LABORATORY OF BIOMEDICAL AND ENVIRONMENTAL SCIENCES
UNIVERSITY OF CALIFORNIA
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MASTER

ANNUAL PROGRESS REPORT

FOR THE PERIOD

JULY 1, 1983 - JUNE 30, 1984

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and the University of California

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LABORATORY OF BIOMEDICAL AND ENVIRONMENTAL SCIENCES

UNIVERSITY OF CALIFORNIA

LOS ANGELES

DIRECTOR

O. R. Lunt

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David E. Kuhl
William J. Moffitt
Philip W. Rundel

FACULTY ADVISORY COMMITTEE
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Associate Vice Chancellor,
Research

LABORATORY OF BIOMEDICAL
AND
ENVIRONMENTAL SCIENCES

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Director

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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

REPORT OF THE DIRECTOR

As will be noted by examination of the contents of this report, our principal investigators published almost 300 technical papers last year. This level of productivity is not only a credit to our investigators but is, in part, a reflection of the involvement of graduate students, postdoctoral trainees, visiting scientists and faculty colleagues in our research.

Of even greater interest is the nature and quality of research information being developed. The reader is referred to the sections dealing with research highlights for brief descriptions of some of the most interesting achievements of the last year. While our focus is primarily on fundamental phenomena, it is evident that some of the information being developed has exciting applied potential in health and environmental areas.

Looking to the future, we do not anticipate major shifts in research programs. Minor shifts will occur as research opens up new avenues of investigation and in response to DOE priorities.

We are indebted to UCLA administration for support and, of course, to the Department of Energy, Office of Energy Research, Office of Health and Environmental Research and other agencies for financial support.

LABORATORY OF BIOMEDICAL AND ENVIRONMENTAL SCIENCES

STATISTICAL SUMMARY

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

Department of Energy

Biomolecular & Cellular Sciences	\$1,075
Environmental Biology	558
Nuclear Medicine	<u>2,150</u>
	\$3,783

Other 2,268

TOTAL OPERATING FUNDING \$6,051

II. STAFFING:

Principal Investigators	26
Scientific Support Staff	15
Others	<u>91</u>
TOTAL	132

III. INSTRUCTION AND OTHER RELATED ACTIVITIES:

Visiting Scientists	14
Fellow and Other Postdoctorals	25
Graduate Students	34
Academic Departmental Staff Appointments	20
Courses to which Laboratory Staff have made significant contributions	69
Number of departments in which these courses were offered	12

*Projected Operating Funding, October 1983 to September 1984. Capital funding excluded.

PROFESSIONAL STAFF

VISITORS

GRADUATE STUDENTS

PRINCIPAL INVESTIGATORS

GEORGE V. ALEXANDER, M.S.

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

JORGE R. 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

HARVEY R. HERSCHMAN, Ph.D.

Regulation of cell division and gene expression by endogenous factors and environmental agents

ACADEMIC DEPARTMENT

Radiological Sciences

Radiological Sciences

Anatomy, Psychiatry
and Behavioral Sciences

Biological Chemistry

Pathology

Biological Chemistry

Radiological Sciences

Medicine

Biological Chemistry

PRINCIPAL INVESTIGATORS

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

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

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

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

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

JOHN C. MAZZIOTTA, M.D., Ph.D.
Animal and human studies of cerebral biochemistry using trace kinetic methods

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

KENNETH A. NAGY, Ph.D.
Vertebrate physiological ecology: energy, water, nutrient metabolism of desert animals

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

AMOS NORMAN, Ph.D.
Medical Physics

ACADEMIC DEPARTMENT

Radiological Sciences

Radiological Sciences

Radiological Sciences

Environmental Sciences
Engineering

Radiological Sciences

Radiological Sciences

Biological Chemistry

Biology

Biology

Radiation Oncology

PRINCIPAL INVESTIGATORS

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

EVAN M. ROMNEY, Ph.D.
Radionuclide and stable element cycling; restoration of vegetation on disturbed desert land

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

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

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

ACADEMIC DEPARTMENT

Radiological Sciences

Biology

Radiological Sciences

ASSOCIATE INVESTIGATORS*

DIVISION

ROBERT ACKERMANN, Ph.D.

Nuclear Medicine

D. FRANK BENSON, M.D.

Nuclear Medicine

JUDITH BERLINER, Ph.D.

Biomolecular and
Cellular Sciences

RICHARD BRUNKEN, M.D.

Nuclear Medicine

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

Nuclear Medicine

ARTHUR GIBSON, Ph.D.

Environmental
Biology

*Co-Investigators who interact with Principal Investigators

ASSOCIATE INVESTIGATORS*

JANINE KRIVOKAPICH, M.D.

ROBERT MARSHALL, M.D.

E. JEFFREY METTER, M.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.

DIVISION

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Nuclear Medicine

Biomolecular and
Cellular Sciences

Nuclear Medicine

Nuclear Medicine

*Co-Investigators who interact with Principal Investigators

SENIOR PROFESSIONAL STAFF

ROBERT ANDERSEN, Ph.D.

DORIS BASS

WADE L. BERRY, Ph.D.

HERBERT HANSEN, B.A.

RICHARD HUNTER, Ph.D.

YUTAKA KOBAYASHI, Ph.D.

SHALINI KUMAR, Ph.D.

HAZEL LEWIS, Ph.D.

DIVISION

Biomolecular and
Cellular Sciences

Biomolecular and
Cellular Sciences

Environmental
Biology

Nuclear Medicine

Environmental
Biology

Biomolecular and
Cellular Sciences

Biomolecular and
Cellular Sciences

Biomolecular and
Cellular Sciences

SENIOR PROFESSIONAL STAFFDIVISION

FREDERICK MEINZER, Ph.D.	Environmental Biology
NIRALA MENON, Ph.D.	Biomolecular and Cellular Sciences
ANTHONY RICCI, A.B.	Nuclear Medicine
RICHARD T. RUETTINGER, Ph.D.	Biomolecular and Cellular Sciences
CAROL SCHNEIDER, Ph.D.	Biomolecular and Cellular Sciences
CARL SELIN, M.S.	Nuclear Medicine
M. R. SHARIFI, Ph.D.	Environmental Biology
GUEY-SHUNG WU, Ph.D.	Biomolecular and Cellular Sciences

VISITING SCIENTISTS

MASAMI BESSHO, Ph.D.	National Institute of Rad. Sciences Chiba-shi, Japan
ETIAN BOGIN, Ph.D.	Kimron Institute Bet-Dagan, Israel
LIANE BOLOGA-GERBER, Ph.D.	University of Berne Berne, Switzerland
JOHN CALLAHAN, Ph.D.	University of Toronto Toronto, Canada
MARTIN B. EPSTEIN, Ph.D.	Cal State University of Los Angeles Los Angeles, California
LAURI V. KARENLAMPI, Ph.D.	University of Kuopio Kuopio, Finland
SHINICHI KITADA, M.D., Ph.D.	Kyoto, Japan
STEPHEN LUNER, Ph.D.	Dalhousie University Nova Scotia

VISITING SCIENTISTS

ERIK T. NILSEN, Ph.D.	Virginia Polytechnic Institute Blacksburg, Virginia
L. J. PAREKH, Ph.D.	University of Baroda Baroda, India
OSERDAN PARODI, M.D.	University of Pisa Pisa, Italy
KANTA SACHAR, Ph.D.	University of Delhi India
JAMES THOMAS, Ph.D.	Iowa State University Ames, Iowa
PAN ZHONG-YUN, M.D.	Beijing Medical College Beijing, China

RESEARCH PARTICIPANTS

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EDMUNDO ACEVEDO, Ph.D.	University of Chile Santiago, Chile
GEORGE A. BARTHOLOMEW, Ph.D.	University of California Los Angeles, California
GARY BELL, Ph.D.	University of California Los Angeles, California
ALBERT F. BENNETT, Ph.D.	University of California Irvine, California
KRISTIN H. BERRY, Ph.D.	U.S. Bureau of Land Management Riverside, California
ADRIAN BRADLEY, Ph.D.	University of Western Australia Perth, Western Australia
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RESEARCH PARTICIPANTS

