DEPARTMENT OF HEALTH AND HUMAN SERVICES NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2013 Budget Request

Witness appearing before the Senate Subcommittee on Labor-HHS-Education Appropriations

Richard J. Hodes, M.D.

Director, National Institute on Aging

Mr. Chairman and Members of the Committee:

I am pleased to present the President's Fiscal Year 2013 Budget request for the National Institute on Aging (NIA) of the National Institutes of Health (NIH). The FY 2013 budget includes \$1,102,650,000, which is \$522,000 over the comparable FY 2012 level of \$1,102,128,000.

Over 40 million people age 65 and older live in the United States, and data from the Federal Interagency Forum on Aging-Related Statistics indicate that their numbers will double by 2040. In less than 50 years, the number of "oldest old" – people ages 85 and older – may quadruple. As record numbers of Americans reach retirement age and beyond, profound changes will occur in our economic, health care, and social systems.

The NIA leads the national effort to understand aging and to identify and develop interventions that will help older adults enjoy robust health and independence, remain physically active, and continue to make positive contributions to their families and communities. We support genetic, biological, clinical, behavioral, and social research related to the aging process, healthy aging, and diseases and conditions that often increase with age. We also carry out the crucial task of training the next generation of researchers who specialize in understanding and addressing the issues of aging and old age.

BUILDING MOMENTUM IN THE FIGHT AGAINST ALZHEIMER'S DISEASE

Estimates of how many people in the United States currently have Alzheimer's disease (AD) range from 2.7 million to 5.1 million, depending on how AD dementia is

defined and measured. However, scientists agree that unless the disease can be effectively treated or prevented, the numbers will increase significantly if current population trends continue.

At the same time, there has never been greater cause for optimism. In recent years, we have expanded our understanding of how the disease takes hold and progresses, identified promising targets for intervention, and developed new models to speed discovery. For example, researchers have developed a mouse model that expresses human tau, one of AD's pathological hallmarks, and discovered that tau pathology is transmitted from cell to cell, beginning in the brain's entorhinal cortex and spreading from one brain region to the next. This discovery provides insight into AD's earliest development and offers a model for testing mechanisms and functional outcomes associated with disease progression. In another study, investigators "reprogrammed" human skin cells into induced pluripotent stem cells, which then differentiated into working neurons; this breakthrough will facilitate the study of AD in human neurons and provide important insight into the etiology of the disease.

Advances in imaging technology, most notably through the NIH-supported Alzheimer's Disease Neuroimaging Initiative (ADNI), have expanded our ability to understand the underlying pathology of AD, diagnose the disease, track the progress of interventions, and even identify individuals at risk. ADNI data were also used last year to develop new, more comprehensive diagnostic guidelines at both the clinical and pathological levels.

NIH currently supports over 35 clinical trials, including both pilot and large scale trials, of a wide range of interventions to prevent, slow, or treat AD and/or

cognitive decline; over 40 compounds are in preclinical development through the AD Translational Initiative. NIA also participates in the NIH Neuroscience Blueprint under which investigators developing new compounds will have access to drug development services not typically available to the academic research community.

Investigators are also "re-purposing" treatments for other diseases as treatments for AD, with encouraging results. For example, a pilot clinical trial recently demonstrated that a nasal-spray form of insulin was able to delay memory loss and preserve cognition in people with cognitive deficits ranging from mild cognitive impairment (often a precursor condition to AD) to moderate AD. In a separate study, the skin cancer drug Bexarotene promoted clearance of amyloid-beta and reversed cognitive deficits in mice. These preliminary findings offer new and exciting possibilities for the effective prevention and treatment of AD.

NIA has been an active participant in the implementation of the National Alzheimer's Project Act, including the development of a National Plan to Address Alzheimer's Disease. A new presidential initiative to boost support for AD research, which will provide an additional \$50 million in FY 2012 and \$80 million in FY 2013 for the disease, will stimulate and support important groundbreaking work in a number of areas, including AD extensive whole genome sequencing to identify genetic risk and protective factors for AD. Our activities will be informed by input from expert advisors participating in the May 2012 Alzheimer's Disease Research Summit.

UNDERSTANDING AGING AT THE MOST BASIC LEVEL

NIA initiatives on the molecular mechanisms of aging, from in-depth study of single cells to the broad study of organisms at the systems level, continue to advance our understanding of the basic underpinnings of the aging process. For example, investigators recently found that it was possible to delay onset of age-related changes in the skeletal muscle, fat, and eye tissues in mice by removing senescent cells – i.e., cells that are alive but no longer functional. The study also found a slowing of progression of age-related disorders in the mice. These results suggest that cell senescence may be a fundamental mechanism that drives aging.

