Our Healthspan Prospects Update

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Healthspan and Lifespan Extension Recent Developments (recap 10/2018)

- **In the previous update, October 2018, I reviewed two major areas of development in age-related diseases:**

  1. Alzheimers and other age-related dementias appear to have multiple causes and may develop over decades without being symptomatic

  - **This research trend continues with no dramatic breakthrough in treatment**
  - **For understanding and possibly warding-off or treating these diseases, I still recommend the work of Dale Bredesen, M.D., represented by his recent book: The End of Alzheimer's: The First Program to Prevent and Reverse Cognitive Decline (2017)**

  2. Senescent cells, dysfunctional cells which can no longer replicate but have bypassed natural self destruction (apoptosis), cause chronic tissue inflammation, a significant risk for age-related diseases including cardiovascular disease, cancer, and sarcopenia.

  - **R&D of senolytics, senescent cell destroyers, continues at numerous academic and pharmaceutical labs. Weak senolytics in the form dietary supplements are multiplying in the marketplace.**

Healthspan and Lifespan Extension Recent Developments, (continued recap 10/2018)

- **The science of aging and related diseases in humans and other animals has been contentious/confused between two concepts:**
  - **diseases of aging as accumulated damage (the body is like a heavily used machine wearing out) and**
  - **aging is governed by a genetically-determined/evolved lifespan which has been our ancestors' responses to their environments.**
- **Both can be true, and can contribute to strategies for avoiding and treating disease.**
- **If you are interested in these topics, I recommend a book by Kris Verburgh, MD: The Longevity Code: Secrets to Living Well for Longer from the Front Lines of Science (2018)**

Cell Reprogramming

- **The key to restoring bodily function in the face of diseases of all kind is knowledge of epigenetics:**
  - **The chemical modulators of gene activity which allow a single cell with one set of genes to develop into a trillion cell organism, each cell with the same set of about 20000 genes, but divided into hundreds of tissues with very distinct appearances and behaviors**
  - **Analogy: our genes are our hardware, replicated in every cell, and epigenetics is the software or program, varying from tissue to tissue**
- **In 2006 Shinya Yamanaka's lab at Kyoto U. published a revolutionary finding (later earning a Nobel Prize)**
  - **activation of only 4 genes, shorthand designation OSKM, was sufficient to reprogram differentiated skin cells (fibroblasts) back to a stem cell which can give rise to all tissues in the body, the pluripotent stem cell, in this case the induced pluripotent stem cell or iPS**
  - **raised the prospect of growing youthful replacement tissues for the human body**
- **Over the next 12 years scientists found the gene combinations to reprogram virtually any cell type to any other type without fully understanding the process (optional for medical progress)**

Cell Reprogramming, continued

- **2008 AAAS Video Story, “Reprogramming Cells”, 0-8m11s**
- **Recently several research teams have reprogrammed cells in situ, inside the body, with the aim of enabling regeneration of damaged/diseased/missing tissue with cells created in a patient’s own body, and, therefore, compatible with their immune system**
- **The research group of Juan Carlos Izpisua Belmonte at the Salk Institute, La Jolla, have been conducting research on cell reprogramming for several years.**
  - **In 2017 they demonstrated relief from a progressive genetic disease, return to a youthful form, and erasure of cellular markers of aging.**
  - **In 2018 they published *In vivo reprogramming of wound-resident cells generates skin epithelial tissue*, the first production of a major organ, the skin, by reprogramming of exposed connective tissue in the open wound. They aim for human trials to develop a technique for closing difficult-to-heal open sores without skin grafts. Such sores are a major problem of the elderly and of burn victims.**
  - **The reprogramming genes are engineered into a virus which then passes them through the cell membrane to infect/activate inside body cells.**

Cell Reprogramming, continued

- **The Center for Regenerative Medicine & Cell-Based Therapies at Ohio State University, under Director Professor Chandan K Sen, has developed another means of introducing reprogramming genes into cells in the body. They use small electrical currents to briefly open the cell membrane (electroporation) to allow entry of small engineered circular chromosomes (plasmids) with the required genes. A 2017 video by OSU introduces the technique, 2m17s: https://www.youtube.com/watch?v=tMQ51Kj2tS0**
  - **They have reprogrammed skin connective tissue to form blood vessels to restore circulation to injured legs in mice.**
  - **They have reprogrammed skin tissue to create neurons also.**
  - **A 2018 NIH grant will support development of devices to reprogram human tissues with an eye toward preparing for clinical trials.**
  - **The technique reprograms cells without the use of an engineered virus to gain entry to the cells.**

Social Consequences of Long Health and Lifespans

- **From Davos 2017, a panel discussion moderated by - Kenji Kohno, Anchor, NHK News Watch9, NHK (Japan Broadcasting Corporation) includes 0-12m of 58m:**
  - **David B. Agus, Professor of Medicine and Engineering, Lawrence J. Ellison Institute for Transformative Medicine of USC, USA**
  - **Lynda Gratton, Professor of Management Practice, London Business School, United Kingdom**
  - **William Francis Morneau, Minister of Finance of Canada**
  - **Yasuhiro Sato, President and Chief Executive Officer; Member of the Board of Directors, Mizuho Financial Group, Japan**

https://www.youtube.com/watch?v=spH9HpIlffA