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E. B. EDNEY, Ph.D.	University of British Columbia Vancouver, British Columbia
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WILLIAM FOLEY, M.A.	University of New England Armidale, NSW, Australia
PAUL FRANCO, M.A.	Oak Ridge National Laboratory Oak Ridge, Tennessee
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DAVID GOLDSTEIN, Ph.D.	University of Arizona Tucson, Arizona
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RESEARCH PARTICIPANTS

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HENRY JOHN-ALDER, Ph.D.	University of California Irvine, California
IAN KAPLAN, Ph.D.	University of California Los Angeles, California
JOHN KEELEY, Ph.D.	Occidental College Los Angeles, California
STERLING KEELEY, Ph.D.	Los Angeles County Museum Los Angeles, California
JAMES G. KENAGY, Ph.D.	University of Washington Seattle, Washington
DANI KOBAYASHI, B.A.	University of California Los Angeles, California
DANIEL KOHL, Ph.D.	Washington University St. Louis, Missouri
THOMAS H. KUNZ, Ph.D.	Boston University Boston, Massachusetts
A. K. LEE, Ph.D.	Monash University Clayton, Victoria, Australia
E. LEIGH, Ph.D.	Smithsonian Tropical Research Institute Panama
JAY A. LEVY, Ph.D.	University of California San Francisco, California
LLOYD LOOPE, Ph.D.	U.S. National Park Service Haleakala National Park, Maui

RESEARCH PARTICIPANTS

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BRIAN OBST, B.A.	University of California Los Angeles, California
DAVID PARSONS, Ph.D.	U.S. National Park Service Sequoia National Park, California
EDGAR QUERO, M.S.	Centro de Investigacion Saltillo, Coahuila, Mexico
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

RESEARCH PARTICIPANTS

IAN ROOKE, Ph.D.	University of Western Australia Perth, Western Australia
GORDON SANSON, Ph.D.	Monash University Clayton, Victoria, Australia
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R. K. SCHULZ, Ph.D.	University of California Berkeley, California
E. D. SCHULZE, Ph.D.	Universitat Bayreuth Bayreuth, West Germany
VAUGHAN H. SHOEMAKER, Ph.D.	University of California Riverside, California
ROY SIEGFRIED, Ph.D.	University of Cape Town Cape Town, South Africa
A. SMITH, Ph.D.	University of Miami Coral Gables, Florida
S. D. SMITH, Ph.D.	University of Reno Reno, Nevada
JAY STEMMLER, M.A.	University of Washington Seattle, Washington
GRAEME SUCKLING, Ph.D.	Monash University Clayton, Victoria, Australia
ROSS VIRGINIA, Ph.D.	University of California Riverside, California
WESLEY W. WEATHERS, Ph.D.	University of California Davis, California
PATRICK WELTON, M.D., Ph.D.	University of California Los Angeles, California
WALTER G. WHITFORD, Ph.D.	New Mexico State University Las Cruces, New Mexico
G. C. WHITTON, Ph.D.	University of Hawaii Honolulu, Hawaii
JOSEPH WILLIAMS, Ph.D.	Pepperdine University Malibu, California

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RORY WILSON, B.A.	University of Cape Town Cape Town, South Africa
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STEVE WITTMER	University of California Los Angeles, California
STANLEY YOKOTA, Ph.D.	University of Arizona Tucson, Arizona
T. YOUNG, Ph.D.	University of Miami Coral Gables, Florida
ALLAN ZIMMERMAN, M.A.	University of Texas Austin, Texas

POSTDOCTORALS

SUSAN ABERNATHY, Ph.D.
DEBORAH BANKER, Ph.D.
PETER BECKER, Ph.D.
MICHAEL BOWERS, Ph.D.
HOWARD W. CALKIN, Ph.D.
BARRY DORFMAN, Ph.D.
MALEAH GROVER, M.D.
SIRPA KARENlampi, Ph.D.
ATSUSHI KATO, Ph.D.
S. CHUAN KEE, Ph.D.
CAROLYN KIMME-SMITH, Ph.D.
HAZE LEWIS, Ph.D.
ROBERT LIM, Ph.D.
ANDRE LUXEN, Ph.D.
ROBERT NAKAMURA, Ph.D.
TERRY L. RITCHIE, Ph.D.
JAMES R. ROPCHAN, Ph.D.
RUSSEL SANETO, Ph.D.
N. SATYAMURTHY, Ph.D.
HERZL SCHWALB, Ph.D.
HEINZ SOCHOR, M.D.
JOHN G. WILLIAMS, Ph.D.
CHARLES WISDOM, Ph.D.
DORIS WU, Ph.D.
DONALD R. YOUNG, Ph.D.

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Jorge R. Barrio
Philip W. Rundel
Jean de Vellis
Jorge R. Barrio
Jean de Vellis
Jorge R. Barrio
Armand J. Fulco
Heinrich R. Schelbert
Park S. Nobel
Philip W. Rundel
Jean de Vellis
Park S. Nobel

GRADUATE STUDENTSDEPT.DEG. OBJ.SPONSOR

YAIR AIZENMAN	Neuroscience	Ph.D.	Jean de Vellis
JEFFREY B. BARTON	Radiological Sciences	Ph.D.	Edward J. Hoffman
BRUCE BIRREN	Biological Chemistry	Ph.D.	Harvey R. Herschman
HANNES CALLISEN	Medical Physics	Ph.D.	Amos Norman
DIANE CHUGANI	Pharmacology	Ph.D.	Jorge R. Barrio
ALLISON COLLINS	Biology	M.A.	Kenneth A. Nagy
MAGNUS DAHLBOM	Radiological Sciences	Ph.D.	Edward J. Hoffman
EVAN DENERIS	Nutrition	Ph.D.	James F. Mead
AUGUSTO FRANCO	Biology	Ph.D.	Park S. Nobel
GARY N. GELLER	Biology	Ph.D.	Park S. Nobel
JEAN M. GUDAS	Public Health	Ph.D.	Oliver Hankinson
BRIAN HENEN	Biology	Ph.D.	Kenneth A. Nagy
EMILY HOFFMAN	Pathology	Ph.D.	Oliver Hankinson
EMILY HOLMES	Anatomy	Ph.D.	Jean de Vellis
RANDY E. KEEN	Radiological Sciences	Ph.D.	Jorge R. Barrio
KAREN LEE	Biology	M.A.	Kenneth A. Nagy
J. C. MITCHELL	Medical Physics	M.S.	Amos Norman
LINDA O. NARHI	Biological Chemistry	Ph.D.	Armand J. Fulco
MADELEINE PINCU	Medical Physics	Ph.D.	Amos Norman
SARAH PIXLEY	Anatomy	Ph.D.	Jean de Vellis
DEBBIE O. RAPHAEL	Biology	Ph.D.	Park S. Nobel
ANTHONY R. RICCI	Radiological Sciences	Ph.D.	Edward J. Hoffman
SHERYL ROSENTHAL	Nutrition	M.S.	James F. Mead
DERRICK SCHMIDT	Radiological Sciences	Ph.D.	Jorge R. Barrio
KAREN SINGER	Biology	Ph.D.	Park S. Nobel
MARK A. STENE	Pathology	Ph.D.	Oliver Hankinson
SUSAN TAPLITZ	Biological Chemistry	Ph.D.	Harvey R. Herschman
ERNEST TERWILLIGER	Biological Chemistry	Ph.D.	Harvey R. Herschman
LORRAINE UTTER	Biology	Ph.D.	Philip W. Rundel
BRIAN VARNUM	Biological Chemistry	Ph.D.	Harvey R. Herschman
ALLAN J. WATSON	Public Health	Ph.D.	Oliver Hankinson
PATRICK WELTON	Physiology	M.D., Ph.D.	John C. Mazziotta
LONG-PING WEN	Biological Chemistry	Ph.D.	Armand J. Fulco
DORIS WU	Anatomy	Ph.D.	Jean de Vellis

STAFF RECOGNITION AND HONORS

STAFF RECOGNITION AND HONORS

JORGE R. BARRIO

Invited Lecturer: American Chemical Society of Pharmacology and Experimental Therapeutics (Symposium Organizer), Philadelphia, Pennsylvania, August 1983;

Third International Symposium on Radiopharmacology, Freiburg, West Germany, September 1983;

Workshop on Medical Applications of Positron Emission Tomography, Uppsala, Sweden, May 1984;

Society of Nuclear Medicine, Los Angeles, California, June 1984;

Collegium Internationale Neuropsychopharmacologicum (Symposium on Brain Imaging Techniques), Florence, Italy, June 1984.

