be studying the "Regulation of the Pulmonary Circulation by Endothelin." His principal advisor is Albert L. Hyman, M.D., Professor of Pharmacy, Medicine and Surgery.

Jonathan Hartman, University of California at San Francisco. Mr. Hartman will focus on "Hypoxic-ischemic Neuronal Damage: Attenuation by Oxidative Modulation of the N-methyl-D-aspartate Receptor." His fellowship supervisor is Stuart A. Lipton, M.D., Ph.D., Associate Professor of Neurology.

Mitzi Hemstreet, Brown University Medical School (one year). Ms. Hemstreet's research involves "Sigma



Carl Peck, Ph.D., Director, Center for Drug Evaluation and Research, FDA, and Clinical Pharmacology Advisory Committee Chairman Paul Calabresi, M.D., intently discuss affairs at the Annual Awardee Banquet, held February 13, 1991.

Receptor Heterogeneity in Rat Brain: Anatomical, Physiological and Functional Differentiation." Her principal advisor is Dr. J. Michael Walter, Associate Professor of Psychology and Neural Science.

Frances Eun-Hyung Lee, Johns Hopkins University School of Medicine (one year). Ms. Lee will research "Brequinar: A Potentially New Anti-malarial Agent." Her fellowship advisor is Paul S. Lietman, M.D., Ph.D., Director, Division of Clinical Pharmacology, Professor of Medicine, Pharmacology and Molecular Science.

Robert E. Martell, University of Michigan Medical School (one year). Mr. Martell's research is entitled, "Calcitriol-mediated Regulation of Nuclear Phosphoprotein Binding to the c-myc Oncogene." His fellowship supervisor is Robert U. Simpson, Ph.D., Associate Professor of Pharmacology.

Susan S. Smyth, University of North Carolina, Chapel Hill, School of Medicine (one year). Ms. Smyth's research will focus on "Reconstitution of the Fibrinogen Binding Properties of GP IIb-IIa in a Cell Free System." Her principal advisor is Dr. Leslie V. Parise, Ph.D.

Clinical Pharmacology Unit Support

This program assists directors of clinical pharmacology units established within a two-year period preceding the award, or units that have acquired a new director during that period. In 1991, the Clinical Pharmacology Advisory Committee recommended and the PMA Foundation Board approved an increase in this award from \$50,000 per award to \$100,000, effective for 1992 awards. The grant, in 1991, provides a total of \$50,000 which may be used at any time over a three-year period. The purpose of the program is to provide supplementary funds to assist the unit's research efforts until other research grants are obtained. The first grants were made in 1978. The total number of awards made to date is twenty-two. Two awards were made for 1991.



Howard R. Knapp, M.D., Ph.D., Director, Division of Clinical Pharmacology, Department of Internal Medicine and Associate Professor of Medicine and Pharmacology, University of Iowa.

Current research in the division focuses on the clinical pharmacology of N-3 fatty acids, with particular emphasis on their potential therapeutic utility in patients with vascular disorders. Functional studies on hypertension and vascular occlusion will be coupled to mechanistic investigations using combined gas chromatography/mass spectrometry to assess the release of eicosanoids and other cell mediators in response to vascular stimuli in vivo. They have described changes in the patterns of both baseline and stimulated eicosanoid release with dietary fishoil supplementation in patients undergoing coronary angioplasty, and in those with essential hypertension. Finally, the synthesis of novel vasoactive eicosanoids

derived from fish oil fatty acids will be explored in both patients with vascular disease and normal subjects. A major part of their research effort is to define how the altered functional responses are related to changes in the synthesis of such mediators, and to determine optimal dosing regimens for N-3 supplements in different patient groups.



James J. Lipsky, M.D., Director, Clinical Pharmacology Unit, Department of Pharmacology and Consultant in Medicine and Pharmacology. One focus of research for the Unit is on an understanding of

the mechanism of antibiotic-associated hypoprothrombinemia. A metabolite of certain cephalosporin antibiotics has been shown to inhibit a step in coagulation factors synthesis as well as related reactions in vitamin K metabolism. This metabolite is a sulfhydryl compound. Studies will be conducted into the nature of the metabolite, what it inhibits, and why only certain individuals are susceptible to the development of hypoprothrombinemia. Another focus of research is an investigation of the clinical utility of the newly described assay for debrisoquin metabolism. Although debrisoquin itself is not a clinically significant drug in the United States, at least 20 other drugs with greater clinical use have been found to be metabolized by the same isoenzyme which uses debrisoquin as a substrate. This enzyme demonstrates a genetic polymorphism such that some individuals metabolize drugs slowly and therefore have higher levels of the drug. Recently a polymerase chain reaction (PCR) assay has been developed which can identify poor metabolizers of debrisoquin. Dr. Lipsky's Unit will determine the clinical utility of the new PCR assay.

BASIC PHARMACOLOGY

Faculty Development Awards in Basic Pharmacology

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

The first awards were made in 1973 and continue to be for a two-year period. The program provides salary and fringe benefits. The Foundation has set a ceiling of \$30,000 on the amount of its participation in the total yearly salary and fringe benefits for awardees. The total number of awards made to date is 52.

Recipients of the 1991 Faculty Development Awards in Pharmacology are:



Stewart N. Abramson, Ph.D., Assistant Professor, University of Pittsburgh, School of Medicine—"Molecular Characterization of Nicotinic Acetylcholine (NA) Receptors." The acetylcholine-recognition site

of nicotinic acetylcholine receptors is the site of action of clinically useful drugs, diagnostic reagents, abused substances, and insecticides. Dr. Abramson's research will be, therefore, directed towards a molecular characterization of this pharmacologically important site. The experimental approach will utilize active-site directed affinity reagents, active-site directed crosslinking reagents, and structure/activity studies to identify amino acids within the acetylcholine-recognition site and to determine their three-dimensional topographical relationship. In addition, the functional role of the identified amino acids will be evaluated by pharmacological characterization of receptors altered by site-directed mutagenesis. Integration of experimental pharmacology, protein chemistry, and molecular biology will allow the construction of a threedimensional map of the acetylcholinerecognition site. As a result, such studies will aid in the design of new agonists and antagonists with enhanced selectivity.



