Programmed Aging and the Emerging Reality of Anti-Aging Medicine

Theodore C. Goldsmith

4/20/2016
Age-Related Diseases and Conditions

• Incidence of age-related diseases and conditions drastically increases with age (example: death from cancer is approximately 270 times more likely in an 80-year-old than in a 20-year-old).
• Age-related diseases cause at least \( \frac{3}{4} \) of all deaths in developed countries.
• The majority of current medical research and health care costs are directed at age-related diseases.
• Examples of highly age-related diseases and conditions:
  – Heart disease
  – Cancer
  – Stroke
  – Alzheimer’s
  – Arthritis
  – Reduced immune response
  – Loss of strength
  – Cataracts; other vision and hearing loss
  – Type 2 diabetes
  – Osteoporosis
  – Some mental deficits
Biological Aging Theories

- **Biological aging theories** attempt to explain observations about aging while simultaneously explaining how aging relates to the process of evolution.
- **Evolutionary mechanics** refers to the “how it works” nature of the evolution process.
- Darwin’s survival-of-the-fittest evolutionary mechanics theory as described by Darwin and currently widely taught is incompatible with observations about aging and certain other observations such as animal altruism and sexual reproduction. Scientific arguments about evolutionary mechanics and the evolutionary nature of aging still persist more than 150 years after Darwin’s theory appeared.
- Discoveries, especially in genetics, exposed other issues with Darwin’s mechanics.
- Consequently modern aging theories are based on **modifications** to Darwin’s evolutionary mechanics developed since 1950.
- Modern aging theories fall into two classes: **Non-Programmed** and **Programmed**.
Non-Programmed Aging Theories

- Modern non-programmed aging theories (beginning ~1950) contend that each species only has an evolutionary need to live for a particular species-specific and internally determined lifespan.
- Many different natural deteriorative processes cause the many observed age-related diseases and conditions.
- Consequently, species only evolved and retained the internal ability to oppose each deteriorative process to the extent necessary to allow for the necessary lifespan.
- If, for example, heart disease was causing deterioration or death at too early an age, a species would evolve better anti-heart-disease mechanisms.
- Living organisms are known to have many different maintenance and repair mechanisms: wounds heal, cells are replaced, infectious diseases are combatted.
- Explains why different mammals have very different lifespans even though biochemically very similar; mammals have lifespans differing by a factor of more than 200 to 1 between some whales and some mice. Fish have lifespans differing by more than 1300 to 1.
- Explains why age-related diseases and conditions are similar between different mammal species. It is the anti-deterioration mechanisms that differ.
- Modern medicine has developed myriad different ways to treat different deteriorative processes such as cancer, heart disease, etc.
Modern Programmed Aging Theories

- Modern programmed aging theories (beginning ~1990) contend that beyond the lifespan needed by each species there is an evolutionary *disadvantage* to living and reproducing longer.
- Consequently, species, including humans, evolved mechanisms (*aging programs*) that purposely limit their lifespans and ultimately cause the many age-related diseases and conditions.
- This idea is an extension of the earlier non-programmed concept to the effect that each species only has an evolutionary need for a certain lifespan.
- Programmed mammal aging theories are based on the idea that a purposely limited lifespan, while adverse from the viewpoint of an *individual* organism, *benefits a population* of those organisms by increasing the probability that the population will avoid extinction. This benefit caused the evolution of suicide mechanisms. Theorists have suggested many population benefits of a purposely limited lifespan.
- Some programmed theories contend that such a program would be similar to many other biological programs (e.g. reproduction program) and similarly involve signaling (such as hormones, pheromones, nervous signals) and the ability to detect and adapt to temporary or local external or internal conditions that affect the optimum lifespan for a species.
Major Medical Implications

- **Non-programmed theories** suggest that any attempt to treat an age-related disease must be designed for and applied to a particular disease. Generally speaking, there is no **treatable common factor** linking age-related diseases. This is the traditional medical approach.

- **Programmed theories** suggest that, in addition to disease-specific interventions, it is possible to develop agents and protocols that generally **delay aging by interfering with the aging program**.

- Programmed theories support **Anti-Aging Medicine**. Just as a food, existing pharmaceutical agent, vitamin store product, or new drug might be effective in treating a particular age-related disease or condition such an agent might also be effective in generally delaying aging and therefore the appearance of all or most age-related diseases and conditions.
History of Programmed vs Non-Programmed Aging

- As late as 2002 programmed aging (initially proposed in 1882) was thought to be theoretically impossible because of evolutionary mechanics considerations.
- The immediate causes of age-related diseases and conditions are obviously different.
- Medical efforts against specific diseases (surgery, pharmaceuticals, other treatment approaches) have been successful.
- Therefore medical research has been directed by non-programmed theories.
- Some physicians and health researchers especially those not specifically concerned with aging or aware of recent developments still consider programmed aging and anti-aging medicine to be scientifically ridiculous.
- However, there now exists substantial and increasing evidence of programmed aging. Since about 2005 multiple modern programmed aging theories have appeared and multiple modern evolutionary mechanics theories support programmed aging. Senior proponents of non-programmed aging are no longer claiming programmed aging is “impossible.”
- There are now substantially funded medical research efforts based on programmed aging theories ($billions).
- Thousands of anti-aging medical practices now exist.
Programmed Aging Research

