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LABORATORY OF BIOMEDICAL AND ENVIRONMENTAL SCIENCES
UNIVERSITY OF CALIFORNIA
900 VETERAN AVENUE
LOS ANGELES, CALIFORNIA 90024

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ANNUAL PROGRESS REPORT
FOR THE PERIOD
JULY 1, 1982 - JUNE 30, 1983

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LABORATORY OF BIOMEDICAL AND ENVIRONMENTAL SCIENCES

UNIVERSITY OF CALIFORNIA

LOS ANGELES

DIRECTOR

O. R. Lunt

ASSOCIATE DIRECTORS

**David E. Kuhl
Harvey R. Herschman
William J. Moffitt
Philip W. Rundel**

**FACULTY ADVISORY COMMITTEE
TO THE LABORATORY**

**John Dean O'Connor - Chairman
Associate Dean, Life Sciences/Biology**

**Frederick Allen
School of Engineering and Applied Sciences**

**Richard H. Gold
Department of Radiological Sciences**

**Donald J. Jenden
Chairman, Department of Pharmacology**

**Sherman Mellinkoff
Dean, School of Medicine**

**John G. Pierce
Department of Biological Chemistry**

**Phillip Thornber
Chairman, Department of Biology**

EX-OFFICIO MEMBER

**Albert A. Barber
Associate Vice Chancellor - Research**

REPORT OF THE DIRECTOR

RESEARCH PROGRAMS

The research program of the Laboratory of Biomedical and Environmental Sciences is carried out in three laboratory units:

- (1) The Laboratory of Biomolecular and Cellular Sciences focuses on fundamental cellular processes such as proliferation, differentiation, gene expression and oncogenic transformation, particularly as related to endogenous factors and energy-related exogenous factors.
- (2) The Laboratory of Environmental Biology uses two primary study sites to address basic arid-region process studies. The long range goal of this program is the generation of data which will lead to the development of models having predictive value. Knowledge of physiological processes in both plants and animals, particularly as influenced by environmental conditions, is required to understand the structure and dynamics of the ecosystems. The carbon, nutrient and hydrological cycles require greater attention and will be the subject of research programs in the near future.
- (3) The Laboratory of Nuclear Medicine measures the physiological behavior of small parts of the brain and heart in health and disease using radioactive tracer techniques employing emission computed tomography. The method is developed technically by rapidly synthesizing biological indicators labeled with short-lived positron emitting radionuclides produced in the laboratory cyclotron. Mathematical models are developed to explain the body distributions of these indicators which are imaged with emission tomographs. This multi-disciplinary effort finally produces cross-section pictures of body biochemistry obtained non-invasively in living patients. It is expected that this approach will result in earlier diagnosis of disease and more careful monitoring of treatment.

REPORT OF THE DIRECTOR (continued)

OPERATIONS

Principal Investigators develop their research programs using technicians, graduate students, postdoctoral students and visiting scientists. Additionally, there are collaborating professional colleagues. The Associate Directors play a vital role as scientific leaders and coordinators of the various individual programs within major laboratory research objectives. Non-DOE support makes a large contribution to our basic DOE program.

LABORATORY OF BIOMEDICAL AND ENVIRONMENTAL SCIENCES

STATISTICAL SUMMARY

I. FUNDING (\$1,000's):

Department of Energy

Biomolecular & Cellular Sciences	\$1,200
Environmental Sciences	700
Nuclear Medicine	2,000
	<u>3,900</u>

<u>Other</u>	<u>1,200</u>
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Total Operating Funding	<u><u>\$5,100</u></u>
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II. STAFFING:

Principal Investigators	24
Scientific Support Staff	86
Others	<u>49</u>

Total	159
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III. INSTRUCTION AND OTHER RELATED ACTIVITIES:

Visiting Scientists	13
Fellow and Other Postdoctorals	28
Graduate Students	36
Academic Departmental Staff Appointments	20
Courses to which Laboratory Staff have made significant contributions	67
Number of departments in which these courses were offered	13

I. Projected Operating Funding, October 1982 - September 1983.
Capital funding excluded.

PROFESSIONAL STAFF

VISITORS

GRADUATE STUDENTS

LABORATORY OF BIOMEDICAL
AND
ENVIRONMENTAL SCIENCES

O. R. Lunt, Ph.D.
Director

Philip W. Rundel, Ph.D.
Associate Director
Laboratory of
Environmental Biology

Harvey R. Herschman, Ph.D.
Associate Director
Laboratory of Biomolecular
and Cellular Sciences

David E. Kuhl, M.D.
Associate Director
Laboratory of
Nuclear Medicine

PRINCIPAL INVESTIGATORS

GEORGE V. ALEXANDER, M.S.

Distribution of tracer elements in biological systems, development of spectrometric methods and equipment; computer applications

JORGE BARRIO, Ph.D.

Development of new radiopharmaceutical indicators for diagnostic imaging and physiologic study

GERALD BIDA, Ph.D.

The development of targetry for the production of short-lived positron emitters using a small accelerator and research into gaining an understanding of the phenomena governing formation of selected precursors for use in radiopharmaceutical synthesis

JEAN S. de VELLIS, Ph.D.

Developmental neurotoxicology

ARMAND J. FULCO, Ph.D.

Control of lipid biosynthesis; characterization and induction of bacterial cytochrome P-450 and epoxide hydratase enzymes

OLIVER HANKINSON, Ph.D.

Genetic control of carcinogen metabolism

ISAAC M. HARARY, Ph.D.

Control of mammalian cell development and specific function

RANDALL HAWKINS, M.D.

Studies of brain physiology and neuropathology with positron tomography

ESTHER F. HAYS, M.D.

Leukemia, etiology and pathogenesis; cadmium effects on hematopoietic cells

ACADEMIC DEPARTMENT

Radiological Sciences,
Pharmacology

Radiological Sciences

Anatomy, Psychiatry,
and Behavioral
Sciences

Biological Chemistry

Pathology

Biological Chemistry

Radiological Sciences

Medicine

PRINCIPAL INVESTIGATORS

ACADEMIC DEPARTMENT

HARVEY R. HERSCHMAN, Ph.D.
Regulation of cell division and gene
expression by endogenous factors and
environmental agents

Biological Chemistry

EDWARD J. HOFFMAN, Ph.D.
Development of new radionuclide instrumentation
for diagnostic imaging and physiologic study

Radiological Sciences

HENRY HUANG, D.Sc.
Mathematical modeling for radionuclide
imaging of physiologic systems

Radiological Sciences

DAVID E. KUHL, M.D.
Development of new radionuclide techniques
for diagnostic imaging and physiologic
study of local organ function

Radiological Sciences

ROBERT G. LINDBERG, Ph.D.
Physical ecology of desert rodents;
environmental effects of solar thermal
power systems

Environmental Sciences
and Engineering

NORMAN S. MAC DONALD, Ph.D.
Development and production of radionuclides
with a compact cyclotron, for medical
research, diagnostic applications and
physiological studies