Rodney Kawahara,

Ph.D., Assistant Professor, University of Nebraska Medical Center— "Transcriptional Regulation of JE, a PDGF Inducible Gene." Stimulation of fibroblasts with plateletderived growth factor

(PDGF) results in the increased transcription of the JE gene. JE encodes a protein which is the murine homolog of Monocyte Chemotactic Protein-1 (MCP-1) and is a member of a growing superfamily of related inducible cytokines. JE/MCP-1 has been identified as the major monocyte specific chemotactic factor from smooth muscle cells and various tumor cell lines and may play an important role in the pathogenesis of atherosclerosis, in would healing and in the inflammatory process. Potent anti-inflammatory glucocorticoids inhibits the PDGF induction of the JE gene with the same rank order of potency consistent with its pharmacology as an antiinflammatory agent. Deletions and mutations of the DNA sequences flanking or within the JE gene will be made to identify key regulatory sequences responsible for the transcriptional induction by PDGF and the repression by glucocorticoids. Transcriptional factors which bind to these sequences will be identified and preliminarily characterized. Experiments designed to distinguish between four model mechanisms of glucocorticoid mediated transcriptional repression will be performed.



Scott A. Waldman, M.D., Ph.D., Assistant Professor, Thomas Jefferson University, Jefferson Medical College— "Molecular Characterization of E. coli Toxin Receptors." Diarrheal disease accounts for five

to ten million deaths worldwide annually. The leading bacterial pathogen responsible for this disease, E. coli, secretes a heatstable toxin (ST) which activates guanylate cyclase in intestinal cell membranes, elevating intracellular cyclic GMP. Cyclic GMP alters fluid and electrolyte secretion in the intestine resulting in diarrhea. ST regulates guanylate cyclase by binding to protein receptors in intestinal cell membranes. Dr. Waldman's research will elucidate the molecular mechanisms underlying ST receptor function. Different ST receptors will be purified and characterized to determine the structural basis for differences in subunit configuration, subcellular localization, ligand binding, and receptor-effector coupling. Also, monoclonal antibodies to different isoreceptors will be generated for study.

Those who received awards beginning July 1990 are:

James J. Galligan, Ph.D, Assistant Professor, Department of Pharmacology and Toxicology, Michigan State University.

Anna T. Riegel, Ph.D., Assistant Professor, Department of Pharmacology, Georgetown University, School of Medicine.

Philip C. Smith, Ph.D., Assistant Professor of Pharmacy, College of Pharmacy, University of Texas at Austin.

Those who entered the second year of their award beginning July 1990 are:

Peter J. R. Cobbett, Ph.D., Assistant Professor, Department of Pharmacology, Michigan State University. **Robert A. Nicholas, Ph.D.,** Assistant Professor, University of North Carolina at Chapel Hill.

Those who ended their award in 1990 are:

Serrine S. Lau, Ph.D., Assistant Professor, Department of Pharmacology, University of Texas at Austin.

Paul H. Ratz, Ph.D., Assistant Professor, Eastern Virginia Medical School.

Jonathan G. Scammell, Ph.D., Assistant Professor, Department of Pharmacology, University of South Alabama, College of Medicine.



Edward J. Cafruny, M.D., Ph.D., addresses a group during the Annual Awardee Program. Dr. Cafruny is Scientific Consultant to the Foundation and Emeritus Distinguished University Professor, University of Medicine and Dentistry of New Jersey.

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

This program, offered initially in 1977, is designed to assist those candidates who expect to complete the research for their doctoral dissertations.

For 1990-91, the fellowship program provides a stipend of \$10,000 a year and \$500 a year for incidentals directly associated with preparation of the dissertation. Twelve awards are budgeted by the Basic Pharmacology Advisory, however, in 1991, the committee elected to give five additional awards, totaling 17. The program, since its inception, has awarded a total of 168 fellowships.

Those who have been awarded 1991 fellowships beginning between January and July are:

Michael A. Barry, Dartmouth Medical School. Mr. Barry's research is entitled "Mechanisms of Cell Death by Pharmacologic Agents." His principal advisor is Dr. Alan Eastman, Associate Professor, Department of Pharmacology. **Cynthia Cheng,** Thomas Jefferson University, Jefferson Medical College. Ms. Cheng will investigate "Mechanisms of Enhanced Fibrinolytic Effect Associated with Chemical Modifications of Fibrinogen." Her principal advisor is Thorir D. Bjornsson, M.D., Ph.D., Director, Division of Clinical Pharmacology.

Alison F. Dobrenski, Georgetown University, School of Medicine. Ms. Dobrenski will study "Transcriptional Regulation of the POMC Gene by Immune Modulators." Her principal advisor is Anna Tate Riegel, Ph.D., Assistant Professor, Department of Pharmacology.

Carrie Teresa Drake, University of Washington, School of Medicine. Ms. Drake's research focuses on the "Actions of Opioids on Identified Hippocampal Interneurons." Her principal advisor is Charles Chavkin, Ph.D., Assistant Professor, Department of Pharmacology.