JEAN S. De VELLIS

Appointments and Elections: Treasurer, American Society for Neurochemistry;

President, California Tissue Culture Association;

Associate Editor, Journal of Neuroscience Research;

Editorial Board, Neurochemical Research;

Reviewer, Brain Research/Developmental Brain Research, Journal of Neurochemistry, Journal of Cellular Physiology, Science, Rapid Communications in Cell Biology, Journal of Cellular Biochemistry.

Invited Lecturer: Workshop on "Neurochemistry of Development in Tissue Culture," International Society for Neurochemistry, Vancouver, Canada, July 1983;

"Astroglial Growth Factors," Symposium on Astrocytes, International Society for Neurochemistry, Vancouver, Canada, July 1983;

"Isolation and Characterization of Glial Cells," International Course: Tissue Culture in Neurobiology, Department of Anatomy, University of Saskatchewan, Saskatoon, Canada, July 1983;

"Growth Factors in Central Nervous System Regeneration," 29th Annual Meeting, American Paraplegia Society, Las Vegas, Nevada, August 1983;

JEAN S. De VELLIS (Continued)

"Cellular and Trophic Interactions During Development and Regeneration," Mental Retardation Research Center Annual Conference, Arrowhead, California, October 1983;

Asilomar Conference on Brain Tumor Research and Therapy, Monterey, California, October 1983;

"Update on Central Nervous System Regeneration," Symposium on Update of Rehabilitation Medicine, American Congress of Rehabilitation Medicine, Annual Scientific Meeting, Los Angeles, California, November 1983;

Lectures in Neurochemistry (30 hr), visiting Professor, Graduate Department of Biochemistry, University of Baroda, India, under UNESCO/UNOP program for centers of excellence, November/December 1983;

"Growth, Differentiation and Neoplastic Transformation of Rat Brain Cells in Cell Culture," Department of Pathology, University of Colorado Health Sciences Center, Denver, Colorado, February 1984;

"Glial Growth Factors," in Neurochemistry of Regeneration Symposium, Veterans Administration, Mt. Hood, Oregon, March 1984;

"Cell Culture Attachment Factors" (Chair), Workshop at the 15th Annual Meeting of the American Society of Neurochemistry, Portland, Oregon, March 1984;

"Growth Factors Affecting Glial Cells," Workshop, *ibid*;

"Myelin Pathology in Normal and Abnormal Development," Workshop, *ibid*;

Moderator, Roundtable Discussion on "Past, Present and Future of Growth Factors," 31st Symposium, Tissue Culture Association, California, Santa Monica, California, April 1984;

"New Horizons in Central Nervous System Regeneration," Spinal Cord Society, Glendale, California, May 1984;

"Astrocyte Cell Lineage," International Workshop convened by Drs. S. Federoff and G. Edelman, Neuroscience Institute, Rockefeller University, May 1984;

"Development and Differentiation of Astrocytes," Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas, June 1984;

JEAN S. de VELLIS (Continued)

"The in vitro Neoplastic Transformation of Glial Cell Subpopulations, Symposium on "Experimental Biology of Brain Tumors," (Chair and Speaker), at Physiological and Pharmacological Control of Nervous System Development, 5th International Meeting ISDN, Chieti, Italy, June 1984.

Recognition and Honors: UNESCO/UNDP Visiting Professor to Department of Biochemistry, Baroda University, India, to teach, review and promote Neurochemistry program.

OLIVER HANKINSON

Public Service Activities: Chairman, UCLA Chemical Safety Committee, 1982 to present;

Principal Investigator for Chemical Carcinogenesis Containment Laboratories of the Jonsson Comprehensive Cancer Center, UCLA, 1982 to present.

ESTHER F. HAYS

Appointments and Elections: Associate Dean for Academic Planning, UCLA School of Medicine, 1984.

Member, Educational Policy and Curriculum Committee, Surgical Sciences, Invited Lecturer, Department of Biology, Kansas State University, 1983;

Public Service Activities: Interviewer and Judge for California Museum of Science and Industry's Annual Junior Science and Humanities Symposium (JSHS) for Student Fellow Research Program, 1984.

HARVEY R. HERSCHMAN

Appointments and Elections: Scientific Advisory Board, Hereditary Diseases Foundation, 1982 to present;

Editorial Board, Journal of Cellular Physiology, 1983;

Director for Basic Research, UCLA-Jonsson Comprehensive Cancer Center, 1983 to present;

Member, Executive Policy Committee of the UCLA-Jonsson Comprehensive Cancer Center, 1983 to present.

HARVEY R. HERSCHMAN (Continued)

Invited Lecturer: Seminar, University of California, Berkeley, 1983;

Seminar, University of California, Riverside, 1983;

Invited Speaker, FASEB Conference on Somatic Cell Genetics, 1984.

Public Service Activities: NIH Special Study Section, Molecular Cytology, March 1984

NIH Special Study Section, Molecular Biology, Bethesda, Maryland, March 1984.

EDWARD J. HOFFMAN

Appointments and Elections: Editorial Board of the Journal of Nuclear Medicine, 1983;

External Review Committee for the Medical Physics Graduate Program for the University of California, Irvine;

Technical Committee on Medical Instrumentation for the IEEE Nuclear Society.

Invited Lecturer: Symposium on "Research Issues in Positron Emission Tomography," National Institutes of Health, Bethesda, Maryland, June 1983;

10th Annual Meeting of the American College of Nuclear Physicians, San Diego, California, February 1984;

Symposium on "Metabolism and Imaging of the Brain," Foundation for the Study of the Central and Peripheral Nervous System, Geneva, Switzerland, March 1984.

HENRY HUANG

Invited Lecturer: Department of Medical Physics, University of California, Irvine, November 1983;

Clinical Cardiology International Symposium on Regional Myocardial Metabolism by Positron Tomography, Santa Barbara, California, May 1984.

DAVID E. KUHL

Appointment and Elections: Editorial Board, Journal of Cerebral Blood Flow and Metabolism;

National Scientific Advisory Board, John Douglas French Foundation for Alzheimer's Disease (Executive Committee);

Commission, Association for Research in Nervous and Mental Disease, Inc.;

Scientific Advisory Board (Fachbeirat), Max-Planck Institute for Neurological Research, Cologne, West Germany;

Imaging Advisory Committee, Department of Psychiatry, College of Physicians and Surgeons of Columbia University;

Chairman, Neurology, Clinical Session of the 31st Annual Meeting of the Society of Nuclear Medicine, Los Angeles, California, June 1984.

