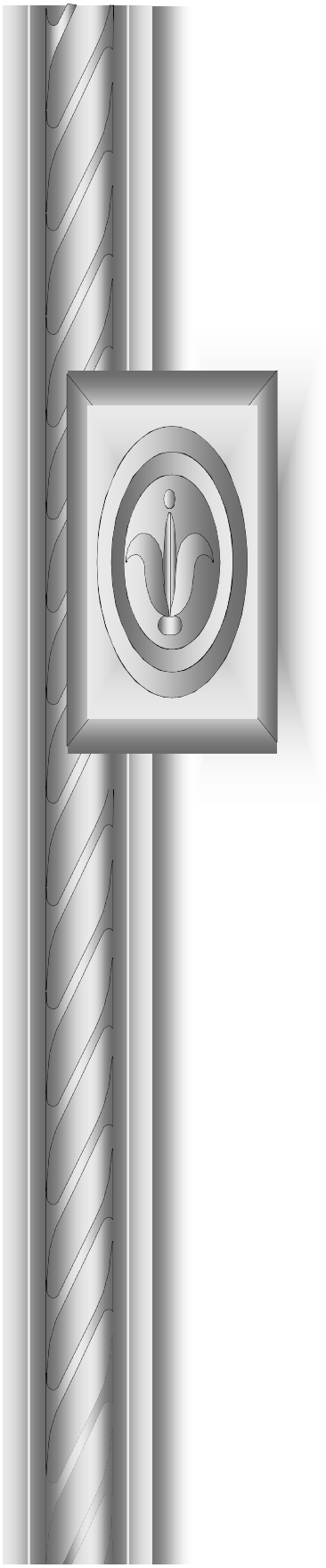

National Institute on Aging

Guide to Research and Training Programs

July 2003

NIA Guide to Research and Training Programs: Contents

About the National Institute on Aging

Richard J. Hodes, M.D., Director

Since 1974, the National Institute on Aging (NIA) has led the federal effort on aging research. The NIA's mission is to improve the health and well-being of older Americans through research, and specifically to:

- Support and conduct high quality research on:
  -aging processes
  -age-related diseases
  -special problems and needs of the aged
- Train and develop highly skilled research scientists from all population groups
- Develop and maintain state-of-the-art resources to accelerate research progress
- Disseminate information and communicate with the public and interested groups on health and research advances and on new directions for research

Since the Institute's founding, we have learned much about the biological, behavioral, and social changes that occur with advancing age. We now know that aging itself is not the cause of disease, disability, and frailty. Rather, disease and disabling processes, influenced by age-related changes in the body and by unhealthy choices and sedentary lifestyles, are the most important factors in compromising the quality of life for older people. This fundamental shift in thinking was reinforced most recently through findings from the NIA-supported National Long Term Care Survey, which documented a dramatic decline in both physical and cognitive disability among older Americans from the 1980s through the mid-1990s. The challenge now is to maintain – or even accelerate – the trend in declining disability and to reduce rates of disease in the face of a rapidly aging U.S. population.

NIA supports extramural research through programs in the Biology of Aging, Behavioral and Social Research, Geriatrics and Clinical Gerontology, and Neuroscience and Neuropsychology of Aging. The NIA Intramural Research Program conducts basic and clinical research in laboratories both in Baltimore and on the NIH campus in Bethesda.

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America's Aging Population

Millions of Americans over age 65 remain healthy, active, and productive well into old age. More people than ever before are enjoying robust health and productivity well into their seventies, eighties, and even beyond.[1] Life expectancy, around 49 years in 1900, has increased over the past century to approximately 76, thanks to improvements in health care, nutrition, and the overall standard of living for most people, and nearly three quarters of people 65 and older rate their health as "good," "very good," or "excellent."

But good health is far from a universal reality for older Americans. The latest national surveys indicate that about one-fifth of people age 65 and older — more than 7 million people — report some disability.[2] Chronic disease, memory impairment, and depressive symptoms affect large numbers of older people and the risk of such problems significantly rises with age. Nearly half of those age 85 and older suffer from Alzheimer's disease.[3] These millions of less fortunate older people struggle with daily activities as simple as bathing and dressing, with families and friends taking on the difficult and often costly role of caregiver.

[1] Federal Interagency Forum on Aging Related Statistics. *Older Americans 2000: Key Indicators of Well-Being*. 2000.
[2] Manton KG et al. Chronic disability trends in elderly United States populations: 1982-1994. Proc Nat Acad Sci USA 94: 2593-2598, 1997.
[3] Evans DA et al. Prevalence of Alzheimer's disease in a community population of older persons; higher than previously reported. JAMA 262: 2551-2556, 1989.

Understanding the differences between advanced years that are active and independent and those that are characterized by frailty and dependence is at the heart of the National Institute on Aging's (NIA's) research program. Since the Institute's founding in 1974, research has shed considerable light on aging and health. It is now known that aging itself is not the cause of disease, disability, and frailty. Indeed, the converse is true: It is disease and disabling processes, influenced by age-related changes in the body and by unhealthy choices and sedentary lifestyles, that are the most important factors in compromising the quality of life for older people. This fundamental shift in thinking was reinforced most recently with insights from the National Long Term Care Survey. According to this study, the rate of disability among older Americans dramatically declined from the 1980s through the mid 1990s, even among people age 85 and older. These findings, along with evidence from a number of clinical trials and studies testing specific interventions, suggest more strongly than ever that disease and disability are not inevitable consequences of aging.

The challenge now is to maintain and even accelerate the trend in declining disability and to reduce rates of disease amid a steep rise in the number and proportion of older people. The task is urgent. Demographic projections show that the U.S. population is beginning to age at a rapid pace, with the first baby boomers turning 65 in 2011. Between now and the year 2030, the number of

individuals age 65 and older will likely double, reaching 70.3 million and comprising a larger proportion of the entire population, up from 13 percent today to 20 percent in 2030.[4] Of great interest is the explosive growth anticipated among those most at risk for disease and disability, people age 85 and older. Their ranks are expected to grow from 4.3 million in 2000 to at least 19.4 million in 2050. These demographic factors combined threaten to increase the burden of age-related diseases and conditions on individuals, families, and society. Unless new understandings and interventions are developed and implemented to reduce disease and disability, the costs, in both human and financial terms, could be extraordinary.

In the 20th century, health research and improved public health practices did much to extend life and improve health. At the start of this new millennium, the NIA's research portfolio is aimed primarily at increasing "health span," or years of healthy, active life expectancy. Aging research is well poised to build upon the work of recent years to improve the lives of older Americans and their families. Toward that end, NIA's overall program is wide-ranging and includes research on: the biochemical, genetic, and physiological mechanisms of aging in humans and animal models; the structure and function of the aging nervous system; social and behavioral aspects of aging processes and the place of older people in society; and the pathophysiology, diagnosis, treatment, and prevention of age-related diseases, degenerative conditions, and disabilities. The NIA is also the lead federal agency for Alzheimer's disease research.

In close collaboration with the National Advisory Council on Aging and other public and private organizations, the NIA has developed a strategic plan for aging research to identify goals for the years 2001–2005. These goals address scientific areas with the greatest promise for advancing knowledge. The NIA also recently completed a strategic plan on disparities in health status of older Americans of different racial and ethnic backgrounds.

[4] Federal Interagency Forum on Aging Related Statistics. *Older Americans 2000: Key Indicators of Well-Being*. 2000.

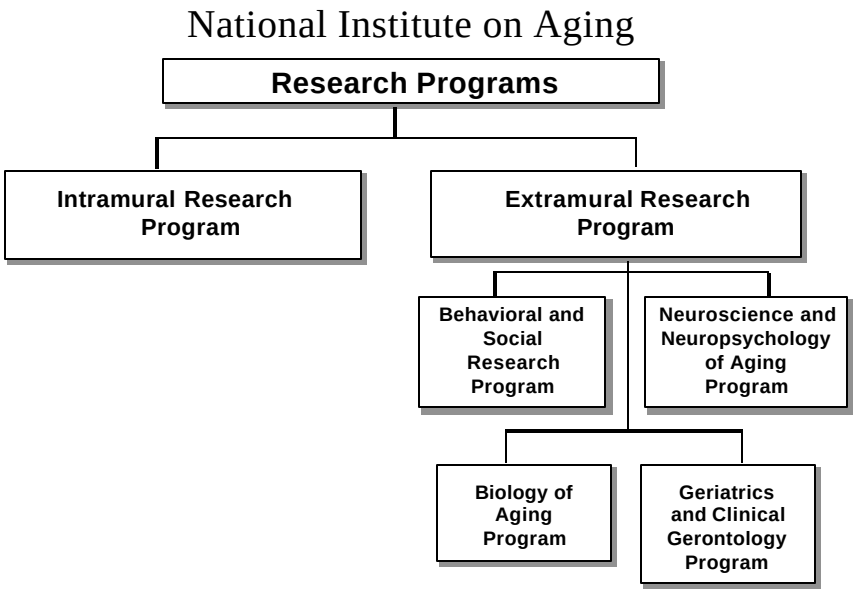
Program Organization

The National Institute on Aging (NIA) includes both extramural and intramural research programs. The four extramural programs are the Biology of Aging Program, the Behavioral and Social Research Program, the Geriatrics and Clinical Gerontology Program, and the Neuroscience and Neuropsychology of Aging Program. The Intramural Research Program comprises eleven research laboratories and a research resources branch.

The Extramural Research Program funds research in universities and other research centers across the country and, in some circumstances, internationally. It also supports training of future research scientists. Extramural Program staff also conduct workshops and other activities to identify promising areas for research and to coordinate the development of research initiatives.

To stimulate research in selected areas, the NIA issues Program Announcements (PA) intended to focus research grant applications on scientific areas of interest. Requests for Applications (RFA) are issued when research is needed on specific topics of major importance to the Institute; each RFA includes a budget set-aside.

NIA intramural scientists conduct basic and clinical research on the NIH campus in Bethesda, MD, and in Baltimore, MD, at the Gerontology Research Center, home of the 45-year-old Baltimore Longitudinal Study of Aging.



BIOLOGY OF AGING PROGRAM

Huber R. Warner, Ph.D., Associate Director

(*For further information, contact* BAPquery@nia.nih.gov*)*

The Biology of Aging Program (BAP) supports research to enhance and extend the human health span by:

- **Identifying opportunities** to better understand the mechanisms of aging,
- **Facilitating creative approaches** to changing needs within the field, and
- **Providing service and funding** to investigators within the aging research community.

The overall objective of BAP's programs is to elucidate the biochemical, genetic and physiological mechanisms of aging and age-related changes in humans and animal models. This includes investigations of the gradual or programmed alterations of structure and function that characterize normal aging, as well as investigations of the adverse changes that are risk factors for or accompany age-related disease states.

Although the research emphasis in BAP is on aging in mammals, lower organism (*e.g. Drosophila, C. elegans*, yeast) research that is related to aging is also supported. The value of the comparative approach in studying aging has been well demonstrated by the Longevity Assurance Gene (LAG) Interactive Network of investigators, and the insights they are providing about the genetic basis of aging in humans.

The Program also includes the Office of Biological Resources and Resource Development (OBRRD) which coordinates the acquisition, maintenance and provision of resources supporting aging research, including cell and tissue banks, aged rodent colonies and non-human primate models.

Office of the Associate Director

Huber R. Warner, Ph.D., Associate Director

Animal Models Program - *Nancy L. Nadon, Ph.D.* The objective of the Animal Models Program is to identify and develop new animal models, both mammalian and lower organism, for use in aging research. These models include rats, mice, rabbits, non-human primates, fish, birds, insects, nematodes, and yeast. Mutant and genetically-engineered rodent models of both normal aging and specific age-related pathologies are of particular interest.

Nathan Shock Centers for Excellence in the Basic Biology of Aging - *Huber R. Warner, Ph.D.* This program was established in 1995 to enhance well-developed institutional programs in basic research on aging by providing state-of-the-art research resources to create the strongest environment possible for the conduct of basic aging research.

Training Grant Program - *Huber R. Warner, Ph.D.* NIA recognizes a continuing and expanding need to train new researchers in aging research, and the institutional training grant program is an important mechanism for accomplishing this. Training grants provide individual and institutional support for graduate students and post-doctoral fellows. Support for individual trainees is usually limited to 3 years.

Genetics and Cell Biology Branch

Anna McCormick, Ph.D.

Aging Research Technologies Program - *Felipe Sierra, Ph.D.* This program supports the development of new molecular research technologies of potential use in aging research.

Cell Structure and Function Program - *Felipe Sierra, Ph.D.* The objectives of the Cell Structure and Function Program are to support research on the molecular basis of age-related changes in:

- signal transduction mechanisms, including membranes/receptors
- changes in gene expression/transcription factors
- translational and post-translational control, protein turnover
- microenvironment/extracellular matrix
- cell senescence
- apoptosis and cancer

Metabolic Regulation Program - *David Finkelstein, Ph.D*. Areas of investigation in the Metabolic Regulation Program include:

- nutrition/metabolism
- age-related changes in mitochondrial function/dysfunction
- mechanism of life span extension by caloric restriction
- generation of free radicals and oxidative stress

Genetics Program - *Anna McCormick, Ph.D*. The objectives of the Genetics Program are to support research on:

- identification and characterization of longevity assurance genes (LAGs)

and senescence assurance genes (SAGs)
- genome stability
- genomics/functional genomics
- mouse mutagenesis
- telomere biology
- Werner syndrome

Systems Branch

Jill Carrington, Ph.D.

Cardiovascular Biology Program - *David Finkelstein, Ph.D*. The objectives of the Cardiovascular Biology Program are to support basic research on:

- age-related changes in cardiovascular function
- factors affecting cell death/cell division in cardiovascular tissue
- age-related changes in cardiac gene expression

Endocrinology Program - *Frank Bellino, Ph.D*. The Endocrinology of Aging Program supports basic molecular and cellular research into the causes and effects of age-related changes in the endocrine system. Areas of investigation in this program include:

- age-related changes in hormone production, metabolism, and action
- diabetes
- reproductive aging, including the biology of menopause and animal models of menopause
- age-related changes in control of prostate growth
- endocrine aspects of age-dependent tumors

Immunology Program - *Rebecca Fuldner, Ph.D.* This program supports research directed toward understanding the age-related regulation of immune function in health and disease, including:

- changes in immune cell proliferation and action related to aging
- response of immune system to biochemical stimuli
- autoimmune disease and other immunopathologies related to aging
- molecular basis of the age-related decline in immune function
- interventions to retard and/or correct age-related decline in immune function

Musculoskeletal Biology Program - *Jill Carrington, Ph.D.* This program supports basic molecular and cellular research toward development of preventative and intervention strategies to extend the health span of the elderly. Areas of investigation in this program include:

- age-related changes in osteoblast and osteoclast function and bone matrix
- age-related changes in muscle structure and function
- age-related changes in cartilage, soft connective tissue, and skin
- molecular mechanisms of the above age-related changes
- molecular and cellular basis of osteoporosis, osteoarthritis, Paget's disease, and osteoporosis imperfecta as these diseases relate to aging

Physiology Program – *Frank Bellino, Ph.D.* BAP's Physiology Program supports research on underlying age-related biologic changes that affect the function of organs and systems that

impact the health of middle-aged and older people, including:

- adrenal function
- renal function
- non-hormonal aspects of male and female reproductive tissue
- blood pressure
- electrolyte balance and transport

BEHAVIORAL AND SOCIAL RESEARCH PROGRAM

Richard M. Suzman, Ph.D., Associate Director

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The **Behavioral and Social Research (BSR)** program supports basic social and behavioral research and research training on the processes of aging at both the level of the individual and the society. It focuses on how people change over the adult life course, on the interrelationships between older people and social institutions, and on the societal impact of the changing age composition of the population. Emphasis is placed upon the dynamic interplay between the aging of individuals and their changing social and physical environments and on multi-level interactions among psychological, physiological, social, and cultural levels. Collaboration and coordination with other NIA programs is emphasized.

The BSR program is administratively organized into two branches – Individual Behavioral Processes and Population and Social Processes. A section devoted to research resources and development is housed within the Office of the Associate Director.

Individual Behavioral Processes Branch

Richard Suzman, Ph.D., Sidney Stahl, Ph.D., Jeffrey Elias, Ph.D., Jennifer Harris, Ph.D., & Kathy Koepke, Ph.D.

The Individual Behavioral Processes Branch supports research and training on:

- biopsychosocial processes linking health and behavior
- cognitive functioning
- human factors
- integrative approaches to the study of social, psychological, and physiological influences on health and well-being over the life course
- personality and social/interpersonal relationships as causal variables and as mediators or moderators of the relationship between social/structural characteristics and health outcomes

Behavioral Medicine and Interventions
This unit focuses on the dynamic interrelationships among aging, health, and behavior processes. Major research topics include:

- disease recognition, coping, and management, including physiological consequences of life stresses and burdens
- social, behavioral, and environmental interventions for health promotion, disease prevention, and disability postponement

Cognitive Aging - This section supports research on changes in cognitive functioning over the life course. Major research topics include:

- higher-order cognitive processes (e.g., problem solving, decision making)
- social cognition
- memory strategies
- perceptual skills
- reading and speech comprehension
- the role of individual difference factors in cognitive functioning (e.g., motivation, self-efficacy, beliefs about aging, emotions, sensory limitations, experience, and expertise)

Staff frequently collaborate with the NIA Neuroscience and Neuropsychology of Aging (NNA) Program to encourage research at the intersection of behavioral science and neurocognition.

Psychological Development and Integrative Science - This section promotes research that applies an integrative approach to the study of health, behavior, and well-being over the life course. Examples include the effects of sociocultural, psychological (social, personality), biological, and genetic processes on behavioral and functional aging. In addition, research exploring individual factors that influence aging are welcomed.

Population and Social Processes Branch

Richard Suzman, Ph.D., Laura Shrestha, Ph.D., Georgeanne Patmios, M.A., Angie Chon-Lee, M.P.H., Rachel Permuth, M.S.P.H., and Elayne Heisler, M.A.

This branch supports research and training on the antecedents and impact of changing social, demographic, economic, and health characteristics of the older population. Research is also supported on the effects of particular health care settings and other social institutions upon the health, well-being, and functioning of people in the middle and later years. Comparative research is often appropriate, and interconnections with individual behavioral processes are encouraged.

Demography and Epidemiology - This section covers such topics as:

- medical and biodemography
- changes in the age structure of populations
- prevalence and incidence of disease and disability; age trajectories of health
- life expectancy and active life expectancy
- forecasting functioning, disability, morbidity, and mortality
- migration and geographic concentrations of older people; rural-urban comparisons
- distributions of health services and the long-term care system
- race, ethnic, and socioeconomic variations
- genetic epidemiology and population genetics

Health and Retirement Economics - This unit concentrates on the economics of aging, including:

- economic and health antecedents and consequences of work and retirement
- pensions and savings
- health insurance and health care expenditures
- Medicaid, Medicare, and Social Security
- interrelationships between health and economic status, including issues related to wealth, poverty, productivity, human capital development, and economic development; the economic costs of disability
- cost-effectiveness of interventions
- effects of taxation policies on older people
- cross-national comparisons

Health and Social Institutions - This unit encourages research on:

- the impact of a wide range of formal health care and related services, with particular emphasis on long-term care systems and settings and on the health and well-being of older persons
- how social institutions (e.g., work, family, religion, community, living arrangements) influence health outcomes in the later years
- the ways in which people influence and are influenced by the network of cultural and social institutions surrounding them

Office of Research Resources and Development

Richard Suzman, Ph.D. and Laura Shrestha, Ph.D.