Jeffrey Keefer, Vanderbilt University, School of Medicine. Mr. Keefer will study the "Mechanisms for Alpha₂ Adrenergic Receptor Polarization in Renal Epithelial



A lighter moment during the Poster Session at the Annual Awardee Meeting is shared by Scientific Advisory Committee Chairman Frederick M. Radzialowski, Ph.D., Searle, and former Awardees Penelope A. Fenner-Crisp and Claire M. Lathers.

Cells." His principal advisor is Dr. Lee Limbird, Professor, Department of Pharmacology.

Kristine A. Kimball, University of Arkansas for Medical Sciences. Ms. Kimball will investigate the "Effect of Diabetes on Control of Cardiac Pacemaking Activity." Her principal advisor is Richard H. Kennedy, Ph.D., Associate Professor, Department of Pharmacology/Toxicology.

Galina Kuznetsov, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey. Ms. Kuznetsov's research will focus on the "Demonstration and Characterization of a Ca²⁺ Requirement for Post-translational Protein Processing in Intact Mammalian Cells." Her principal advisor is Margaret A. Brostrom, Ph.D., Professor of Pharmacology.

Barbara W. LeDuc, Tufts University School of Medicine. Ms. LeDuc's research involves "Identification of Cytochrome P-450 Isozymes Active in Cocaine Metabolism." Her principal advisor is Dr. Louis Shuster, Acting Chairman, Department of Pharmacology.

Matthew V. Lorenzi, University of Miami School of Medicine. Mr. Lorenzi will study the "Regulation of Two Species of Choline Acetyltransferase (ChAT) mRNA by Nerve Growth Factor." Mr. Lorenzi's thesis advisor is William L. Strauss, Ph.D., Assistant Professor.

Lisa Ellen Rubin, Cornell University Graduate School of Medical Sciences. Ms. Rubin will examine the question, "Do Bradykinin and ACE Inhibitors Play a Protective Role in Immediate Hypersensitivity Reactions of the Heart." Her principal advisor is Dr. Roberto Levi, Professor, Department of Pharmacology.

John Donald Roback, The University of Chicago School of Medicine. Mr. Roback will investigate "Regulatory Factors Involved in NGF and NGF Receptor Expression in the Brain." His principal advisor is Bruce H. Wainer, M.D., Ph.D., Professor and Associate Chairman, Department of Pharmacological and Physiological Sciences.

Thomas Riley Shannon, University of Missouri - Columbia, School of Medicine. Mr. Shannon will perform "Molecular Cloning of the Cardiac Endothelin-I Binding Site." His principal advisor is Dr. Calvin C. Hale, Assistant Professor.

Grace A. Stafford, Cornell University, New York State College of Veterinary Medicine. Ms. Stafford will study the "Regulation of L-Type Voltage-dependent Calcium Channels." Her principal thesis advisor is Gregory A. Weiland, Ph.D., Associate Professor, Department of Pharmacology.

Marilyn Eileen Thompson, University of South Alabama. Ms. Thompson's research will focus on the "Regulation of the Chromogranins/Secretogranins in GH_4C_1 Pituitary Tumor Cells." Her principal advisor is Jonathan G. Scammell, Ph.D., Assistant Professor, Department of Pharmacology.

Richard Regis Vaillancourt, University of Wisconsin Medical School-Madison. Mr. Vaillancourt's research will examine the "Characterization of Hormone Receptor and Effector Protein Domains Associated with the GTP-binding Protein, Transducin." His principal advisor is Dr. Arnold E. Rooho.

David E. Wildman, Yale University School of Medicine. Mr. Wildman will investigate "G Protein bd-subunit Specificity for Receptors." His thesis advisor is Dr. John K. Northup, Assistant Professor of Pharmacology.

Barbara Y.R.H. Williams, University of Texas Medical School. Ms. Williams will study the "Function of the Bombesin Receptor and Cellular Desensitization to Bombesin in a Human Gastrointestinal Cancer Cell Line." Her principal advisor is Dr. Agnes Scohonbrunn, Professor of Pharmacology.

Those who received fellowships in 1990 are:

Lori Ann Birder, Department of Pharmacology, University of Pittsburgh.

Rebecca M. Brawley, Department of Pharmacology, Northwestern University Medical School.

Jin Chen, Laboratory of Toxicology, Harvard University.

Marilyn N. Friedemann, Department of Pharmacology, University of Colorado Health Sciences Center.

Laurie Ann Hanson, D.V.M., Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center.

Barbara A. Hill, Division of Pharmacology, College of Pharmacy, The University of Texas at Austin.

Jeffrey R. Huth, Department of Pharmacology, University of Michigan Medical School.

Patrick J. Pagano, Department of Pharmacology, New York Medical College. His advisor is Alberto Nasjletti, M.D., Professor.

John E. Pawlowski, Department of Pharmacology, University of Pennsylvania.

Jennifer Pohl, Department of Pharmacology, University of Nevada, Reno, School of Medicine.

Steven L. Roberds, Department of Pharmacology, Vanderbilt University School of Medicine.

Lynda Hamlington Spinolo, Department of Pharmacology, University of Tennessee, College of Medicine.

Teresa Wilson Wilborn, Department of Pharmacology and Biochemistry, University of Alabama at Birmingham.

Lena Wu, Department of Pharmacology, Stanford University Medical Center.

Fellowship Awards in Pharmacology-Morphology

The aim of this program is to increase our knowledge about the actions of drugs by direct study of their effects on cells and tissues; to correlate the morphological changes; and, concurrently, to uncover associations observed with functional parameters of cells and tissues.

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. First offered in 1968, 81 awards have been made.

In order to be eligible for an award, the candidate must possess formal training in a morphologic specialty or in pharmacology. However, subsequent training in the complementary discipline, during the period of the fellowship, may be informal. On completion of the program, the fellow should be able to use the tools and concepts of both disciplines.