Invited Lecturer: "The Contribution of Physics to the Developing Imaging Modalities of Nuclear Medicine," President's Symposium, 25th Anniversary Annual Meeting of the American Association of Physicists in Medicine, New York City, New York, August 1983;

Positron Emission Tomography (PET) in the Diagnosis of Alzheimer's Disease," First Annual Frontiers in Alzheimer's Disease Symposium, University of California, San Diego, September 1983;

"Emission Computed Tomography of the Heart and Brain," Grubbe Award Lecture, Chicago Medical Society, Chicago, Illinois, October 1983;

"Positron Emission Tomography of the Functioning Brain in Health and Disease," Michael Reese Hospital, Chicago, Illinois, October 1983;

"Clinical Experience with Emission Tomography of the Brain" UCLA Postgraduate Course in Diagnostic Imaging; Santa Monica, California, October 1983;

"Newer Progress and Diagnosis of Dementias," International Conference on Alzheimer's Disease - Senile Dementia of Alzheimer's Type Aging of the Brain," WHO Kellogg Program, University of Copenhagen, Copenhagen, Denmark, November 1983;

(1) Commission member and panel discussant, (2) "Regional Brain Glucose Utilization in Huntington's Disease," 63rd Annual Meeting of Association for Research in Nervous and Mental Disease, Inc., New York, New York, December 1983;

DAVID E. KUHL (Continued)

"New Directions for Success with SPECT and PET," Workshop on Functional Imaging with SPECT, Diagnostic Imaging Research Branch, National Cancer Institute, NIH, Bethesda, Maryland, January 1984;

"Nuclear Medicine and Positron Emission Tomography," New Horizons in Radiology Symposium on the 100th Anniversary of Montefiore Medical Center, New York, New York, January 1984;

"Positron Emission Tomography in the Study of Dementia," Montefiore Medical Center, *ibid*;

"Metabolic Studies of Depression and Dementia," Albert Einstein College of Medicine, New York, New York, January 1984;

"CNS: Function, Metabolism and Blood Flow," in Symposium "Past, Present and Future of Clinical Nuclear Medicine," 10th Anniversary Meeting of the American College of Nuclear Medicine Physicians, San Diego, California, February 1984;

"Positron Emission Tomography in the Study of Dementia," Brain Imaging Dedication, The Russell H. Morgan Department of Radiology and Radiological Sciences, The Johns Hopkins Medical Institutions, Baltimore, Maryland, March 1984;

"Positron Emission Tomography in Dementia," Conference on Parkinson's Disease and Dementia, Sanders-Brown Research Center on Aging, University of Kentucky and Department of Neurology, Ohio State University, Ohio, April 1984;

"Positron Emission Tomography in the Study of Dementia," Veterans' Administration Medical Center, Sepulveda, California, May 1984;

"Positron Emission Tomography of the Brain in Health and Disease," Olive View Medical Center, Van Nuys, California, June 1984.

Recognition and Honors: Emil H. Grubbe Gold Medal Award, The Chicago Medical Society and Chicago Radiological Society.

OWEN R. LUNT

Appointments and Elections: Short term technical expert, Kenya, United Nations International Atomic Energy Agency;

Reviewer, American Society of Agronomy.

JAMES F. MEAD

Appointments and Elections: Editorial Boards of Lipids Editorial Advisory Board, Journal of Neurochemistry and Associate Editor of Physiological Chemistry and Physics, Progress in Lipid Research, AGE, and the Journal of Nutrition, Growth and Cancer;

Chairman, Academic Senate Committee on Research, University of California, Los Angeles;

Member, Fellowships Committee, UCLA Medical School, Los Angeles, California;

Chairman, Session on Aging, Longevity Society, Los Angeles, California, September 1983;

Chairman, Session on Free Radical Reactions, 13th Annual Meeting of American Aging Association, Washington, D.C., October 1983;

Invited Lecturer: (1) "Relationships of Free Radicals, Lipid Peroxidation and Vitamin E and Other Antioxidants to the Aging Process," (2) "Vitamin E and Aging," American Longevity Society, Los Angeles, California, September 1983;

"Free Radical Mechanisms in Lipid Peroxidation and Prostaglandins, 13th Annual Meeting of the American Aging Association, Washington, D.C., October 1983;

Free Radical Mechanisms in Cell Damage and Aging, Cal State Northridge, California, November 1983;

"Vitamin E: Insulation Against Aging?," New Approaches to Health, Santa Barbara Community College Adult Education, Santa Barbara, California, March 1984.

KENNETH A. NAGY

Invited Lecturer: North Texas State University, September 1983;

University of California, Los Angeles, October 1983;

Loyola Marymount University, Los Angeles, October 1983;

University of California, Riverside, April 1984

University of California, Los Angeles, May 1984;

Department of Energy, Washington, D.C., June 1984;

Physiological Ecology Annual Meeting, Bishop, California, June 1984.

KENNETH A. NAGY (Continued)

Public Service Activities: Committee Member and Merit Badge Counselor, Boy Scouts of America.

PARK S. NOBEL

Appointments and Elections: Member, United Nations Environment Programme Committee;

Member, Editorial Board of Plant, Cell and Environment.

Invited Lecturer: CIBA Foundation, London, July 1983;

6th International Congress on Photosynthesis, Brussels, August 1983;

Ecological Society of America Annual Meeting, Grand Forks, North Dakota, August 1983;

Cabot Symposium on Evolutional Constraints on Primary Productivity, Harvard Forest, August 1983;

Symposium on North American Succulents, Fort Worth, October 1983;

Conference on Biology of Desert Plants, Palm Desert, October 1983;

Symposium on Contemporary Research in Plant Biology, Boulder, April 1984;

2nd International Rangeland Congress, Adelaide, May 1984.

MICHAEL E. PHELPS

Appointments and Elections: Co-Program Chairman, Positron Tomography Symposium, World Congress of Psychiatry, Vienna, Austria, July 1983;

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

Chairman, Commission of the Association for Research in Nervous and Mental Disease, 1983;

Jennifer Jones Simon Endowed Chair and Professorship, 1983 to present;

MICHAEL E. PHELPS (Continued)

Chairman, Instrumentation Session, Society of Nuclear Medicine, 1984.

Invited Lecturer: "Strategies and Problems in the Use of PET to Study Normal and Abnormal Cerebral Function," University of Michigan, Ann Arbor, Michigan, September 1983;

"The Use and Impact of PET Scanning in Epilepsy," 3rd Annual Merritt-Putnam Symposium, Washington, D.C., September 1983;

"Update on TIA and Stroke," American Heart Association 51st Annual Symposium, Los Angeles, California, September 1983;

"Cognitive Neuroscience: Study of Sensory, Behavioral and Pharmacologic Responses - Autoradiography and Positron CT," 13th Annual Meeting, Society for Neuroscience, Boston, Massachusetts, November 1983;

"Human Neuropsychological Imaging Studies of Local Brain Metabolism and Blood Flow: Strategies and Results," 63rd Annual Meeting of the Association for Research in Nervous and Mental Disease, New York, New York, December 1983;

"The Study of Human Brain Function with Positron Computed Tomography," Smithsonian Institute Scientific Lecture Series, Washington, D.C., December 1983;

"Strategies for Experimental Design and Data Analysis with Positron CT," National Institutes of Health, Bethesda, Maryland, March 1984;

"Clinical Applications and Potential of Positron CT," New Imaging Modalities, Annenberg Center for the Health Sciences, Palm Springs, California, March 1984;

"Positron CT Studies of Cerebral Metabolic Responses to Complex Motor Tasks," 36th Annual Meeting of the American Academy of Neurology, Boston, Massachusetts, April 1984.

Recognition and Honors: Ernest O. Lawrence Memorial Award for Outstanding Contributions in the Field of Atomic Energy, awarded by Secretary of Energy, Donald P. Hodel, U.S. Department of Energy, Washington, D.C., 1983;

Special Award for Individual Distinction from the American Nuclear Society, New Orleans, 1984.

EVAN M. ROMNEY

Invited Lecturer: U.S. Department of Energy, Nevada Operations Office, Las Vegas, Nevada, April, June 1984.

U.S. Department of Energy, Office of Health and Environmental Research, Washington, D.C., June 1984.

PHILIP W. RUNDEL

Appointments and Elections: Panel Member, National Science Foundation Ecology Program;

National Park Service Personnel Review Committee.

Invited Lecturer: AIBS, Ecological Society of America. University of North Dakota, August 1983;

Symposium, Tropical Alpine Ecosystems, University of California, Los Angeles, February 1984;

Symposium, National Center for Intermedia Transport Research, University of California, Los Angeles, February 1984;

Symposium, Acid Rain Research, Sequoia National Park, February 1984;

Symposium, Arid Zone Research, U.S. Department of Energy, Washington, D.C., June 1984.

