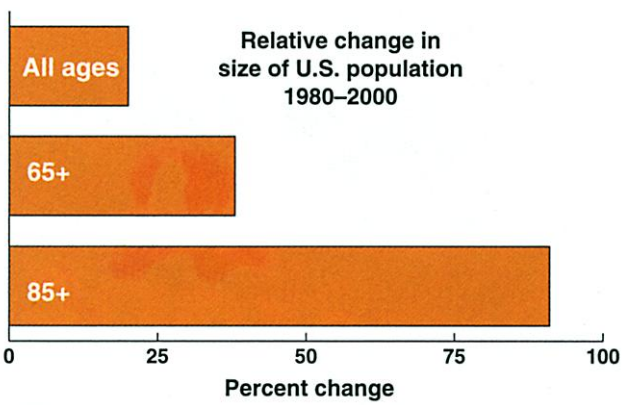
Frontiers of Aging

After a long and sometimes painful incubation period, biochemical research on aging has done what we all do eventually: It's come of age. The goal of the field is a deeper understanding of the fundamental mechanisms that lead to the slow, insidious postmaturational declines in structure and function observed in most organisms. Evolutionary biologists appear to be unanimous in their conclusion that senescent phenotypes are still in the population because they have escaped the force of natural selection. But we also know that life history parameters, including variable rates of aging, are highly plastic. Given the opportunity, such as a new ecological niche for the evolution of alternative gene actions, nature can devise clever methods for superior maintenance of the soma. It is our job to reveal these secrets in order to enhance our health spans as well as our life-spans. To facilitate this process, on 3 October *Science* launched a new knowledge environment focused squarely on the biology of aging. Named SAGE KE (Science of Aging Knowledge Environment), this Web site (at sageke.sciencemag.org) is designed to help scientists in and outside of the field of aging stay abreast of the diverse facets of aging research.

To push our understanding of the aging process ahead will require the recruitment of a wide range of scientists, including those who have not yet thought of their work in the context of aging. Nucleic acid, protein, carbohydrate, and lipid biochemists; endocrinologists; neuroscientists; geneticists; organ and integrative physiologists; population biologists; and many others—we want them all to join us in this quest. Models of aging can offer some special advantages for their research. Phenotypes in old cells and animals can act as amplifiers of signals that would otherwise escape detection. The emerging innovations in genomics and proteomics will help us define these signals. That task has only just begun. There is currently a flurry of activity regarding the use of expression microarrays in aging tissues of many organisms. The rapid progress in the characterization of human single-nucleotide polymorphisms has made genome-wide linkage and association studies more feasible for the detection of important alleles for senescent phenotypes and for unusual longevity. There will be full employment for human statistical geneticists for years to come, as we try to confirm controversial results!



U.S. census estimates

Meanwhile, I urge the funding agencies to continue their support of research on aging in model organisms. The most exciting recent advances in biogerontology have made use of simple organisms that are amenable to genetic analysis. The remarkable potential of allelic variants at the *daf 2* pathway to modulate the life-span of the nematode *Caenorhabditis elegans* was quickly shown to have a counterpart in the fruit fly *Drosophila melanogaster*, and there is evidence that comparable mechanisms may be operative in mice. This makes a strong case that at least one class of genetic "geromodulators" has been evolutionarily conserved. The best bet is that it evolved to maximize reproductive fitness in "feast or famine" environments. These results also point to a powerful central neuroendocrine control of life history strategies, although research on Werner syndrome is consistent with peripheral mechanisms of somatic cell aging that are independent of central controls. Clearly, there is not one process of aging but multiple processes.

We are far from having magic elixirs to prevent or reverse aging. But such interventions may not be out of the question for the distant future; for example, superoxide dismutase/catalase mimetics (which inactivate damaging reactive oxygen species) or caloric restriction can extend the life-span of model organisms. We will know more about this possibility when we understand the precise molecular mechanisms that respond to variations in fuel utilization.

The encyclopedic nature of the field and the exponential rates at which scientific information relevant to the biology of aging is increasing make it difficult to keep up with the literature. Fortunately, the age of digitized data and the Internet has arrived in the nick of time. The SAGE KE is designed to help digest these rich fruits of past and current research. Although we offer no panaceas, like so many of the translational products of aging research we do provide a measure of palliation!

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