Radiological Sciences

JAMES F. MEAD, Ph.D.
Lipid metabolism in normal, aging,
and malignant tissue; membrane peroxidation
and properties

Biological Chemistry,
Public Health

KENNETH A. NAGY, Ph.D.
Vertebrate physiological ecology

Biology

PARK S. NOBEL, Ph.D.
Plant physiological ecology, biophysical
ecology, and plant distribution

Biology

AMOS NORMAN, Ph.D.
Medical Physics

Radiation Oncology

PRINCIPAL INVESTIGATORS

ACADEMIC DEPARTMENT

MICHAEL E. PHELPS, Ph.D.
Development and application of new instrumentation labeled compounds and tracer kinetic models for physiologic studies and diagnostic imaging; study of normal and altered states of cerebral function with positron tomography

Radiological Sciences

EVAN M. ROMNEY, Ph.D.
Radionuclide and stable element cycling in plants and soils and restoration of disturbed desert land

PHILIP W. RUNDEL, Ph.D.
Plant physiological ecology, plant nutritional cycles, fire ecology

Biology

HEINZ SCHELBERT, M.D.
Development of new radionuclide techniques for diagnostic imaging and physiologic study of local organ function

Radiological Sciences

FREDERICK B. TURNER, Ph.D.
Biology of desert vertebrates; environmental effects of energy development

ARTHUR WALLACE, Ph.D.
Plant physiology, particularly desert plant biology; trace elements in nutrition

ASSOCIATE INVESTIGATORS*

LABORATORY

ROBERT ACKERMANN, Ph.D.

Nuclear Medicine

JUDITH BERLINER, Ph.D.

Biomolecular
and Cellular Sciences

D. FRANK BENSON, M.D.

Nuclear Medicine

JEROME ENGEL, JR. M.D., Ph.D.

Nuclear Medicine

ARTHUR C. GIBSON, Ph.D.

Environmental Biology

EBERHARD HENZE, M.D.

Nuclear Medicine

*Co-Investigators who interact with Principal Investigators

ASSOCIATE INVESTIGATORS*

JANINE KRIVOKAPICH, M.D.

ROBERT MARSHALL, M.D.

JOHN C. MAZZIOTTA, M.D., Ph.D.

JAMES F. MC GINNIS, Ph.D.

E. JEFFREY METTER, M.D.

HENRY PADGETT, Ph.D.

JOSEPH PERLOFF, M.D.

MARKUS SCHWAIGER, M.D.

KENNETH SHINE, M.D.

ROBERT A. STEIN, Ph.D.

JAN TILLISCH, M.D.

CLAUDE WASTERLAIN, M.D.

GUEY-SHUANG WU, Ph.D.

LABORATORY

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Biomolecular
and Cellular Sciences

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Biomolecular
and Cellular Sciences

Nuclear Medicine

Nuclear Medicine

Biomolecular
and Cellular Sciences

*Co-Investigators who interact with Principal Investigators

SENIOR PROFESSIONAL STAFF

ROBERT ANDERSEN, Ph.D.

SAIL A. BAKER, M.A.

DORIS BASS, Ph.D.

LABORATORY

Biomolecular
and Cellular Sciences

Environmental Biology

Biomolecular
and Cellular Sciences

SENIOR PROFESSIONAL STAFF

WADE L. BERRY, Ph.D.
RICHARD HUNTER, Ph.D.
YUTAKA KOBAYASHI, Ph.D.
SHALINI KUMAR, Ph.D.
NIRMALA MENON, Ph.D.
ANTHONY RICCI, A.B.
RICHARD T. RUETTINGER, Ph.D.
CARL SELIN, M.S.

LABORATORY

Environmental Biology
Environmental Biology
Biomolecular
and Cellular Sciences
Biomolecular
and Cellular Sciences
Biomolecular
and Cellular Sciences
Nuclear Medicine
Biomolecular
and Cellular Sciences
Nuclear Medicine

VISITING SCIENTISTS

ETIAN BOGIN, Ph.D.	Kimron Institute Bet-Dagan, Israel
JOHN CALLAHAN, Ph.D.	University of Toronto Toronto, Canada
BRUCE MAHALL, Ph.D.	University of California Santa Barbara, California
ROBERT S. MATSON, Ph.D.	University of Southern California Los Angeles, California
PHILOMENA MC ANDREW, M.D.	University of California Los Angeles, California
ERIK T. NILSEN, Ph.D.	Virginia Polytechnic Institute Blacksburg, Virginia
OBERDAN PARODI, M.D.	University of Pisa Medical School Pisa, Italy

VISITING SCIENTISTS

JARIYA PRASATSRI SUPAB	Department of Agriculture Bangkok, Thailand
SACHAR, KANTA, Ph.D.	University of Delhi Delhi, India
SRINIVASA RAO PYATA, Ph.D.	National Institute of Nutrition Hyderabad, India
PATRICIA M. STEVENSON, Ph.D.	University of Western Australia Perth, Western Australia
JAMES THOMAS, Ph.D.	Iowa State University Ames, Iowa
MAURICE VAN DER STEE, L.M.A.M., M.S.	University of Groningen The Netherlands

RESEARCH PARTICIPANTS

RONALD ABRAMS, M.A.	University of Cape Town Cape Town, South Africa
EDMUNDO ACEVEDO, Ph.D.	University of Chile Santiago, Chile
IGNACIO BADILLA, Ph.D.	University of Chile Santiago, Chile
F. J. BAUMGARTER, Ph.D.	University of California Los Angeles, California
ALBERT F. BENNETT, Ph.D.	University of California Irvine, California
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RESEARCH PARTICIPANTS

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BEVERLY DUGAN, Ph.D.	University of Tennessee Knoxville, Tennessee
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HUGH ELLIS, Ph.D.	University of Hawaii Honolulu, Hawaii
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BETH FLINT, B.A.	University of California Los Angeles, California
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ROBIN FOSTER, Ph.D.	Field Museum of Natural History Chicago, Illinois
PAUL FRANCO, M.A.	Oak Ridge National Laboratory Oak Ridge, Tennessee

RESEARCH PARTICIPANTS

DAVID GRABER, Ph.D.	USNPS University of California Davis, California
BRIAN GREEN, Ph.D.	CSIRO Canberra, Australia
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DEAN HECTOR, B.A.	Department of Biology University of California Los Angeles, California
STEVEN HUBBELL, Ph.D.	University of Iowa Ames, Iowa
RAYMOND B. HUEY, Ph.D.	University of Washington Seattle, Washington
ROBERT HYMAN, Ph.D.	Salk Institute La Jolla, California
NADINE JACOBSEN, Ph.D.	University of California Davis, California
WESLEY JARRELL, Ph.D.	University of California Riverside, California
HENRY JOHN-ALDER, Ph.D.	University of California Irvine, California
IAN KAPLAN, Ph.D.	Earth and Space Sciences University of California Los Angeles, California
ROBERT KNOBLER, Ph.D.	Scripps Research Foundation La Jolla, California
DANI KOBAYASHI, B.A.	Biology Department University of California Los Angeles, California
DANIEL KOHL, Ph.D.	Washington University St. Louis, Missouri