The BSR Office of Research Resources and Development (ORRD) coordinates and implements initiatives related to research data and resources. ORRD manages the Health and Retirement Study (see page 49), the National Archive of Computerized Data on Aging (see page 49), and all Interagency Agreements. ORRD also serves as NIA's administrative site for the Federal Interagency Forum on Aging-Related Statistics (see page 58), which encourages cooperation among federal agencies responsible for the collection, analysis, development, and dissemination of data on the aging population.

GERIATRICS AND CLINICAL GERONTOLOGY PROGRAM

Evan C. Hadley, M.D., Associate Director

(For further information, contact GCGquery@nia.nih.gov*)*

The Geriatrics and Clinical Gerontology (GCG) Program supports research on health and disease in the aged and research on aging over the human life span and its relationships to health outcomes. GCG comprises three branches: Geriatrics, Clinical Gerontology, and Clinical Trials.

Geriatrics Branch

Evan Hadley, M.D.

This branch is focused primarily on health issues regarding the aged, and deals with research on disease and disability in older persons, including both specific conditions and issues related to multiple morbidity. Examples of current research areas addressed by this branch and future directions are:

- multifactorial geriatric syndromes, such as falls, frailty, and various types of disability
- effects of comorbidity and polypharmacy
- effects of age-related changes on clinical or functional disease outcomes or treatment responses
- effects of physical activity on disease and disability in older persons
- elucidation, diagnosis, and treatment of previously unappreciated pathologic changes in old age (e.g., sarcopenia, vascular stiffening, diastolic dysfunction)

Clinical Gerontology Branch

Chhanda Dutta, Ph.D.

This branch is focused primarily on clinically-related issues regarding aging, and deals with research on aging changes over the life span. A major focus is on the determinants of rates of progression of age-related changes that affect disease risk, particularly those affecting risk for multiple age-related conditions. Examples of areas addressed by this branch are:

- healthy aging across the life span, including exceptional longevity
- protective factors against multiple age-related conditions
- longitudinal studies of factors affecting aging changes at different points in the life span
- translational human research to follow up findings from basic research on aging processes
- long-term effects of current or new interventions that may be administered over a large part of the life span (e.g., antihypertensives, statins)
- long-term effects of physical activity throughout the life span

Clinical Trials Branch

Charles Hollingsworth, Dr. P.H.

This branch plans and administers larger-scale and some medium-scale clinical trials on age-related issues that require extensive specialized clinical trials expertise. Examples of current and possible future interventions for trials are:

- interventions to prevent or treat "geriatric syndromes," disability, and complications of comorbidity or polypharmacy
- trials to detect age- or comorbidity-related differences in responses to interventions against conditions found in middle age and old age
- interventions for problems associated with menopause and other mid- and late-life changes
- interventions that may affect rates of progression of age-related declines in function in early and mid-life
- interventions with protective effects against multiple age-related conditions

GCG Staff Liaisons

In addition to the branch staff contacts, the GCG Program has designated staff liaisons who provide interface with organ-system and disease research communities and NIH components for areas such as cardiovascular research, diabetes, cancer, and arthritis. For contact information, see page 5.

Rehabilitation -- Stanley Slater, M.D.
Infectious Diseases/Immunology -- Stanley Slater, M.D.
Cardiovascular -- André Premen, Ph.D.
Cancer -- Rosemary Yancik, Ph.D.
Diabetes -- Chhanda Dutta, Ph.D.
Exercise -- Chhanda Dutta, Ph.D.
Osteoarthritis -- Chhanda Dutta, Ph.D.
Osteoporosis – Sherry Sherman, Ph.D.
Genetics -- Winifred Rossi, M.A.
Bioengineering -- Winifred Rossi, M.A.

NEUROSCIENCE AND NEUROPSYCHOLOGY OF AGING PROGRAM

Marcelle Morrison-Bogorad, Ph.D., Associate Director

(For further information, contact NNAquery@nia.nih.gov*)*

The **Neuroscience and Neuropsychology of Aging (NNA)** program supports a broad spectrum of research and training aimed at obtaining a better understanding of age-related normal and pathological changes in the structure and function of the nervous system and how such changes affect behavior. The basic mission of the program is to expand knowledge on the aging nervous system to allow improvement in the quality of life of older individuals. This mission includes basic and clinical studies of the nervous system, clinical trials of therapeutic modalities, and epidemiologic research to identify risk factors and to establish prevalence and incidence estimates of pathologic conditions. Additionally, NNA supports research relevant to geriatric problems arising from psychiatric and neurologic disorders associated with aging.

Although NNA conducts and supports activities related to a wide range of diseases and conditions, a major focus within NNA is on the neurodegenerative disorder Alzheimer's disease (AD). NNA supports research on the etiology, treatment, and diagnosis of AD, as well as treatment and prevention clinical trials.

Neurobiology Branch

Andrew A. Monjan, Ph.D.

This branch fosters a broad spectrum of research aimed at elucidating how the nervous system is affected by both normal and pathological aging. Research focused on Alzheimer's disease is *not* supported here. Major research areas include:

Fundamental Neuroscience - *Bradley C. Wise, Ph.D.* This section supports research at the cellular, molecular, and genetic levels that will elucidate age-related structural and functional changes. Of particular interest is selective vulnerability of neural cells to loss of function or neurodegeneration that may occur in aging. Research areas include:

- specific mechanisms of neuronal cell death such as endogenous and exogenous neurotoxicants
- neuroplasticity
- molecular genetics of brain aging (genomics and proteomics)
- mechanisms of neuronal cell death
- mitochondrial energy metabolism and oxidative stress
- glial cells in brain aging
- neural stem cells and cell repair/replacement in the brain
- molecular mechanisms involved in neuronal plasticity in response to environmental influences and age
- proteolytic enzymes and kinases in the regulation of cell membrane components
- cellular and molecular mechanisms involved with permanent changes in neuronal function as a result of external stimuli

Integrative Neuroscience - *Andrew A. Monjan, Ph.D.* This section focuses on:

- neural mechanisms underlying age-related changes in endocrine functions
- epidemiology, etiology, pathogenesis, diagnosis, prevention, and treatment of neurodegenerative diseases of aging associated with infectious agents (e.g., HIV, herpes viruses, and prions)
- neural control of the senescence of female reproductive function
- reciprocal control of the relevant hypothalamic regions by the gonadal hormones
- brain, endocrine, and immune system interactions

Sleep and Biological Rhythms - *Andrew A. Monjan, Ph.D.* This section encompasses epidemiology, etiology, pathogenesis, diagnosis, treatment, and prevention of sleep disorders in older people. Of interest to this section are studies involving:

- age-related mechanisms that underlie sleep-wakefulness cycles and their behavioral sequelae in the aged
- effects of normal and disordered circadian rhythms and other biorhythmicity upon the aging nervous system
- cellular and molecular mechanisms controlling these biological rhythms
- how sleep disorders in older people affect neural processes and cognition

Sensory and Motor Processes - *Judith A. Finkelstein, Ph.D.* This section supports research on age-related changes or impairments in sensory functions and

modalities and on the cellular and molecular mechanisms underlying pathological and nonpathological sensory functioning. Sensory systems covered in this program include vision, hearing, taste, smell, vestibular, somatosensory, and proprioception functions, as well as pain. Areas of special research interest include:

- elucidation of underlying mechanisms of age-associated changes or impairments in sensory functions and modalities
- cellular and molecular mechanisms underlying pathological and nonpathological sensory functioning
- molecular and cellular mechanisms of neuromotor control of striated and nonstriated muscles
- disruptions of central integrative processes and/or reflex mechanisms at spinal and supraspinal levels
- motor neuron diseases and Parkinson's disease
- effects of vestibular and other sensory-motor changes in aging, including the neural control of posture, balance and gait, and falling

Neuropsychology Branch

Andrew A. Monjan, Ph.D., Acting

The mission of the Neuropsychology Branch is to expand understanding of the mechanisms and processes underlying cognitive, affective, and perceptual behavior over the adult life-course. The branch fosters research on interactions between the brain and behavior, endeavoring to understand how pathological occurrences as well as normal aging processes may affect neurologic, psychiatric, and psychological capacities.

Cognitive and Systems Neuroscience - *Molly V. Wagster, Ph.D.* This section emphasizes human, computational, and animal research to examine the underlying causes for the cognitive changes that occur with aging and/or experience. The use of neuroimaging technologies and computational approaches to elucidate mechanisms, track perturbations, and assess interventions is encouraged. Studies in this area include research on:

- attention
- memory
- learning
- language
- spatial skills
- problem solving
- other higher-order cognitive capacities
- psychometric studies and clinical testing in normal aging
- affect (e.g., depression and other psychiatric functions)

Dementias Branch

Neil S. Buckholtz, Ph.D.

This branch fosters basic, clinical and epidemiological studies of Alzheimer's disease, mild cognitive impairment, cerebro-vascular disorders and stroke, multi-infarct dementias, vascular dementias, fronto-temporal dementia, Lewy body dementia, and other brain disorders of older people, including psychiatric disorders such as depression and delirium.

Basic Research - *D. Stephen Snyder, Ph.D. and Marilyn Miller, Ph.D.* This section supports research on:

- the etiology of Alzheimer's disease and other age-related dementias and neurodegenerative disorders
- identification of genetic loci associated with inherited forms of these diseases
- biochemical and molecular genetic analysis of the components of amyloid plaques, neurofibrillary tangles, and other abnormal structures found in the brains of patients with AD and other dementias of aging
- mechanisms of neuronal dystrophy and death

Population Studies - *Neil S. Buckholtz, Ph.D. and Dallas Anderson, Ph.D.* This section supports research in the epidemiology of Alzheimer's disease and on models for large-area registries for Alzheimer's disease, mild cognitive impairment, and other dementing diseases of later life. Areas of special interest include:

- domestic and international epidemiologic studies of the age-specific incidence and prevalence rates and risk and protective factors for Alzheimer's disease, mild cognitive impairment, and other dementias of aging
- familial aggregation studies
- development of sensitive and specific cognitive and diagnostic screening instruments for use in heterogeneous and culturally varied populations

Clinical Studies - *Neil S. Buckholtz, Ph.D., Elisabeth Koss, Ph.D., and Susan Molchan, M.D.* This section supports research on the diagnosis, treatment, and management of patients with Alzheimer's disease, as well as research on possible preclinical stages. Research topics include:

- development and evaluation of reliable and valid multidimensional diagnostic procedures and instruments
- identification and testing of preclinical and antemortem biological, chemical, and behavioral markers for Alzheimer's disease
- refinement of the diagnosis of Alzheimer's disease, including studies of neuropsychological batteries, neuroimaging techniques, and clinical and neuropathological concordance studies
- improved understanding of the clinical course, signs, and symptoms of Alzheimer's disease
- preclinical drug discovery and development of compounds to treat and prevent Alzheimer’s disease and other dementias of aging
- clinical trials for the treatment and prevention of Alzheimer’s disease and other dementias of aging

Research Centers - *Creighton Phelps, Ph.D. and Elisabeth Koss, Ph.D.* This section supports the Alzheimer's Disease Research Centers (ADRC), the Alzheimer's Disease Core Centers (ADCC), the National Alzheimer’s Coordinating Center (NACC), and the National Alzheimer’s Cell Bank. See page 39 for more information on these programs.

The NIA Office of Nutrition

Judith A. Finkelstein, Ph.D.

This office coordinates nutrition-related activities throughout the Institute and provides liaison with other agencies. The major focus is to increase the awareness of the scientific community and the public of the importance of nutrition and aging research and to stimulate and encourage support of research and training in this area. Caloric restriction research supported through NNA includes the impact of caloric restriction on the central nervous system, as well as the central nervous system mediation of the longevity effects of caloric restriction.

INTRAMURAL RESEARCH PROGRAM

Dan L. Longo, M.D., Scientific Director

(For further information, visit our web site: www.nih.gov/nia/research/intramural*)*

NIA's Intramural Research Program (IRP) includes eleven scientific laboratories, two scientific research sections, a clinical research branch, and a research resources branch. Scientific disciplines include biochemistry, cell and molecular biology, structural biology, genetics, behavioral sciences, epidemiology, and statistics; medical disciplines include neurobiology, immunology, endocrinology, cardiology, rheumatology, hematology, oncology, and gerontology. The IRP's central focus is to understand age-related changes in physiology and the ability to adapt to environmental stress; this understanding is then applied toward gaining insight into the pathophysiology of age-related diseases. Thus, common age-related diseases are under study (e.g., Alzheimer's disease, atherosclerosis, osteoarthritis, diabetes, cancer), while determinants of healthy aging are being defined.

Most IRP research is conducted at the Gerontology Research Center (GRC) in Baltimore, Maryland, with two laboratories and one scientific research section located on the NIH campus in Bethesda. IRP laboratories provide a stimulating environment for age-related research. The IRP also offers many excellent training opportunities in both laboratory research and clinical medicine for investigators at all stages of their career.

Laboratory of Cardiovascular Science

Edward Lakatta, M.D.

The overall goals of the Laboratory of Cardiovascular Science (LCS) are to:

- study myocardial structure and function and determine how age interacts with chronic disease states to alter function
- study basic mechanisms in excitation-contraction coupling and heart regulation and how these are modulated by surface receptor signaling pathways in cardiac muscle
- determine the mechanisms controlling the movement of ions through ionic channels and pumps present in myocardium, and how these are affected by aging and disease
- determine mechanisms that govern physiological and behavioral aspects of hypertension
- determine mechanisms of normal and abnormal function of vascular smooth muscle and endothelial cells
- establish the potentials and limitations of new therapeutic approaches such as gene transfer and stem cell implantation techniques.

In meeting these objectives, studies are performed in human volunteers, intact animals, and isolated heart and vascular tissues, isolated cardiac and vascular cells, and subcellular organelles.

The LCS contains two sections:

Behavioral Hypertension Section – *David E. Anderson, Ph.D.* The goal of the research in this section is to identify physiological and biochemical mechanisms by which behavioral interactions with the environment compromise the ability of the kidneys to regulate dietary sodium and thereby contribute to the development of chronic hypertension. From such studies may come interventions to reduce the risk of heart disease, stroke, and kidney disease in older persons.

Cardiac Function Section – *Edward Lakatta, M.D.* Research in this section emphasizes cardiac dynamics and basic studies on isolated myocardial cells, as well as the influence of age on the intact cardiovascular system, with special attention to the human myocardium. Researchers in this section also conduct studies on the vascular structure, function, and mechanisms of atherosclerosis, as well as on gene therapy for age-related cardiovascular disease. The Cardiac Function Section is organized into nine functional units:

- Cardiovascular Biology Unit (Edward G. Lakatta, M.D.)
- Cardiovascular Gene Therapy (Mark Talan, M.D., Ph.D.)
- Calcium Signaling Unit (Heping Cheng, Ph.D.)
- Cardioprotection Unit (Steven Sollott, M.D.)
- Cellular Biophysics Unit (Michael D. Stern, M.D., SBRS)
- Human Cardiovascular Studies (Samer Najjar, M.D.)
- Hypertension Unit (Alexei Bagrov, M.D., Ph.D.)

- Molecular Cardiology (Kenneth R. Boheler, Ph.D.)
- Receptor Signaling (Rui-Ping Xiao, M.D., Ph.D.)

Laboratory of Cellular and Molecular Biology

Myriam Gorospe, Ph.D., Acting Chief

The ultimate goal of the Laboratory of Cellular and Molecular Biology (LCMB) is to uncover knowledge that can be applied to prevent or delay the onset of age-related disabilities and disease processes, and/or provide new strategies for their diagnosis or treatment. Major areas of emphasis common to the individual programs across the LCMB include:

- elucidation of signal transduction processes and gene regulatory mechanisms involved in mediating cellular responses to environmental signals such as growth factors, cytokines, and stress stimuli
- determination of mechanisms contributing to the maintenance of cellular homeostasis and cell cycle control
- contribution of dysregulated gene expression, or loss of critical gene functions, to the development of cancer

A wide variety of in vitro and in vivo models are being employed to approach these issues. Specialized expertise in a variety of approaches used to analyze or manipulate gene expression is also available within the LCMB. Individual research programs include:

Cancer Molecular Genetics Unit – *Patrice J. Morin, Ph.D.* This unit focuses specifically on research related to the molecular genetics of ovarian cancer and the role of the APC/ß-catenin pathway in human cancer.

Cell Cycle Control Unit – *Myriam Gorospe, Ph.D.* The efforts of this unit are two-fold: 1) to search for RNA-binding proteins, target mRNA regions, and signaling pathways involved in regulating the stability of mRNAs encoding proliferative and cell cycle-regulatory genes, and 2) to elucidate the tumor suppressive role of the von Hippel-Lindau gene product by investigating its influence on gene expression.

DNA Repair Unit – *Michele K. Evans, M.D.* The focus of this unit's work is to understand the role of DNA repair in cellular senescence and tumorigenesis and to use DNA repair capacity as a clinical tool in the diagnosis and treatment of cancer and age-related disease and disability. Specific areas of investigation include the role of oxidative damage and base excision repair in breast and prostate cancers.

T Lymphocyte Signaling Unit – *Ronald L. Wange, Ph.D.* The long-term goal of this unit is to gain a better understanding of the mechanisms through which immunosenescence arises in aging animals.

Laboratory of Clinical Investigation

Darrell R. Abernethy, M.D., Ph.D.

The Laboratory of Clinical Investigation (LCI) chiefly focuses on translational research to identify therapeutic targets and develop treatments for age-related diseases. This clinical work includes cross-sectional studies in a variety of disease areas, including diabetes, metabolism, cardiovascular disease, neurological disease, and cancer.

Bioanalytical Chemistry and Drug Development Section – *Irving W. Wainer, Ph.D.* The overall goals of this section are the development of novel bioanalytical methods, their application to the etiology and diagnosis of diseases in the aging population, and the optimization of treatment protocols for these diseases. Through these activities, investigators in the section hope to participate in the improvement of existing therapies and to lay the basis for the development of new approaches to clinical treatment.

Diabetes Section – *Josephine M. Egan, M.D.* This section focuses on developing and improving methods for treating type 2 diabetes. Because it is most likely that elevated blood sugar levels lead to the complications of diabetes, this section's endeavors are directed towards improving insulin secretion or restoring insulin action, and particularly towards developing and understanding insulinotropic agents as potential treatments for diabetes.

