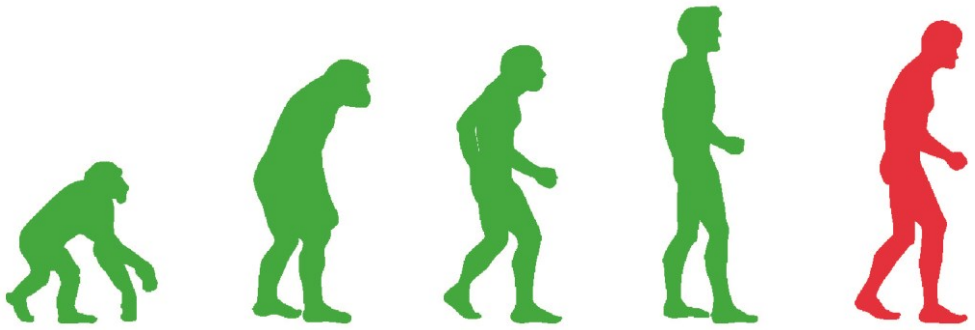

New Evolution Concepts Are Changing How We Think About Biological Aging

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New thinking about the evolutionary nature of biological aging will profoundly affect medical research on age-related diseases – here's why.

Before Darwin nobody thought that the origin of lifespan was different from that of all of a species' other traits. Whatever caused a rat to have a long tail and beady eyes also caused it to have a particular lifespan, which like tails and eyes varied a lot between different species. Mammal lifespans vary from less than a year for some mice to more than 200 years for some whales.

In 1859 Darwin's survival-of-the-fittest concept changed that idea. Now organisms were evolving myriad traits that each caused them to live longer and/or breed more. Because living longer and breeding more was indefinitely advantageous, organisms were presumably evolving toward reproductive immortality. By the present, after billions of years of evolving longer lives, why weren't organisms immortal or at least all similarly limited by some universal and fundamental law of physics or chemistry that could not be overcome by the evolution process? Why would lifespans vary so much among even biochemically similar organisms? Contemporaries actually wrote Darwin and asked this question! Biotheorists have been laboring ever since to develop a theory that fits with evolution theory and simultaneously matches empirical evidence such as the lifespan observations.

Most gerontologists and medical researchers now believe one of two main aging theory concepts that eventually resulted: Programmed aging theories, first proposed in 1882, say that species generally possess a *lifespan regulation mechanism* that purposely limits lifespan to a species-specific value in order to obtain an evolutionary benefit.

Non-programmed theories proposed that each species only has an evolutionary need to live to a particular lifespan and therefore only evolved the ability to overcome natural deteriorative processes to the extent necessary to live to that age. Both concepts explain why species have such different lifespans; both require modifications to the survival-of-the-fittest idea that we all learned in high school biology class.

Modern non-programmed theories are based on an idea by Nobel-laureate Peter Medawar who proposed in 1952 that beyond a certain species-specific age there is no further evolutionary benefit to living or reproducing longer. In effect, survival-of-the-fittest only applies to young organisms where "young" is defined relative to the age at which the organism is first able to reproduce. Nature doesn't care what happens to old organisms. Death and deterioration are not an evolutionary disadvantage unless they occur before the critical age.

For most people who paid any attention in biology class, programmed aging, the idea that we possess a sort of suicide mechanism that purposely pro-actively limits lifespan, appears to be even more patently ridiculous and more obviously incompatible with the whole *survival*-of-the-fittest idea than modern non-programmed aging theory. Indeed, as late as 2002 some prominent biologists were still writing that programmed aging in mammals was literally theoretically impossible. Consequently, steadily increasing evidence of programmed aging such as genes that *cause* aging was largely ignored by medical researchers. "Impossible" trumps any amount of evidence.

Meanwhile, beginning in the 1960's a number of other theorists were working on trying to explain some *other* apparent conflicts between observations and evolutionary mechanics theory. Darwin's theory says that every *individual* animal is fighting *for* the survival of itself, its mate, and direct descendants and *against* competitors from its own species. An individual surviving longer and breeding more produced more descendants having its individual design than competitors and thus better propagated its individual traits. This is the "individual benefit clause" or the "dog eat dog" aspect of Darwinian evolution theory. There was very wide agreement that deterioration and death caused by aging did not represent any evolutionary benefit from the point of view of an individual mammal!

