The Longevity Dividend: 
Geroscience Meets Geropolitics
When the NIH was founded in 1930, the average human life expectancy from birth was about 60 years in the United States (see, e.g., University of Oregon Mapping History Project, n.d.). By the turn of the last century, life expectancy from birth had increased to about 77 years (see, e.g., University of Oregon Mapping History Project). The earliest achievements in life expectancy resulted from improvements in sanitation and treatments for infectious diseases—parts of the original mission of the NIH when it was formally created from the Hygienic Laboratory. The NIH has been extremely successful in recognizing and responding to the emergent health issues of each era while also supporting fundamental advances in basic biological research. Addressing public-health issues and therapies designed to counteract the effects of infectious and acute diseases, which were the major scourges of an earlier time, also led to dramatic decreases in mortality at young ages.

However, in part because of the success of NIH-led programs that have increased life expectancy, the burden of diseases affecting the U.S. population has also changed. As stated on the occasion of the 100th anniversary of the American Cancer Society, “Back in 1913...cancer was a lesser threat for most Americans. The biggest killers then were flu, pneumonia, tuberculosis, and stomach bugs. At a time when average life expectancy was 47, few lived long enough to get cancer” (Associated Press, 2013, ¶ 2). Now, the biggest killers in the United States and worldwide are heart disease and cancer, and the major causes of disability are chronic diseases and conditions—including diabetes, obesity, sarcopenia, osteoporosis, and dementias (among others)—that are found most often in elders.

Since its inception, the NIH has responded to the shifting landscape of health concerns and diseases by establishing and reorganizing institutes and centers that are capable of responding forcefully both to widespread diseases and to rare illnesses. The NIH has supported, in parallel, fundamental research in basic biology and application of these findings in clinics and clinical trials. What, then, are the current and future challenges of aging that the NIH could address, given that aging is not a disease but encompasses all parts of the body while putting that body at greater risk of disease and death?

For the NIH, the challenges of aging are not new. The National Institute on Aging (NIA) was established in 1974 as a component of the NIH. From its inception, the mission of the NIA has encompassed many aspects of aging, including physiological, behavioral, social, and economic factors (in essence, gerontology); clinical approaches to the diseases of aging (in essence, geriatrics); and the basic biology of the processes and molecular mechanisms of aging, as well as the basis for understanding age-related disease (geroscience). Two fundamental discoveries in geroscience have occurred over the past 2 decades that may underpin innovative approaches to aging across the NIH: Life spans...
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are influenced by genetics, and life spans can be altered pharmacologically. Moving forward from these two discoveries is a third important (but still tentative) observation: Life spans that have been increased by interventions or by genotypes appear to coincide with improved health.

For centuries, people have known that life span could be extended (probably within limits) simply by adopting a moderate diet and exercise. Basic research and clinical studies both support very strongly the potential for improved health during aging, even when faced with chronic diseases (see, e.g., National Institute on Aging, 2013). In an extreme approach—more suitable to experimental systems with laboratory animals than would be practical on a large scale for human populations—substantially reduced caloric intake extends life span. Generally, these behavioral interventions yielding longer life have been coupled with improvements in health at older ages. As described in some studies of human centenarians and their kindred, survival to old age may coincide with a lower burden of disease—an outcome that is encouraging (Atzmon et al., 2004). However, knowledge about the extent to which any given intervention that extends life span reduces the burden of disease or increases the tolerance for disease remains incomplete. For example, despite recent successes for encouraging behavioral interventions that improve health—most notably a reduction in smoking tobacco and an increase in wearing seatbelts in cars—reversing the trends from immoderate diets and too little exercise are still works in progress for most people.

Furthermore, longevity has long been known to run in families, and geroscience has identified many of the genes and biochemical pathways that can increase life span. Much of this knowledge is based on work done primarily in model experimental systems (laboratory animals) whose genes can be manipulated, but it also comes from studies of long-lived human families and populations. Indeed, multiple animal studies (Bartke, 2011; Kenyon, 2010; Selman & Withers, 2011) have shown that life span is quite malleable and can be extended significantly by manipulation of one or more among a few hundred genes linked to aging (most of which belong to three or four well-defined molecular pathways).

In addition, this type of research has shown that some behavioral modifications that extend life span, such as caloric restriction, function through one or more of these pathways (Fontana, Partridge, & Longo, 2010). In concert with these findings on the genetics of life span are studies on whether life span can be extended by pharmacological agents known to interact with one or more of the molecular pathways linked to life span (Chung, Manganiello, & Dyck, 2012; Fernández & Fraga, 2011; Harrison et al., 2009; Lam, Peterson, & Ravussin, 2013; Park et al., 2012). Thus, a handful of pharmacological agents—including sirtuin activators, rapamycin, and others—have been shown to alter life span in tests using laboratory animals. Prominent among this research is the work done by the NIA-supported Interventions Testing Program (Nadon et al., 2008), which has been critical in producing a turning point in thinking about health in relation to interventions that increase life span.

A recent discovery is the extent to which targeting specific molecular processes that increase life span are also important in the development of most chronic diseases (Baker et al., 2011; Jeck, Siebold, & Sharpless, 2012). In searching for ways to translate basic research into treatments that can meet the major health challenges of an aging population, the NIA has been the lead institute for Alzheimer’s disease, in particular, and dementias and cognitive declines in general, with substantial involvement from the National Institute of Neurological Disorders and Stroke and the National Institute of Nursing Research. Other NIH institutes have been leaders focused on specific diseases and conditions; because many of these diseases are found predominantly in elders, the NIA also supports research in these areas.

As their names indicate, many NIH institutes have been developed in response to emerging health needs identified by specific diseases. For example, the National Institute of Allergies and Infectious Diseases takes the lead on research about allergies and infectious diseases, but also on declining immunity with age; the National Heart, Lung, and Blood Institute takes the lead on studies of heart failure; the National Cancer Institute takes the lead on cancer research; and so forth. However, because one or another aspect of biology affects more than one disease or condition, NIH institutes sometimes work in parallel, and often together, to address specific shared interests. Several examples of research areas—categorized as important in the basic biology of aging—are illustrative: cellular senescence is one important process by which cells lose vigor and increase the risk of tumor formation, and at least four institutes of the NIH deal with this area of research (although the main ones are the National Cancer Institute and the NIA). Another facet
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of the biology of aging involves regeneration of damaged tissue, which declines with aging in most but not all animals. One broadly shared goal is to translate knowledge of the biology of regeneration (in animals that do versus do not retain this capacity) to improve regeneration in humans (whose regenerative capacity diminishes with aging); 13 institutes of the NIH are involved in this area. Likewise, 16 institutes of the NIH support research on inflammation, which can be both acute and chronic; the two forms of inflammation serve seemingly contradictory functions in health, on the one hand promoting healing but on the other hand increasing the risk for disease.

As the increase in survival to older ages becomes more an expectation than a dream, there is a greater need to understand how to improve and maintain health during aging. The NIH has always promoted and supported turning discovery into health via translating research to practice. The trans-NIH GSIG, for example, seeks to apply this credo to promote healthier aging. With an aim toward efficiency, the NIH has always promoted and supported turning discovery into health via translating research to practice.

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References


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