Hematology/Oncology Section – *Eric H. Westin, M.D.* Researchers in this section seek to develop novel anti-tumor therapies and evaluate these and conventional therapies in an aging population. Studies are planned to explore DNA repair and other potential predictive factors in the treatment of lymphoma and breast cancer. A **Cancer Immunology Unit** led by Igor Espinoza-Delgado, M.D., explores "mini-transplant" approaches to treatment – for example, whether immune reconstitution can be accelerated in diseases such as chronic lymphocytic leukemia.

Molecular and Clinical Pharmacology Section – *Darrell R. Abernethy, M.D., Ph.D.* This section studies the role of age- and disease-related changes in calcium signaling in vascular smooth muscle on vascular responses in aging, hypertension, and atherosclerosis and seeks to understand how such changes affect drug responses. In addition, studies of the role of inflammation and skeletal muscle atrophy in osteoarthritis are conducted, with the goal of identifying therapeutic targets related to the early inflammatory process. Within this section, the ***In Vivo* Nuclear Magnetic Resonance Unit,** led by Richard Spencer, Ph.D., M.D., conducts imaging studies of connective tissue biophysics (whole cartilage, chondrocytes in culture, and in vivo cartilage imaging), spectroscopic studies of muscle metabolism under a variety of pharmacological and physiological conditions, and imaging of transgenic mice to noninvasively determine phenotype.

Laboratory of Epidemiology, Demography, and Biometry

Richard J. Havlik, M.D., M.P.H.

The Laboratory of Epidemiology, Demography, and Biometry (LEDB) conducts research on aging and age-associated diseases and conditions using population-based epidemiologic and biometric methods. The mission of LEDB is to:

- elucidate the etiology of diseases of old age by combining epidemiologic data with information from other disciplines
- evaluate the consistency of epidemiologic data with etiologic hypotheses developed either clinically or experimentally
- provide the basis for developing and evaluating preventive procedures and public health practices

These general principles have guided a research agenda that emphasizes three important and interrelated areas: Physical Function and Disability, Cognitive Function and Dementia, and Age-Associated Diseases and Conditions (including successful or effective aging). In each area, studies are influenced by results of current LEDB-sponsored studies and by opportunities created by advances in biology.

Laboratory staff work collaboratively both within and among three sections:

Epidemiology and Demography Section – *Jack Guralnik, M.D., Ph.D.* This section plans and conducts studies on chronic diseases, functional status, and disability in the older population.

Neuroepidemiology Unit – *Lenore Launer, Ph.D.* This section conducts interdisciplinary research on the association of genetic, molecular, and behavioral factors in relation to brain disease in old age.

Geriatric Epidemiology Section – *Tamara Harris, M.D., M.S.* This section carries out interdisciplinary studies of the association of molecular and genetic risk factors with health outcomes in old age, including discrete diseases, disability, and mortality.

Laboratory of Experimental Gerontology

Donald K. Ingram, Ph.D.

The Laboratory of Experimental Gerontology (LEG) is the newest laboratory within the IRP. The LEG conducts basic research in experimental models focused on interventions that retard aging processes. Major research initiatives include:

- a longitudinal study of the potential beneficial effects of calorie restriction on aging in nonhuman primates
- identification of protective mechanisms invoked by caloric restriction in cellular and rodent models
- a standardized research program coordinated through the NIA extramural program to evaluate various aging interventions (pharmaceuticals, hormones, dietary supplements, genes) in mouse models to assess effects on lifespan, pathology, and functional capacity at older ages

- creation and evaluation of behavioral assays of aging in rodents and nonhuman primates with focus on motor and memory performance, as well as the development and assessment of targeted pharmaceuticals to improve the function of these behavioral systems

Laboratory of Genetics

David Schlessinger, Ph.D.

The research program of the Laboratory of Genetics (LG) is based on the view that the aging process has genetic determinants, with a profound dependence on processes that are initiated in utero. LG's major areas of study include:

- transitions between immortal and mortal cells – for example, the transition of immortal embryonic stem cells to mortal differentiating cells
- cohorts of genes involved in the development of "nonrenewable" systems such as the skin
- mechanisms and treatment of heritable connective tissue disorders
- nuclear organelles that determine large-scale chromatin remodeling events
- genes involved in embryonic events that prefigure aging-related phenomena
- the genetics of aging-related complex conditions (through the SardiNIA study – see page 50)

Laboratory components include:

Human Genetics Unit – *David Schlessinger, Ph.D.* Investigators in this program analyze developmental processes critical for the aging of specialized mammalian cells and concomitant aging-related phenomena. The studies include analyses of the regulation of cohorts of genes involved in the development and overall growth control of selected tissues, including ovary and skin.

Human Genetics and Integrative Medicine Section – *Clair A. Francomano, M.D.* The research program of this section focuses on the clinical and molecular aspects of human hereditary connective tissue disorders, including the skeletal dysplasias. Investigators research the molecular processes involved in skeletal development in both health and disease. Clinical studies are designed to elucidate the natural history of these disorders and to understand the relationship of phenotype to mutation and pathophysiology. This section is also exploring applications of alternative and complementary medicine to the diagnosis and treatment of patients with hereditary connective tissue disorders and other genetic conditions.

Developmental Genomics and Aging Section – *Minoru S.H. Ko, M.D., Ph.D.* The long-term goal of this section is to understand the fundamental mechanisms for the maintenance of self-renewal, immortality, and pluripotency of early mouse embryos and stem cells.

Gene Recovery and Analysis Unit – *Ramaiah Nagaraja, Ph.D.* This unit produces state-of-the-art gene materials, along with informatics and related technology for gene analysis. The technology initiatives include the adaptation of phage display to recover reagents that specifically detect and permit quantitation of individual proteins in cells. Two research endeavors are designed to extend relevant current technology: Recovery of Genes in Chromatin Form and Sequence and Gene Analysis in the Mouse T-Complex.

Transcription Regulation and Remodeling Unit – *Weidong Wang, Ph.D.* This unit studies selected nuclear regulatory complexes, including chromatin-remodeling complexes that participate in gene regulation and recQ DNA helicase complexes involved in genome instability syndromes.

Laboratory of Immunology

Dennis D. Taub, Ph.D., Acting

The interests of the Laboratory of Immunology (LI) cover a wide range of topics devoted to a greater understanding of the biological, biochemical, and molecular alterations in immune functions that occur within individuals during both normal and disease-associated aging processes. A common goal of these research programs is the elucidation of the age-related deficits in immune function that could be targeted by various therapeutic strategies. Areas being studied include:

- the role(s) of various cytokines, hormones, and chemokines in leukocyte trafficking, cellular activation, and apoptosis
- the biological function and molecular composition of lipid rafts and the plasma membrane derived from the immune cells of young and elder populations
- the physiological and molecular mechanisms associated with age-related immunosuppression and thymic involution
- the preclinical development and clinical monitoring of immunologically-based protocols with a focus on modulating immune responses in elder populations and cancer patients
- the molecular examination of telomere length and telomerase activity in lymphocyte populations at various stages of activation and differentiation
- the study of the various factors and genes that appear to be differentially regulated during human lymphocyte development, differentiation, and activation
- identification and characterization of immunosuppressive factors associated with cancer-based immunosuppression
- defining the role(s) of oncogenes and signaling/cytoskeletal components involved in various signaling pathways with lymphocytes
- the biological and molecular mechanisms associated with the development of the B-cell repertoire

Clinical Immunology Section – *Dennis D. Taub, Ph.D.* The research interests of this section are focused in several areas, including the intersection of chemokines, immune responses, and aging; differential entry, propagation, and apoptosis induced by HIV in aged immune cells; the role of lipid rafts and cholesterol in cellular activation and trafficking; molecular profiling of aging immune cell subsets, lymphoid organs, and tissues; and optimizing vaccine responses in the elderly.

Lymphocyte Differentiation Unit – *Nan-Ping Weng, M.D., Ph.D.* The research interests of this unit are focused on three areas: 1) molecular and cellular mechanisms of lymphocyte differentiation and immunological memory; 2) regulation of telomerase and telomere length in young and aged lymphocyte subsets; and 3) molecular basis of learning and memory formation in various age groups.

Lymphocyte Cell Biology Unit – *Dan L. Longo, M.D.* Research in this unit focuses on several areas, including the regulation of tumor cell growth and progression; mechanisms of tumor-induced immunosuppression; cyclosporine A-resistant costimulation of T cells; the role of NF?B variants and caveolin in lymphocyte function; and mutant p53 in TGFß-mediated lymphoma growth suppression.

Laboratory of Molecular Gerontology

Vilhelm A. Bohr, M.D., Ph.D.

The Laboratory of Molecular Gerontology (LMG) investigates DNA-related mechanisms such as genomic instability, DNA repair, DNA replication, and transcription.

DNA Repair Section – *Vilhelm A. Bohr, M.D., Ph.D.* This section conducts research on a variety of topics, including DNA repair processes, oxidative DNA damage and mitochondrial functions, and premature aging diseases such as Werner syndrome and Cockayne syndrome.

Unit of Oxidative DNA Damage Processing and Mitochondrial Functions – *Vilhelm A. Bohr, M.D., Ph.D.* This unit focuses on DNA repair processes of oxidative damage in nuclear and mitochondrial DNA and how these processes change with aging.

DNA Helicases Unit – *Robert M. Brosh, Jr., Ph.D.* This unit focuses on the roles of DNA helicases in genomic stability and diseases with the premature aging phenotype, e.g., Werner syndrome.

Unit of Structure and Function in Base Excision Repair – *David M. Wilson III, Ph.D.* This group focuses on the molecular and biochemical processes involved in the removal of oxidative DNA damage.

Antibody Diversity Unit – *Patricia J. Gearhart, Ph.D.* Researchers in this unit investigate the mechanism of somatic

hypermutation and its interrelationships with DNA repair pathways and proteins.

Gene Targeting Section – *Michael Seidman, Ph.D.* The goal of the Gene Targeting Section is the development of robust technologies for the facile manipulation of sequences in the genome of living cells. The approach is based on oligonucleotides that can form triple helical structures with specific target sequences.

Laboratory of Neurogenetics

John Hardy, Ph.D.

The Laboratory of Neurogenetics (LNG) focuses on understanding major neurodegenerative diseases using genetic approaches. LNG's activities include:

- identification of risk factor genes for age-related neurological conditions, including Alzheimer's disease and Parkinson's disease
- identification of biochemical pathways leading to disease pathogenesis
- creation of animal models of disease

Complex Genetics Section – *Andrew Singleton, Ph.D.* This section's goal is to identify genetic mutations that lead to neurological disease. At present the foci of the section's work are dystonia, especially Lubag, and Parkinsonism. Lubag is an X-linked Parkinsonism dystonia that occurs in Filipino men.

Cell Biology and Gene Expression Section – *Mark Cookson, Ph.D.* The goal of this section is to develop an understanding of the proteins involved in disease pathogenesis, and in particular, to try and elucidate which biochemical pathways are impacted by pathogenic mutations. Currently, the two major projects in the lab focus on the torsin A gene and the possible biochemical interactions among the proteins encoded by the genes involved in Parkinson's disease.

Transgenic Modeling Section – *Huaibin Cai, Ph.D.* The goal of the Transgenic Modeling Section is to develop and characterize animal models of neurodegenerative diseases; these models will be useful in examining in vivo consequences of the underlying genetic mutations of human diseases and for testing potential therapeutics. In particular, this section is interested in using animal models to explore the molecular pathogenesis of Alzheimer's disease and amyotrophic lateral sclerosis.

Laboratory of Neurosciences

Mark P. Mattson, Ph.D.

Two major goals of research in the Laboratory of Neurosciences (LNS) are to understand normal aging of the nervous system at the cellular and molecular levels and to identify the mechanisms responsible for age-related neurodegenerative disorders. Knowledge gained in such basic research is then used in preclinical studies to develop interventions such as changes in diet and lifestyle and development of drugs and cell therapy techniques to prevent and treat these

disorders. LNS scientists are conducting research in:

- oxidative stress and calcium regulation
- apoptotic and neuroprotective signaling pathways
- neural regulation of energy metabolism and stress responses
- synaptic signaling and plasticity
- stem cell biology
- telomerase
- invertebrate genetics
- inflammatory processes
- behavior
- diet and lifestyle

Cellular and Molecular Neurosciences Section – *Mark P. Mattson, Ph.D.* This section employs a multifaceted array of experimental models of aging and age-related neurodegenerative disorders in order to establish the molecular and biochemical changes that occur during aging and in disorders such as Alzheimer's, Parkinson's, and Huntington's diseases and stroke.

Invertebrate Molecular Genetics Unit – *Catherine A. Wolkow, Ph.D.* The primary research focus of this unit is to identify and characterize genetic pathways controlling aging and life span, with particular emphasis on studies in *C. elegans.*

Stem Cell Biology Unit – *Mahendra S. Rao, Ph.D.* Research in this unit focuses on the cellular and molecular mechanisms that regulate the proliferation, differentiation, and survival of neural progenitor cells in the brain and spinal cord during development and in the adult.

Synaptic Physiology Unit – *Katsutoshi Furukawa, M.D., Ph.D.* Research in this unit aims to understand the molecular basis for synaptic dysfunction and degeneration in aging and age-related neurological disorders.

Drug Design and Development Section – *Nigel H. Greig, Ph.D.* Research in this section is designed to develop novel agents against rate-limiting steps involved in the pathophysiology of nervous system diseases, with particular interest in Alzheimer's disease.

Laboratory of Personality and Cognition

Paul Costa, Jr., Ph.D.

Few phenomena are more basic than the fact that human beings differ—in health, in rates of aging, in cognitive ability, in personality, in happiness, and in life satisfaction. The fundamental scientific paradigm guiding research in the Laboratory of Personality and Cognition (LPC) is the analysis of individual differences. The LPC:

- conducts basic and clinical research on individual differences in cognitive and personality processes and traits
- investigates the influence of age on these variables and their reciprocal influence on health, well-being, and adaptation
- employs longitudinal, experimental, psychophysiological, epidemiological, and behavior and quantitative genetic methods in the analysis of psychological and biological issues of aging, including health and illness, predictors of

intellectual competence and decline, models of adult personality, and correlates of disease risk factors

The LPC is composed of two sections and a unit.

Personality, Stress, and Coping Section – *Paul Costa, Jr., Ph.D.* Investigators conduct basic and applied research on personality as it relates to aging, including studies of stress and coping, mental and physical health risks and outcomes, adaptation, and well-being. Basic research centers on a taxonomic model of personality traits and its assessment. Cross-cultural and genetic analyses are also employed.

Emotions and Quantitative Psychophysiology Unit – *Julian F. Thayer, Ph.D.* Research in this unit is largely focused on the areas of neural control of the cardiovascular system and cardiovascular reactivity, including autonomic characteristics of anxiety and mood disorders.

Cognition Section – *Alan B. Zonderman, Ph.D.* Investigators conduct studies that attempt to distinguish pathological from healthy age-related changes in a broad range of cognitive tasks, including short-term and long-term memory, visuo-spatial rotation, attention, and decision tasks. In addition, structural and functional brain changes are examined using MRI and PET.

Brain Physiology & Metabolism Section

Stanley I. Rapoport, M.D.

The Brain Physiology & Metabolism Section (BPMS) studies brain phospholipid metabolism in intact animals and humans, as well as synaptic integrity and function in aging and Alzheimer's disease. There are two major areas of research: brain lipid metabolism in signal transduction and neuroplasticity, and synaptic dysfunction in aging and Alzheimer's disease.

Molecular Dynamics Section

Joseph M. Rifkind, Ph.D.

The research program in the Molecular Dynamics Section (MDS) focuses on the interplay between structure and dynamics and how these influence biological function. The section is presently involved in studying the structural and dynamic factors in hemoglobin that regulate the binding of oxygen, the uptake and release of nitric oxide, and autoxidation with its associated release of superoxide.

Clinical Research Branch

Eric H. Westin, M.D.

The Clinical Research Branch (CRB) conducts and provides the infrastructure for clinical research within a coordinated multi-disciplinary environment that provides a model for geriatric research programs. This branch is responsible for management and support for research on the cause, diagnosis, prevention, and treatment of age-associated diseases, as well as translation of advances in basic science from other NIA-IRP laboratories into

clinical applications. Major research initiatives of the CRB include the longstanding Baltimore Longitudinal Study of Aging (BLSA) and the new Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) initiative. The focus of other studies supported or initiated by investigators and staff within the branch include examination of risk and progression of diseases such as osteoarthritis, as well as studies in a variety of age-related diseases, including cancer, diabetes, and neurologic and cardiovascular diseases.

Longitudinal Studies Section – *Luigi Ferrucci, M.D., Ph.D.* Under its newly-recruited head, this section is responsible for the scientific design and evolution of the BLSA (see page 51). Current research interests of scientists within the section focus on the muscular, neuromuscular, bone, and physical functioning aspects of the aging process, with plans for new initiatives in the genetics underlying the aging process as well as defining physical- and laboratory-based correlates of frailty during aging. In addition, a variety of projects are ongoing using historical and newly-collected data which intersect with the interests of a number of other laboratories within the NIA-IRP.

Health Disparities Research Section – *Michele K. Evans, M.D.* This section is responsible for ongoing studies examining health disparities and their influence on cardiovascular disease, cerebrovascular disease, age-associated changes in cognition, strength and physical functioning, and psychophysiology and nutrition. Central to this section is the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) Program (see page 54), which is a community-based research effort designed to evaluate health disparities in minority and socio-economically diverse populations.

Research Resources Branch

Alan B. Zonderman, Ph.D., Chief

The Research Resources Branch **(**RRB**)** provides centralized research resources and research support services essential to the productive conduct of biomedical research by the Intramural Research Program. The branch is divided into sections that focus on particular specialties or types of service:

- Central Laboratory Services, including cDNA arrays, bioinformatics, confocal microscopy, flow cytometry, and mass spectrometry
- Comparative Medicine, including animal husbandry for a variety of species, among them transgenic and knockout rodents
- Instrumentation, Design, and Fabrication
- Library and Information Services
- Network, Computing, and Telephony
- Media and Graphic Art Services
- Statistical and Experimental Design

Although this branch largely provides research services, there are several investigator-initiated projects conducted by RRB scientists. These projects include studies on array-based

technology development, changes in gene expression over the life span, and the identification of novel markers and signaling pathways in a variety of tissues and non-human hematopoietic stem cells.

Major NIA Initiatives by Research Area

Alzheimer's Disease (AD)

As the lead federal agency for AD research, NIA conducts and supports an extensive program of research on the etiology, prevention, and treatment of AD, as well as fundamental neuroscience. Several laboratories in the NIA Intramural Research Program have AD as an important focus. In the Extramural Program, AD research is largely concentrated in the Neuroscience and Neuropsychology of Aging (NNA) program, although activities with relevance to AD are found throughout the Institute.

Some of NIA's major intramural and extramural initiatives devoted to AD are described below.

