**Longevity Research**

This document summarizes the various articles I found while working on the background to the Rejuvenation story. Based on these articles, it would seem like we are pretty much ready to eliminate old age. But of course, these all hint at pieces of a big complex process. Tinkering with it before we fully understand it can't be good, right?

This should tell you all you need to know:

Jeff Bezos Invests in Anti-Aging Biotech Start-up Altos Labs (marketrealist.com)

By Rachel Curry, September 7, 2021

'Bezos Expeditions—Jeff Bezos's investment office—has funded Altos Labs alongside Russian-Israeli venture capitalist Yuri Milner's foundation. Milner himself has talked about "rejuvenating" humans and other animals. Given Bezos's investment, he might be of the same dogma.'

'In 2013, billionaire Google co-founder Larry Page announced a similar company called Calico Labs. To date, any progress that Calico has made is speculative, although the company has admitted it's dabbling in reprogramming as well. That means healthy competition for early-stage Altos Labs, which started with an idea but has quickly turned into a well-funded venture.'

The above are excerpts from Rachel Curry's article. It is only one of several articles about this. Apparently, researchers in longevity research are commanding eye-watering salaries to join these new companies.

The following summarizes what I learned about the aging process.

**The Hayflick Limit**. Scientists in the 1960's noticed that cells cannot go on dividing forever. After a certain number of cell divisions, they stop dividing and die. Human cells at birth have the capacity to divide between 40 and 60 times. This phenomenon, poorly understood at the time, was called the Hayflick limit. Since the maintenance and regeneration of our tissues throughout our lives depends on this cell division, it is thought that the Hayflick limit puts a hard stop on human (or any animal) longevity.

**Telomeres:** Research on our chromosomes identified a section of repeating DNA bases at the ends of each chromosome. At an initial length of over ten thousand bases in humans, this stretch of DNA forms the telomere, a protective cap on the ends of our chromosomes. Our chromosome is a long string of DNA, wound up tightly, folded in on itself many times. At the ends of the chromosome, the ends of these folded strands are exposed. Like the end of a shoelace that is missing its little plastic tube, the aglet. Without the aglet the threads of the shoelace will unravel and be damaged. The same is true for the ends of the chromosome. The telomere forms the cap or aglet of the chromosome.

Further research revealed that the Hayflick limit appears to be tied to the telomere. Each time a cell divides, the telomere gets shorter. Eventually after many divisions, the telomere has become too short to properly protect the ends of the chromosome. The cell stops dividing and dies.

**Telomerase:** From www.nobelprize.org/prizes/medicine/2009/blackburn/facts/ In 1982, Elizabeth Blackburn, Carol Greider and Jack Szostak discovered an enzyme in certain cells that seem to have unlimited ability to divide. This enzyme restored the telomere to its original length, avoiding the Hayflick limit. They called this enzyme telomerase. The genes to make telomerase lie dormant in all of our cells, being active in our germ cells, and places in the body where a continuous production of cells is essential such as in the bone marrow to make blood cells. This raises thoughts of by-passing the Hayflick limit if we could just figure out how to reactivate the telomerase genes in all of our cells to reset the length of our telomeres. I think you wouldn't have to reactivate all of you cells just a small fraction in each tissue. These will divide and push out the old cells.

**New Blood/Old blood:** In 2012, Sauk Villeda et all. of Stanford University found that blood from young mice, infused into older mice, reversed some effects of aging in the older mice. Learning and memory scores improved for the older mice. Something carried in the younger blood endowed 'youthfulness' on the older mice.

**Newscientist, August 13, 2022: by Chris Stokel-Walker**: “Young mice age when given blood from older animals: Transfusing young mice with blood from older rodents triggers cellular aging, suggesting aging isn’t all down to wear and tear. Irina Conboy at the University of California, Berkeley, and her team transfused blood between young mice, aged 3 months, and old mice, which were nearly 2 years old. Two weeks later, the young mice have an increased number of senescent cells, ones that are damaged and stop dividing but don’t die. These cells accumulate as a normal part of aging, beginning after a few years of life in humans. Strength tests also revealed the young mice became weaker after receiving the older rodent’s blood…”

**Newscientist March 19, 2022:** Clue to rejuvenating effects of young blood:
Extracellular vesicles are little bags of chemicals that cells shed. These bud off from a cell and can travel in the blood and fuse to distant cells, releasing their contents. The proteins and RNA from the vesicle can turn on and off genes in the destination cell. Recent studies suggest that these vesicles are involved in aging in good and bad ways. The content of vesicles can change as the cell ages. Those from senescent cells (see below) may accelerate aging. A study injected vesicles from young stem cells into old mice twice, a week apart. A month later, the mice showed increased grip strength, more endurance. Even regrew hair faster. 2 months after the injections, the effects had faded.

**Senescent Cells:** These are interesting beasts. When cells are old or damaged, they shut themselves down. In youthful animals, the immune systems clean out these senescent cells. But as we get older, the cleaning out isn’t as effective or stops completely. The senescent cells accumulate in our tissues. They may exude compounds that damage other cells, making them senescent as well. Sort of a zombie effect. These cells appear to rob our tissues of their vitality. Given this, would it not be better to find a way to eliminate them?

**Senolytics:** There are compounds called senolytics. These compounds trigger the self-destructive mechanism in senescent cells. The cells are destroyed, stopping them from doing their damage. Should we be taking mouthfuls of these compounds? The jury still seems to be out.

**Ultrasound?** Another article (see below) describes a study that found that low frequency ultrasound appears to restore senescent cells to full vigour. This restores youthfulness to mice. But should we be waking up zombie cells? Nature must put them into a senescent state for a good reason.

**Newscientist, January 21, 2023, Ultrasound Rejuvenates Cells by Michael Le Page**: Low frequency ultrasound appears to have rejuvenating effects on animals. As well as restarting cell division in aging human cells, it has reinvigorated old mice, improving their physical performance in tests such as running on a treadmill and making one old mouse with a hunched back move around normally again. Michael Sheetz at the University of Texas Medical Branch, whose team is planning to start a small trial in people to see if the technique is safe and can help treat age-related diseases.... Sheetz's team has found that low-frequency ultrasound makes senescent cells from monkeys and human resume dividing and halts the secretion of chemicals that promote senescence.

**Microbiome:** Then there is the microbiome. The microflora and fauna that live within us. Apparently, we have more of these cells in us than the cells that make us up. (So, what are we?) Apparently a 'healthier' microbiome can turn down diseases of old age. There is also a suggestion that it can rev up our immune systems so that they can get back to the business of ridding our tissues of senescent cells.

**Newscientist, December 3, 2022, Gut Reactions by Jessica Bond**: "If the gut microbiome is like a pharmacy, postbiotics are the medicines it dispenses…..Patrice Cani at the Catholic University of Louvain in Belgium and his colleagues conducted a clinical trial involving 32 overweight or obese volunteers. It showed that regardless of whether the bacteria were dead or alive, they led to improved insulin sensitivity,

which can reduce the risk of type 2 diabetes, lower blood cholesterol and lower body weight compared to people who took a placebo.”