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Executive Summary

The Genomics of Longevity

Genes associated with increased lifespan give drug discovery companies new insight into how to tackle age-related diseases.

Entrepreneurs hoping to translate the science of anti-aging into profitable businesses have been a bit like the optimist combing through a crate of horse manure and saying, "there's got to be a pony in here." On the one hand, the demographics and economics of an aging population are tantalizing. Chronic diseases and other conditions of aging, like cardiovascular disease, cancer, diabetes, and the consequences of physical inactivity, account for 75% of health care costs each year. Costs will continue to increase too; today, 13% of the US population is over 65 and the Centers for Disease Control and Prevention projects that the elderly will account for 20% of the population within 30 years. Today's Baby Boomer, a consumer activist concerned with quality of life, is the senior of tomorrow, and such customers will certainly drive demand for new interventions that address the frailties of aging.

But positioning anti-aging drug development strategies has always been awkward. Companies that want to develop products with anti-aging claims have no place to sell them but the nutraceuticals market, where large consumer advertising budgets rather than scientific studies hold sway. On the pharmaceutical side, the challenge has always been how to create a sustainable business around the science of aging; how to develop products for which efficacy (delayed aging) must be measured over decades, and how to position products that slow the aging process in a health care system that is largely based on the treatment, not the prevention, of individual diseases.

Historically, therefore, the clinical community and the companies that serve it have viewed aging as the sum total of a number of different diseases that develop through mechanisms that are independent of each other. The conventional belief is that diseases cause aging. But now, the genetics of longevity has a select group of converts believing that it's the other way around: aging causes diseases.

The discovery that certain genes can be altered to increase the lifespan of organisms like yeast, nematodes, and mice has led some researchers to believe that aging is not just a build-up of cellular damage that leads to organ failure. Aging might be, they suggest, an innate part of the cellular machinery, a program that can be switched on or off to speed up or slow the aging process, and in so doing affect particular diseases. One hint of a connection between the phenomenon of aging and age-related diseases: restricting the calorie intake of mice lengthens lifespan, and those abstemious rodents don't get cancer.

Prominent anti-aging researchers are aligning themselves with new companies that hope to use a molecular understanding of longevity to develop drugs against age-related diseases. Several companies have rallied around calorie restriction (CR) and are characterizing genetic and phenotypic changes associated with CR—BioMarker Pharmaceuticals Inc. to develop pharmaceuticals that achieve the same effect, and LifeGen Technologies Inc. and Longenity Inc. to create biomarkers of aging that will prove useful in future studies of aging and age-related diseases. Chronogen Inc. is the licenser of genes (discovered by Siegfried Hekimi, PhD, professor of biology at McGill University), that appear to lengthen lifespan in model systems by reducing oxidative stress. Elixir Pharmaceuticals Inc. has rights to different genes (discovered by Leonard Guarente, PhD, of the Massachusetts Institute of Technology and Cynthia Kenyon, PhD, of the University of California, San Francisco), that lengthen the lifespan of model animals and also, encouragingly, have human homologs.

These companies aim to use knowledge of the aging process as a tool for gene-based discovery to create compounds that treat particular age-related diseases by new mechanisms, which they can sell to pharma.

Investors in the new companies are looking at a difficult business with far-off horizons to profitability. Indeed, not clear yet is the extent to which new companies will be able to identify, much less match to specific diseases, mechanisms that increase lifespan, or whether they will be successful in developing efficacious compounds based on gene targets, particularly since physiological mechanisms are often redundant. The diseases of aging are also among the toughest in which to run clinical trials; many are degenerative and develop over many years, with changing biology along the way, and many of them lack measurable endpoints by which to demonstrate efficacy in the short term. The biggest unknown of all may be whether findings related to longevity in animals will correlate to human experience. Researchers must rely on animal models whose lifespans are short enough to run experiments—three weeks for nematodes, three years for mice. The predictability of animals is always a question in drug discovery, but here, the animal-to-human connection isn't validated.

But if genomics does light up the path between aging and disease, start-ups will be in a position to address multi-billion dollar primary care markets.