Alzheimer's Disease Centers. NIA currently funds 29 Alzheimer's Disease Centers (ADCs) at major medical institutions across the nation. In addition, there are three Affiliate Centers. Researchers at these centers are working to translate research advances into improved care and diagnosis for AD patients while focusing on the program's long-term goal - finding ways to treat and possibly prevent AD. Investigators conduct basic, clinical, and behavioral research and train scientists and health care providers new to AD research, and areas of investigation range from the basic mechanisms of AD to managing the symptoms and helping families cope with the effects of the disease. Many ADCs have satellite facilities, which offer diagnostic and treatment services and collect research data in underserved, rural, and minority communities.

Although each center has its own unique area of emphasis, a common goal of the ADCs is to enhance research by providing a network for sharing new ideas and research results. Collaborative studies draw upon the expertise of scientists from many different disciplines. The National Alzheimer's Coordinating Center (see below) coordinates data collection and fosters collaborative research among the ADCs.

AD Cooperative Study. NIA's major AD clinical trials effort is the Alzheimer's Disease Cooperative Study (ADCS). Initially funded in 1991, the ADCS conducts clinical trials on compounds in which large pharmaceutical companies would generally not be interested. These include drugs that are off patent, or were patented and marketed for another use but might be useful for treatment of AD, or novel compounds from individual investigators or from small companies without adequate resources for clinical trials. It remains the major government initiative for AD clinical trials, addressing treatments for both cognitive and behavioral symptoms.

Alzheimer's Disease Education and Referral Service (ADEAR). This service offers information and publications on diagnosis, treatment, patient care, caregiver needs, long-term care, education and training, and research related to AD. ADEAR staff members answer telephone and written requests and make referrals to local and national resources.

AD Genetics Initiative. The NIA created the Alzheimer's Disease Genetics Initiative in order to move the field of Alzheimer's disease genetics forward more rapidly. A major component of this initiative is the collection of family-based, population-based, and case-control sample sets. To facilitate collection of the family-based sample set, administrative supplements were awarded last year to ten Alzheimer's Centers to identify families with two or more affected members and to collect blood and information from them for archiving in the National Cell Repository for Alzheimer's Disease (NCRAD). DNA and information on these individuals will be made available, with appropriate controls to ensure participant confidentiality, to the research community. The information gained through this initiative will be invaluable to the discovery of AD-related genes, which will in turn help us identify pathways affecting AD development or progression.

AD Prevention Initiative. This trans-NIH initiative has the ultimate intent of developing interventions to prevent AD in susceptible individuals. It encompasses a number of interrelated efforts, including basic, epidemiological, behavioral, and clinical research.

Healthy Brain Project (Cognitive and Emotional Health Project). NIA, the National Institute on Mental Health, and the National Institute of Neurological Disorders and Stroke have partnered to create a new initiative designed to explore components of cognitive and emotional health in adults, often referred to as "The Healthy Brain Project." The goals of the project are to identify and evaluate what is known about predictors of cognitive and emotional health in older adults and risk factors that may point to cognitive decline or emotional instability. One ongoing activity for achieving this goal is an assessment of the state of longitudinal and epidemiological research on demographic, social, and biologic determinants of cognitive and emotional health in aging adults and the pathways by which cognitive and emotional health may reciprocally influence each other. Activities also include efforts to accelerate the pace of scientific discovery in these areas.

Minority-Based Satellite/Diagnostic Centers. NIA's Satellite Diagnostic and Treatment Clinics, part of the Alzheimer's Disease Centers Program, serve as vehicles for the recruitment, diagnosis, and management of AD patients and their families, who are then offered the opportunity to participate in research protocols and clinical drug trials. Outreach efforts particularly focus on members of special and/or underserved populations. These clinics

do not conduct research themselves. The satellite program is designed to increase the diversity of the research patient pool and to enhance the research capabilities of the ADCs through extension of the activities of the clinical cores. From an initial four sites, the program has expanded to include some 26 funded satellites across 18 ADCs.

National Alzheimer's Coordinating Center (NACC). The NACC was established in 1999 in a cooperative agreement with the University of Washington at Seattle to facilitate collaborative research, including standardized data collection, across the ADCs. Statistics on over 54,000 participants enrolled in ADC studies since 1984 are now accessible on the NACC website (http://www.alz.washington.edu). New procedures have recently been adopted for widening access to the database by non-Center scientists wishing to use the data. The confidentiality of individual study participants' data is scrupulously maintained.

REACH. NIA supports a large, multi-site clinical trial, REACH (Resources for Enhancing Alzheimer's Caregiver Health), to examine the effectiveness of various interventions to strengthen family members' capacity to care for individuals with AD. REACH is designed to show us what works to support caregivers and at what cost; the first phase of the study has been completed, and a second phase began recently.

Clinical Trials in Alzheimer's Disease. NIA is currently conducting a number of AD clinical trials, including large-scale prevention studies. A chart describing these trials can be found on pages 42-45.

Alzheimer's Disease Clinical Trials – 2003

Study*	Drug: Generic (Brand name) Dosage/day	Duration	N	Sex	Age	Subjects
AD Anti-Inflammatory Prevention Trial (**ADAPT**)	Celecoxib (Celebrex) 200 mg bid Naproxen (Aleve) 220 mg bid	5-7 years	2,625	both	≥70	healthy elderly w/family history of AD or dementia
AD Estrogen Prevention Trial (**PREPARE**)	Hyst/estrogen (Premarin) .625 mg Non-hyst/estrogen+progesterone (Pempro) 2.5 mg	5 years	900	F	>65	healthy elderly w/family history of dementia
Estrogen Treatment Trial	17-β estradiol 50 or 100 µg transdermal (with or w/o progesterone 2.5 mg)	1 year; f-up @ 15mos.	160	F	55 - 85	mild/moderate AD
Multicenter Osteoporosis Raloxifene Evaluation (**MORE**)	Retrospective and prospective analysis of MORE data	5 years	7,705	F	≥65	post menopausal white women
Mild Cognitive Impairment (MCI) Trial	Vitamin E 2,000 IU or Donepezil (Aricept) 10 mg	36 mos.	720	both	55 - 90	MCI

Women's Antioxidant Cardiovascular Study (**WACS**)	Vit E (600 IU every other day), Vit C (500 mg), B12 (1 mg), Beta carotene (50 mg every other day), Folate (2.5 mg), B6 (50 mg)	5 years	3,445	F	>65	Women at high risk of cardiovascular disease
Women's Health Study (**WHS**)	Aspirin (100 mg every other day) Vit E (600 IU every other day)	5 years	7,441	F	>65	Healthy women
Physician's Health Study II (**PHS II**)	Beta carotene 50 mg every other day**,** Vit E 400 IU every other day, Vit C (500 mg), multivitamin w/folate	4 years	6,012	M	>65	Healthy men
Slow Progression in Down Syndrome	Vit E 2000 IU	3 years	750	Both	>50	slow rate of cognitive/functional decline in persons w/Down Syndrome
Ginkgo Evaluation of Memory Study (**GEM**) (NCCAM primary)	Ginkgo biloba: 240 mg	6 years	3,000	both	≥75 ≥71 Afr-Am	non-demented
Non-steroidal anti-inflammatory treatment	Rofecoxib (Vioxx) 25 mg or Naproxen 200 mg	1 year w/ f-up @14 mos	320	both	≥55	Probable AD
Propranolol for agitation in AD	Propanolol (Inderal) up to 120 mg titrated	8 weeks	120	both	>65	Nursing home pts with agitation & AD

Brain imaging & age-associated memory impairment (AAMI)	Donepezil (Aricept) 10 mg/day	2 years	138	both	65-90	AAMI & family hx of dementia
Divalproate therapy for agitation in nursing home residents with dementia	Divalproate (Depakote), up to 500 mg/day	6 weeks + 6 wks open label	150	both		Nursing home pts with agitation
AD Pilot Clinical trial: Drug inhibition of Aβ induced immune responses	Hydroxychloroquine (6.5 mg/kg) or Dapsone (2 mg/kg) or Thalidomide (2 mg/kg)	1 year	45	both	≥55-90	Mild-moderate AD
AD Pilot Clinical trial: Cognitive treatment for Early AD	Cog rehab + Donepezil (Aricept) 10 mg	12 weeks; 3& 6 mos post eval	120	both	40-90	Mild AD
AD Pilot Clinical trial: Vitamin therapy for hyperhomocystenemia in AD	Phase I: case-control; Phase IIa: low dose B6/B12/folate followed by Phase IIb: high dose B6/B12/folate	12 weeks	Phase I (300); Phase II (200)	both	≥60-85	Mild-moderate AD
Prevention of AD by Vitamin E and Selenium **(PREADVISE)**	Vit. E (400 mg) Selenium (200 mg)	5 years	10,000	M	>60	Healthy men
Testosterone on Memory in Aging and AD	Testosterone 50-300 mg/week	5 years	270	M	>55	Healthy and demented men
AD Pilot Clinical Trial: Pioglitazone in AD	Pioglitazone 15-45 mg	3 years	30	Both	>50	Mild AD

AD Pilot Clinical Trial: Huperzine A in AD	Huperzine 400 ug	3 years	80	Both	>55	Mild AD
Simvastatin Study	Simvastatin 20 mg for 6 weeks, then 40 mg	18 mos	400	Both	>50	Mild-moderate AD
Homocysteine Study	Vitamins B6 (25 mg) and B12 (1 mg) and folate (95 mg)	1 year	400	Both	>50	AD patients

*: Randomized, placebo-controlled trial unless otherwise noted

Arthritis

Multisite Osteoarthritis Study. In September 2001, NIA funded the seven-year Multisite Osteoarthritis Study (MOST). The overall goal of MOST is to evaluate longitudinally the effects of biomechanical factors, bone and structural factors, and nutritional factors on the progression of symptomatic and radiographic knee OA in men and women ages 50 to 70 years. A noteworthy aspect of MOST is that it is the first longitudinal study of knee OA to incorporate both state-of-the-art radiographic techniques and magnetic resonance imaging.

Osteoarthritis Initiative. NIA is also collaborating with the National Institute of Arthritis and Musculoskeletal and Skin Diseases in supporting the Osteoarthritis Initiative (OAI). OAI's objective is to pool public and private scientific expertise and funding to collect, analyze, and make widely available the largest research resource to date of clinical data, radiologic information, and specimens from individuals with early and progressing OA. The goal is to create a public resource to validate imaging and biochemical biomarkers and ensure that validated biomarkers are widely available to further drug development and improve public health.

Coordination and collaboration between these two large initiatives is expected.

Basic Biology

Nathan Shock Centers for Excellence in Basic Biology of Aging. These Centers consist primarily of research resource cores to support specialized technologies such as animal colonies, bioinformatics, gene expression microarray analysis, shared equipment, etc. Funds are also provided to these Centers for scientific program enrichment such as seminar programs and research development in the form of pilot grants. The Centers are named after Nathan Shock, a pioneer in the study of gerontology in the United States. There are currently four funded Centers; these are located at:

- The University of Michigan – John Faulkner, PI
- The University of Rochester – Howard Federoff, PI
- The University of Texas Health Science Center, San Antonio – Arlan Richardson, PI
- The University of Washington – Peter Rabinovitch, PI

The Centers each currently receive about $750,000 per year per Center, and support at this level is committed through July 2005. Two of the Centers (Michigan, UTHSCSA) have programs specifically targeted for training minority investigators; these components are funded by the National Center on Minority Health and Health Disparities.

Cancer

Recognizing that close to 58 percent of all newly-diagnosed malignant tumors and 71 percent of all cancer deaths occur in persons 65 years and older, the NIA participates in a number of research efforts on cancer in the elderly. Frequently, the NIA collaborates with the National Cancer Institute (NCI) on cancer-related initiatives, and may take a leadership role in such partnerships, depending on the topic. Some projects are large-scale research initiatives and/or co-sponsored workshops on research areas chosen to address knowledge gaps on discrete topics identified by the NIA, while others involve establishing working relationships with individual NCI staff to develop key questions for research in specific areas. Ongoing initiatives include joint program announcements and the inclusion of NIA-supported studies within the NCI Cooperative Group system (a network of consortia throughout the U.S. that collaborate frequently on clinical trials for a variety of common cancers).

Two new collaborative efforts were initiated in September 2002. Both are based on the June 2001 NIA/NCI workshop "Exploring the Role of Cancer Centers for Integrating Aging and Cancer Research." As part of one initiative, the 61 NCI-designated Cancer Centers were invited to submit research planning and development grant applications to develop and establish formal interdisciplinary research programs directed at the aging/cancer interface. Five to seven awards are expected to be made in FY2003.

A second initiative, organized for the extramural scientific community at large, invites grant applications from individual scientists for studies on cancer in older persons. The research will expand the knowledge base on cancer prevention, treatment, early detection, care, and survival for individuals in the age group most vulnerable to cancer. For more on this initiative, see http://grants1.nih.gov/grants/guide/pa-files/PA-02-169.html.

For a full report on the June 2001 workshop, see http://nia.nih.gov/health/nianci.

Cardiovascular Disease

NIA's extramural research program in cardiovascular disease (CVD) currently emphasizes diastolic heart failure and acute coronary syndromes in the elderly. In the Intramural Program, the Laboratory of Cardiovascular Science conducts extensive research on the mechanisms of the cardiovascular system, and research on CVD is a major aspect of the HANDLS study (see page 54). The NIA also supports several studies that assess cognitive function in individuals who have, or who are at risk for, cardiovascular disease; many of these are ancillary to National Heart, Lung, and Blood Institute (NHLBI)-led research initiatives such as the Cardiovascular Health Study, the Framingham Heart Study, and the Women's Health Initiative. The NIA

also recently co-sponsored a workshop with both NHLBI and the National Institute on Neurological Disorders and Stroke to explore the bases of and potential interventions for cognitive decline after coronary bypass graft surgery, a procedure that is becoming increasingly common among individuals over age 65.

Other initiatives include:

Bogalusa Heart Study. In FY 2000, NIA began support for the Bogalusa Heart Study, the only long-term community study of heart disease that is examining a biracial (black-white) population beginning in childhood. The goal of this study is to characterize traits in a biracial population reaching middle age that influence the sub-clinical cardiovascular disease process in normal aging. Study participants include 1,200 individuals born between 1959 and 1969, who have been examined at least four times since childhood. During the first year of funding, the project focused on updating the patient registry of some 3,400 individuals, including 1,708 patients eligible for the NIA project. To date, 407 patients have been successfully screened and examined.

B-Vitamin Atherosclerosis Intervention Trial. This is a study of B-vitamin supplementation in healthy men and women 40 years of age and older. The trial is designed to assess the effect of lowering the amino acid homocysteine via B-vitamin supplementation on the risk of CVD in healthy individuals without preexisting CVD. Recruitment of participants is on schedule, and the trial is ongoing and being monitored by a Data Safety and Monitoring Board.

Vascular Dementia. The NIA supports a large program of research on vascular dementia at the University of Southern California. To date, over 550 individuals have been enrolled into the study. The multi-project study focuses on cognitive impairment due to small-vessel cerebrovascular disease (s-CVD). The goals of this project are to improve the understanding of the pathogenesis of subcortical ischemic vascular dementia (SIVD) and its interactions with Alzheimer's disease, and to develop and validate clinical and neuroimaging markers that inform clinical diagnosis and prognosis. To our knowledge, there is no other SIVD cohort in the world with serial neuropsychological and quantitative neuroimaging studies that is being followed to autopsy.

Demography/Statistics

Demography of Aging Centers. NIA supports 11 Demography of Aging centers that provide a research base for many of the nation's leading scholars in aging and health services research and in the social and behavioral sciences. The Centers bring together and enhance a significant number of large-scale research and database development activities in aging already taking place at each of the participating academic institutions. In addition to this coordinating role, the Centers promote research development in new areas

through small, focused pilot project funding; they support improved data resources on older people in the United States and around the world; they foster international collaborations of research scholars; they provide the advanced data management and data security arrangements for investigators to be able to access and analyze sensitive and restricted data sources that would not otherwise be available for academic research; they promote cross-disciplinary engagement and collaboration both within and across institutions; they facilitate the dissemination of important research findings to a broad public audience; and they provide a premier environment for training the most prominent emerging scholars in aging-related research.

Health and Retirement Study. The Health and Retirement Study (HRS) is a biennial survey of more than 22,000 Americans over age 50. The study paints an emerging portrait of an aging America's physical and mental health, insurance coverage, financial status, family support systems, labor market status, and retirement planning. HRS is increasingly recognized as the premier longitudinal data set in the U.S., and perhaps the world, for the community of scientific and policy researchers who study the health, economics, and demography of aging.

National Archive of Computerized Data on Aging (NACDA). NACDA's mission is to advance research on aging by helping researchers profit from the under-exploited potential of a broad range of datasets. NACDA acquires and preserves data relevant to gerontological research, processing as needed to promote effective research use, disseminates the data to researchers, and facilitates their use. By preserving and making available the largest library of electronic data on aging in the United States, NACDA offers opportunities for secondary analysis on major issues of scientific and policy relevance.

Diabetes

Diabetes is one of the major debilitating diseases that affect older people, and remains a priority of the Institute. Among the elderly, type 2 diabetes is the most common; it occurs when pancreatic beta cells produce insufficient insulin or when the body cannot use its insulin efficiently.

NIA-supported researchers participated in the Diabetes Prevention Program, a major, multi-institutional study that was initiated by the National Institute on Diabetes and Digestive and Kidney Diseases and was designed to identify interventions that could prevent or delay the development of type 2 diabetes. The researchers found that people who are at high risk for diabetes can sharply reduce their risk by adopting a low-fat diet and moderate exercise regimen. This effect was most pronounced among study participants age 60 and over. Treatment with the drug metformin (Glucophage®) also reduced diabetes risk among study participants, but for unknown reasons was less effective among older participants. Nearly half of the study

participants were members of racial and ethnic groups that suffer disproportionately from type 2 diabetes. With other participating NIH Institutes, we are continuing to follow the DPP participants to determine long-term effectiveness of these interventions.

Genetics of Aging

The Age, Gene/Environment Susceptibility Study (AGES). In collaboration with the Icelandic Heart Association, investigators from the NIA Intramural Research Program have initiated a major study that will examine the genetic contribution to commonly occurring age-related diseases. Research will focus on four areas: neurocognitive health (cognition, dementia, depression, vision, hearing); cardiovascular health (atherosclerosis, arterial distensibility, ventricular and valvular disease); muscoloskeletal conditions (spine and hip osteroporosis, hip osteoarthritis, strength and function); and body composition and metabolic disease (obesity, sarcopenia, hyperglycemia, diabetes). As part of the study, over 9,000 participants will be examined in a three-day clinic examination using imaging and other physiologic measures to phenotype for the focus health conditions. Extensive health records including birth weight, mid-life cardiovascular risk factors, and medical records will be incorporated into the study and a biorepository for specimens is also planned. Scientific collaboration to complement the research hypotheses of the study is invited and can be facilitated by contacting Dr. Tamara Harris or Dr. Lenore Launer in the Intramural Research Program.