Recipients of the fellowships beginning July 1991 are:



Charles Allan Fox, Ph.D., Mental Health Research Institute, University of Michigan— "Pharmacological and Molecular Biological Characterization of Circuits Controlling Reinforcement." The

nucleus accumbens is an influential site in the brain, acting as a bridge between the limbic and motor systems. Dopaminergic input to the nucleus accumbens has a prominent role in the control of emotions and the reinforcing properties of some drugs of abuse. In Dr. Fox's studies, the functional dopamine receptive output circuitry of the nucleus accumbens will be investigated. Conventional tract tracing combined with dopamine receptor *in situ*

hybridization will be used to determine the dopamine receptor subtypes expressed by efferent neurons of the nucleus accumbens. This will provide an anatomical foundation upon which more functional studies can be based. Pharmacological manipulation of dopamine receptive cells in the nucleus accumbens, followed by c-fos protein and mRNA detection in accumbens target nuclei, will functionally define the dopamine receptive output circuitry of the accumbens. Finally, a novel approach to examining how neurons respond to pharmacological agents in situ, will analyze how dopamine receptor agonists and antagonists affect dopamine D₂ and D₂ receptor, enkephalin, and dynorphin gene expression.



Laura J. Sim, Ph.D., Department of Physiology and Pharmacology, Bowman Gray School of Medicine, Wake Forest University. A combined anatomical, pharmacological, and molecular biological approach will

be used to study the potential neurotoxic effects of cocaine on the hypothalamic neurosecretory neurons. Cocaine was chosen because it is a known stimulant drug of abuse; a tissue culture model will allow study of its activity on specific cell types. The specific experimental objectives are as follows: (1) To evaluate the acute, dose-related effects of cocaine on cultured hypothalamic neurosecretory cells using cfos activation and peptide secretion as markers for stimulation. (2) To evaluate the effect of chronic administration of cocaine to cultured hypothalamic cells with evaluation of the survival of specific cell types using immunocytochemistry for specific peptides and in situ hybridization for peptide mRNAs. (3) To evaluate the specificity of the responses to cocaine by testing the dose-related effect of adrenergic agonists, antagonists and other amine

uptake inhibitors. The effect of acute and chronic exposure will be examined.



Marie Vivien St-Pierre, Ph.D., Department of Physiology, Tufts University School of Medicine—"The Biology of Hepatic Endothelial Cell Fenestrae." Hepatic endothelial cells uniquely contain holes

(fenestrae) of approximately 110 nm in diameter, which may act as sieves, keeping cells from entering the Disse space but permitting plasma-hepatocyte exchange. The laboratory has demonstrated that fenestrae consist of actin-myosin rings which respond to physiologic/ pharmacologic signals. Serotonin causes fenestral contraction due to binding to a receptor, activating a G protein, which opens a CA++ channel and increases intracellular CA++. Myosin light chain kinase is activated, phosphorylating serine 19 on myosin light chain. Fenestrae are therefore dynamic structures and may exert a role in regulating the microcirculation, substrate access to hepatocytes and regeneration responses. Trained in the above process, Dr. St-Pierre will in particular (1) immortalize the primary cultures of endothelial cells using retroviral constructs; (2) quantitate the fenestral response to other potential agonists (peptide hormones, adrenergic agonists, phospholipase A2 activators) and antagonists (anti-peptide antibodies, phosphatase activators); (3) evaluate the role of fenestral contraction in vivo using a labeled microsphere method; (4) The laboratory has observed that fenestrae develop in these cells within one day after being placed in culture. Dr. St-Pierre will explore the mechanism of de novo formation of fenestrae, wherein plasma membrane unites with pre-existing cytoskeletal ring like structures resulting in membrane fusion and fenestral development.



Foundation Board Member Theodore Cooper, M.D., Ph.D., and Former FDA Commissioner—and former PMAF Award Recipient—Arthur Hayes, M.D., share a moment at the Awardee Banquet.

Recipients of the fellowships which began in 1990 are:

Andrew Bean, Ph.D., Departments of Histology and Neurobiology, Karolinska Institute.

Ellen B. Cornbrooks, Ph.D., Department of Anatomy and Neurobiology, College of Medicine, University of Vermont.

Meredith Mason Garcia, Ph.D., Department of Anatomy, Tulane University School of Medicine.

Kathleen Gogas, Ph.D., Department of Anatomy, University of California, San Francisco.

Bruno C. Jubelin, M.Sc., Ph.D., Department of Anatomy and Cell Biology, College of Physicians and Surgeons of Columbia University. Individuals who entered the second year of their awards in 1990 are:

Karen J. Axt, Ph.D., The Johns Hopkins University, Department of Neuroscience. Melissa Rogers, Ph.D., Dana-Farber Cancer Institute, Harvard University.

Paul R. Wade, Ph.D., Columbia University, College of Physicians and Surgeons, Department of Anatomy & Cell Biology.

Those who ended their awards in 1990 are:

Dennis J. Paul, Ph.D., Department of Neurology, Memorial Sloan-Kettering Cancer Center.

Jean-Jacques Soghomonian, D.E.A., Medical College of Pennsylvania.

David W. Schulz, Ph.D., Harvard Medical School, Department of Biological Chemistry and Molecular Pharmacology.



Advisory Committee Member William B. Abrams, M.D., Executive Director for Clinical Research at Merck Sharp & Dohme Research Laboratories, absorbs the data in the poster presentation.

Faculty Awards in Toxicologic Pathology

Initiated in 1983, this award 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 support veterinary and comparative pathologists who will devote two years to research with drugs. In 1990 this program offered \$30,000 per year for two years' salary and fringe benefits. Two awards were made in 1991, bringing the total number to 17.