RESEARCH PARTICIPANTS

L. J. LANE, Ph.D.	USDA/ARS Southwest Rangeland Watershed Research Center Tucson, Arizona
A. K. LEE, Ph.D.	Monash University Clayton, Victoria, Australia
JAY A. LEVY, M.D.	University of California San Francisco, California
CAROL L. MACLEOD, Ph.D.	University of California San Diego, California
BRUCE MAHALL, Ph.D.	University of California Santa Barbara, California
ROGER MARTIN, B.A.	Monash University Clayton, Victoria, Australia
WILLIAM MAUTZ, Ph.D.	University of California Irvine, California
GEROLD MERKER, M.A.	University of California Riverside, California
G. GENE MONTGOMERY, Ph.D.	Smithsonian Tropical Research Institute Panama
H. A. MOONEY, Ph.D.	Stanford University Stanford, California
KEITH MORRIS, M.A.	University of Western Australia Perth, Western Australia
BRIAN OBST, B.A.	Department of Biology University of California Los Angeles, California
DAVID PARSONS, Ph.D.	USNPS University of California Davis, California
FINN SKOU PEDERSEN, Ph.D.	University of Aakhus Denmark

RESEARCH PARTICIPANTS

RICHARD L. PERRINE, Ph.D.	Department of Systems Engineering University of California Los Angeles, California
A. STANLEY RAND, Ph.D.	Smithsonian Tropical Research Institute Panama
ROBERT RICKLEFS, Ph.D.	University of Pennsylvania Philadelphia, Pennsylvania
ROBERT ROBICHAUX, Ph.D.	University of California Berkeley, California
IAN ROOKE, Ph.D.	University of Western Australia Perth, Western Australia
GORDON SANSON, Ph.D.	Monash University Clayton, Victoria, Australia
DERRICK SCHMIDT, Ph.D.	University of California Los Angeles, California
R. K. SCHULZ, Ph.D.	University of California Berkeley, California
GEORGIA SHEARER, Ph.D.	Washington University St. Louis, Missouri
VAUGHAN H. SHOEMAKER, Ph.D.	University of California Riverside, California
ROY SIEGFRIED, Ph.D.	University of Cape Town Cape Town, South Africa
ANDREW P. SMITH, Ph.D.	Monash University Clayton, Victoria, Australia
CLIFFORD SMITH, Ph.D.	University of Hawaii Honolulu, Hawaii
GRAEME SUCKLING, Ph.D.	Monash University Clayton, Victoria, Australia
DEE TAKEMOTO, Ph.D.	Kansas State University Kansas City, Missouri

RESEARCH PARTICIPANTS

ROSS VIRGINIA, Ph.D.	University of California Riverside, California
WESLEY W. WEATHERS, Ph.D.	University of California Davis, California
G. C. WHITTOW, Ph.D.	University of Hawaii Honolulu, Hawaii
JOSEPH WILLIAMS, Ph.D.	Pepperdine University Malibu, California
RORY WILSON, B.A.	University of Cape Town Cape Town, South Africa
STANLEY YOKOTA, Ph.D.	University of Arizona Tucson, Arizona

POSTDOCTORALS

SUSAN ABERNATHY, Ph.D.
HOWARD W. CALKIN, Ph.D.
ATSUSHI KATO, M.D.
BOK-HOI KIM, M.D.
CAROLYN KIMME-SMITH, Ph.D.
SHINICHI KITADA, M.D., Ph.D.
LOUISE LE DUC, Ph.D.
HAZEL LEWIS, Ph.D.
ALEXANDER LIN, M.D. Ph.D.
MARK MANDELKERN, M.D., Ph.D.
JOHN C. MAZZIOTTA, M.D., Ph.D.
DOMINIC MONTISANO, Ph.D.
RICHARD MORRISON, Ph.D.
HENRY C. PADGETT, Ph.D.
JOHN PILETZ, Ph.D.
TERRY RITCHIE, Ph.D.
RONALD ROBBERECHT, Ph.D.
JAMES ROPCHAN, Ph.D.
ALBERTO SALCEDO, M.D.
RUSSELL SANTEO, Ph.D.
N. SATYAMURTHY, Ph.D.
MARCUS SCHWAIGER, M.D.

SPONSOR

Harvey R. Herschman
Park S. Nobel
Esther F. Hays
Armand J. Fulco
Amos Norman
James F. Mead
Harvey R. Herschman
Amos Norman
David E. Kuhl
David E. Kuhl
Michael E. Phelps/David E. Kuhl
Oliver Hankinson
Jean de Vellis
Jorge Barrio
Harvey R. Herschman
Jean de Vellis
Park S. Nobel
Jorge Barrio
David E. Kuhl
Jean de Vellis
Jorge Barrio
Heinrich Schelbert

POSTDOCTORALS

HERZL SCHWALB, Ph.D.
 M. RASOUL SHARIFI, Ph.D.
 STANLEY D. SMITH, Ph.D.
 JOSEPH WAPENSKI, M.D.
 DANIEL WEINGARTEN, Ph.D.
 CHARLES WISDOM, Ph.D.

SPONSOR

Armand J. Fulco
 Philip W. Rundel
 Park S. Nobel
 David E. Kuhl
 Jean de Vellis
 Philip W. Rundel

GRADUATE STUDENTSDEPT.DEG. OBJ.SPONSOR

YARI AIZENMAN	Neuroscience	Ph.D.	Jean de Vellis
WAYNE BARCIKOWSKI	Biology	M.A.	Park S. Nobel
JEFF BARTON	Medical Physics	Ph.D.	Edward Hoffman
BRUCE BIRREN	MBI	Ph.D.	Harvey R. Herschman
HANNES CALLISEN	Medical Physics	Ph.D.	Amos Norman
RICHARD CARSON	Biomathematics	Ph.D.	Sung-Cheng Huang
DIANE CHUGANI	Pharmacology	Ph.D.	Jorge Barrio
ALLISON COLLINS	Biology	M.A.	Kenneth A. Nagy
MAGNUS DAHLBOM	Medical Physics	Ph.D.	Edward Hoffman
EVAN DENERIS	Div. of Nutrition	Ph.D.	James F. Mead
RUSSELL DOLLINGER	Dept. of Anatomy	Ph.D.	James F. Mead
GARY N. GELLER	Biology	Ph.D.	Park S. Nobel
DAVID GOLDSTEIN	Biology	Ph.D.	Kenneth A. Nagy
JEAN GUDAS	Public Health	Ph.D.	Oliver Hankinson
BRIAN HENEN	Biology	Ph.D.	Kenneth A. Nagy
EMILY HOLMES	Anatomy	Ph.D.	Jean de Vellis
VIRTUE T. ISHIHARA	Biology	M.A.	Park S. Nobel
PETER W. JORDAN	Biology	Ph.D.	Park S. Nobel
RANDY E. KEEN	Radiol. Sciences	Ph.D.	Jorge Barrio
SHERMAN LAMBERT	Biology	Ph.D.	Philip W. Rundel
KIRK MAHONEY	Biomathematics	M.S.	Sung-Cheng Huang
BROOKS C. MICHAELS	Biological Chemistry	Ph.D.	Armand J. Fulco
CAMERON MITCHELL	Medical Sciences	Ph.D.	Amos Norman
LUISA MONTESANO	Biological Chemistry	Ph.D.	Harvey R. Herschman
LINDA O. NARHI	Biological Chemistry	Ph.D.	Armand J. Fulco
JORY OLSEN	Biological Chemistry	Ph.D.	Harvey R. Herschman
MADELEINE PINCU	Medical Physics	Ph.D.	Amos Norman
SARAH K. PIXLEY	Anatomy	Ph.D.	Jean de Vellis
DEBBIE O. RAPHAEL	Biology	Ph.D.	Park S. Nobel
DERRICK SCHMIDT	Radiol. Sciences	Ph.D.	Jorge Barrio
RACHEL SCHWAB	Computer Sciences	M.A.	John C. Mazziotta
MARK STENE	Pathology	Ph.D.	Oliver Hankinson
SUSAN TAPLITZ	Biological Chemistry	Ph.D.	Harvey R. Herschman