Longevity Assurance Gene Initiative/Interactive Network. The Longevity Assurance Gene Initiative and the LAG Interactive Network of Investigators promote research on unraveling the genetic and molecular basis of longevity and aging. Advances include identification of several conserved biological processes and biochemical pathways involved in the modulation of aging and longevity in both invertebrates and mammals. The LAG Interactive Network serves as a model for the organization of multidisciplinary and crosscutting research initiatives to define common themes and biological processes in aging biology.

The SardiNIA Project. Because of the relative homogeneity of its population, the island of Sardinia provides a favorable location in which to study the genetics of age-associated diseases and conditions. Investigators from NIA's Intramural Research Program have initiated a five-year study of the genetics of risk factors for age-associated traits in this special population. The ongoing study is being conducted in Sardinia under the direction of investigators at the Instituto di Ricerca sulle de Talassemie et Anemie Mediterrane (IRTAM) Cagliari – Consiglio Nazionale delle Recerche (CNR).

Healthy Aging

ACTIVE. Advanced Cognitive Training for Independent and Vital Elderly

(ACTIVE) is a multi-site cooperative trial of cognitive interventions designed to maintain independence in older African Americans and Caucasians. The trial investigates whether three common cognitive interventions (memory, reasoning and speed of processing) can maintain or improve functioning in unimpaired, community-dwelling older adults. A total of 2,832 people are participating in this trial.

Baltimore Longitudinal Study of Aging (BLSA). The NIA supports the BLSA, America's longest-running scientific study of human aging. The study, which opened in 1958, has more than 1,300 men and women ages 20 to 90+ enrolled. Current studies within the BLSA focus on changes in physical function, glucose metabolism, body and bone composition, cardiovascular function, and cognition and personality during the aging process. Additional research topics include immune function with aging, including response to prior vaccinations such as smallpox and pneumonia; predisposition to osteoarthritis; and muscular and neuromuscular changes with aging.

Behavioral Change Consortium. This loosely federated project, of which NIA supports three components, examines multiple lifestyle factors and innovative approaches to increase health promoting behaviors (exercise, healthy weight management) and decrease debilitating behaviors (smoking, poor diet).

CALERIE (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy). Caloric restriction (CR), or consumption of a diet containing 30-50% fewer calories than normal, has proven effective in every animal model in which it has been adequately tested in slowing down aging and increasing longevity. The CALERIE study will explore the effects of CR on physiology, body composition, and risk factors for age-related pathologies in non-obese humans. Plans are also underway to establish a Coordinating Center for CALERIE because a high level of coordination will be required for appropriate oversight of site-specific protocols, as well as for the standardization of common measures across the study sites.

Edward R. Roybal Centers for Research on Applied Gerontology. The Edward R. Roybal Centers for Research on Applied Gerontology, initiated in 1993, are designed to translate behavioral and social research findings into practical outcomes for older adults. Each of the six Roybal Centers addresses one or more central themes (e.g., cognitive influences on physician/patient interaction affecting medical compliance; safe driving behavior; social role adjustment upon retirement). Administrative cores, dissemination cores, and advisory boards at each site provide integration, facilitate scientific findings reaching the general public, and ensure that research is applicable to real-world problems.

Older Americans Independence Centers. The development of effective interventions to reduce disability and increase independence may offer

immense physical and emotional benefits to older Americans, as well as significant saving in health care costs. The OAICs are "centers of excellence" that provide support for basic and clinical research to enhance the ability of older persons to maintain their independence. They provide core support for research to develop and test interventions directed at disorders and diseases associated with aging. They also train individuals in research approaches to develop and test methods of maintaining and increasing independence.

HIV/AIDS

With the establishment of an NIA-wide Workgroup on HIV/AIDS and Aging, this area of research has become an Institute priority. Several activities have been undertaken since 1997 to stimulate research in this area, including conferences, co-sponsorship of a trans-NIH RFA on human immunology and AIDS issues, and supplementation of several research grants to pursue related research. In FY 2000, NIA, in conjunction with the National Institute on Mental Health, entered into an interagency agreement with the Veterans Administration to explore the feasibility of conducting the Veterans with HIV/AIDS Cohort Study (VACS). In FY 2002, NIA funded the National Academy of Sciences to convene a workshop on aging issues in sub-Saharan Africa that will highlight the devastating impact of AIDS in this region. This workshop is in the planning stage at present. As HIV/AIDS is a serious problem among older Americans and internationally, we anticipate that this will remain an important area of research for the Institute.

Special Populations

The health status of racial and ethnic minority groups in the U.S. has improved steadily over the last century. Despite this progress, disturbing disparities in health persist between majority and minority populations. In 1997, for example, average life expectancy at age 65 was 16.1 years for African Americans and 17.8 years for Caucasians. Demographic projections predict a substantial change in the racial and ethnic makeup of the older population, heightening the need to examine and reduce differences in health and life expectancy. Research to date has shown that health disparities are associated with a broad, complex, and interrelated array of factors. Disease risk, diagnosis, progression, response to treatment, caregiving, access to care, and overall quality of life each may be affected by variables such as race, ethnicity, gender, socioeconomic status, age, education, occupation, country of origin, and possibly other lifetime and lifestyle differences.

The NIA is committed to addressing health disparities, with many initiatives supported in partnership with the National Center on Minority Health and Health Disparities. Minority aging research is conducted throughout the Institute's research programs. For example:

- Satellite Diagnostic and Treatment

Centers, part of the national Alzheimer's Disease Centers (ADC) Program, have successfully recruited African Americans, Hispanics, Native Americans, and American Indian/Alaska Natives to AD prevention and treatment studies.

- Researchers on the NIA's Religious Orders Study have made a major effort to enroll African American members of the Catholic clergy; the nature of the study population enables the etiology and pathology of AD to be established among individuals with similar educations, occupations, socioeconomic status, and lifestyles.
- Five ADCs received funding in 2000 and 2001 specifically to encourage minority-related research.
- NIA's R03 Pilot Grant Program specifically invites researchers to submit grant applications that deal with "research leading to the identification of underlying mechanisms, including cellular and molecular mechanisms, linked to racial/ethnic differences in late-life function or disease. . ." This program announcement invites applications from new or established investigators to conduct pilot research that is likely to lead to a subsequent individual research project grant (R01) that is focused on a significant aspect of aging research. In 2002, each awardee received $50,000 in direct costs for one year.
- The NIA supports several specific programs to assist in the development of research careers for minority investigators whose research topics are relevant to the NIA mission. These include dissertation awards for minority doctoral students and awards to institutions hoping to increase their numbers of students from underrepresented populations.
- In 2001, half of the NIA Director's Reserve funds, which encourage collaborative research projects, were allocated to minority-focused research.
- NIA is initiating a new project, "Promoting Research Participation Among Black and Hispanic Seniors." This year-long project will: (1) explore ongoing and completed Yale-Older Americans Independence Center recruitment and retention data to identify characteristics of Black and Hispanic study participants and non-participants, (2) interview key informants with intimate knowledge about ways to promote research participation among the targeted samples, and (3) conduct focus group discussions on the topic of recruitment and retention of minority older adults into aging-related research among representatives of the type of Black and Hispanic older adults participants likely to be targeted by studies of multi-factorial geriatric health conditions. The data emerging from these sources will then be synthesized into a monograph describing recommended practices to improve the recruitment of minority seniors into health-related research.

Other NIA initiatives are designed to increase the number of minority investigators involved in aging research. The NIA-supported **Resource Centers for Minority Aging Research** (RCMARs) continue to be one of the Institute's most visible and focused efforts to build the national research infrastructure for minority aging research. The six RCMARs maintain active involvement in activities addressing the program's original mission of establishing a research mentoring mechanism in minority health, enhancing professional diversity in minority health research, evaluating/developing measurement tools tailored to minority populations, and developing strategies for recruiting and retaining minority research participants.

The need to understand the driving factors behind persistent black-white health disparities in many age-related diseases and overall longevity has led to the development of the NIA **Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS)** study, a community-based research effort designed to focus on evaluating health disparities in minority and socio-economically diverse populations. Among the questions to be addressed are: What is the influence of SES on normal age-related declines in function? What is the influence of SES on the incidence of age-related diseases? What is the influence of SES on the natural history of common age-related diseases? How does SES contribute to health disparities? Are there early biomarkers of age-related health disparities that may enhance our ability to prevent or ameliorate the severity of these diseases? In particular, the researchers are studying cardiovascular disease, cerebrovascular disease, age-associated changes in cognition, strength and physical functioning, and psychophysiology and nutrition, in a diverse population in Baltimore, Maryland. To facilitate the study, NIA has designed and implemented the use of two mobile medical research vehicles (MRVs) to enhance recruitment and retention of non-traditional research participants.

The Wave 1 pilot phase of this study, completed December 2001, was successful in addressing its primary goal of assessing the feasibility of conducting a community-based study using a mobile medical research vehicle. The pilot has allowed us to refine the logistical requirements for the conduct of clinical research focused on several scientific and clinical domains among a diverse socioeconomic sample. The second goal of the pilot was to begin data collection for the study. Wave 2 of the pilot will permit further logistical assessments of the mobile medical research vehicles, evaluation of retention strategies, and 3-year interim follow-up of participants to verify and expand on findings from Wave 1. The lead investigators are currently working with a panel of experts from a wide range of disciplines, including survey statisticians, epidemiologists, sociologists, behaviorists, nutritionists, health services researchers, and biostatisticians, to design and implement the population-based phase

of this study, which is scheduled to begin in early 2004.

Recently, the NIA completed a year-long review of health disparities among older Americans and developed a comprehensive strategic plan to address health disparities in the older population. In addition, the Minority Aging Research Review Committee (a panel composed of extramural scientists and senior NIH staff), in partnership with the National Advisory Council on Aging, developed a series of recommendations for action that should improve understanding of how to improve the health status of minority elders and expand participation by under-represented scientists in aging research.

The strategic plan on health disparities can be found at http://www.nia.nih.gov/strat-planhd/2000-2005/.
For more information, contact J. Taylor Harden, Ph.D. (HardenT@nia.nih.gov).

Women's Health

Women make up a majority of the older population: 58 percent of the population age 65 and older, and 70 percent of those 85 and older, are women. However, older women are more likely to live alone (a potential indicator or risk factor for isolation, lack of caregivers, or lack of support), are institutionalized earlier on average than men, and live in poverty at a disproportionately high rate. In particular, the death of a husband often marks the point of acute economic reversals for the surviving wife.

The NIA supports a diverse portfolio of research on older women's health, including studies elucidating the risks and benefits of hormone replacement therapy for relief of premenopausal symptoms. Other areas of inquiry include:

- Alzheimer's disease and other types of dementia
- menopause and hormone therapy
- osteoporosis and age-related muscle loss
- physical disability
- caregiver burden (research has shown that caregivers are more likely to be women)
- decline in function of older women
- hip fractures
- cancer in older women

Significant long-term research programs in women's health at NIA include the following:

Prevention of Cognitive Decline in Women. In the United States, 5 percent of women over age 60, and 28 percent over 85, likely have some form of dementia. Furthermore, while advances have been made to delay Alzheimer's disease progression, additional research is needed to study the earliest stages of cognitive decline, which might be most susceptible to intervention, in healthy women. The investigators of this study are examining prospectively how estrogen use, antioxidant intake, and anti-inflammatory drugs influence cognitive decline in non-demented women; they will examine the duration

and dose of these agents, and explore interactions with genetic factors. The investigation is being conducted within the Nurses' Health Study, which began in 1976 with 121,700 women. The Nurses' Health Study provides a highly cost-efficient setting to examine lifestyle and genetic influences that may be instrumental in preventing or delaying early decline in cognitive function.

Study of Women's Health Across the Nation (SWAN). The goal of SWAN is to characterize the biological processes, health effects, psychosocial influences, and sequelae of the pre- to peri- to postmenopausal transition in Caucasian, African American, Chinese, Japanese, and Hispanic women. SWAN is supported by the NIA, the National Institute of Nursing Research, the National Heart, Lung and Blood Institute, the National Institute of Mental Health, the National Center for Complementary and Alternative Medicine, and the NIH Office of Research on Women's Health.

The **Study of Osteoporotic Fractures (SOF)** is a community-based prospective study in a cohort of 9,704 older women. Data from SOF have served for: (1) developing osteoporosis guidelines, (2) estimating the cost-effectiveness of screening for osteoporosis, and (3) planning trials of osteoporosis therapies. Current research directions include the evaluation of bone mineral density as a predictor of future hip fractures and an exploration of possible common etiologies between osteoporosis and breast cancer.

The **Women's Health and Aging Study II (WHAS II)**, currently in its seventh year, is the source of an ongoing study of risk factors for physical disability in aging women. This longitudinal study was designed to determine the characteristics of early functional decline in initially high-functioning older women (70-79 years of age at baseline), and how the diseases and other conditions associated with aging contribute to this early decline and its progression to full disability and dependency. Findings thus far indicate that there is a preclinical stage of decline in mobility function which is identifiable, prevalent, and predictive of who goes on to become disabled in mobility over a relatively short time frame of 1.5 years. Future findings from this study will evaluate how mobility difficulty progresses to difficulty in daily tasks, and what factors cause that to happen.

NIA's Collaborative Activities

NIA staff participate in collaborative activities both within the Institute and with other organizations, including other NIH Institutes. Collaboration within NIA often is facilitated by Working Groups, which include:

- Aging and Cancer
- AIDS and Aging
- Alzheimer's Disease
- Cardiovascular Aging
- Clinical Trials
- Endocrinology/Menopause
- Genetic Basis of Aging
- Minority Aging

There are also NIA offices that coordinate Institute research activities in specific areas, including the NIA Office of Nutrition (based in the Neuroscience and Neuropsychology of Aging program) and the Office of Research Resources and Development (based in the Behavioral and Social Research program.) In other areas, such as women's health, disease prevention, and international activities, a staff member has been designated as Institute coordinator.

Collaborations with Other Federal Agencies

Many research projects funded by NIA are conducted collaboratively with federal agencies outside of NIH. Discussed below are some of the agencies NIA works with to support aging-related research.

The **Federal Interagency Forum on Aging-Related Statistics** was initially established in 1986 with the goal of bringing together Federal agencies that share a common interest in improving aging-related data. The Forum has played a key role by critically evaluating existing data resources and limitations, stimulating new database development, encouraging cooperation and data sharing among Federal agencies, and preparing collaborative statistical reports. The specific goals of the Forum are to improve both the quality and use of data on the aging population by:

- widening access to information on the aging population through periodic publications and other means;
- promoting communication among data producers, researchers, and public policymakers;
- coordinating the development and use of statistical databases among federal agencies;
- identifying information gaps and data inconsistencies;
- investigating questions of data quality;
- encouraging cross-national research and data collection on the aging population; and
- addressing concerns regarding collection, access, and dissemination of data.

NIA is one of nine federal participants in the Federal Interagency Forum, and one of three "core participants." Their first chartbook, *Older Americans 2000: Key Indicators of Well-Being*, was produced in 2000. New data are released each year, and the next version of the Chartbook is scheduled for release in 2004.

Two additional working groups have been formed as part of the Interagency Forum. The first working group focuses on the complex issues surrounding the production and use of integrated data for aging-related research. The working group's first project is to assemble a compendium that includes (1) a listing and description of all such data sources, and (2) the conditions that are required for access to these data sources. The second working group concentrates on filling some of the data gaps that were identified in *Older Americans 2000*. Future plans include examining the problems associated with defining different types of long-term care facilities and measuring the transitions that occur into and between these "institutionalized" residences.

Social Security Administration (SSA) funds are supplementing an NIA grant to the University of Michigan to support the Health and Retirement Study (HRS) for data collection and development

costs, and to support the work of the HRS Design and Data Monitoring Committee. The surveys are developing longitudinal data on work and retirement, job characteristics, health and disability status, Social Security and private pension benefits, Medicare and other health benefits, economic well-being, and other characteristics related to retirement, health and aging.

NIA collaborates with the **U.S. Census Bureau** on a number of endeavors. For example, the Census Bureau provides funds to NIA to co-fund a **National Academy of Sciences (NAS)** study of race and ethnicity with respect to aging-related issues. This secondary analysis of Census Bureau data will focus on: 1) the nature and extent of racial and ethnic disparities in life expectancy, health, and disability in later life; 2) the extent to which disparities can be attributed to lifestyle risk factors, access to health care, and other biological, social, and economic factors; 3) an examination of immigrant populations who appear to be in better health than mainland Americans of comparable racial and ethnic groups; and 4) recommendations for future research on racial and ethnic disparities. The Census Bureau is also a key participant in the Federal Interagency Forum, and coordinates aging-related activities and materials through its Domestic Aging Program.

In collaboration with the **National Academy of Sciences (NAS)**, NIA has convened an expert panel to recommend a prioritized national research agenda on elder abuse and neglect. Other agencies with significant interest in the panel include the Agency for Healthcare and Research Quality (AHRQ), the Office of Behavioral and Social Science/National Institutes of Health (OBBSR/NIH), and the Office of Research on Women's Health/National Institutes of Health (ORWH/NIH), and the Department of Justice (DoJ).

NIA also collaborates with NAS on an **Institute of Medicine** study on the use of complementary and alternative medicine by the American public. The study will provide a comprehensive overview of the use of CAM therapies by the American public; identify scientific and policy issues; and develop a conceptual framework to guide decision-making on CAM-related issues and questions.

NIA participates in an NIH-wide collaboration with the **National Aeronautics and Space Administration** (NASA) to support both ground-based and in-flight research on basic, applied, and clinical biological and behavioral problems that could benefit from using the space environment as a laboratory and that are relevant to human space flight and human health on Earth. Over the past several decades, space flight and ground-based research have begun to provide new perspectives on the biological basis of living and evolving in gravity and on the fundamental biomedical mechanisms of the response and adaptation to the space environment.

The **National Science Foundation (NSF)** conducts the Panel Study of

Income Dynamics (PSID), a nationally representative longitudinal study that collects information on US households. Notably, the PSID contains information on approximately 5,000 heads of households and spouses who are baby boomers (born 1945-1964) – a cohort not yet represented in the Health and Retirement Study (HRS). Continued data from the PSID will shed light on individual household saving behavior of the baby boom generation and its neighboring age cohorts.

The NIA originally provided funds to the **National Center for Health Statistics (NCHS)** to create the *Longitudinal Study of Aging (LSOA).* This study was based on re-interviews of respondents ages 70 and over to the 1984 Supplement on Aging in 1986, 1988, and 1990. In 1994, NIA provided NCHS with additional funds to create a second LSOA cohort. The LSOA II data, when used in conjunction with data from the original LSOA, enables researchers to track trends in disability, as well as the impact of changes in the health care system on disability. The second follow-up wave of interviewing, "Wave 3," was completed July 1, 2000. Wave 3 includes a reworking of the Health Care Coverage and Utilization sections, an addition of expectation and engagement questions, and placement of the Childhood Health and Family Longevity section within the main body of the questionnaire.

The NIA also provides funds to NCHS to develop a dynamic information system on health and aging using data from NCHS and a number of other data systems, to disseminate this information using modern technologies, to analyze and interpret the information for the Federal Interagency Forum on Aging-Related Statistics as well as other consumers, and to train junior researchers.