IMPROVING THE HEALTH AND WELL-BEING OF OLDER AMERICANS

As the American population continues to age, it is imperative that we identify the optimal means to address the unique health needs of older individuals. For example, the Centers for Disease Control and Prevention reports that fully half of older Americans have at least two chronic health conditions that compromise quality of life. NIA is participating in a trans-NIH initiative to develop interventions to modify behavior and improve health outcomes among individuals with three or more chronic conditions.

Increased adherence to recommended medication regimens promises substantial improvements in public health as well as savings in healthcare costs. NIA-supported investigators found that simply encouraging people to write down the time and date when they plan to receive a flu vaccination can significantly increase vaccination rates. NIA also participates in an NIH-wide initiative to identify practical interventions to improve medication adherence in the primary care setting.

Studies have shown that regular physical activity can improve physical performance in older people, but definitive evidence that physical activity can prevent mobility disability is lacking. The NIA supports the Lifestyle Interventions and Independence for Elders Study to assess the effects of a structured physical activity program in 1,600 sedentary older individuals. With the U.S. Surgeon General, the NIA has also launched its nationwide *Go4Life* campaign to motivate older Americans to engage in physical activity and exercise.

In the past year, preliminary results were released from the "Oregon Lottery" study, in which randomly-selected low-income Oregon residents were able to enroll in the state's Medicaid program. Compared to a control group, the new Medicaid enrollees reported improved health and well-being, as well as reduced financial strain. Use of important types of health care services such as preventive care also increased.

EMPOWERING THE NEXT GENERATION OF AGING RESEARCHERS

The need for health care professionals who specialize in the unique needs of older individuals is becoming ever more urgent. We must not only increase the number of practicing physicians trained in geriatrics and in subspecialty fields related to the health problems of elders, but also foster the development of the next generation of physician-scientists whose clinical research will lead to improved care and more effective treatment options for older patients with complex medical conditions.

Recently, NIA established the Grants for Early Medical/Surgical Subspecialists'

Transition to Aging Research (GEMSSTAR) program to promote future leaders in clinical aging research through support of physicians who seek to become clinician-

scientists in geriatric aspects of their subspecialty. NIA has also established a program targeting undergraduate students from diverse backgrounds in order to advance their interest in and knowledge of aging issues.

Richard J. Hodes, M.D.

Director, National Institute on Aging

Richard J. Hodes, M.D., directs the research program of the National Institute on Aging (NIA) at the National Institutes of Health. A leading immunologist, Dr. Hodes was named Director of the NIA in 1993, to oversee studies of the basic, clinical, epidemiological and social aspects of aging.

Under Dr. Hodes' stewardship, the NIA budget has surpassed \$1 billion, reflecting increased public interest in aging as America and the world grows older. Dr. Hodes has devoted his tenure to the development of a strong, diverse, and balanced research program, focusing on the genetics and biology of aging, basic and clinical studies aimed at reducing disease and disability, including Alzheimer's disease and age-related cognitive change, and investigation of the behavioral and social aspects of aging. Ultimately, these efforts have one goal -- improving the health and quality of life for older people and their families.

In the past decade, the NIA has worked in new and innovative ways to conduct research and to translate research findings into practical interventions and public information. In biology, research conducted and supported by the NIA examines the genetic and other factors influencing lifespan and age related diseases and conditions. Research in geriatrics is uncovering new ways to combat frailty with age, and social and demographic research is deepening understanding of the individual behaviors and

societal decisions that affect well-being. In Alzheimer's disease (AD), new initiatives to find genes involved in AD and to identify biomarkers are expected to considerably reduce the length and cost of clinical trials, thereby speeding up the testing of new therapies for AD.

Dr. Hodes is a graduate of Yale University and received his M.D., from Harvard Medical School. He completed training in Internal Medicine at Massachusetts General Hospital and in Oncology at the National Cancer Institute. Dr. Hodes is a Diplomate of the American Board of Internal Medicine. In 1995, he 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' research laboratory in the National Cancer Institute focuses on the cellular and molecular mechanisms that regulate the immune response, with major fields of current emphasis in: 1) the function of costimulation in T and B cell lineage development and function, and 2) regulation of telomere length, and its functional consequences, in both human and mouse model systems. Additional background is available at the lab's website, http://ccr.cancer.gov/Staff/Staff.asp?StaffID=472.