<u>GRADUATE STUDENTS</u>	<u>DEPT.</u>	<u>DEG. OBJ.</u>	<u>SPONSOR</u>
ERNEST TERWILLIGER	Biological Chemistry	Ph.D.	Harvey P. Herschman
JOHN VAN GURP	Pathology	Ph.D.	Oliver Hankinson
LONG-PING WEN	Biological Chemistry	Ph.D.	Armand J. Fulco
DORIS K. WU	Anatomy	Ph.D.	Jean de Vellis

STAFF RECOGNITION AND HONORS

STAFF RECOGNITION AND HONORS

JORGE R. BARRIO

Appointment and Elections: Nuclear Medicine Program Review Committee (Sloan Kettering Institute), Department of Energy, January 1983.

Invited Lecturer: VII Nobel Conference on Positron Emission Tomography, Stockholm, Sweden, May 1983;

Los Alamos National Laboratories, Los Alamos, New Mexico, May 1983;

University of California, San Diego, Department of Pharmacology, June 1983;

Recognition and Honors: Georg von Hevesy Prize from the Georg von Hevesy Foundation, Zurich Switzerland, August 1982.

JEAN DeVELLIS

Appointments and Elections: Treasurer, American Society for Neurochemistry, re-elected 1983;

Program Chairman, Winter Conference on Brain Research, 1982-1983;

Scientific Advisory Council, American Paralysis Association, 1982-1983;

Vice President, California Tissue Culture Association, 1983-1984;

Program Committee, International Society for Developmental Neuroscience, 1982-1983;

Regional Secretary, International Society for Developmental Neuroscience, 1981-present;

Associate Editor, Journal of Neuroscience Research, 1980-present;

Guest Editor, Special Issue on Growth and Trophic Factors, Journal of Neuroscience Research, 1982-present.

Invited Lecturer: Cold Spring Harbor Neurobiology Courses, Cold Spring Harbor, New York, August 9-15, 1982;

28th Annual Meeting of the American Paraplegic Association, Las Vegas, Nevada, September 19-22, 1982;

JEAN DeVELLIS (continued)

First European Conference on Serum-Free Cell Culture, University of Heidelberg, West Germany, October 7-9, 1982;

First International Symposium, Recent Achievements in Restorative Neurology, Houston, Texas, October 27-30, 1982;

16th Annual Winter Conference on Brain Research, Keystone, Colorado, January 22-29, 1983;

International Workshop on Immune Responses to Cell Membrane Receptors and their Ligands as Causes of Neurological Disease, Rancho Mirage, California, February 23-26, 1983;

14th Annual Meeting of the American Society for Neurochemistry, Honolulu, Hawaii, March 22, 1983;

American Paralysis Association, Pacific Grove, California, April 25-27, 1983;

Department of Physiology and Society for Neuroscience, University of California, Davis, May 12, 1983.

ARMAND J. FULCO

Invited Lecturer: Selected as the Plenary Lecturer for the Japanese Conference on the Biochemistry of Lipids, to be held in Niigata, Japan, July 1984.

Recognition and Honors: Biography published in current edition of "Who's Who in America".

OLIVER HANKINSON

Appointments and Elections: Chairperson, Chemical Safety Committee, University of California, Los Angeles, 1982-present.

ESTHER F. HAYS

Appointments and Elections: Chairman, Human Subject Protection Committee, University of California, Los Angeles, 1983;

Member, Human Subject Protection Committee, University of California, Los Angeles, 1983;

ESTHER F. HAYS (continued)

Attending Physician, Medical Ambulatory Care Center, University of California, Los Angeles, 1983;

Member, Day Nursery Auxillary Assistant League of Southern California, 1983;

Director, Vivarium, Laboratory of Biomedical and Environmental Sciences, 1983;

Member, Selection Committee, 22nd Annual Junior Science and Humanities Symposium for Student Fellow Research Program, California Museum of Science and Industry, 1982;

Judge, 23rd Annual Junior Science and Humanities Symposium for Student Fellow Research Program, California Museum of Science and Industry, December 1982;

Pathology B Study Section, National Institutes of Health, Bethesda, Maryland, 1983.

HARVEY R. HERSCHMAN

Appointments and Elections: Nominations Committee, Tissue Culture Association, 1983;

Scientific Advisory Board, Hereditary Diseases Foundation, 1982-present.

Invited Lecturer: ICN-UCLA Symposium on Evolution of Hormone Receptor Systems, Squaw Valley, California, March 1982;

Gordon Research Conference on "Microbial Toxins and Microbial Pathogens", New Hampshire, August 1982;

The La Jolla Symposium, La Jolla, California, (co-organizer), September 1982;

Winter Conference on Brain Research, Keystone, Colorado, January 1983;

Immune Responses to Cell Membrane Receptors and Their Ligands as Causes of Neurological Disease, Palm Springs, California, February 1983;

HARVEY R. HERSCHMAN (continued)

EMBO Conference on "Growth Control in Normal and Transformed Cells", Oxford, England, April 1983;

NATO Advanced Study Institute on "Receptor Mediated Targeting of Drugs", Cape Sounion Beach Resort, Greece, June 1983.

Public Service Activities: Testified before the Subcommittee on Natural Resources, Agriculture Research and Environment of the U. S. House of Representatives' Committee on Science and Technology.

EDWARD HOFFMAN

Recognition and Honors: Georg von Hevesy Prize from the Georg von Hevesy Foundation, Zurich, Switzerland, August 1982.

HENRY HUANG

Invited Lecturer: Workshop on time-of-flight positron emission computed tomography, St. Louis, Missouri, May 1982;

Stroke Director's Workshop in San Diego, February 1983.

Recognition and Honors: Georg von Hevesy Prize from the Georg von Hevesy Foundation, Zurich, Switzerland, August 1982.