- Google subsidiary Calico and pharmaceutical giant AbbVie are engaged in a multi-billion dollar anti-aging research effort based on programmed aging concepts.
- The U.S. National Institutes of Health/ National Institute on Aging is operating a search for anti-aging agents called the Interventions Testing Program (ITP). Testing is performed on potential oral anti-aging agents using mice.
- Moscow State University is doing extensive research including human clinical trials based on programmed aging concepts. Director of this effort Dean Vladimir Skulachev is a leading proponent of programmed aging.
Programmed Aging Mechanisms

• If aging is a biological function that evolved to serve a purpose it is likely implemented in a manner similar to other biological functions like reproduction. Such functions include a mechanism to determine when to perform the function (a “biological clock”), means for sensing and responding to internal or external conditions that affect the optimum operation of the function (e.g. seasons), and means for coordinating the operation of various systems and tissues in executing the function such as chemical (hormone) or nervous signaling.

• There is wide agreement that temporary or local internal and external conditions such as famines, predation, and changes in reproductive behavior would alter the optimum lifespan for an organism.

• Therefore an evolved programmed aging mechanism would be expected have the capabilities suggested above.

• Non-programmed theories suggest that differences in each of many anti-disease (maintenance and repair) mechanisms are responsible for the huge observed differences in lifespan between similar species.

• Some programmed theories suggest that the anti-disease mechanisms are in turn controlled by a common aging program that differs between species to explain the lifespan differences and other observations.

• A complex control program would involve many points at which anti-aging intervention could be attempted.
Programmed Aging Mechanisms

Biological Clock Functions

Sensory Functions

External Conditions
- Time-of-Year
- Predator Stress
- Caloric Restriction

Programmed Mammal Aging Mechanism Functional Diagram

Signaling

Maintenance Functions
- Anti-Cancer Functions
- Anti-Heart Disease Functions
- Anti-Arthritis Functions
- Anti-Cataract Functions
- Anti-Diabetes Functions
- Other Maintenance and Repair Functions
- Age-Related Phenotypic Changes
- Reproductive Functions
  - Puberty Age
  - Mating seasons
Evidence of a Treatable Common Cause of Aging

• Caloric restriction effect: dietary restriction generally delays aging
• Stress effect: Exercise appears to generally delay aging
• Progeria and Werner Syndrome: Human genetic diseases that simultaneously accelerate many symptoms of aging suggesting a defect in a common control mechanism.
• Concentrations of many hormones vary with age: Fits with programmed concept. Suggests some form of hormone replacement/ modification may be a treatment for aging.
• Some “negligibly senescent” species apparently do not age, a problem for non-programmed theories. Programmed theories suggest these species are the result of an inherited genetic defect in their aging program.
• Genes that cause aging: Disabling certain genes in simple GMO organisms (Roundworm) has resulted in lifespan increases of as much as a factor of 10.
The practice of anti-aging medicine can be divided into two aspects: Behavioral or **lifestyle protocols** and **anti-aging agents**.

**Lifestyle protocols** include:
- **Dietary (caloric) restriction**: Many animal studies suggest lifespan is extended by caloric restriction. Some programmed theories suggest that the caloric restriction effect is a trait that evolved because it increases a population’s ability to survive famines.
- **Exercise** including physical and mental activity is widely thought to generally delay aging. Some programmed theories suggest that this response to stress evolved to increase a population’s ability to survive temporary or local increases in predation.
- Lifestyle protocols are not very controversial; most physicians favor less obesity, healthy diet, more exercise, and avoiding dangerous behaviors like alcoholism and drug abuse.

**Anti-Aging Agents:**
- Under programmed theory anti-aging agents can be found or manufactured that generally delay aging. Multiple agents including some existing prescription pharmaceuticals are suspected of having anti-aging properties.
- Some potential anti-aging agents: rapamycin, metformin, resveratrol, vitamin D3, deprenyl
- **Hormone replacement/ modification**
- Potential for existence of anti-aging agents is still rejected by followers of non-programmed theories and some physicians.

The **American Academy of Anti-Aging Medicine (A4M)** provides certifications and continuing medical education to 26,000 physicians and researchers.
Conclusion

• The emergence of programmed aging and anti-aging medicine is a very exciting development for two reasons:
  – **A Parallel Path to Treatments**: Anti-aging medicine represents a second path toward treatment and prevention of highly age-related diseases that can be exploited in addition to traditional disease-specific approaches.
  – **The Low-Hanging Fruit Effect**: Because programmed aging and anti-aging medicine represent a new approach to treatment and prevention of age-related diseases we can reasonably expect rapid initial progress.
Further Reading