Public Service Activities: Advisory Panel on Landscape Horticulture, University of California, Irvine Extension;

Newport Backbay Advisory Panel, California Division of Fish and Game;

Reviewer: Ecology, Bryologist, Quaternary Research, Mycologia, American Journal of Botany, Botanical Gazette, NSF, Universidad Catolica de Santiago, Chile.

HEINRICH R. SCHELBERT

Appointments and Elections: Member, Cardiovascular Pulmonary Study Section, National Institutes of Health, Bethesda, Maryland;

Member, Steering Committee, Bethesda Conference #14: "Noninvasive Diagnostic Instrumentation in the Assessment of Cardiovascular Disease in the Young;"

HEINRICH R. SCHELBERT (Continued)

Member, Scientific Program Committee, Council on Clinical Cardiology, American Heart Association;

Member, Steering Committee on "Workshop on Metabolic Imaging," National Institutes of Health, Bethesda, Maryland;

Member, Editorial Board of International Journal of Cardiac Imaging;

President, Clinical Cardiology International Symposia Series, "Regional Myocardial Metabolism by Positron Tomography," Santa Barbara, California, May 1984;

Member, Medical Research Service Merit Review Board for Cardiovascular Studies, The Veterans Administration, Washington, D.C.;

Journal Reviewer for Journal of Nuclear Medicine, Circulation, Circulation Research, Journal of Computer Assisted Tomography, American Heart Journal.

Recognition and Honors: Listed in "Who's Who in Science Frontier and Technology."

Invited Lecturer: "Positron Emission Tomography in the Young," 14th Bethesda Conference, "Non-Invasive Diagnostic Instrumentation in the Assessment of Cardiovascular Disease in the Young," The American College of Cardiology and the National Heart and Lung Institute, Bethesda, Maryland, September 1983;

(1) "Phase Analysis of Equilibrium Radionuclide Angiograms for Accurate Detection of Regional Myocardial Ischemia," and (2) "Probing into Myocardial Biochemistry with Positron Emission Tomography," Symposium, "New Perspectives in Cardiac Imaging," Michigan Heart Association, Dearborn, Michigan, September 1983;

"Detection of Ischemic but Viable Myocardium with Positron Emission Tomography," 8th Annual Nuclear Cardiology Symposium, University of Wisconsin, Madison, Wisconsin, October 1983;

"Regional Metabolic Alterations in Myocardial Ischemia Assessed by Positron Tomography," Research Seminar, Division of Cardiology, University of California at San Diego, October 1983;

"Diagnostic Imaging: Recent Advances in Radionuclide Evaluation of the Heart," Postgraduate Course, Department of Radiological Sciences, University of California, Los Angeles, Santa Monica, California, October 1983;

HEINRICH R. SCHELBERT (Continued)

"Noninvasive Assessment of Myocardial Ischemia and Reversible Ischemic Injury," Division of Nuclear Medicine, University of Geneva School of Medicine, Geneva, Switzerland, October 1983;

"Functional and Metabolic Recovery During Reperfusion After Transient Myocardial Ischemia," 4th International Workshop on Regional Myocardial Blood Flow, Division of Cardiology, University of Hannover School of Medicine, Celle, West Germany, October 1983;

(1) Chairman, "Cardiovascular Radiology: Radionuclide Imaging II," and (2) Discussion Leader and Presenter, "Imaging of Myocardial Perfusion by Single Photon and Positron Tracers," 56th Scientific Session, The American Heart Association, Anaheim, California, November 1983;

"PET, Metabolic Studies of the Myocardium," Cardiovascular Nuclear Medicine Symposium, Southern California Chapter of the Society of Nuclear Medicine and the Cancer Foundation of Santa Barbara, Santa Barbara, California, December 1983;

Visiting Professor to the University of Washington at Seattle, Division of Nuclear Medicine, December 1983;

"Positron Emission Tomography of the Heart: What Can It Do? What Are Its Limitations?," Department of Nuclear Medicine, National Institutes of Health, Bethesda, Maryland, February 1984;

Co-Chairman of Scientific Session, "Assessment of Myocardial Metabolism," 33rd Annual Scientific Session, The American College of Cardiology, Dallas, Texas, March 1984;

Seminar on Cardiovascular Imaging Techniques, Division of Cardiology, Cedars Sinai Medical Center, Los Angeles, California, April 1984;

(1) "Regional Myocardial Metabolism by Positron Tomography," (2) "Assessment of Myocardial Fatty Acid Metabolism with C-11 Palmitic Acid," (3) Assessment of Myocardial Blood Flow with N-13 Ammonia," (4) "Normal Alterations in Substrate Metabolism Demonstrated by Positron CT," (5) Positron-CT Studies in Cardiomyopathies," Clinical Cardiology International Symposia Series, Santa Barbara, California, May 1984;

"Cardiovascular VI: Myocardial Metabolism," Session Moderator, 31st Annual Meeting, Society of Nuclear Medicine, Los Angeles, California, June 1984;

HEINRICH R. SCHELBERT (Continued)

"Positron Emission Tomography," for Session "Positron Tomography as a Clinical Service," 31st Annual Meeting, Society of Nuclear Medicine, *ibid.*

Public Service Activities: Vice Chairman, Research Committee, American Heart Association, Greater Los Angeles Affiliate.

FREDERICK B. TURNER

Public Service Activities: Assisted Kristin Berry with preparation of report to the U.S. Fish and Wildlife Service on the status of the desert tortoise in U.S.

ARTHUR WALLACE

Recognition and Honors: Adjunct Professor of Soil Science, Utah State University, 1981 to present;

Adjunct Professor of Agronomy, Brigham Young University, 1981 to present;

Consulting editor, Soil Science, 1982 to present.

DIVISION
OF
BIOMOLECULAR AND CELLULAR SCIENCES

DIVISION OF BIOMOLECULAR AND CELLULAR SCIENCES

RESEARCH HIGHLIGHTS

Research in the Laboratory of Biomolecular and Cellular Sciences deals with proliferation, gene expression and differentiation in normal cells and in cells exposed to pollutants, carcinogens or tumor promoters.

At the cellular level our studies emphasize normal and abnormal control of cell division and the responses of organ-specific, differentiated cellular functions to hormones, growth factors, drugs, carcinogens, tumor promoters, metals and other agents. Peptides that differentially regulate growth of neuronal sub-populations, astrocytes or oligodendrocytes are being purified from brain, pituitary and glial-cell conditioned media, using responses of purified cell populations in culture for assay. An endogenous, physiological inducer of aryl hydrocarbon hydroxylase activity has been observed. We are currently trying to purify this activity. Cloned murine and human epithelial cell lines have been shown to secrete T cell maturation factors. Thymic stromal cell grafts from leukemic and preleukemic mice appear to play a causal role in leukemogenesis.

A fourth complementation group for the induction of aryl hydrocarbon hydroxylase has been discovered. Complementation analysis of epidermal growth factor non-responsive variants of 3T3 cells has demonstrated that two variants are non-complementing and recessive, while one variant is dominant to wild-type.

Receptors for normal and abnormal lipoproteins have been identified on large blood vessel endothelial cell walls. Treatment with abnormal lipoproteins causes increased cholesterol content and resistance to insulin action. Endothelial cells produced a chemotactic factor for monocytes (important agents in vascular disease); production of the factor was accelerated in cholesterol-loaded cells. Insulin stimulates DNA synthesis in small vessel endothelial cells. Cholesterol loading of these cells occurred in response to normal lipoproteins (e.g., LDL), also leading to insulin resistance. A subcellular fraction of rat liver produces isoprene from mevalonic acid and ATP, via the intermediate dimethylallyl pyrophosphate (or the corresponding alcohol). Isoprene may, therefore, be alternate to cholesterol synthesis. Cloned populations from a model murine T lymphoma have distinguishable phenotypes characteristic of different stages in the T-cell differentiation pathway. We have now developed, as a research model, the most highly leukemogenic (higher incidence, shorter latent period, under strain susceptibility) of all AKR-derived oncogenic viruses. Studies of the function of heart cells using the video/computer system have shown that calcium and agents such as ouabain, nifedipine and calmodulin-regulating drugs (all previously shown to affect arrhythmia) also affect pacemaker shifting and synchrony. We have recently found that heart cells in culture exist in two

quantitatively distinct states, characterized by slow and rapid beating. Differences in glycogen metabolism and calcium responses exist between these two populations of cells.