Beginning their awards July 1991 are:



Renate Reimschuessel, V.M.D., Ph.D., Assistant Professor, Department of Pathology, School of Medicine, University of Maryland—"Development of Newly Formed Nephrons in Fish Following Nephrotoxin Admin-

istration: A Marker for Environmental Contaminants?" Recent research at Maryland University demonstrated that hexachlorobutadiene-induced nephrotoxicity in the goldfish was followed by regeneration along the nephron and by development of new nephrons. The aim of Dr. Reimschuessel's research is to explore this phenomenon and to determine if the development of new nephrons is a general response of the fish kidney to tubular cell injury. This project investigates the morphologic response of the kidneys of different species of adult fish following chemical and drug induced nephrotoxicity. The patterns of injury, repair and regeneration will be characterized by light and electron microscopy. Alterations in the rate of cellular proliferation in the different tubular segments will be determined using bromodeoxyuridine immunohistochemical labeling. These

studies could lead to a valuable nonmammalian model for studying the effects of chemicals and drugs on development and adult nephrons.



Thomas J. Rosol, Assistant Professor, Department of Veterinary Pathobiology, The Ohio State University— "Effects of Mithramycin on Bone Metabolism In Vivo and In Vitro." Mithramycin is an

antitmor drug used to treat embryonal carcinoma of the testes. Its side effects include hypocalcemia, thrombocytopenia, as well as liver and kidney toxicity. Hypocalcemia is thought to be due to drug-induced inhibition of osteoclastic bone resorption. The hypocalcemic action of mithramycin has been utilized to treat life-threatening elevations in serum calcium in patients with cancer-associated hypercalcemia. The overall goal of the research plan is to investigate the mechanisms by which mithramycin induced the potentially useful side effect of hypocalcemia. The effects of mithramycin will be determined on: (1) the rates of bone resorption and formation in rats in vivo; (2) intracellular messenger production in osteoblasts and osteoclasts in vitro; (3) formation of osteoclasts in vitro; and (4) synthesis of mRNA and secretion of a newly discovered hypercalcemic hormone (parathyroid hormone-related protein) by tumor cells. These objectives will be valuable to further define the toxic mechanisms of mithramycin on bone cell physiology and exploit its effects for the treatment of cancer-associated hypercalcemia.

Individuals who began their awards in July 1990 are:

Dale C. Baker, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Colorado State University. Mary K. Reinhard, D.V.M., Assistant Professor and Director of Clinical Medicine, Department of Comparative Medicine, Medical University of South Carolina.

Entering the second year of their awards in July 1990 are:

Deborah Gillette, D.V.M., Ph.D., Assistant Professor of Pathology, School of Veterinary Medicine, University of Pennsylvania.

Matthew A. Wallig, D.V.M., Ph.D., Assistant Professor of Pathology, College of Veterinary Medicine, Department of Pathobiology, University of Illinois at Urbana-Champaign.

Ending their awards in 1990 are:

Evelyn Anne Kazacos, D.V.M., Ph.D., Department of Veterinary Microbiology, Pathology and Public Health, Purdue University School of Veterinary Medicine.

James Arthur Render, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Michigan State University.

Fellowship for Advanced Predoctoral Training in Pharmaceutics

This program was initiated in 1987 to assist candidates who have one or two years remaining in their predoctoral training, the time during which they are engaged in dissertation research.

The fellowship program provides a stipend of \$10,000 a year and \$500 a year for incidentals directly associated with the preparation of the dissertation. The program has been funded to provide eight fellowships each year. Five fellowships were awarded for 1991 bringing the total number of awards to 29.

Those who received fellowships beginning between January and August 1991 are:

Christine Gentry, Department of Pharmaceutics, University of Utah School of Pharmacy. Ms. Gentry will investigate "A Model System to Study the Structure and Function of immunoliposomes." Her thesis advisor is James N. Herron, Ph.D., Assistant Professor.



Vincent J. Klaus, PMA's Chief Financial Officer and Controller, and PMAF Secretary-Treasurer Joseph A. Mollica, Ph.D., discuss organizational finances at the Awardee Banquet.

Kathleen M. Hillgren, Department of Pharmaceutical Chemistry, University of Kansas College of Pharmacy. Ms. Hillgren's research is entitled "Isolation and Characterization of the Intestinal Dipeptide Carrier Using the Caco-2 Cell Culture Model System." Her principal advisor is Ronald T. Borchardt, Summerfield Professor and Chairman.

Patrick M. Hughes, Department of Industrial and Physical Pharmacy, Purdue University, School of Pharmacy and Pharmacal Sciences. Mr. Hughes will study the "Ocular Absorption of Acycloguanosine Analogues." His principal advisor is Ashim K. Mitra, Ph.D., Associate Professor of Physical Pharmacy.

Michael Mulski, Department of Pharmaceutics, University of Wisconsin School of Pharmacy. Ms. Mulski's research involves "Peptide Stability in Aqueous Solution: Modification by Cosolvents and Cyclodextrins." His primary advisor is Kenneth A. Connors, Professor.

Susanne M. Peck, Department of Pharmaceutics, University of Maryland School of Pharmacy. Ms. Peck will study the "Effect of Stabilizing Additives and Residual Moisture on T_g of Lyophilized Protein." Her principal advisor is Dr. R. Gary Hollenbeck, Associate Professor.

Continuing their 1990 fellowships into 1991 are:

Janice L. Cacace, Department of Pharmaceutics, University of Florida College of Pharmacy.

Francis J. Nowaczyk, Jr., Department of Pharmacy, Philadelphia College of Pharmacy and Science.