The **Centers for Medicare and Medicaid Service (CMS)** administers Medicare, the federal health insurance program for people age 65 and older and those with certain disabilities. CMS sets eligibility requirements for Medicare recipients, develops claims procedures for health care providers, and regulates the contractors who process Medicare claims. In FY 2002, NIA transferred funds to CMS to support the data processing and logistical arrangements necessary to provide Medicare claims data to NIA's research projects.

NIA Collaboration Within NIH

Whenever feasible, the NIA works jointly with other NIH Institutes and Offices to define needed research areas and fund research on aging-related topics. Collaborative activities may include joint sponsorship of workshops and conferences, contributions to portions of larger studies sponsored primarily by other Institutes, and co-funding of research projects on a variety of topics. Frequently, the NIA collaborates with other Institutes and Offices to issue Program Announcements and Requests for Applications. NIA is currently working — or has worked — collaboratively with every other research entity of the NIH.

Current areas of collaboration with other Offices or Institutes of the NIH include:

- AIDS/HIV
- Alcohol abuse in older persons
- Alzheimer's disease
- Arthritis, including osteoarthritis
- Basic research
- Behavioral and social issues in aging
- Bone and the hematopoietic system
- Cancer and aging
- Caregiving
- Cardiovascular and cerebrovascular disorders
- Diabetes
- Genetics and genetic epidemiology
- End-of-life care
- Health disparities
- Hutchinson-Gilford progeria syndrome and other laminopathies
- Immunology and vaccines
- Language comprehension changes with aging
- Mental health
- Menopause biology
- Mind-body interactions and health
- Obesity
- Pain management
- Rehabilitation
- Restless leg syndrome
- Sleep
- Social, ethical, and legal issues in research
- Stem cell biology
- Technology development

Private-Sector Collaborations

In addition to its collaborations with other Federal agencies, the NIA partners with private organizations from the for-profit and non-profit sectors on a variety of projects. Such projects can include co-sponsorship of workshops, drug development, management of clinical trials, or other initiatives.

The pharmaceutical company **Pfizer/Eisai** and the nonprofit **Institute for the Study of Aging** are providing support for two key offshoots of the ADCS Mild Cognitive Impairment Trial (for more on the ADCS, see page 39). Pfizer/Eisai is providing financial support for adding a third arm to the study to test the drug donezepil (Aricept), while the Institute for the Study of Aging is funding an MRI imaging arm of the study.

In 2001, the NIA partnered with the **Progeria Research Foundation (PRF)** to sponsor a workshop to discuss strategies for elucidating the molecular basis for the Hutchinson-Gilford syndrome, an incurable condition characterized by short stature, abnormal development, and premature death. Researchers at the National Human Genome Research Institute (NHGRI) identified the gene for the condition in November 2002, and the NIA, NHGRI, and PRF are organizing another workshop, scheduled for summer 2003, to discuss how to exploit this important breakthrough.

Researchers in the NIA Intramural Research Program have recently begun a partnership with **the University of Medicine and Dentistry of New Jersey - Robert Wood Johnson Medical School** to examine the influence of the RNA-binding proteins AUF1 and HuR on breast cancer. IRP researchers are also working with **IDEC Pharmaceuticals** on the identification of novel biomarkers and therapeutic targets for the diagnosis and treatment of ovarian cancer, with the ultimate goal of developing a new treatment for ovarian cancer by targeting a novel ovarian tumor-specific gene identified by SAGE.

NIA is collaborating with **ALTEON, Inc.** to evaluate the safety and efficacy of the investigational agent ALT-711 in the treatment of isolated systolic hypertension in older people, and with **Johns Hopkins University Department of Medicine** and **Angiotech Pharmaceuticals, Inc.** to develop microtubule stabilizing agents and local drug delivery systems for the treatment of a variety of fibroproliferative vascular diseases, including atherosclerosis and restenosis.

Agilent Technologies and the NIA are working together to develop high-quality whole-genome mouse DNA microarrays, to optimize the protocol for application to small amounts of cells/tissues, and to further explore the possibility of providing standardized,

low-cost, high-quality whole genome mouse DNA microarrays to the scientific community. A major success of this collaboration has been the development of a commercial oligo chip bearing over 22,000 genes, which is now available to the community. NIA researchers are also collaborating with **Celera Dx**, along with several academic partners, to identify genes that predispose to late-onset Alzheimer's disease. Work on this project is ongoing.

Applying for Funding from NIA: Extramural Grant Mechanisms

For the latest information: http://grants1.nih.gov/grants/oer.htm

Most of NIA's budget is used to support research, training, and career development outside of the NIH. NIA supports a variety of different types of research grants; to qualify for most of these, investigators must be conducting research at the postdoctoral level. There are also grant mechanisms that support multidisciplinary teams of investigators addressing a common theme.

Most research support at NIH is through **Research Project Grants.** Grants are awarded to nonprofit and for-profit organizations, universities, hospitals, research foundations, and agencies. Programs such as the Small Business Innovation Research grants (SBIR), Academic Research Enhancement Awards (AREA), and Minority Access to Research Careers (MARC) grants have been established for certain categories of applicants. Several programs are aimed specifically at encouraging minorities to participate in research.

For more on training and career development at the NIA, see page 68.
For the most current information, check the NIH and NIA web sites.

http://grants1.nih.gov/training/index.htm
http://www.nia.nih.gov/funding/training/

How to Apply for NIA Funding

Before you apply for an NIA research grant, we recommend that you take the following steps:

- *Get advice.* Contact a member of NIA's program staff for information and advice on how to maximize your chances of obtaining funding. Names of program directors are found in the Program Area descriptions on pages 11-38; there's also a comprehensive Contact List on pages 4-7. Also, be sure to contact your institution's research office for grant information and for assistance in completing the application, particularly the administrative and budgetary components.
- *Determine whether NIA is sponsoring a Request for Applications (RFA) or Program Announcement (PA) in your research area.* These special announcements indicate areas of particular interest to the Institute. An up-to-date list of NIA-supported RFAs and PAs can be found at http://www.nia.nih.gov/data/fundbrowse.asp.
- *Visit the NIH Grants Page for general guidance.* All applications for NIA funding are initially processed through the NIH Center for Scientific Review (CSR), a receipt and referral center. The NIH Grants Page contains information about how and where to send your

application, as well as relevant regulations and requirements. It also contains downloadable copies of the standardized forms you'll need to complete your application. See http://grants1.nih.gov/grants/oer.htm.

- *Know when your application is due.* Due dates for applications differ depending on what type of grant you're applying for. A comprehensive calendar can be found at http://grants1.nih.gov/grants/dates.htm.

For more information on applying for research funding from NIA, contact the NIA Office of Extramural Affairs at 301-496-9322.

Resources for Scientists

The NIA provides several resources developed to support research in the field of aging.

- **Aging Rodent Resources:** Because most investigators have neither the facilities nor the resources to develop and maintain colonies of aged animals in a barrier facility, the NIA provides support for both rat and mouse colonies for use by the scientific community. Available rodent resources include: four inbred strains of mice (C57BL/6, BALB/cBy, CBA, DBA/2, all from Jackson Laboratory stock); one hybrid strain of mice (CB6F1); two inbred strains of rats (F344 of NIH stock origin and Brown Norway of TNO Netherlands stock origin); one hybrid rat strain (F344BN F1); and a limited supply of calorically restricted rats (F344, BN, F344BNF1).

  Information on the NIA aged rodent colonies and ordering procedures can be obtained at **http://www.nia.nih.gov/research/resources.htm**. For specific information regarding availability of rodents from any of the NIA colonies, contact:

  Order Desk
  Office of Biological Resources and Resource Development, NIA
  Phone: 301-496-0181
  E-mail: rodents@nia.nih.gov

- **Aged Rodent Tissue Bank:** NIA's Aged Rodent Tissue Bank contains flash-frozen tissue and organs from animals in the aged rodent colonies. Tissues are available from the following strains and ages:

F344 (Fisher 344) rats	4, 12, 18 and 24 months of age
F344BN (F344xBN F1) rats	4, 18, 24 and 32 months of age
C57BL/6 mice	4, 12, 18 and 24 months of age
CB6F1 mice	4, 18, 24, and 32 months of age

  BALB/cBy mice, caloric restricted and ad lib fed controls at various ages
  F344 rats, caloric restricted and ad lib controls, at 4, 18, 24 and 28 months

  Contact the OBRRD Order Desk (above) for more information.

- **NIA Mouse 15K Cloned Gene Set:** A collection of 15,000 mouse genes has been developed, with emphasis on inclusion of genes active in placenta and embryo development. Nearly complete sequences of each gene in the 15K gene set are also available. To facilitate extensive use of this gene collection, the set has been made available as a resource to the scientific community. A related Microarray Facility provides investigators with low-cost access to microarrays developed from the set and will also provide for collecting and analyzing the gene expression findings of multiple investigators.

Complementing the 15K cDNA set is a new collection of 7409 unique genes called the NIA mouse 7.4K cDNA clone set. This collection includes genes from various mouse stem cell lines, mouse early embryos, and mouse newborn organs.

For more information on both clone sets, see http://lgsun.grc.nia.nih.gov/.

- **Non-Human Primates:** The NIA supports approximately 150 rhesus macaques for aging research. Inquiries regarding the use of these animals should be directed to:

  Nancy L. Nadon, Ph.D.
  Phone: 301-496-6402
  e-mail: NadonN@nia.nih.gov

- **Aging Cell Repository:** To facilitate research on cells in culture, the NIA provides support for the NIA Aging Cell Repository located at the Coriell Institute for Medical Research in Camden, New Jersey. The purpose of this repository is to acquire, develop and characterize, store, and supply cell cultures for gerontological research. The catalog for the NIA Cell Repository is available at http://locus.umdnj.edu/nia. For additional information about the Repository, contact:

  Donald Coppock, Ph.D.
  Director, Aging Cell Repository
  Coriell Institute for Medical Research
  401 Haddon Avenue
  Camden, NJ 08103
  Phone: 800-752-3805

- ***C. elegans* Genetic Stock Center:** The NIA provides partial support for the *Caenorhabditis* Genetic Center located at the University of Minnesota. This stock center contains over 1,000 strains of *C. elegans*. To obtain information about this collection contact:

  Robert Herman, Ph.D.
  Caenorhabditis Genetics Center
  Department of Genetics and Cell Biology
  University of Minnesota
  St. Paul, MN 55108
  Phone: 612-624-6203

- **Virtual Repository:** The NIA Virtual Repository provides information on, search capability for, and hyperlinks to NIA-supported studies with collections of human biospecimens available for sharing. The URL is http://www.nia.nih.gov/research/repository.asp.

Training and Career Development

Training and career development awards support the research training of scientists for careers in the behavioral and biomedical sciences, as well as help professional schools to establish, expand, or improve programs of continuing professional education.

NIA participates in a number of NIH-wide training and career development programs aimed at people at all stages of their career, from high school students to senior investigators. Some training programs are extramural – i.e., based at universities, medical schools, and research institutions, while others are intramural, or based in NIA's laboratories.

For more information on intramural training programs at the National Institutes of Health, see http://www.training.nih.gov/. If you would like information about the extramural awards, including K awards, see http://grants.nih.gov/training/extramural.htm.

NIA sponsors several additional programs aimed at training and career development of investigators interested in aging research:

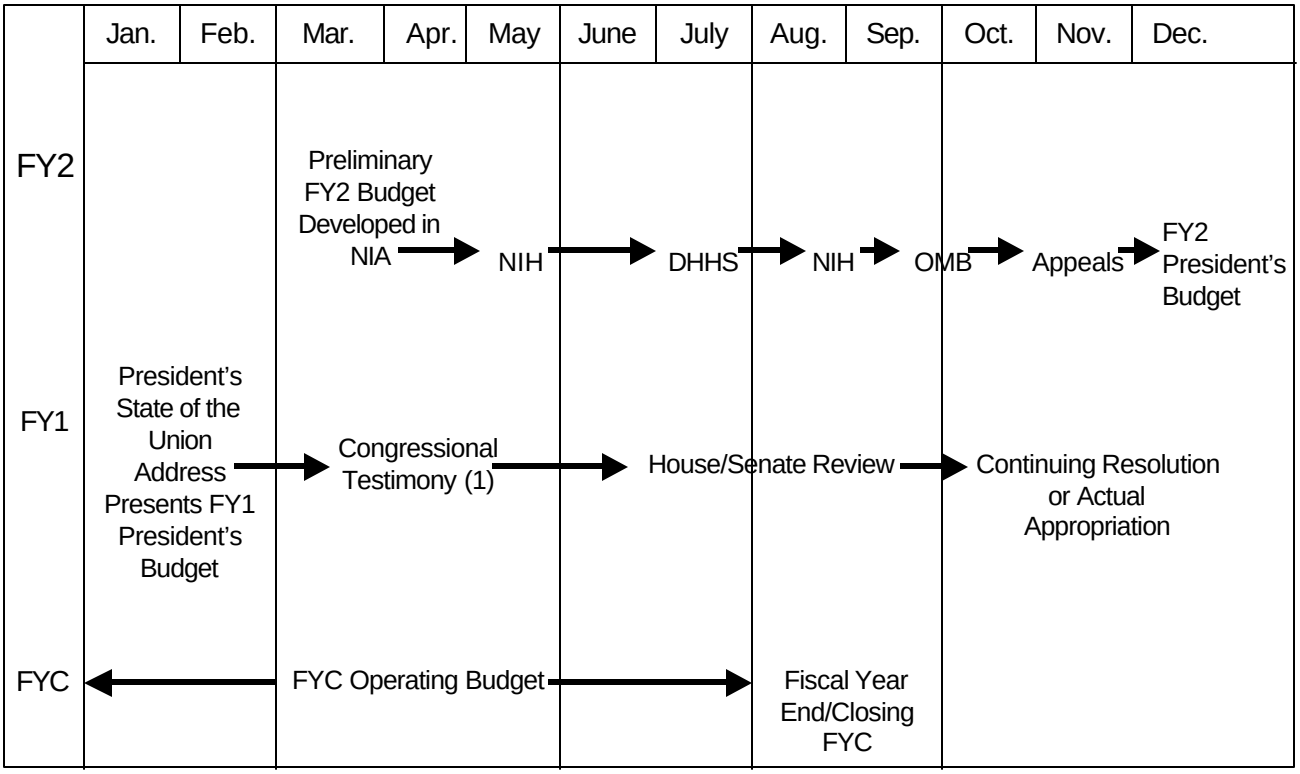
Summer Institute on Aging Research. This annual, one-week event provides junior investigators an opportunity to learn about the substance and methodology of aging research from recognized experts in the field. The goal is to enhance participants' potential for success as independent investigators. Racial and ethnic minority investigators and researchers interested in research on minority health are especially encouraged to apply.

Technical Assistance Workshop. With financial support from the NIH Office of Research on Minority Health, the NIA sponsors an intensive two-day workshop each year on the research grant application process for minority investigators and for scientists with a commitment to ethnic/minority aging research.

Regional Training Meetings. These meetings inform investigators new to aging research about NIA programs. Investigators who are members of groups underrepresented in aging research are also encouraged to attend. The regional meetings are also vehicles for obtaining reactions to ongoing programs and information on research training needs. While this forum is not intended solely for underrepresented populations, it serves as an important avenue of outreach to these groups.

For information on these special programs, contact Dr. Taylor Harden (HardenT@nia.nih.gov).

Budget: The Federal Budget Process



Fiscal Year = October 1 to September 30

FY2=Second Future Fiscal Year

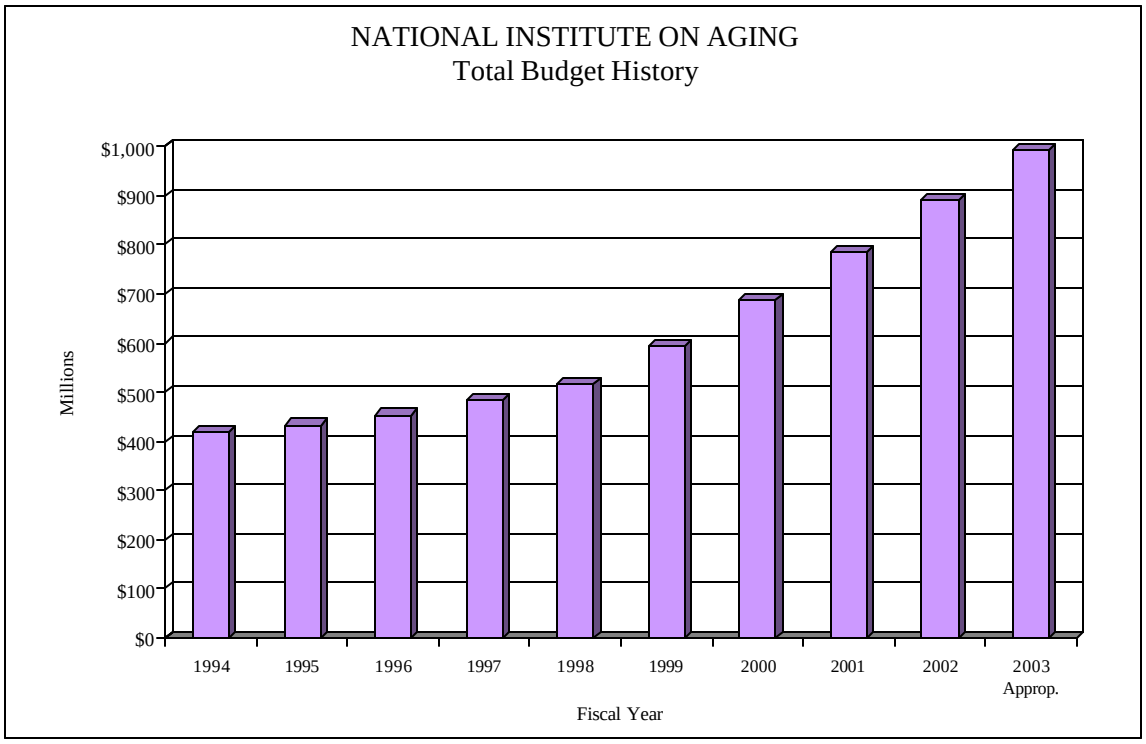
FY1=First Future Fiscal Year

FYC=Current Fiscal Year

(1)NIH Director and NIH Institute Directors provide testimony to the House and Senate Appropriations Subcommittee on Labor, Health and Human Services, and Legislation.

NIA's budget cycle begins each year when the National Institutes of Health, of which NIA is part, submits a preliminary budget to the Department of Health and Human Services for review and adjustment. After DHHS review, revised Institute budgets are sent to the U.S. Office of Management and Budget, where staff prepare the "passback" (i.e., total funding recommended), which will be spread among all the Institutes and Centers. The OMB passback becomes the President's budget request to Congress. After further review, including testimony from Institute Directors about scientific needs and opportunities, Congress sets the final budget for the fiscal year.

