Planting Shade

by Dahl Clark

A man has made at least a start on discovering the meaning of human life when he plants shade trees under which he knows full well he will never sit.
~ Elton Trueblood

I spent years trying to find a treatment for a degenerative genetic disease. Millions around the world knowingly lived and died from it, and yet it took so long to find a treatment because many considered it a "natural" part of life. Too long, I'm sure you know.

It all began the summer before we met, when I worked in Barry Goz's pharmacology/cancer biology lab. Before, genes had been theoretical objects I couldn't see or touch. That idea quickly changed once I learned I could control the growth of cancer using cell-cycle and DNA repair-blocking drugs. That summer, I realized how the disease of aging might be treated. If the genome contained all instructions for a cell's activities, knowing what genes to manipulate meant that any cellular activities could potentially be altered.

However, this newfound fascination with genetics was preceded by another deep interest, physics. My long but fruitful detour back to the genetics of aging began with my first advanced physics course that fall. Then I began my weekly research at Robert Behringer's granular materials lab at Duke, ending high school at the 12th International Young Physicists' Tournament. Physics seemed to be the field for me, especially when Duke gave me a full-tuition scholarship so I could do more.

You never doubted I was a good student, even when my first roommate began keeping me awake with loud music and friends over every night. Without sleep, my work suffered. However, I switched rooms, worked hard, and finished that semester at the top 5% of my class. After that challenging first year, I decided to pursue a biology major after realizing just how strong Duke's biology program was. I also took biomechanics and computer science to continue my training in physics, and learned how to use BLAST, PDB, and other NCBI software. When I graduated and became a biology TA, I had plenty to share with my students. I still remember their looks when I reviewed the physics of light for 20 minutes before photosynthesis lab, or how atomic force microscopy could visualize *and* move proteins.

That year, I also worked in Sönke Johnsen's visual ecology/biophysics lab. I was the only undergraduate to ask him for admission into his graduate photobiology course, later joining his lab for more research experience. Over months I measured variations in the natural color of skylight, so scientists could better understand how light pollution affected nocturnal animals. I didn't have as many research opportunities in genetics/cell biology as I wanted since I had started college in physics, and had to play catch-up in biology. However, the research I did convinced me that I was ready for the next level.

You shared my disbelief when I heard the news. Sönke and I were so sure I would make Duke's 8% admissions cut that I hadn't bothered applying elsewhere. Shortly after, I received my NSF fellowship but had no graduate school to attend. More work was in order. That summer I wrote a paper titled "The Cellular Mechanisms of Aging," still at www.realizen.com/projects/senescence.html. I wrote it to bolster the research component of my application, never thinking it would be so warmly received by the many researchers I met with that year.

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I already knew which over-expressed genes gave rise to the "immortal" but non-cancerous SIK, NIKS, and NM1 human fibroblast lines. After isolating their homologs in *C. elegans*, I used viral vectors to test whether these genes would extend lifespan. Our lab's subsequent paper spurred interest that someday, gene therapy might also lengthen human lifespan.

However, we still had no good treatment for tissues composed largely of senescent cells. It was my experience with cancer cells in Barry Goz's lab that inspired the solution. During my post-doc I used drugs, viral vectors, and antibody tagging to remove senescent cells in mice, replacing them using adult stem cells. Our greatest challenge was having the senescent cell ablation and the cell replacement occur together smoothly, but after working together with cell biology, immunology, and gene therapy researchers, we did it.

You were happy when my post-doc ended, and I found a research position near home. Years later, my new team and I demonstrated a 25% lifespan extension in rhesus monkeys who began treatment in their last quarter of expected life. You shared my amazement when, within days of our announcement, wealthy seniors were calling to volunteer funding and themselves for our first clinical trials.

Soon our senescence vaccine was ready. If given in youth, it could eliminate the genetic causes of aging. Millions could choose to overcome their biological programming, to learn and experience life for an extra 25 years or more. I remember your soft, wrinkled smile as you celebrated with the world's youth, even as you knew the vaccine could not help the old, and the treatment that could was still in testing.

I remember the morning when I learned that my forty years of research had not ripened in time to delay your pruning. You would have wanted to see all that has blossomed as a result of my graduate school research, and the experiences we had along the way.

I think what exemplifies human life most are the steps we're willing to take to ensure our bonds of friendship last as long as possible. I spent much of my life trying to extend yours, while you spent much of yours enriching mine. You've nurtured a seed that has grown into a great tree of discovery, a treatment for aging. I only wish you were here with me to enjoy its bountiful shade.