Cynthia A. Oksanen, Department of Pharmacy, University of Wisconsin-Madison.

Marcelo O. Omelczuk, Department of Pharmaceutics, The University of Texas at Austin, College of Pharmacy.



Frank G. Standaert, Ph.D., and Keith F. Killam, Jr., Ph.D., both members of the Basic Pharmacology Advisory Committee, discuss Dr. Killam's remarks at the afternoon Basic Pharmacology Subgroup Session.

Elaine M. Phillips, Department of Pharmaceutics, Virginia Commonwealth University School of Pharmacy.

Stephen B. Ruddy, Department of Pharmaceutics, University of North Carolina at Chapel Hill, School of Pharmacy.

Steven P. Schwendeman, Department of Pharmaceutics and Pediatric Cardiology, College of Pharmacy, University of Michigan.

Scott W. Smith, Department of Pharmaceutics, College of Pharmacy, University of Utah.

Gary H. Ward, Department of Pharmaceutical Sciences, University of Arizona. His advisor is Samuel Yalkowsky, Ph.D., Professor of Pharmaceutics.

Undergraduate Research Fellowships in Pharmaceutics

For the first time in 1990, the PMA Foundation offered support to undergraduate students in pharmaceutics. This program gives the undergraduate student an opportunity to participate in a meaningful research project with a motivated, inspiring and research-active pharmaceutics faculty member. The award provides a selected pharmaceutics faculty member with a oneyear fellowship for \$5,000 which the faculty member can provide to a qualified undergraduate of their choosing. Twelve awards are budgeted per year and twelve awards were made for 1991.

Faculty and their undergraduate students who will receive fellowships between January and August 1991 are:

Jessie L-S Au, Pharm.D., Ph.D., Associate Professor, Division of Pharmaceutics, Ohio State University College of Pharmacy. Student: Chong Lim—"Pharmacokinetics and Pharmacodynamics of Intravesical Mitomycin C for Superficial Bladder Cancer."

Walter D. Conway, Ph.D., Associate Professor, Departments of Pharmaceutics and Medicinal Chemistry, State University of New York at Buffalo.

Student: Annie Rodriquez—"(1) Alternatives to Higher Animals in Pharmacologic Research; (2) Relationship Between Pharmacodynamic and Anticonvulsive Effect of Anticonvulsive Drugs Against Electroshock-Induced Seizures in Goldfish."

Maureen D. Donovan, Ph.D., Assistant Professor, University of Iowa College of Pharmacy.

Student: Michael Arndorfer—"The Use of a PABA-Peptide (Bentiromide) as a Nasal Absorption Marker."

Anil D'Mello, Ph.D., Assistant Professor, Philadelphia College of Pharmacy and Science. **Student: Maria Marone**—"The Effect of Fluoxetine on the Plasma Protein Binding of Carbamazepine."

David J. W. Grant, D.Sc., Professor, Department of Pharmaceutics, University of Minnesota College of Pharmacy. Student: Jeffrey W. Huotari—"Crystal Engineering of Oral Iron Chelators"

Pardeep K. Gupta, Assistant Professor, Department of Pharmaceutics, Philadelphia College of Pharmacy and Science. Student: Kelly Dowhower—"Capillary Electrophoresis Assay of Erythropoietin Using Indirect Photometric Detection."

Christopher M. Riley, Ph.D., Associate Professor, Department of Pharmaceutical Chemistry, University of Kansas College of Pharmacy.

Student: Steven Elkinton—"A Comparison of the Partition Coefficients of a Series of Quinolone Antimicrobials."

Ronald A. Siegel, Sc.D., Associate Professor, Departments of Pharmacy and Pharmaceutical Chemistry, University of California, San Francisco, School of Pharmacy.

Student: Sherri L. Konzem—"Novel Characterization of Transport and Reaction in Multilaminar Membranes."

Philip C. Smith, Ph.D., Assistant Professor, Department of Pharmaceutics, University of Texas at Austin, College of Pharmacy. Student: Rebecca L. Schuhmacher— "Stability and Covalent Binding of Benoxaprofen Glucuronide to Proteins."

Raj Suryanarayanan, Ph.D., Assistant Professor, Department of Pharmaceutics, University of Minnesota College of Pharmacy.

Student: Mark Heggestad—"Effect of Moisture on the Properties of Carbamazepine Tablets."

Raj Suryanarayanan, Ph.D., Assistant Professor, University of Minnesota College of Pharmacy.



Finding a relaxing moment during the busy Annual Awardee Meeting are Scientific Advisory Committee Member and Member of the Basic Pharmacology Advisory Committee (BPAC) E. Leong Way, Ph.D., Foundation Scientific Consultant Edward J. Cafruny, M.D., Ph.D., and Theodore Brody, Ph.D., also a member of the BPAC.

Student: Chien Huang—"Site Specific Drug Delivery to Brain."

Victor Yang, Ph.D., Assistant Professor of Pharmaceutics, University of Michigan College of Pharmacy.

Student: Allen J. Flynn—"Immobilized Protamine for Extracorporeal Heparin Removal."

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 grants of relatively large amounts for two to five years were made, principally to established investigators, either to extend existing research or to provide "seed" monies to follow a promising lead. In 1971 a change in emphasis within the Foundation shifted the bulk of the funds into educational support programs and, consequently, 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, educational support programs are in fact also supporting research. The Foundation continues to accept requests for research 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.

The Foundation will continue to review research applications that do not fall within the scope of its formal programs, but will not fund them unless they are deemed to be exceptional and novel approaches that have not generated support from conventional sources.