Harlequin staining studies with BrUdR and micronuclear formation are being used to develop methods to estimate low level damage to DNA by UCV, ionizing radiation and chemical carcinogens. A human fertility test which is based on differential intercalation into DNA of sperm of fluorescent dyes has been developed.

A brain-tumor associated antigen of 64K, recognized by a monoclonal antibody, is being characterized. Anti-lymphoma activity of a new plant lectin is being investigated. Retrospective immunoperoxidase staining for S100 protein of lymph nodes from patients with melanoma was compared with H & E; the S100 assay demonstrated 29% of the nodes as tumor positive versus 10% for H & E; the serologic procedures more accurately identified those patients who died within five years of lymphadectomy.

At the molecular level, the phenobarbital induction of bacterial P450 appears to be coordinated with the amplification of a plasmid (one of five present) in *B. megaterium*. Kinetics of induction of the P450 and plasmid amplification in response to phenobarbital are co-ordinate. Inhibition of chromosomal DNA replication does not affect phenobarbital plasmid amplification or P450 induction; inhibition of all DNA replication, including the plasmid, blocks P450 induction by phenobarbital. The A complementation group of murine arylhydrocarbon hydroxylase induction has been shown to code for the protein. The dominant AHH deficient mutant(s) produce a trans-acting repressor of AHH mRNA. An AHH deficiency has been cured in group A and C mutants by DNA transfection. This procedure is now being used to clone the A and C genes. The cDNAs and genes for glutamate synthetase and glycerol phosphate dehydrogenase are being cloned (as specific markers for astrocytes and oligodendrocytes), to study hormonal regulation of these genes in the nervous system. The rat structural gene for metallothionein I has been sequenced, along with (i) a processed pseudogene and (ii) a second genomic sequence that resembles a cDNA of the MT-1 message, but has 5' genomic regulatory sequences as well, suggesting it can be transcribed. Transfection studies to determine if this sequence can be transcribed, as well as differential hybridization studies to determine whether it is normally transcribed, are currently underway.

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1. Andersen, R.D., Birren, B.W., Ganz, T., Piletz, J.E., and Herschman, H.R. 1983. Molecular cloning of the rat metallothionein 1 (MT-1) mRNA sequence. DNA 2:15-22.
2. Andersen, R.D., Piletz, J.E., Birren, B.W., and Herschman, H.R. 1983. Levels of metallothionein messenger RNA in foetal, neonatal and maternal rat liver. Eur. J. Biochem. 131:497-500.
3. Arenander, A.T. and de Vellis, J. 1983. Frontiers of glial physiology. In: R. Rosenberg (ed.), W.D. Willis, Jr. (assoc. ed.) The Clinical Neurosciences. Section V, Neurobiology, Chapter IV, pp. 53-91. Churchill Livingstone, New York.
4. Butzdorf, U., and Mead, J.F. 1983. On the composition of certain lipid tumors of the central nervous system. Western Neurological Society, 29th Annual Meeting, Oct. 1983.
5. Beardsley, T.R., Pierschbacher, M., Wetzel, G.D., and Hays, E.F. 1983. Induction of T-cell maturation by a cloned line of thymic epithelium (TEPI). Proc. Natl. Acad. Sci. USA 80:6505-6009.
6. Bogin, E., Better, O., and Harary, I. 1983. The effect of jaundiced sera and bile salts on cultured beating rat heart cells. Experientia 39:1307-1308.
7. Bressler, J.P., Cahan, L.D., and de Vellis, J. 1982. Cell culture models for the study of brain tumors. UCLA Cancer Bulletin 9(2):5-14.
8. Butler-Gralla, E. and Herschman, H.R. 1983. Glucose uptake and ornithine decarboxylase activity in tetradecanoyl phorbol acetate nonproliferative variants. J. Cell. Physiol. 114:317-320.
9. Butler-Gralla, E., Taplitz, S., and Herschman, H.R. 1983. 12-O-tetradecanoylphorbol-13-acetate stimulates release of arachidonic acid, prostaglandin E2 and prostaglandin F2 α from Res. Comm. 111:194-199.
10. Chandler, C.E. and Herschman, H.R. 1983. Binding, sequestration, and processing of epidermal growth factor and nerve growth factor by PC-12 cells. J. Cell. Physiol. 114:321-328.

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11. Cochran, A.J., Holland, G.N., Wen, D.-R., Herschman, H.R., Lee, W.R., Foos, R.Y., and Straatsma, B.R. 1983. Detection of cytoplasmic S-100 protein in primary and metastatic intraocular melanomas. Investigative Ophthalmology and Visual Science 24:1153-1155.
12. Cochran, A.J., Wen, D., and Herschman, H.R. 1984. Occult melanoma in lymph nodes selected by antiserum to S-100 protein. Intl. J. Cancer (in press).
13. de Vellis, J., Morrison, R.S., Eng, L.F., and Saneto, R.P. 1983. Astroglial growth factors. J. Neurochemistry 41:S3.
14. de Vellis, J., Morrison, R.S., Peng, W.W., and Arenander, A.T. 1982. The use of primary glial cell cultures in developmental studies of the central nervous system. In: A.M. Giuffrida-Stella, B. Haber, G. Nashim, and J.R. Polo (eds.) Nervous System Regeneration. pp. 67-78. Alan R. Liss, New York.
15. de Vellis, J., Peng, W.W., Pixley, S.K.R., and Tiffany-Castiglioni, E. 1983. Oligodendroglial, astroglial and glial tumor-associated antigens defined by monoclonal antibodies. In: H. Peeters (ed.) 30th Annual Colloquium -- Protides of the Biological Fluids. pp. 99-102. Pergamon Press, London.
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17. Duthu, G.S. and Hankinson, O. 1983. The defects in all classes of aryl hydrocarbon hydroxylase-deficient mutant of mouse hepatoma line, Hepa-1, are restricted to activities catalyzed by cytochrome P-450. Cancer Lett. 20:249-254.
18. Edmond, J., Auestad, N.S., Bergstrom, J.D., Cole, R.A., and de Vellis, J. 1983. Lipogenesis from ketone bodies and glucose in developing brain. 4th Int. Cong. Int. Soc. for Develop. Neurosci. July 27, 1983.
19. Edmond, J., Bergstrom, J.D., Robbins, R.A., Cole, R.A., and de Vellis, J. 1983. Substrate utilization by glial cells from developing brain in primary culture. J. Neurochemistry 41:S38.

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20. Eng, L.F., Smith, M.E., de Vellis, J., and Skoff, R.P. 1984. Recent studies of the glial fibrillary acidic protein. Annals of N.Y. Acad. Sci. (in press).
21. Fulco, A.J., Kim, B.-H., Matson, R.S., Narhi, L.O., and Ruettinger, R.T. 1983. Nonsubstrate induction of a soluble bacterial cytochrome P-450 monooxygenase by phenobarbital and its analogs. Mol. Cell Biochem. 53-54:155-162.
22. Hays, E.F. and Beardsley, T.R. 1984. Immunologic effects of human thymic stromal grafts and cell lines. Clinical Immunol. and Immunopath. (in press).
23. Hays, E.F., Kato, A., Hyman, R., Leslie, J., and Schulte, R. 1983. Characterization of the prelymphoma cell in the bone marrow of AKR mice. Blood 62: Suppl. 1, 191a.
24. Hays, E.F. and Levy, J.A. 1984. Differences in lymphomagenic properties of AKR mouse retroviruses. Virology (in press).
25. Hays, E., Streifinger, C., Goodrum, D., and Uittenbogaart, C. 1984. T-cell lymphomas produce their own growth factor. J. Cell Biochem., Suppl. 8A:108.
26. Hays, E., Streifinger, C., and Macleod, C. 1983. Differentiation and metastatic properties of T lymphoma cell lines in vivo. J. Cell. Biochem., Suppl. B:46.
27. Hays, E.F., Swanson, S.K., Hale, L., and Margaretten, N. 1983. The relationship of thymic stroma to lymphomagenesis in AKR mice. In: M.A. Rich (ed.) Leukemia Reviews International. pp. 182-183.
28. Thymic stroma in AKR mice: Its function and virus production. Leuk. Res. (in press).
29. Herschman, H.R. 1983. Selection and characterization of mitogen-specific non-proliferative 3T3 variant cell lines. Cell Biology International Reports 7:493-494.
30. Herschman, H.R. 1983. Teleocidin is not mitogenic for 12-tetradecanoyl-phorbol-13-acetate nonproliferative variants of 3T3 cells. Carcinogenesis 4:489-490.