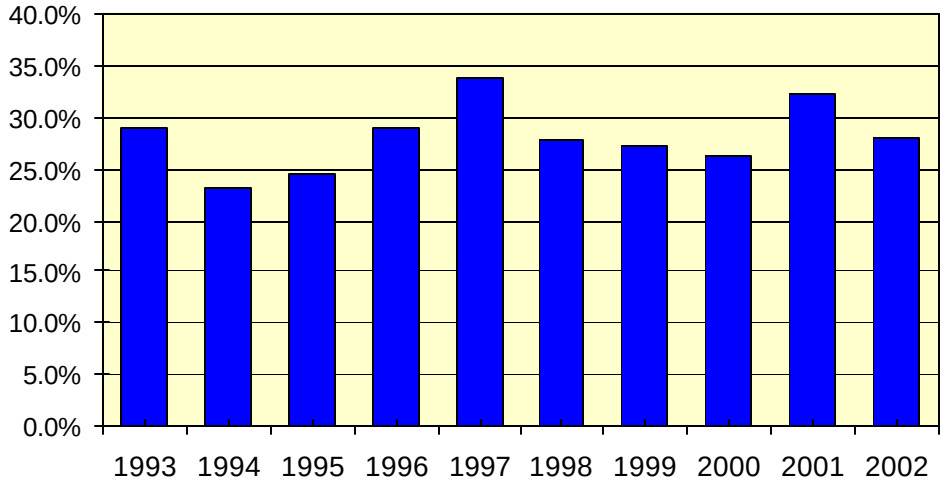
Budget: Trends in NIA Appropriations



Trends in Appropriations. NIA appropriations (the Institute budget, as set by Congress) have risen steadily each year, from $420.3 million in Fiscal Year 1994 to $993.6 million in Fiscal Year 2003.

Source: NIA Budget Office, 2003

Budget: Research Project Grant Success Rates

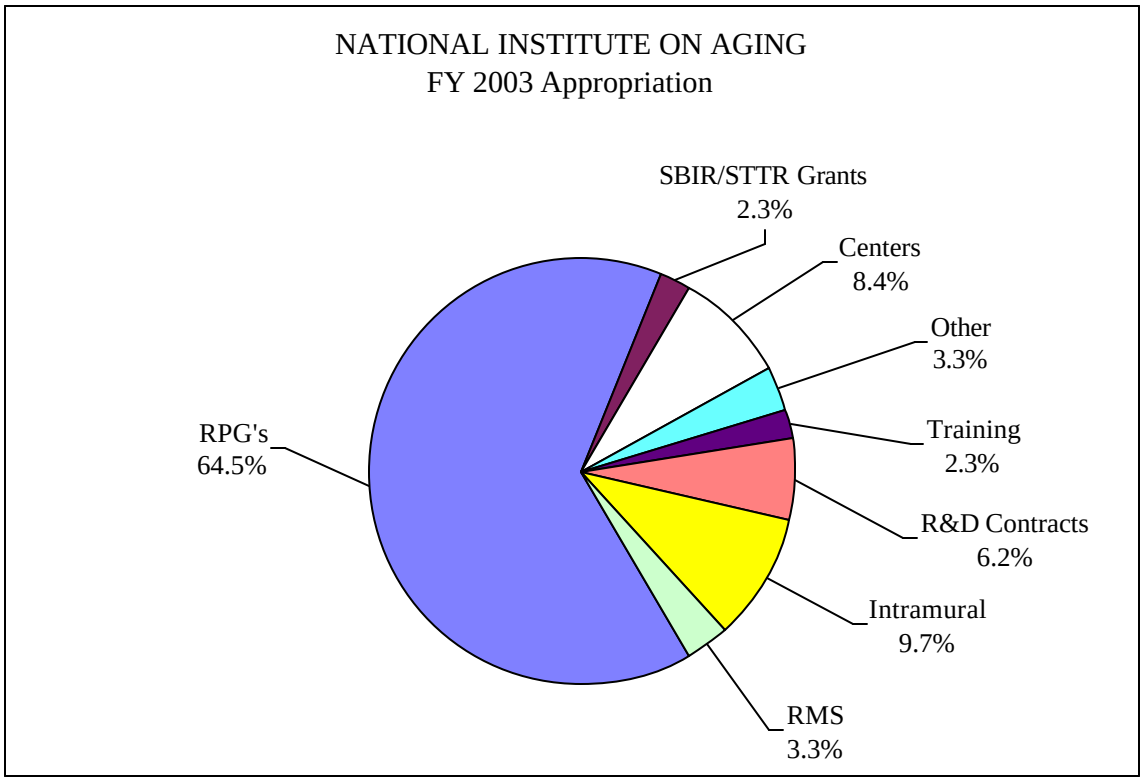


Success Rate=Ratio of applications awarded to applications reviewed

Research Project Grant Success Rates. Research project grants continue to be the highest NIH funding priority, since it is through this mechanism that investigator-initiated research is supported. This chart shows a history of the proportion of NIA applications reviewed that were actually awarded funds from 1993 through the present. This rate fluctuates from year to year; for Fiscal Year 2002, the most recent year for which we have complete data, the rate was around 28 percent.

Source: NIA Budget Office, 2003

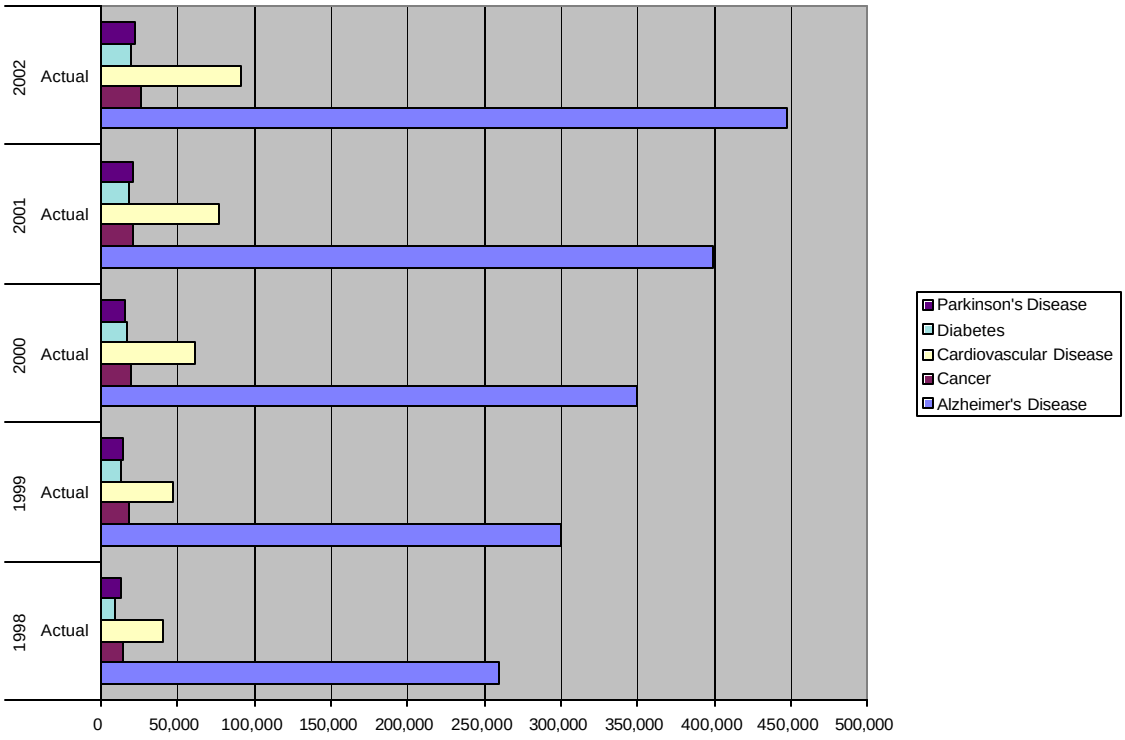
Budget: FY 2003 President's Budget Request by Mechanism



President's Budget Request by Mechanism. Financial obligations are commitments by a government agency to pay a sum of money. This chart shows NIA's distribution of financial obligations by budget category for FiscalYear 2003, based on the President's budget request to Congress. (Exact figures may change when Congress finalizes the Institute budget.) By far the largest portion of NIA's budget goes to fund extramural activities, which include research project grants (RPGs), research centers, research and development (R&D) contracts, and research training.

Source: NIA Budget Office, 2003

Budget: NIA Obligations – Selected Diseases



$ In Thousands

This table shows NIA's obligations for selected diseases and conditions common among older Americans. Dollar figures in these areas for Fiscal Year 2002, the most recent year for which we have complete data, are as follows (dollars in thousands):

Alzheimer's Disease:	$446,936
Cancer:	$25,924
Cardiovascular Disease:	$91,319
Diabetes:	$19,815
Parkinson's Disease:	$21,785

Source: NIA Budget Office, 2003

Administration: Leadership Biographies

Richard J. Hodes, M.D.
Director

Dr. Richard J. Hodes, an eminent immunologist, directs the NIA's research program. He maintains an active involvement in research on the NIH campus in Bethesda, Maryland, through his direction of the Immune Regulation Section, a laboratory devoted to studying regulation of the immune system, focused on cellular and molecular events that activate the immune response. This involvement in campus research also serves to strengthen ties with other NIH scientists involved in studies of age-related diseases.

Dr. Hodes was named Director of the NIA in 1993, but has enjoyed a long career in science at NIH – first as a clinical investigator in the National Cancer Institute, then as the Deputy Chief and Acting Chief of the Cancer Institute's Immunology Branch.

He is a Diplomate of the American Board of Internal Medicine. In 1995 Dr. Hodes was elected as a member of The Dana Alliance for Brain Initiatives; in 1997 he was elected as a Fellow of the American Association for the Advancement of Science; and, in 1999 he was elected to membership in the Institute of Medicine of the National Academy of Sciences.

Dr. Hodes is a graduate of Yale University. He received his M.D. from Harvard Medical School. As author of more than 200 research papers, he is an influential scientist in and contributor to the field of immunology.

Judith A. Salerno, M.D., M.S.
Deputy Director

Judith A. Salerno, M.D., M.S., is the Deputy Director of the National Institute on Aging at the National Institutes of Health. She most recently was the Chief Consultant for Geriatrics and Extended Care for the Department of Veterans Affairs (VA), Washington, D.C. and Associate Clinical Professor of Health Care Sciences and of Medicine at the George Washington University. Prior to her VA appointment, she was Associate Chief of Staff at the VA Medical Center in Washington, D.C. where she developed and implemented an innovative model of geriatric primary care and coordinated geriatric training. Dr. Salerno co-founded the Washington D.C. Area Geriatric Education Center Consortium, a collaboration of more than 160 educational and community organizations within the Baltimore-Washington region that generates educational opportunities for those serving the area's aging. She has extensive experience in the analysis of public sector health programs, specializing in long term care and chronic disease management at the federal and state levels. As Senior Clinical Investigator at the National Institute on Aging, she implemented clinical research protocols for the study of patients with Alzheimer's disease and

geriatric hypertension. Her current research interests include issues related to the inclusion of elderly subjects in clinical trials, and new models of geriatric care; she also serves on several national committees concerned with quality of care in long-term care settings and with geriatric manpower issues. She earned her M.D. degree from Harvard Medical School in 1985 and a Master of Science degree in Health Policy from the Harvard School of Public Health in 1976. Dr. Salerno also holds a Certificate of Added Qualifications in Geriatric Medicine.

Dan L. Longo, M.D., F.A.C.P.
Scientific Director

Dr. Dan L. Longo directs the NIA's Intramural Research Program (IRP). Dr. Longo was named Scientific Director of the NIA in 1995 after an outstanding 18-year career at the NIH conducting research in medicine and immunology at both the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Diseases. His most recent position at the NCI was Director, Biological Response Modifiers Program, and Associate Director, Division of Cancer Treatment, a position he held from 1985-1995.

Dr. Longo is a member of several academic societies. He is a Fellow of the American College of Physicians and currently serves as Chair of its Oncology Subspecialty Committee. Dr. Longo serves as an associate editor or member of the editorial board of a dozen scholarly journals, including *Journal of the National Cancer Institute, American Journal of Medicine,* and *Blood*. In addition, he is editor of *Harrison's Principles of Internal Medicine*, *Cancer Chemotherapy and Biotherapy: Principles and Practice,* and *Clinical Oncology Alert*. He has been listed in every edition of *Best Doctors in America*. Dr. Longo is a Diplomate of the National Board of Medical Examiners and the American Board of Internal Medicine, and is also Board Certified in Medical Oncology (Subspecialty).

Dr. Longo completed medical school at the University of Missouri, Columbia and internal medicine training at the Peter Bent Brigham Hospital and Harvard Medical School in Boston. He is author of more than 660 research papers and book chapters.

Scientific Planning Process

Barbara F. Kellner, M.S.,
Planning Officer

NIA's scientific planning process is multifaceted and covers a multiyear cycle. Its primary goals are to:

- Identify new and emerging areas of scientific opportunity
- Maintain maximum flexibility to enable the Institute to keep pace with rapid scientific progress
- Improve linkage of planning activities to resource allocation decisions

NIA's annual planning calendar can be found on page 78. Key components of the planning cycle include:

- Periodic reviews of NIA programs conducted by the National Advisory Council on Aging (see page 84)
- Regular meetings of NIA's Planning Group, which is composed of senior Institute staff and coordinates program direction and activities
- Twice-yearly planning retreats
- Working Groups on special aging-related topics

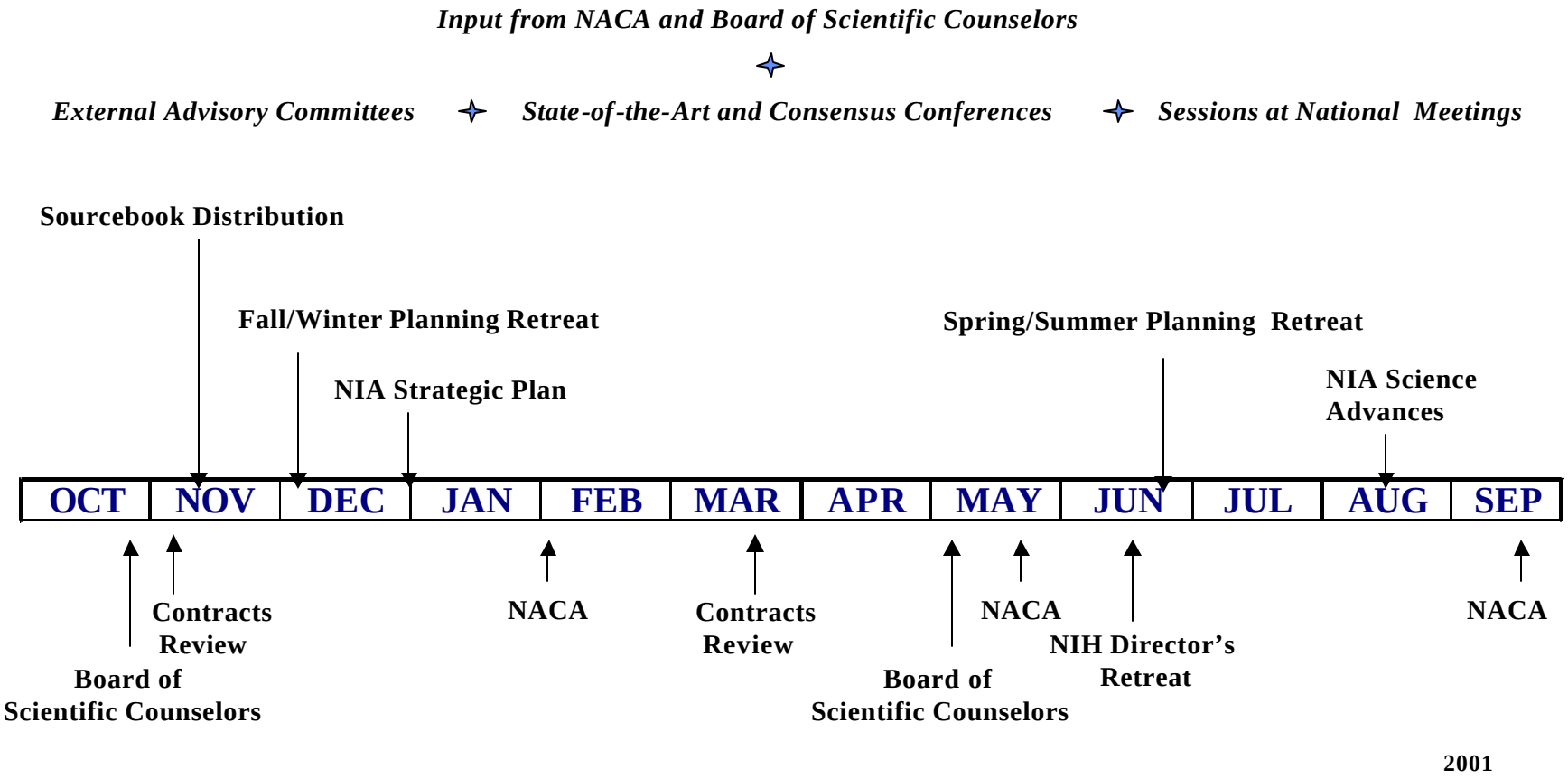
At the planning retreats, NIA staff have the opportunity to provide input into the Institute's scientific programs. At the spring/summer planning retreat, NIA senior management and staff explore implications for the Institute of emerging scientific opportunities. Selected opportunities involving trans-program collaboration are developed and then discussed at the fall/winter planning retreat. The NIA Director's decisions on these initiatives, as well as others submitted by individual programs, are discussed with senior Institute staff at a planning group meeting and broadly announced as soon as possible after the winter retreat. Working groups composed of representatives of participating programs may be formed to coordinate the implementation of trans-program initiatives.

The NIA has completed a five-year strategic plan for aging research. The plan describes the Institute's mission, areas of current and future research opportunities, and plans for maintaining health and independence for older Americans. It includes research goals for Fiscal Years 2001 through 2005 on the biological, behavioral, and social changes that occur with age and their effects on health and disease, with a special emphasis on preventing Alzheimer's disease. A section of the plan is devoted to research aimed at reducing health disparities among older populations, including rural and minority elderly. The plan is available on the NIA web site (http://www.nia.nih.gov/strat-plan/2001-2005/).

NIA Planning Office:
KellnerB@nia.nih.gov

NIA PLANNING CALENDAR

Key Planning Events



2001

Public Information

Jane Shure,
Communications Director

Through its Office of Communications and Public Liaison (OCPL), the NIA educates the public, the research community, physicians, and other health care providers about aging research and the physical and psychological processes associated with aging. These health communication activities increase public awareness of specific aging issues; reinforce specific knowledge, attitudes, or health behaviors; and encourage individual or collective action.