Ethical Considerations

The Scientific Advisory Committee as well as the program advisory committees of the PMA Foundation are sensitive to the appropriate use of experimental subjects, animals and humans, in research. In their deliberations, they consider all aspects of a proposal and may deny support for many reasons. Careful consideration is given to humane use and care of animal subjects. For human and animal research, the project review committee requires, in writing, a statement of adherence to prevailing standards of ethical research practices, including Institutional Review Board approval before initiation of any research project. In addition, for human research, assurance of informed consent will be required.

Research Starter Grants

As part of the change of emphasis in 1971 which sought to direct monies more toward the training of individuals, 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 423 research starter grants have been made, including the 20 awards beginning January 1, 1991.

Recipients of the grants beginning January 1991 are:

Carlos Enrique Catalano, Pharma.D., Ph.D. University of Colorado School of Pharmacy

Bruno Escalante, M.D., Ph.D. New York Medical College

Nicholas R. Ferreri, Ph.D. New York Medical College

Marc W. Harrold, Ph.D. Duquesne University School of Pharmacy

Pamela J. Hornby, Ph.D. Louisiana State University School of Medicine Laurie Grace Hudson, Ph.D. Northwestern University Medical School

Lin Joseph Hymel, Ph.D. Tulane University School of Medicine

Michael James Jamieson, MBChB, MRCP University of Texas Health Science Center

Rodney Kawahara, Ph.D. University of Nebraska Medical Center

Stephen Korn, Ph.D. University of Connecticut



Frank Samuel, Jr., Esq, was the speaker following the Annual Awardee Banquet of February 13, 1991. As former executive of the Health Industry Manufacturers Association, and current consultant to FDA's Advisory Committee, he drew parallels and distinctions—between drug regulation and device regulation by the federal government.

David Michael Lovinger, Ph.D. Vanderbilt University School of Medicine

Kenneth J. Mack, M.D., Ph.D. University of Wisconsin School of Medicine

Bryan L. Roth, M.D., Ph.D. Case Western Reserve University School of Medicine

Chris R. Ross, D.V.M., Ph.D. Kansas State University College of Veterinary Medicine

Theresa A. Shepard, Ph.D. Rutgers University College of Medicine

Thomas E. Smithgall, Ph.D. Georgetown University School of Medicine

Miguel A. Vazquez-Padua, Ph.D. University Central del Caribe School of Medicine

Scott A. Waldman, Ph.D., M.D. Thomas Jefferson University Jefferson Medical College

Linda L. Werling, Ph.D. George Washington University

Mark Jonathan Winn, Ph.D. University of Alabama at Birmingham School of Medicine

Based on need for funds, a review of the 25 research starter grantees whose awards began January 1, 1990 for a second year of the awards resulted in 17 of them having their awards continued. These are:

Dale L. Birkle, Ph.D. West Virginia University

Arthur R. Buckley, Ph.D. Kirksville College of Osteopathic Medicine

David R. Compton, Ph.D. Medical College of Virginia Virginia Commonwealth University **Philip G. Dunbar, Ph.D.** University of Toledo College of Pharmacy

Jonathan E. Freedman, Ph.D. Northeastern University College of Pharmacy

Colin D. Funk, Ph.D. Vanderbilt University School of Medicine

Sharon H. Jones, Ph.D. University of Oklahoma College of Medicine

Leonard Lothstein, Ph.D. University of Tennessee, Memphis School of Medicine

Donald J. Messner, Ph.D. Washington University School of Medicine

Todd D. Porter, Ph.D. University of Michigan Medical School

John W. Regan, Ph.D. University of Arizona School of Pharmacy

Edwin R. Sanchez, Ph.D. Medical College of Ohio

Derek David Smith, Ph.D. Creighton University School of Medicine

Jeffrey M. Voigt, Ph.D. Philadelphia College of Pharmacy and Science

Kenneth B. Walsh, Ph.D. University of South Carolina School of Medicine

Susan E. Wellman, Ph.D. University of Mississippi Medical Center

Marina E. Wolf, Ph.D. Wayne State University School of Medicine



Continuing a Commitment to Careers in Biomedical Research

Photograph courtesy of Syntex Corporation



Photograph courtesy of ICI Pharmaceuticals Group



PURPOSE

he 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 in support of fundamental research on drugs and programs for training personnel in basic and clinical pharmacology, toxicology and pharmaceutics.

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, unless the drug is for an orphan disease. 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 30.

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 11.

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



Report of the Treasurer



Joseph A. Mollica, Ph.D. Secretary-Treasurer

he total income of the Foundation in 1990

was \$2,596,402. Of this amount, \$2,370,000 came from contributions. The balance of \$226,402 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 1990 from PMA Associates and Research Affiliates.

Grants, Foundation-sponsored programs, special meetings and other expenses for 1990 amounted to \$2,330,906. Of this total, \$1,740,441 represents expenditures for grants. The total fund balance as of December 31, 1990 was \$5,089,900. 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, 1990, the contingency liability for 1991-94 was approximately \$3,659,097.

The Foundation's financial position as of December 31, 1990, has been audited by the Washington D. C. accounting firm of Buchanan & Company.