However, In addition to all of the human societal rules, laws, and commandments that limit individuals in favor of wider benefit, theorists observed animal behaviors (*altruism*) in which animals similarly behaved in a way that was counter to their individual best interest, apparently to obtain a wider "group" survival benefit. A number of other apparent discrepancies with the individual benefit clause surfaced. Eventually a number of theories appeared to the effect that benefit to the survival of groups or kin, benefit to the propagation of genes (the selfish gene theory), or benefit to the evolution process itself (evolvability theory) could offset some degree of individual disadvantage

and result in evolution of an individually-adverse (or neutral per Medawar) trait like programmed mammal aging. Multiple programmed aging theories then appeared based on non-individual benefit resulting from a purposely limited lifespan. According to these theories, beyond a species-specific age (also associated with reproductive maturity) there is an evolutionary *disadvantage* from living longer. As only one very simple example, a longer lifespan in many mammal species would lead to decreased genetic diversity. A single long-lived male "king of the hill" might mate with many generations of his own descendants!

Genetics discoveries, some quite recent, exposed additional issues with traditional individual-benefit-only evolutionary mechanics theory. At least two assumptions made by Darwin and critical to the individual/ non-individual issue are now provably false. The emerging reality: the evolution process, rather than being simple and elegant is actually complicated and messy. The reader may have noticed that the two main theories are much closer to each other than to traditional evolutionary mechanics. The argument is over whether beyond the critical age living and reproducing longer creates zero net evolutionary advantage (and therefore species never evolved a longer lifespan) or whether, beyond the critical age further survival creates at least a small disadvantage (and therefore species evolved suicide mechanisms). Arguing about the difference between zero and slightly less than zero is a lot like arguing about how many angels can fit on the head of a pin!

It is now increasingly obvious that programmed mammal aging is the right theory. Programmed aging theories now exist proposing that a panoply of wider evolutionary benefits would result from programmed lifespan limitations. Various logical flaws with popular non-programmed theories have been identified. A number of senior advocates of non-programmed aging have even conceded the validity of the non-individual-benefit evolutionary concepts that are necessary to support programmed mammal aging. This essentially concedes the validity of programmed aging because programmed aging provides a much better fit to experimental evidence.

Why is this development so important? Programmed and non-programmed theories predict very different mechanisms behind the aging process and therefore behind massively age-related diseases like cancer and heart disease. Following the wrong theory is therefore likely to substantially delay development of ways to treat or prevent the age-related diseases that in developed countries are now the *main cause of death* for people over 40! For example, non-programmed theories suggest that the various manifestations of aging are functionally independent of each other and that therefore treatments and prevention techniques must be individually developed for each condition. Programmed theories suggest that, in addition, there is substantial potentially treatable commonality between various manifestations, i.e. the program. If aging is at least partially controlled by a program similar to the one that controls reproductive

functions, we would expect the existence of a "biological clock" that could be medically altered. We would expect the existence of signals such as hormones used to coordinate the activities of various tissues in performing the aging function that could also be altered. Such signals have been identified in aging mechanisms of various organisms.

Researchers following non-programmed theories talk about preventing or contravening damage, usually associated with a particular disease. Followers of programmed theories talk about genes, signals, receptors, interrupting the aging program, and simulating some effect known to delay aging such as caloric restriction or exercise in order to "fool" the aging program.

Most of us have been trained from an early age to believe that the evolution process resulted in the development of all of the "beneficial" characteristics of an organism but that all of the "adverse" aspects came from random deteriorative processes or external forces. It is indeed a giant leap to think that muscle weakness, sensory and mental deterioration, heart disease, cancer, increased susceptibility to infectious diseases, arthritis, and other manifestations of aging are also "beneficial" as seen from the evolution process point of view and therefore ultimately result from the operation of complex evolved mechanisms similar to those that produce the traditionally "beneficial" organism features. However unless we make this leap we will never really understand aging or age-related diseases

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