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32. Herschman, H.R., Goodman, R., Chandler, C., Simpson, D., Cawley, D., Cole, R., and de Vellis, J. 1983. Is epidermal growth factor a modulator of nervous system function In: A.M. Giuffrida-Stella, B. Haber, G. Hashim, and J.R. Polo (eds.) pp. 79-94. Alan R. Liss, New York.
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34. Herschman, H.R., Simpson, D.L., and Cawley, D.B. 1983. Toxic ligand conjugates as tools in the study of receptor-ligand interactions. In: R. Bradshaw and G. Gill (eds.) Evolution of Hormone-Receptor Systems. pp. 129-142. Alan R. Liss, New York.
35. Karenlampi, S.O., Eisen, H.J., Hankinson, O., and Nebert, D.W. 1983. Effects of cytochrome P1-450 inducers on the cell surface receptors for epidermal growth factor, phorbol 12, 13-dibutyrate, or insulin of cultured mouse hepatoma cells. J. Biol. Chem. 258:10378-10383.
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37. Kerk, D., Myers, C.P., and Hays, E.F. 1983. Gentamycin alters Hemat. 11:819-827.
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41. Kumar, S., Weingarten, D.P., Callahan, J.W., Sachar, K., and de Vellis, J. 1984. Regulation of mRNAs for three enzymes in the glial cell model, C6 cell line. J. Neurochem. (in press).
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43. MacLeod, C., Hyman, R., Bourgeois, S., and Hays, E. 1983. Characterization of T-lymphoma cell lines: Differentiation and metastatic properties. Midwinter Conference of Immunologists.
44. MacLeod, C., Hyman, R., Bourgeois, S., Streifinger, C., and Hays, E. 1983. Characterization of T-lymphoma cell lines: Differentiation and metastatic properties. In: M.A. Rich (ed.) Leukemia Reviews International. pp. 192-193.
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47. Menon, N.K., Baker, N., and Mead, J.F. 1984. Differences in the β -oxidation of palmitate in liver mitochondria of normal and lymphoma-bearing AKR mice. Fed. Proc. 43:620.
48. Menon, N.K. and Dhopeswarkar, G.A. 1984. Incorporation of [U- 14 C] isoleucine into myelin in essential fatty acid (EFA) deficiency in the rat. Nutrition Reports International 29:783.
49. Menon, N.K., Dhopeswarkar, G.A., and Mead, J.F. 1984. Restriction of maternal food intake inhibits fatty acid activation in developing rat hearts. Lipids 19:122.
50. Morrison, R.S. and de Vellis, J. 1983. Preparation of a chemically defined medium for purified astrocytes. In: G. Sato, D. Sirbasku, and D. Barnes (eds.) Methods for Serum-Free Culture of Neuronal and Lymphoid Cells. pp. 15-22. Alan R.

PUBLICATIONS (Continued):

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DIVISION
OF
ENVIRONMENTAL BIOLOGY

DIVISION OF ENVIRONMENTAL BIOLOGY

RESEARCH HIGHLIGHTS

The research program of the Laboratory of Environmental Biology presents an integrated approach to studies of the functional interactions of the physical and biotic components of arid land ecosystems. While the overall focus is that of an ecosystem perspective, with special attention toward modelling, the individual research activities of the staff cover a wide range of activities including ecosystem processes studies, the environmental physiology of desert plants and animals, primary production studies and population biology. The core research support from the Department of Energy has been supplemented heavily by major competitive research grants and contracts from a wide variety of federal, state and private organizations. Six areas of research can be highlighted in Environmental Biology.

Primary Production Processes:

Intensive studies at Deep Canyon on the Sonoran Desert of Southern California have been investigating the environmental, nutritional and physiological controls on primary production in a wash woodland ecosystem dominated by Dalea spinosa (smoke tree) and Cercidium floridum (palo verde). While both of these are woody legumes, the former is an active nitrogen fixer while the latter does not fix nitrogen. During the unusually wet year of 1983 an unusual opportunity presented itself to study the effect of atypical summer rains on production and water relations of a variety of desert species. Heavy winter and spring rains occurred in 1983 at a level likely to occur only once or twice a century. Contrary to "conventional wisdom" on desert plant growth, in California, all of the dominant species in both wash woodland and bajada habitats are able to maintain physiological activity with summer rains, and indeed the net production from summer growth was higher in many species than from normal spring growth. Many herbaceous legumes germinated in areas where they were not previously known to occur and provided sufficient cover to allow up to $6-8 \text{ kg ha}^{-1}$ of net nitrogen accretion through fixation. These data provide the first quantitative data on the mechanisms of nitrogen input to some of these habitats and suggests the importance of long-term studies of ecosystem properties. Since water is the most important limiting factor in desert ecosystems, ongoing studies of the differential ability of desert perennials to osmotically adjust to seasonal changes in water availability are providing a new insight into mechanisms of drought adaptation. These studies are separating the relative importance of individual cations, anions, amino acids, sugars, organic acids and other organic compounds in osmotic adjustment.

Plant-Environment Interactions:

Research on plant-environment interactions has ranged from water relations to thermal tolerances to productivity. Again, the modeling approach to physiology that has been developed over the past few years was emphasized. Intraspecific competition for water was demonstrated for the common C_4 bunchgrass of the western Sonoran Desert, Hilaria rigida, and seasonal change in transpiration and photosynthesis was documented for the characteristic plant of the Mojave Desert, the C_3 arborescent monocot Yucca brevifolia. Desiccation tolerance of CAM plants was shown to be enhanced by preferential loss of water from the internal parenchyma. The highest thermal tolerances ever reported for vascular plants (69°C) were demonstrated for two species of Ferocactus, and an interesting acclimation of high-temperature tolerances was found in all 14 species examined. A major study of the relation between nutrient levels, nocturnal acid accumulation, and growth of cacti was completed, and a study of elemental stresses on desert CAM plants was initiated. Also, the relationship between photosynthetically active radiation and productivity for Opuntia ficus-indica and other succulent plants was reported. Studies by Dr. Nobel in England on root responses of desert plants to water and in Germany on cellular events for cacti during salinity stress were also completed.

Environmental Physiology of Desert Animals:

The physiological and behavioral mechanisms that desert animals use to survive and reproduce have been revealed last year as the result of long-term studies of several species of birds, mammals and reptiles, and two species of beetles. Avoidance of harsh desert conditions is critically important to the success of many species. These animals must then accomplish their chores of feeding, reproducing, etc. during the milder times of the year or day. A relatively few species are active during the most stressful times, and these animals possess remarkable adaptations for conserving and for obtaining scarce water, energy and nitrogen. These animals also have spectacular means of dealing with the problem of overheating, including using their tails as parasols, storing heat in their bodies and tolerating large fluctuations in body temperature, and making use of colors and skin structures that reduce heat input. Careful behavioral selection of favorable microhabitats is central to survivorship of many desert animals.