To inform the public about NIA's research efforts, OCPL staff members perform a variety of activities to ensure that the American people are kept abreast of the latest biomedical advances and findings of aging research. These activities include:

- writing and disseminating newspaper articles, items for technical bulletins, and press releases
- responding to information requests via phone, letters, and e-mail, and distributing booklets and brochures
- writing professional education material
- creating lay-language fact sheets about specific conditions and illnesses related to aging
- conducting news conferences and press briefings, and arranging interviews for media outlets
- publicizing NIA-supported conferences, lectures, and workshops
- developing and distributing public service announcements
- maintaining a collection of news clippings, photographs, slides, videotapes
- using NIA research to increase web accessibility for older people
- creating online learning modules about specific conditions and illnesses related to aging for adults 60 and older

The OCPL identifies, collects, analyzes, and catalogs science articles for the Alzheimer's disease subfile of the Combined Health Information Database (CHID). At the direction of Congress, NIA established the **Alzheimer's Disease Education and Referral (ADEAR) Center** to respond to a growing need for information about Alzheimer's disease, its impact on families and health professionals, and research into possible causes and cures. It is an information clearinghouse that distributes NIA publications in response to public and professional requests.

- To request information related to Alzheimer's disease and memory problems, call the ADEAR center at 1-800-438-4380.

- To request information related to other needs of older people or aging research, call NIA's Information Center at 1-800-222-2225.

Aging Health Policy and Legislative Point of Contact

Tamara Jones, Ph.D., R.N.

The NIA interacts with associations and advocacy groups, academic and professional groups and members and staff of Congress relative to the development, analysis, and review of current and proposed policies relating to research on aging. The management of these activities is the responsibility of the Public Health Analyst, who is part of the NIA Office of the Deputy Director.

In addition, the Public Health Analyst:

- serves as liaison to aging-related advocacy groups, professional organizations, scientific organizations, and other federal agencies
- analyzes policies related to NIA program goals and objectives as well as proposals with direct relevance to NIA programs in the biomedical, behavioral and social sciences
- serves as NIA point of contact for Congressional staff working on aging public health policy issues
- monitors and analyzes proposed legislation and scientific policies that directly affect the NIA mission
- keeps NIA staff up-to-date about the status and implications of upcoming or proposed legislation and public health policy
- prepares testimony, statements, presentation materials, and other documents based on analysis of a variety of issues for NIA and NIH staff on such important and sensitive topics as Alzheimer's disease, Parkinson's disease, stem cell research, and elder abuse and neglect

Recent congressional testimony delivered by NIA officials is posted on the NIA home page at http://www.nih.gov/nia/about/legislation.

In addition, the Public Health Analyst provides outreach to outside organizations that have an interest in the NIA mission, including advocacy groups, professional societies, and non-profits. Activities include responding to inquiries and preparing and reviewing materials for use by the groups' constituencies.

NIA Public Health Analyst and Legislative Point of Contact:
tamjones@mail.nih.gov

International Activities

Marta Campbell, M.P.P., Director

By 2050, more than 20 percent of the world's population will be over age 60, and the number of very old — those over 85 — will increase six-fold. As an effect of global aging, non-communicable chronic diseases likely will replace communicable, perinatal, maternal, and nutritional conditions as the world's leading causes of death and disability. These epidemiological predictions highlight a worldwide need to separate chronic disease states from healthy aging, and to develop effective preventive and treatment strategies against the chronic diseases and disabilities often associated with aging.

The NIA Office of International Activities (OIA) serves as a liaison with international agencies, foreign organizations, and foreign scientists involved in aging research. It also coordinates aging research activities under agreements between the U.S. and other countries, promotes strategies to build global aging research capacity, and supports collaborative research projects.

The OIA administers the Global Health Research Initiative Program (GRIP) for new foreign investigators within NIA. GRIP is an extramural program that helps NIH intramural fellows establish independent research careers when they return home to their developing countries. The program enhances aging research infrastructure in these countries while advancing global health.

Sponsoring and participating in international meetings and workshops are also among the office's responsibilities.

Office of International Activities:
CampbelM@nia.nih.gov

Office of Extramural Affairs

Miriam F. Kelty, Ph.D.,
Associate Director

The **Office of Extramural Affairs (OEA)** is often the first point of contact for applicants requesting information on how to apply for federal support or who wish to know if their research ideas may be of interest to NIA. The OEA:

- coordinates NIA's extramural programs and ensures that policies and procedures are implemented in a uniform and fair way
- oversees grants and contract administration, scientific review, and committee management
- provides grants policy information
- serves as primary liaison for NIA with the NIH Office of Extramural Research and with other NIH Institutes that share research interests
- coordinates NIA's extramural training programs, career development programs, small business initiatives, and other special programs
- handles appeals, as well as scientific integrity and other ethical issues involved in the conduct of research
- organizes meetings of the National Advisory Council on Aging (NACA) and related groups

Within OEA, the **NIA Training Officer** has central responsibility for the overall direction of research training and career development activities at the Institute, including policies related to the types of mechanism supported, the eligibility of particular classes of student and investigator, and the structure of research support within the individual mechanisms. The Training Officer also develops and manages initiatives to increase the number of underrepresented students and researchers trained in aging research.

The **NIA Small Business Innovation Research (SBIR) coordinator** performs a similar role for SBIR programs. SBIR program funding supports small

businesses that conduct research on, and develop and test, health-related products and services with commercial potential that target older Americans or organizations that serve them.

OEA's **Scientific Review Office (SRO)** is responsible for initial peer review of mission-specific research applications assigned to the NIA. These include grant applications for Centers, program projects, special initiatives, and training and career development. SRO scientific staff prepare a summary of each review and make it available to the principal investigator.

While the SRO interacts with applicants prior to the award of grants, the **Grants and Contracts Management Office (GCMO)** works with scientists and institutional research administrators to manage grant awards from issuance through completion of research. GCMO staff members provide guidance on administrative and fiscal policies and practices for the investigator and for the institutional research administrators. The GCMO has legal responsibility for the fiscal management of the Institute's extramural grants and contracts.

Office of Extramural Affairs: 301-496-9322

Initial Scientific Review (Peer Review)

In support of research, research training, and career development related to aging, the NIA awards grants to universities, hospitals, and research organizations throughout the U.S. and abroad. Approximately 80 percent of NIA's budget is disbursed through these extramural awards. Competition for this funding is intense; for example, over the past ten years, NIA has been able to fund about one in three of the research project grant applications it received. To ensure that the research funded is of the highest quality and serves the health needs of the nation, peer review committees composed of scientific experts from outside the NIA are brought together to review proposed and ongoing research.

Extramural Grant Review

The first stop for all applications for NIA funding is the NIH Center for Scientific Review (CSR), a review and referral office. Applications that are focused on aging are assigned to NIA for funding consideration. Many of these are reviewed by groups of experts that CSR organizes. Others are reviewed by NIA-organized groups. These latter applications include:

- applications for program project grants
- applications for center grants
- career development award applications
- small (R03) grant applications (until winter 2004)
- institutional training grant applications
- applications submitted in response to RFAs issued by the NIA

Whether the applications are reviewed at the CSR or at the NIA, committees of experts, including NIH grantees, assess the quality and originality of the

proposed science. Reviewers also assess applications for the qualifications of the investigators, quality of the proposed facilities, animal welfare (if relevant), and, for research involving humans, protection of human subjects and proposed plans for recruiting women and minorities to the studies. The judgment of the group on these parameters is summarized in a report (**summary statement**) and overall rating (**priority score**) of the application. These reports are provided to the applicants and to NIA officials. Following initial scientific review, applications receive a second level of review by the National Advisory Council on Aging (see box, page 84).

Grant applications over $50,000 must receive NACA recommendation for funding. In its deliberations, the NACA reviews summary statements to evaluate the fairness and appropriateness of the initial review of grant applications, and considers the scientific and public health importance of the proposed work. A small number of applications are discussed individually in the Council; most are acted on en bloc.

Once the Council provides its recommendations, the NIA Director may approve payment of applications that have been favorably reviewed and for which sufficient funds are available. Primary weight is given to the scientific quality of the application as judged by initial peer review. Consideration is also given to the proposed research's relevance to NIA priorities and to the timeliness of the research.

Intramural Scientific Review

The Board of Scientific Counselors

The investigators and projects of the Intramural Research Program (IRP) are reviewed on a regular basis for quality and productivity by NIA's Board of Scientific Counselors (BSC). Past performance as well as future research plans are included in the review, as are issues affecting recruitment and retention of scientists. A review of each IRP laboratory takes place every four years.

The BSC consists of nine members with outstanding scientific credentials who provide rigorous and objective on-site reviews. New BSC members are appointed by the NIH Director based upon recommendations from current BSC members and senior NIA and NIH scientists. The BSC advises the NIH Director and Deputy Director for Intramural Research, and the NIA Director and Scientific Director. BSC members are invited to serve for overlapping terms of five years. *Ad hoc* external reviewers with specialized expertise are routinely invited to supplement the BSC membership.

The Institute annually provides a written report to the National Advisory Council on Aging that describes research reviewed by the BSC and the results of that review. Based upon this report, the NACA may make recommendations to the NIA Director regarding IRP research and the peer review it undergoes.

National Advisory Council on Aging

Congress created the National Advisory Council on Aging (NACA) in 1975, when the Institute was established, to provide advice on programmatic and policy matters – specifically:

"To advise, consult with, and make recommendations to the Secretary, DHHS; the Assistant Secretary for Health; the Director, NIH; and the Director, NIA on matters relating to the conduct and support of biomedical, social, and other programs with respect to the aging process and the diseases and other special problems and needs of the aged."

In addition to reviewing grant applications to the NIA, Council members serve as a conduit for insights into the concerns and opinions of the research community, and assist in keeping the scientific community, Congress, and the public knowledgeable about the activities of the NIA.

The NACA meets three times each year to review applications for grants and cooperative agreements for research and training. The group consists of 18 members appointed by the DHHS Secretary and 5 non-voting *ex officio* members. Of the 18 appointed members, 12 are leading representatives of the health and scientific disciplines and are leaders in the fields of public health and the behavioral or social sciences. Six members are leaders from the general public in the fields of public advocacy, law, health policy, economics, and management. Members are invited to serve for overlapping four-year terms.

Appendix A:
National Advisory Committee on Aging Roster (June 2003)

Richard J. Hodes, M.D., Chair
Director, National Institute on Aging

Dennis A. Ausiello, M.D.
Massachusetts General Hospital

John D. Cambier, Ph.D.
University of Colorado Health Sciences Center
National Jewish Medical & Research Center

Judith Campisi, Ph.D.
University of California - Berkeley

Rose Dobrof, D.S.W.
Hunter College of the City of New York

David V. Espino, M.D.
University of Texas Health Science Center

F. Michael Gloth, III, M.D.
Victory Springs Senior Health Care
Reisterstown, Maryland

Eugene M. Johnson, Jr., Ph.D.
Washington Univ School of Medicine

Lewis H. Kuller, M.D., Dr.P.H.
University of Pittsburgh

Ronald D. Lee, Ph.D.
University of California - Berkeley

Peter W. Nauert, J.D.
Insurance Capital Management, Chicago

Stanley B. Prusiner, M.D.
University of California - San Francisco

Judith A. Riggs, M.A.
Washington, DC

Ilene C. Siegler, Ph.D., M.P.H.
Duke University

Leon C. Thal, M.D.
University of California - San Diego

Myron L.Weisfeldt, M.D.
Johns Hopkins Univ School of Medicine

David A. Wise, Ph.D.
National Bureau of Economic Research

Phyllis M. Wise, Ph.D.
University of California-Davis

Appendix B:
Board of Scientific Counselors Roster (June 2003)

Leslie J. Berg, Ph.D., Chair
University of Massachusetts Medical School

Leonard P. Guarente, Ph.D.
Massachusetts Institute of Technology

James S. Jackson, Ph.D.
Institute for Social Research

J. Larry Jameson, M.D., Ph.D.
NMH/NUMS, Chicago

Arlan Richardson, Ph.D.
University of Texas Health Center

Sangram Singh Sisodia, Ph.D.
University of Chicago

Susan Swain, Ph.D.
Trudeau Institute

Rudolph E. Tanzi, Ph.D.
Charlestown, MA

Douglas C. Wallace, Ph.D.
University of California - Irvine

Appendix C: Glossary of Acronyms

ACTIVE	Advanced Cognitive Training for Independent and Vital Elders
AD	Alzheimer's Disease
ADC	Alzheimer's Disease Centers
ADCC	Alzheimer's Disease Core Centers
ADCS	Alzheimer's Disease Cooperative Study
ADEAR	Alzheimer's Disease Education and Referral Center
ADRC	Alzheimer's Disease Research Centers
AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired Immunodeficiency Syndrome
AREA	Academic Research Enhancement Awards
BAP	Biology of Aging Program
BLSA	Baltimore Longitudinal Study on Aging
BPMS	Brain Physiology and Mapping Section
BSC	Board of Scientific Counselors
BSR	Behavioral and Social Research Program
CALERIE	Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy
CAM	Complementary and Alternative Medicine
CC	Warren Grant Magnuson Clinical Center
CHID	Combined Health Information Database
CMS	Centers for Medicare and Medicaid Services
CR	Caloric restriction
CSR	Center for Scientific Review
CVD	Cardiovascular disease
DHHS	Department of Health and Human Services
FDA	Food and Drug Administration
FY	Fiscal Year: October 1 - September 30
GCMO	Grants and Contract Management Office
GCG	Geriatrics and Clinical Gerontology Program
GRC	Gerontology Research Center
HANDLS	Healthy Aging in Neighborhoods of Diversity across the Life Span
HIV	Human Immunodeficiency Virus
HRS	Health and Retirement Study
IOM	Institute of Medicine
IRP	Intramural Research Program
IRTA	Intramural Research Training Award
LAG	Longevity assurance gene
LEDB	Laboratory of Epidemiology, Demography, and Biometry
LCMB	Laboratory of Cellular and Molecular Biology
LCI	Laboratory of Clinical Investigation
LCS	Laboratory of Cardiovascular Science

LEG	Laboratory of Experimental Gerontology
LG	Laboratory of Genetics
LI	Laboratory of Immunology
LMG	Laboratory of Molecular Genetics
LNG	Laboratory of Neurogenetics
LNS	Laboratory of Neurosciences
LPC	Laboratory of Personality and Cognition
LSOA	Longitudinal Study of Aging
MARC	Minority Access to Research Careers Program
MBRS	Minority Biomedical Research Support Program
MDS	Molecular Dynamics Section
MERIT	Method to Extend Research in Time Award
MOST	Multisite Osteoarthritis Study
MRI	Magnetic resonance imaging
NACA	National Advisory Council on Aging
NACDA	National Archive of Computerized Data on Aging
NACC	National Alzheimer's Coordinating Center
NAS	National Academy of Sciences
NASA	National Aeronautics and Space Administration
NCCAM	National Center for Complementary and Alternative Medicine
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NCMHD	National Center on Minority Health and Health Disparities
NCRR	National Center for Research Resources
NEI	National Eye Institute
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD	National Institute of Child Health and Human Development
NIDA	National Institute on Drug Abuse
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
NIOSH	National Institute of Occupational Safety and Health
NLM	National Library of Medicine

NLTCS	National Long Term Care Survey
NNA	Neuroscience and Neuropsychology of Aging Program
NRSA	National Research Service Award
NSF	National Science Foundation
OA	Osteoarthritis
OAICs	Claude D. Pepper Older Americans Independence Centers
OAR	Office of AIDS Research
OBRRD	Office of Biological Resources and Resource Development
OBSSR	Office of Behavioral and Social Sciences Research
OCPL	Office of Communications and Public Liaison
OD	Office of the Director
OEA	Office of Extramural Affairs
OIA	Office of International Activities
OPAE	Office of Planning, Analysis, and Evaluation
ORRD	Office of Research Resources and Development
ORWH	Office of Research on Women's Health
PA	Program Announcement
PET	Positron emission tomography
PI	Principal Investigator
PSID	Panel Study of Income Dynamics
R&D	Research and Development
RCMAR	Resource Centers for Minority Aging Research
REACH	Resources for Enhancing Alzheimer's Caregiver Health
RFA	Request for Applications
RFP	Request for Proposals
RM&S	Research Management and Support
RPG	Research Project Grant
RRB	Research Resources Branch
SAG	Senescence assurance genes
SBIR	Small Business Innovation Research
SES	Socioeconomic status
SOF	Study of Osteoporotic Fractures
SRO	Scientific Review Office
SSA	Social Security Administration
STTR	Small Business Technology Transfer
SWAN	Study of Women's Health Across the Nation
VA	Veterans Administration
VACS	Veterans with HIV/AIDS Cohort Study

Appendix D: Glossary of Terms

Appropriation - An act of Congress that allows federal agencies to incur obligations and make payments from the United States Treasury for specified purposes. An appropriation usually follows enactment of authorizing legislation and is the most common means of providing budget authority. Appropriations do not represent cash actually set aside in the Treasury for purposes specified in the appropriation act; they represent limitations of amounts that agencies may obligate during the period of time specified in the respective appropriation acts. At the NIH, each Institute and Center receives its own appropriation.

Competing Applications - New applications and those competing for renewal.

Constant Dollars - Current dollars for a fiscal year adjusted for inflation with reference to a base year, according to the Biomedical Research and Development (R&D) Price Index.

Extramural Research - Research performed by investigators outside the NIH and supported by the NIH. It includes grants, cooperative agreements, or contracts from NIH to scientific investigators or organizations in support of biomedical or behavioral research and research training related to health and disease.

Fiscal Year (FY) - Any yearly accounting period, without regard to its relationship to a calendar year. The fiscal year for the federal government (including NIA) begins October 1 and ends the following September 30. (For example, FY 2003 covers the period October 1, 2002 – September 30, 2003).

Initiative - Research activities of NIH Institutes such as workshops, Program Announcements (PA), Requests for Applications (RFA), Requests for Proposals (RFP), or other mechanisms that support biomedical or behavioral research or research training.

Intramural Research - Research performed by investigators within the NIH community or its extensions.

NIH Guide to Grants and Contracts - The NIH Guide announces scientific initiatives in the form of PAs, RFAs, and RFPs and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by NIH.

Obligations - Commitments by a government agency to pay a particular sum of money for orders placed, grants and contracts awarded, services received, and similar transactions during a given period of time.

Program Announcement (PA) - PAs are issued by one or more NIH Institutes to stimulate research in specific areas for

which grant applications are invited. PAs are published in the "NIH Guide to Grants and Contracts," and are intended to encourage research in stated topics. Unlike RFAs, PAs do not have an expiration date and do not have funding set aside for specific period of time. Meritorious applications sent in response to PAs are funded based on successful peer review and availability of funds.

Request for Applications (**RFA**) **-** An RFA invites applicants to apply for a research grant in a specific scientific area. The RFA has a designated submission date and funds set aside for a certain number of awards.

Research Management and Support (RM & S) - Management of extramural programs, Office of the Director, and certain management costs applicable to cover operations.

Request for Proposals (RFP) - Solicits contracts from for-profit organizations to acquire specific services or products. Research contract awards may be made for the development and support of research or data resources or for the conduct of research that fulfills a specific research need.

Success Rate - Ratio of applications awarded to applications reviewed.