DAVID E. KUHL

Appointments and Elections: Editorial Board - International Journal of Nuclear Medicine and Biology;

Editorial Board - Journal of Cerebral Blood Flow and Metabolism;

Scientific Advisory Board, the John Douglas French Foundation for Alzheimer's Disease.

Invited Lecturer: World Congress of Nuclear Medicine and Biology, Paris, France, August 29, 1982;

Radionuclides and Brain Disease Meeting, World Health Organization, Valais, Switzerland, September 8, 1982;

DAVID E. KUHL (continued)

Brain Imaging Discussion Group, Malinckrodt Research and Development Program, St. Louis, Missouri, October 4, 1982;

Western Regional Meeting, Society of Nuclear Medicine, San Diego, California October 9, 1982;

Radiological Society of North America, Chicago, Illinois, November 30, 1982;

U. S. VA Medical Center, Sepulveda, California, January 5, 1983;

International Symposium on Regional Cerebral Blood Flow, Cedar-Sinai Medical Center, February 9, 1983;

Harvard Medical School and Brigham & Women's Hospital, Boston, Massachusetts, March 8, 1983;

American College of Nuclear Physicians, Dorado, Puerto Rico, March 11, 1983;

Psychopharmacology Unit, Brentwood VA Medical Center, Brentwood, California, April 12, 1983;

American Academy of Neurology, San Diego, California, April 27, 1983;

Indiana University School of Medicine, Indianapolis, Indiana, April 29, 1983;

Nobel Conference VII, Karolinska Institute, Stockholm, Sweden, May 17-20, 1983;

Abo Akademi & Turku University School of Medicine, University Central Hospital, Turku, Finland, May 23, 1983;

Kuopio University School of Medicine, University Central Hospital, Kuopio, Finland, May 24, 1983;

Annual Meeting of the Society of Nuclear Medicine, St. Louis, Missouri, June 6-10, 1983;

Conference on Research Issues in Positron Emission Tomography, National Institutes of Health, Bethesda, Maryland, June 16-17, 1983.

DAVID E. KUHL (continued)

Recognition and Honors: First Annual Philip M. Johnson Memorial Lecturer, College of Physicians and Surgeons, Columbia University;

Annual Orator, Radiological Society of North America;

Fellow of the American College of Nuclear Physicians;

Merrill C. Sosman Lecturer, Harvard Medical School.

Public Service Activities: Program Director, Los Angeles Nuclear Medicine Conferences.

ROBERT G. LINDBERG

Public Service Activities: Chairman, American Institute of Biological Sciences Sub-Panel on Biological, Behavioral and Social Sciences for "AAAS Review of NSF Bilateral Cooperative Science Programs", 1983;

Member, Biological Resource Workshop (Mojave Desert), California Energy Commission/Bureau of Land Management, Riverside, California, 1982.

JAMES F. MEAD

Invited Lecturer: Basic Science Foundations in Endocrinology Lecture Series, Harbor-UCLA Medical Center, "The Mechanism of Essential Fatty Acid Action", January 1983;

Introductory Talk at Workshop on Oxygen Free Radicals and Lipid Peroxidation in the Nervous System, 14th Annual Meeting, American Association of Neurochemistry, Honolulu, Hawaii, March 1983.

Public Service Activities: Nutritional Advisory Committee, Frito-Lay Corporation;

Member, Award Committee, Supelco-AOCS;

Research Award, 1983-present

Editorial Board of 5 publications: Lipids; Physiological Chemistry and Physics; J. American Aging Association; Progress in Lipid Research; and J. Nutrition, Growth and Cancer.

PARK S. NOBEL

Invited Lecturer: Symposium devoted to different kinds of stress on photosynthesis, Sint-Trinden, Belgium, August 1982;

Society of Experimental Biology meeting regarding plant temperature, Dublin, Ireland, July 1982.

MICHAEL D. PHELPS

Appointments and Elections: Chairman, Neurology Section, Basic Sciences, Society of Nuclear Medicine, St. Louis, June 1983;

Chairman, Instrumentation Section, International Society of Cerebral Blood Flow and Metabolism, Paris, June 1983;

Chairman, Nobel Symposium, Stockholm, Sweden, May 1983;

Academic Council, The Society of Nuclear Medicine, 1983-present;

Member, Science Advisory Board of NINCDS Intramural Program at NIH, 1982;

Member of Council and Founding Member, International Society of Cerebral Blood Flow and Metabolism, 1982-present.

Invited Lecturer: Central Chapter of the Society of Nuclear Medicine, Chicago, Illinois, March 1983;

Winter Brain Conference, January 1983;

Academy of Neurology, April 1983;

Nobel Symposium, Stockholm, Sweden, May 1983;

Society of Nuclear Medicine, June, 1983;

American Society Pharmacology and Therapeutics, July 1983.

Recognition and Honors: Georg von Hevesy Prize, Georg von Hevesy Foundation, Zurich, Switzerland, 1982;

The Paul Aebersold Award for Outstanding Achievement in Basic Science Applied to Nuclear Medicine, Society of Nuclear Medicine, 1983;

MICHAEL D. PHÉLPS (continued)

Jennifer Jones Simon Endowed Chair and Professorship, 1983;
Benedict Cassen Memorial Lecture, Society of Nuclear Medicine,
May 1983;
Chairman, 1983 Nobel Symposium, Stockholm, Sweden.

EVAN M. ROMNEY

Invited Lecturer: Southwest Rangeland Watershed Research Center,
Tucson, Arizona, October 1982;
University of Nevada, Las Vegas, Nevada, June 1983.

PHILIP W. RUNDEL

Appointments and Elections: Visitng Professor in Tropical
Ecology, Universidad de Los Andes, Merida, Venezuela,
April 1983.
Invited Lecturer: National Park Service, Symposium on Research
in California National Parks, September 1982;
Forest Sciences Laboratory, Oregon State University, November 1982;
Center for Intermedia Transport, University of California,
Los Angeles, March 1983;
Departamento de Ecologia Vegetal, Universidad de Los Andes,
Merida, Venezuela, April 1983;
Program in Global Ecology, NASA Ames Laboratory, Mountain View,
California, May 1983;
OHER, U. S. Department of Energy, Washington, D.C., May 1983.

HEINRICH SCHELBERT

Appointments and Elections: Medical Research Service Merit
Review Board for Cardiovascular Studies, The Veterans
Administration, Washington, D.C., 1982;

HEINRICH SCHELBERT (continued)

Vice-Chairman, Scientific Program Committee, 30th Annual Meeting of Society of Nuclear Medicine, The Society of Nuclear Medicine, New York, 1983;

Vice-Chairman of Research Committee, Greater Los Angeles Affiliate of the American Heart Association, Los Angeles, California, 1982-present;

Member, NIH Cardiovascular-Pulmonary Study Section, National Institutes of Health, Bethesda, Maryland, 1983-present.