Animal Population Biology:

Research on the desert tortoise in the eastern Mojave continued during 1984. Mean clutch size was 4.17 in 1983 and 4.28 in 1984 (an insignificant difference). The mean number of clutches laid in 1983 was 1.89; in 1984 it was 1.56. These figures imply an approximate 12% reduction in the number of eggs produced per female in 1984. The 1983 season was an unusually good one in terms of rainfall and forage production, that of 1984 very poor--gauged by the same criteria. Given the distinct differences in the two seasons, we view the 1984 egg production as remarkable. Other work in this Division suggests that female tortoises may be able to capitalize on late summer rainfall--as occurred in August 1983--and carry over energy derived from dried summer forage to the ensuing breeding season. We found that tortoises lay eggs in the bottom of their burrows, and almost never in the open. Over 60 eggs were removed from nests and placed in predator-proof containers to incubate. We will thus measure natural hatching rates of eggs directly.

Applied and Land Research:

Work underway during FY84 has focused on the transport of long-lived fission products and transuranic elements from contaminated land by water and wind erosion processes, and on the importance of vegetation cover in reducing such transport. Experimental results will be used to develop predictive capability for runoff, sediment yield and contaminant transport. This work is conducted at the Nevada Test Site in collaboration with investigators from Lawrence Livermore National Laboratory, Los Alamos National Laboratory, and USDA/ARS-Tucson. This past year has also been the final year of applied studies of the environmental effects of solar power plants in the Mojave Desert. This multiyear project is now in the stage of synthesis and analysis.

Integrated Ecosystem Studies:

Synthesis efforts of many years of data from the Nevada Test Site have been actively underway. This site is perhaps the most intensively studied desert site in the world and these long-term data are an invaluable resource for initiating conceptual models of ecosystem function and stability. The future focus of the Laboratory will be increasingly toward the development and refinement of such conceptual models. We are aiming to be at the forefront of research groups in the world in the area of modelling arid zone ecosystems.

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DIVISION
OF
NUCLEAR MEDICINE

DIVISION OF NUCLEAR MEDICINE

Research Highlights

In the Nuclear Medicine program of this laboratory, the theme has been one of expanding the capability of positron emission tomography 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.

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.

Primary emphasis of the Chemistry Section is on the use of short-lived cyclotron produced radionuclides for labeling physiological substrates or their functional analogs. This activity includes (a) planning and development of appropriate synthetic pathways, and chemical radionuclides identity and purity for the target compounds; (b) relate chemical structure to biological activity in the development of new ways to explore local organ metabolism and neuroreceptor localization employing radioactive compounds and positron computed tomography; (c) development of the required enzyme technology, biochemical assays and autoradiographic procedures for metabolic and receptor studies; (d) development of remote systems for synthesis and chemical processing of large quantities of cyclotron produced radionuclides for the safe preparation of selected test agents and, on a laboratory scale, for their evaluation in animals and man; and (e) preparation of radiopharmaceuticals in sterile, pyrogen free form suitable for human use.

In the Physical Sciences Section, the principles of the new positron tomograph have been experimentally verified with the tomographic simulator. The results show that the new system, with very high resolution detectors, will have resolution and signal to noise characteristics an order of magnitude better than our present system. The tomograph, itself, is nearing completion and initial testing should begin in September 1984. Basic concepts for future developments in positron tomography are under study, involving new detector materials and new methods of extracting the signals from detectors with low noise solid state photodetectors. The new detector materials are being carefully characterized relative to their use in positron tomography, and the photodetectors, in a more primitive state of development, are

being fabricated in a variety of ways to optimize their light collection capabilities.

The focus of tracer kinetic modeling has been on 1) the characterization of the accuracy of the O-15 water method for cerebral and myocardial blood flow measurements and 2) the further refinement of the FDG method for measurement of glucose utilization. Animal models are used in the characterization of the blood flow techniques. Standard microsphere technique is used simultaneously with the positron CT technique to provide direct comparisons. In the estimation of glucose utilization with FDG, the effect of vascular volume has been examined and a parameter representing the vascular volume has been incorporated into the FDG model that allows estimation of vascular volume and glucose utilization simultaneously. Models for O-15 oxygen (oxygen utilization), C-11 palmitate (free fatty acid utilization), C-11 leucine (protein synthesis), and F-18 spiperone (neuroreceptor binding) are also being developed.

In the Neuroscience Section tracer kinetic methods are used in animal and human studies of cerebral biochemistry and physiology. Human studies involve the use of positron computed tomography for the evaluation of both normal and abnormal brain function. In the realm of normal brain physiology we are actively involved in the development of paradigms to stimulate sensory, motor, cognitive, and memory systems so as to learn the structure-function relationships of the normal brain performing routine tasks. These tasks once developed will be used as probes in patient populations where deficiencies or abnormalities in any of these functional systems have been identified. Studies in patients include those with both adult and childhood forms of epilepsy, dementing diseases such as Alzheimer's disease, multiple infarct dementia and others, affective disorders (unipolar depression and bipolar illness), cerebral infarction as it affects language function, cerebral neoplasms with particular emphasis on glucose transport, metabolism and blood-brain barrier permeability, and movement disorders with specific emphasis on Huntington's Disease, Parkinson's Disease, tardive dyskinesia and inborn errors of metabolism such as glycogen storage disease type I (Von Gierke's Disease).

Animal studies have been and continue to be used for the validation of tracer kinetic methods and for understanding the phenomena measurable with these methods in electrophysiological or biochemical terms. These studies employ the use of both noninvasive (tomographic) and invasive (autoradiography, tissue biopsy, arterial-venous difference studies) techniques. Primate studies are under way to validate the measurement of cerebral blood flow with Oxygen-15 labeled water by the combined use of Oxygen-15 labeled water injections and radio labeled microspheres in non human primates. Autoradiographic studies in combination with electrophysiological measurements are presently under way to

understand the changes in glucose metabolism associated with electrophysiological inhibition and excitation. Studies of ligand systems in the brain with particular emphasis on the dopaminergic system are being performed to explore the differences and similarities between the in vivo and in vitro determination of receptor number and binding affinity. Concomitant studies are being performed on human brain tissue excised from patients with surgically intractable epilepsy who are candidates for a temporal lobe resection.

In the Cardiovascular Imaging Section progress has continued in adopting already established tracer kinetic models to the heart as well as developing new tracer kinetic models for the measurement of regional myocardial fatty acid metabolism and blood flow. Other studies in isolated perfused hearts have contributed to a better understanding of the metabolic fate of the C-11 and N-13 label attached to amino acids and provided new insights into myocardial amino acid metabolism. Major advances were made in the area of myocardial ischemia, acute myocardial infarction and reperfusion of transiently ischemic tissue. Metabolic activity in reperfused tissue early after ischemic injury invariably predicted in dogs studied over a 4 to 5 week period subsequent improvement in segmental function despite an initial transient deterioration, attesting to the significance of metabolic characterization of ischemic tissue injury. A metabolic pattern characteristic for ischemia has been defined in patients with chronic ischemic heart disease and been found useful in predicting beneficial effects of surgical revascularization on functional improvement. Other studies have emphasized the value of metabolic tracers over more conventional ones in characterizing viable and non-viable myocardium. In patients with recent Q-wave infarctions, sustained metabolic activity in infarcted myocardium has been observed. The subsequent fate of such a segment is two-fold: some improve function spontaneously while in others, metabolic activity together with regional function deteriorates with time and tissue necrosis occurs. The findings in patients with chronic ischemic heart disease as well as with recent myocardial infarction are clinically of potential importance. They may become decisive in choosing between a more conservative or more aggressive course of treatment.

The new high temporal and spatial resolution positron emission tomograph will be available this Fall. It will allow cross-sectional imaging perpendicular to the long axis of the left ventricle and thus minimize partial volume effect, bidirectional cross-contamination between myocardium and cardiac blood pools and allow measurements of regional wall thickness. With this device more accurate measurements of regional indicator tissue concentrations can be obtained. Studies in patients with recent myocardial infarction and chronic ischemic heart disease will continue with this device and tracer kinetic models already existing or under development further validated in experimental

animals and humans. Research with this new device will also focus on measurements of regional myocardial blood flow and oxygen metabolism.

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