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Joseph A. Mollica, Ph.D. Secretary-Treasurer, PMA Foundation President and Chief Executive Officer The DuPont Merck Pharmaceutical Company

Statement of Income and Expenditures For the Year Ended December 31, 1990

Income

Contributions Income from investments Miscellaneous Income	2,370,000 196,514 29 888
Total Income	2,596,402
Expenditures	
Grants—Note A	
Clinical Pharmacology Faculty Awards	265,000
Clinical Pharmacology Fellowships	109,492
Clinical Pharmacology Unit Support	99,756
Basic Pharmacology Faculty Awards	157,500
Medical Student Research Fellowships	18,000
Pharmacology-Morphology Fellowships	141,076
Research Starter Grants	400,000
Advanced Predoctoral Fellowships in Pharmacology	239,617
Toxicologic Pathology Faculty Awards	107,500
Advanced Predoctoral Fellowships in Pharmaceutics	142,500
Undergraduate Fellowships in Pharmaceutics	60,000
Total Administrative February Awardee	1,740,441
Meeting, Annual ASPET Meeting and Other Expenses	590,465
Total Expenditures	2,330,906
Excess of income over expenditures Operating fund balance at January 1, 1990 Operating fund balance December 31, 1990 Future Commitment Fund (Reserve Fund) — Note B	265,496 2,490,499 2,932,995 2,156,905
Total fund balance at December 31, 1989	5,089,900

Note A— In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 31, 1990, the amounts still to be disbursed with respect to these grants amounted to aggregated \$3,659,097 with approximately \$1,907,774 of this to be disbursed during 1991; \$1,289,823 in 1992; \$401,500 in 1993; and \$60,000 in 1994.

Note B—The Future Commitment Fund is a reserve fund established by the Foundation to ensure the continuation of existing grants.

Income from Investments	145,671
Gain on Sale of Stock	63,148
Less: Trust Commission Expense	208,819 21,754
Future Commitment Fund Balance at	187,065
January 1, 1990	2,146,840
Future Commitment Fund Balance at December 31, 1990	2,156,905



ORGANIZATION AND ADMINISTRATION

1991 Officers



Sheldon G. Gilgore, M.D. Chairman PMA Foundation Chairman of the Board, President and Chief Executive Officer G&D Searle & Co. Skokie, Illinois The PMA Foundation operates through its officers, Board of Directors and six advisory committees. In April, 1991, Sheldon G. Gilgore, M.D, Chairman of the Board, President and Chief Executive Officer of G.D. Searle & Co., was re-elected Chairman. Charles A. Sanders, M.D., Chief Executive Officer of Glaxo, Inc., was elected Vice Chairman. Joseph A. Mollica, Ph.D., President and Chief Executive Officer, The Du Pont Merck Pharmaceutical Company, was re-elected Secretary-Treasurer.

Mr. Maurice Q. Bectel again served as the Foundation's President and Donna Moore served as Associate. Edward J. Cafruny, M.D., Ph.D., and C. Joseph Stetler, Esq., continue to serve as Foundation consultants—Dr. Cafruny as scientific consultant and Mr. Stetler as staff counsel.



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Pausing momentarily in front of his poster is Ullrich Schwertschlag, M.D., former Awardee and currently with Lilly Laboratory for Clinical Research.

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APPLICATIONS

he 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:

Mr. Maurice Q. Bectel President Pharmaceutical Manufacturers Association Foundation, Inc. 1100 Fifteenth Street, N. W. Washington, D. C. 20005

PMA Foundation Current Programs for 1992

Name of Program/ Year of First Awards	Number of Awards Budgeted Yearly/ Length of Award	Program Budget	Deadline Announcement Date Starting Time
Clinical Pharmacology Advisory Committe	ee		
(1) Faculty Awards in Clinical Pharmacology (1967)	3 budgeted/ 3 years	\$360,000 total \$ 40,000 per award per year	October 1 December 15 July 1
(2) Fellowships for Careers in Clinical Pharmacology (1973)	4 budgeted/ 2 years	\$192,000 total \$ 24,000 per award per year	October 1 December 15 July 1
(3) Medical Student Research Fellowships (1974-Amended 1982)	8 budgeted/ 3 months to 24 months	 \$ 60,000 total \$ 833 per month maximum \$10,000 	January 15 March 15 July 1
(4) Development Grants for Clinical Pharmacology Units (1978)	1 budgeted/ 3 years to use funds	\$100,000 per award	January 15 March 15 July 1
Basic Pharmacology Advisory Committee			
(5) Faculty Awards in Basic Pharmacology/Toxicology (1973)	3 budgeted/ 2 years	\$180,000 total \$ 30,000 per award per year	September 15 December 15 July 1
(6) Research Starter Grants (1972)	20 budgeted/ 2 years	\$400,000 total \$ 10,000 per award per year	September 1 November 15 January 1
(7) Advanced Predoctoral Fellowships in Pharmacology/Toxicology (1978)	12 budgeted/ 1 or 2 years	\$240,000 total \$ 10,000 per award per year	September 15 December 15 January-July 1
Pharmacology-Morphology Advisory Com	mittee		
 (8) Fellowships in Pharmacology- Morphology including Cell Biology (1968) 	3 budgeted/ 2 years	\$126,000 total \$ 21,000 per award per year	January 15 March 15 July 1
Toxicologic-Pathology Advisory Subcomm	ittee		
(9) Faculty Development Awards in Toxicologic-Pathology (1982)	2 budgeted/ 2 years	\$120,000 total \$ 30,000 per award per year	September 1 November 15 July 1
Pharmaceutics Advisory Committee			
(10) Advanced Predoctoral Fellowships in Pharmaceutics (1987)	8 budgeted/ 1 or 2 years	\$160,000 total \$ 10,000 per award per year	October 1 December 15 January-July
(11) Undergraduate Research Fellowships in Pharmaceutics (1990)	12 budgeted/ 1 year	\$ 60,000 total \$ 5,000 per award	October 1 December 15 January-July
(12) Postdoctoral Fellowships in Pharmaceutics (1992)	2 budgeted/ 1 or 2 years	\$100,000 \$ 25,000 per award per year	October 1 December 1 January-December

All of the above programs will accept applications for research on drugs for rare diseases



1 Action

Pharmaceutical Manufacturers Association Foundation 1100 Fifteenth Street, N.W. Washington, D.C. 20005