Invited Lecturer: Southwest Regional Medical Education Center, The Veterans Administration, Long Beach, California, July 10, 1982;

Chair Person, 29th Annual Scientific Meeting of the Society of Nuclear Medicine, Miami Beach, Florida, June 1982;

The Chinese Medical Association, 1982 Congress and Scientific Meeting, Taipei, Taiwan, Republic of China, July 1982;

World Federation of Nuclear Medicine and Biology; Third World Congress of Nuclear Medicine and Biology, Paris, France, August 1982;

St. Johns Hospital and Health Center, Santa Monica, California, 4th Annual Postdoctoral Assembly, September 1982;

University of Wisconsin, Milwaukee, School of Medicine, 7th Annual Nuclear Cardiology Symposium, September 1982;

Hammersmith Hospital, Department of Cardiology, Royal Postgraduate School of Long, London, United Kingdom, September 4, 1982;

Luncheon Panelist, The Greater Los Angeles Affiliate of the American Heart Association, 50th Anniversary Fall Symposium, September 1982;

American Heart Association, 55th Scientific Session, Dallas, Texas, November 1982;

Workshop of Merck, Sharp and Dohme Cardiovascular Faculty, Annual Meeting, Palm Springs, California, January 1983;

HEINRICH SCHELBERT (continued)

The American College of Cardiology, The Heart House Learning Center, Bethesda, Maryland, February 1983;

The American College of Cardiology, 32nd Annual Scientific Session, New Orleans, Louisiana, March 1983;

Department of Cardiology, University of Heidelberg, International Titisee Conference on "Myocardial Ischemia", Titisee, West Germany, March 1983;

Western Regional Chapter of the Society of Nuclear Medicine, Hawaii Spring Conference, Hawaii, April 1983;

The Society of Nuclear Medicine, 30th Annual Meeting, Session Chairman, St. Louis, Missouri, June 1983;

Abo Academy and the University of Turku: Third Symposium on Medical Applications of Cyclotrons, Turku, Finland, June 1983;

Visiting Professor, The Division of Nuclear Medicine, Massachusetts General Hospital, Boston, Massachusetts, February 1983.

Recognition and Honors: Fellow, Council on Basic Science, The American Heart Association, 1983;

Georg von Hevesy Prize, Georg von Hevesy Foundation, Zurich, Switzerland, 1982;

Group Investigatorship Award, The Greater Los Angeles Affiliate of The American Heart Association, December 1982;

ARTHUR WALLACE

Recognition and Honors: Honorary Fellow, Indian Society for Plant Nutrition, 1982;

Adjunct Professor of Soil Science, Utah State University, 1981-present;

Adjunct Professor of Agronomy, Brigham Young University, 1981-present.

Public Service Activities: Co-chairman, Second Biennial Symposium on Iron in Plants, Utah State University, Logan, Utah, 1983.

**RESEARCH HIGHLIGHTS
PUBLICATIONS**

**LABORATORY
OF
BIOMOLECULAR AND CELLULAR SCIENCES**

LABORATORY OF BIOMOLECULAR AND CELLULAR SCIENCES

RESEARCH HIGHLIGHTS

Research in LBCS is concerned -- at the organismal, cellular and molecular level -- with proliferation, gene expression and differentiation in normal cells and in cells exposed to pollutants and/or carcinogens.

At the organismal level we have investigated the origin of isoprene in human breath, presuming it derives from cholesterol precursors. However, labeling experiments suggest this is not the case. Labelled precursors are now being used to look for a new pathway of isoprenoid synthesis. In other systemic studies, long term oral administration of cadmium caused bone-marrow hypoplasia, resulting in anemia and granulocytopenia. Animals did not develop overt/aplastic anemia; there was no increase in mortality. We have also investigated the effect of acute Cd^{++} administration on synthesis and degradation of metallothionein, the metal and steroid inducible metal-binding protein, in three mutant strains altered in trace metal metabolism and have characterized developmental appearance of this protein.

Cellular studies emphasize both control of growth and the regulation of differentiated, organ-specific function by hormones, carcinogens, tumor promoters, metals, drugs, and other agents. We described the minimal set of growth factors required for survival, proliferation and maturation of CNS neurons, astrocytes and oligodendrocytes. Receptors for epidermal growth factor, a potent mitogen, were restricted primarily to astrocytes. Thymic growth factors were shown to be essential for the transformation into lymphoma cells of a minor sub-population of prelymphoma bone marrow thymocyte progenitors carrying murine leukemia viruses. Variant 3T3 cell lines non-responsive to specific growth factors have been selected. Biochemical defects unique to cells non-responsive to the potent mitogen/tumor promoter tetradecanoyl phorbol acetate (TPA) have been partially described; and a somatic cell genetic analysis has been initiated. These cells have been used to demonstrate that a second tumor promoter, teleocidin, works through the same pathway as TPA. Complementation analysis of the variants has begun. The biochemical basis for the activation of the polycyclic aromatic hydrocarbon (PAH) carcinogens is also being analyzed in cell culture. Mutants defective in PAH induction of aryl hydrocarbon hydroxylase (AHH, P450), the PAH activating enzyme, have been isolated from a murine cell line. Using somatic cell genetic techniques the mutants have been divided into four groups: one dominant and three recessive and complementing one

another. Using a reverse selection, revertants were isolated from each class, demonstrating their mutagenic origin. Induction of another P450 monooxygenase by barbiturates, a second class of inducers, is being studied in *B. megaterium*. This is a unique phenomenon in which, in bacteria, a non-substrate inducer regulates a gene product. The parallels between this procaryotic system and similar barbiturate-inducible eucaryotic P450 monooxygenases make this an attractive system for evolutionary studies in structure, gene regulation and cellular detoxification. Structure-function studies have suggested a two-step induction mechanism, one of which involves barbiturate intercalation into membranes. Abnormal gene expression in tumors has been exploited by extending the analysis of S100 protein, a nervous-system specific protein previously found to be present in melanomas, to an immunohistological analysis of metastatic cells in lymph nodes. The plasticity of tumor cells is also being studied by characterizing the heterogeneity, with respect to growth and metastasis, of murine T cell lymphomas. Phenotypic heterogeneity in normal cells has been demonstrated with hormone-toxin conjugates, which have proved to be differentially toxic to various target cells carrying the same receptor. Heterogeneity of normal and neoplastic tissue is also investigated with monoclonal antibodies directed to separate classes of CNS cells and tumors. The effects of calcium blockers, cardiac glycosides, ion concentrations and a variety of hormones on cardiac function are being probed using a video computer program to analyze cultured beating heart cells. A new program which is able to analyze rhythmicity and arrhythmicity has demonstrated the central role of calcium flux in mediation of a variety of pharmacologic agents that affect network rhythmicity.

At the molecular level the cDNA for one (of two) rat metallothioneins has been cloned and sequenced. The gene family for this protein has been recovered from a genomic library and the structure of the gene(s) and pseudogenes is under way. The molecular basis for regulation of expression of metallothionein is being studied by examining messenger RNA expression. A molecular analysis of the PAH-induced AHH in mutant cell lines is also underway, and has demonstrated production of normal levels of AHH mRNA in one of the AHH non-inducible (in terms of enzyme activity) mutant classes. Genes for two enzymes under hormonal regulation in brain are also being cloned, to extend our cell biological and endocrine studies to the molecular level in this system.

PUBLICATIONS

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LABORATORY
OF
ENVIRONMENTAL BIOLOGY

LABORATORY OF ENVIRONMENTAL BIOLOGY

RESEARCH HIGHLIGHTS

The research activities of the laboratory of Environmental Biology broadly cover a range of topics including ecosystem process studies, environmental physiology of desert plants and animals, and population biology. We are currently moving to better focus research activities toward an integrated ecosystem approach with emphasis on modelling. The synthetic efforts toward integrating existing data sets for the Rock Valley site in Nevada have been an important staff activity. Individual foci of major research fell into five areas.

Primary Production Processes: Over the past two years Dr. Rundel has been investigating the relationship of dynamic cycles of N and water availability to net primary production (NPP) of mesquite woodlands in the Sonoran Desert of Southern California. A multidisciplinary research group (including plant ecologists, soil scientists and N₂-fixation specialists) has quantified a number of significant aspects of the ecosystem processes which control productivity in relatively pure stands of *Prosopis glandulosa* (mesquite) at the primary study site near the Salton Sea in the Sonoran Desert. There have been a number of significant results to date including the following: both biomass and aboveground NPP are remarkably high for desert ecosystems (14,000 kg ha⁻¹ and 3700 kg ha⁻¹ yr⁻¹ for 980 respectively), high NPP is possible for mesquite because it is able to decouple itself from normal limiting factors of both water and N availability, the phreatophytic habit of mesquite allows it to tap permanent groundwater supplies, Nitrogen-fixing root nodules are present on mesquite in the field and our natural ¹⁵N abundance measurements have established that approximately 60% (36 kg N ha⁻¹) of the net annual increment of N accumulation comes from N₂-fixation, high levels of N₂-fixation have produced a positive net flux of N into mesquite woodland soil such that very high levels of both total soil N (1020 g m⁻²) are present under mesquite canopies, assuming a maximum age of 500 years, the minimum annual increase in the total ecosystem N pool has been 6 kg ha⁻¹ yr⁻¹ (19.5 kg ha⁻¹ yr⁻¹ on a canopy basis).

Plant-Environmental Interactions: Dr. Nobel's program entitled "Plant-Environment Interactions" has focused on the physical factors affecting desert plants, with particular emphasis on modeling and physiological responses. Initially, most effort was devoted to studying water relations, which are of paramount importance for understanding desert plants. This involved determining which years were suitable for seedling establishment based on rainfall records and tissue tolerances

to dehydration, e.g., for the common desert agave, Agave deserti, only one year in 17 was suitable for seedling establishment in the western Sonoran Desert. The water-use efficiency (g CO₂ fixed per kg H₂O transpired) was studied for representative plants from all three photosynthetic pathways (C₃, C₄ and CAM), so that productivity could be predicted.

The next major research phase, which overlapped with the above studies, was a modeling effort to predict the temperature of plant parts under various environmental conditions using energy budget models. For succulent plants like cacti and agaves this entailed development of new computing methodology. We are now examining the tissue tolerances to extreme temperatures so that the computer output can be used to predict range boundaries, especially for succulent plants.

The final environmental parameter examined was light, more specifically photosynthetically active radiation (PAR). It was determined that cacti and agaves, which are CAM plants characteristic of the desert, are on the verge of being PAR-limited, even in the high radiation environment of the desert. This program has also involved a major modeling effort whereby it is possible to predict the total daily PAR intercepted by a surface facing in any direction at any season and any latitude.

Presently, an investigation of the various physical factors mentioned above is being completed and studies are underway on the last major variable, i.e., nutrients. Temperature effects on metabolic processes and the acclimation of optimal temperatures are being further examined. The next phase will be to examine the interaction of two factors (e.g., dehydration and high temperature, which often occur together in the desert), which has been done on a limited basis for C₃ plants. Finally, the various factors will be synthesized into models predicting the overall response of desert plants to the physical environment, including any trends caused by natural or man-induced changes.

Ecological Physiology of Desert Vertebrates: In Dr. Nagy's program predictive models, based on measurements of representative animals, are being generated for food, energy and water requirements of birds and mammals living in their natural habitats. Effects of natural stresses (droughts, heat) on desert tortoises and lizards at Rock Valley, Nevada are being analyzed. New projects on an important desert lizard and kidney physiology of desert tortoises are being initiated. These results will form part of the data base needed in analyzing nutrient cycles and critical processes on the consumer portion of the desert ecosystem. We are attempting to obtain fundamental measurements on

all the major vertebrate consumers in this habitat. Predictive models for nutrient requirements of desert reptiles have just been published.

Soil-Plant-Animal Transport of Energy Pollutants: The objective of Dr. Romney's research project is to develop better understanding of the critical pathways and transfer mechanisms involved in abiotic and biotic transport of energy-derived pollutants in desert environments. Field studies are done in contaminated areas at the Nevada Test Site and in surrounding areas exposed to fallout from nuclear weapon tests. These studies are designed to improve understanding of potential health hazards resulting from the cycling of radionuclides and toxic element pollutants among soil, plant and animal components of the natural ecosystem.

Wildlife Issues in Non-Nuclear Development: A 5-year study of coal ash on native desert plants was completed by Dr. Turner. Ash was applied to treated plots in amounts ranging from 5 to 100 metric tons per hectare. Our lowest dose was about 28 times higher than the worst-case estimate of aerial deposition of stack-emitted particulates over the 30-year lifetime of a hypothetical coal burning power plant. The dividing line between no observed effects and clearly distinguishable effects lay between treatments of 5 and 10 mt/ha of ash. The pH of surface soils was increased significantly in plots receiving from 10-100 mt/ha of ash. Populations of annual plants were affected by application of 10, 30 and 100 mt/ha of ash, but not by 5 mt/ha. Numbers of species and of individuals were strongly reduced in 30 and 100 mt/ha plots. Effects of ash were most pronounced about 9 months after the last increment of ash was applied. At this time, aggregate densities of annual plants in 100 mt/ha plots were only 2-4% of those in untreated plots. During the last two years of the study there was some recovery in treated plots, apparently owing to weathering of ash. Experiments in which germination success of seeds of annual plants was compared in natural soil and in soil-ash mixtures, showing that ash generally inhibited germination. Some species were more tolerant than others and these species assumed greater relative importance in ash-impooverished floras.

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**LABORATORY
OF
NUCLEAR MEDICINE**

LABORATORY OF NUCLEAR MEDICINE

Research Highlights

During the past year, members of our laboratory have been singled out by their peers for special recognition. For a second time, a team of our investigators received the prestigious Von Hevesy Award at the World Congress of Nuclear Medicine and Biology, held this year in Paris. Dr. Michael Phelps was named the first Jennifer Jones Simon Professor of Biophysics at UCLA and received the Paul C. Aebersold Award of the Society of Nuclear Medicine for outstanding work in basic science applied to nuclear medicine.

In the nuclear medicine program of this laboratory, the theme has been one of expanding the capability of positron emission tomography particularly, but of single-photon emission computed tomography also, so as to provide a means of accurately documenting local alterations in blood flow and metabolism in the normal brain and heart and the local response in these organs to disease. The laboratory approach advances these methods by combining methods in cyclotron science, physics, instrumentation, chemistry, physiological tracer kinetics, and clinical investigation. The branching impact of this program on other University programs is suggested by patterns of collaboration. In addition to principal investigators in nuclear medicine, there are 15 formally identified associate investigators from the faculties of Internal Medicine and Neurology.

In the Cyclotron Section, short-lived isotopes of oxygen, nitrogen, carbon, and fluorine are prepared in multiple runs daily to satisfy the requirements of the overall research program. Special attention is now being directed to the development of new gas targets which will permit the production of anhydrous HF which is necessary for the very special requirements of receptor assessment in the brain and heart.

In the Chemistry Section, the primary emphasis is on labeling selected physiological substrates or their functional analogs with short-lived radionuclides prepared in the cyclotron. This requires the development of appropriate synthetic pathways, relating chemical structure to biological activity, developing the required technology and assay methods for measuring in metabolic studies, and finally development of remote systems for

both synthesis and processes of large quantities of radiopharmaceuticals appropriately pure for human use. A series of automated systems has been developed for 18-FDG, 11-CDG, and 11-C palmitic acid production on a regular basis. Increasing emphasis is now be given to the fluorine chemistry necessary to introduce very high specific activity indicators for assessment for neurotransmitter receptors.

In the Physical Sciences Section, new instrumentation has been introduced for more accurate and precise positron emission tomography and tracer kinetic models have been developed for accurate measurement of physiological parameters from scan and blood data. A tomographic simulator is used for designing new tomographic systems and developing the fundamental relationships of the match between measured data and activity concentrations within the human body. This system was used to design the present tomographic brain scanner and extend these principles to a hypothetical machine necessary for accurate imaging of the heart. The analysis showed that dramatic improvements can be expected in both resolution and reduction of image noise by employing principles termed "signal amplification technique". Novel light gathering devices are under development which should permit the use of very thin detection crystals in future scanners. In tracer kinetic modeling, extensive error sensitivity analyses have been applied to new assessments of blood flow, glucose utilization, oxygen utilization, and protein synthesis in the brain and blood flow, fatty acid utilization, and glucose utilization in the myocardium. A model, along with autoradiography and biochemistry studies in animals, is being developed for ligand assays of neuroreceptors.

In the Brain Imaging Section, the overall goal is to improve understanding of normal human cerebral physiology and the pathophysiology of cerebral disorders by means of positron emission tomography or single-photon emission computed tomography. Recently, experience with FDG brain imaging here has indicated that predictable patterns of local brain metabolism can be identified in response to normal sensory manipulations such as auditory and visual stimulation. Cerebral metabolic patterns were determined for aging effect and distinguishing features among depressed and demented patients. In Huntington's disease, a caudate nucleus hypometabolism was found to be characteristic of the disease and noted in some asymptomatic children of patients with the disorder. Application of the FDG method to a large group of patients with partial

epilepsy confirmed the initial prediction that the method would be extremely useful in localizing part of the brain responsible for seizure activity and has helped in the surgical treatment of these patients. After validation of a single-photon tomographic method for measuring local cerebral blood flow, it was suggested that this combination may prove to be a less expensive technique capable of more widespread use in hospitals. More recent highlights of progress include the following new information obtained from FDG brain imaging with positron tomography: (1) In Parkinson's disease, the overall metabolism of the brain is only slightly reduced, but the relative distribution of this metabolism is normal, whether or not the patient is medicated; (2) Metabolic scans are characteristic in elderly patients with multiple infarct dementia, and Alzheimer's disease, suggesting that these scans may help differentiate these disorders early in the course of disease from normal aging or depression; (3) Patients with unipolar depression and bipolar manic-depressive disorders appear to have metabolic distinct subgroups by FDG scan; (4) Patients with Wilson's disease have global cerebral hypometabolism and metabolic patterns different from those noted in Huntington's disease; (5) Memory or decision functions appear correlated with measures of local cerebral metabolism; and (6) The significance of local brain metabolism during epileptic seizures has been further clarified by studies in humans and in rats. These results confirm the "technological transfer" of this project from research laboratory to patient care.

In the Cardiovascular Imaging Section, major advances were made in characterizing myocardial substrate utilization, especially related to ¹¹C amino acid metabolism, myocardial metabolic rate for glucose during anaerobic glycolysis, and the use of ¹¹C palmitate for the evaluation of regional myocardial fatty acid metabolism. The primary goal of this project is to gain an improved understanding of cardiovascular physiology in man and to achieve earlier diagnosis of cardiac disease by means of an atraumatic study technique which can accurately and precisely determine regional myocardial performance in terms of blood flow, metabolism, and mechanical function. Progress has been good in applying improved models for characterizing the metabolic state of the heart as well as the efficiency of converting chemical to mechanical energy. These new studies should allow further characterization of metabolic changes associated with acute myocardial ischemia and other cardiac diseases. For example, under normal conditions the myocardium

prefers fatty acids as an energy substrate. During ischemia, however, glucose utilization increases disproportionately even in excess of oxygen availability. The presence of residual metabolic activity in ischemic tissue can be determined and may be useful for defining and predicting potential reversibility. With the current interest in reperfusion in patients with acute myocardial infarction and salvage of ischemically injured myocardium, this form of metabolic imaging may become useful in monitoring the recovery and for selecting new therapeutic strategies.

Future plans of Nuclear Medicine Program; The overall theme of this nuclear medicine program will remain the same: a systematic development of chemistry, instrumentation, and mathematical modeling directed to increasing an evolution of quantitative emission computed tomography and applying this method to important physiological problems leading to an eventual exploitation in clinical medicine. The cyclotron and chemistry efforts will be directed more and more to fluorine chemistry because of its importance in ligand labeling for receptor assessment. Physical Sciences efforts will be increased in the area of concern for the requirements to handle very large amounts of image data. This will require new computer hardware and the development of software routines far more advanced than now in use. Brain Research will concentrate more on disordered brain function in aging, dementia, and affective disorders, as well as a continuing interest in seizure disorders. Special features of these studies will include the cerebral responses to activating manipulations, drug responses, and longitudinal studies. The PET brain scanner will be improved in capability and a new single-photon emission computed tomography unit will be added to improve technological transfer to patient care. Cardiovascular imaging research will continue to focus on the interrelationship of blood flow and substrate utilization in ischemic heart disease and myocardiopathies. It is anticipated that a new cardiac PET scanner will be acquired next year; this improvement is essential to proper exploitation of the method in heart disease.

It is expected that the research program of the Laboratory of Nuclear Medicine will continue to maintain a leadership role in this exciting area of study.

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