Telocyte Newsletter
Q1 2019

Telocyte focuses on Alzheimer's disease. Once we have engaged in our phase 1 FDA trial, currently slated for 2020, we plan to engage with other age-related diseases, including other dementias as well as cardiovascular disease, osteoarthritis, etc. At the most fundamental level, all of the diseases that we target share one coming feature: aging. Aging is no mere chronological measure, but an underlying process that occurs at the genetic – and epigenetic – level. Realistically, the only way we can cure age-related disease is by intervening in the aging process. One might say that we can only reverse age-related diseases by reversing aging itself.

Why then is Telocyte narrowly focused on disease and not on longevity?

Some twenty years ago, the FDA circulated a private white paper on the issue of age-related disease. Shorn of the explanations and the data, the outcome was simple: they would take the stance that they would not consider any interventions aimed at "aging", but they WOULD consider interventions aimed at age-related diseases. Frankly, both then and now, I agree with that stance. After all, it is not the years that bother us but the discomforts. The measure of importance is, after all, the loss of ease or the "dis-ease" that accompanies aging. Putting it differently, the practical measure of any intervention aimed at aging must be its ability to prevent and cure the diseases of aging.

Longevity, for example, is not the measure of success. In Greek mythology, it was Tithonus (*Τιθωνός*) who received the "gift" of eternal life without eternal youth: he had longevity without health. Pure length of life – longevity – is neither attainable without health nor is it desirable. The measure of our lives, from the medical if not the philosophical standpoint, is how healthy we are, not how long we can prolong unhealthy lives.

As a result, we believe that our critical focus must lie with improving health, not with extending lives. We have nothing against longevity – far from it – but that longevity must be secondary to optimal health, not to years that are merely long, perhaps even all-too-long. When Telocyte focuses on age-related disease, it is not really the diseases we focus on, but the age-related health that we create by curing and preventing those diseases.

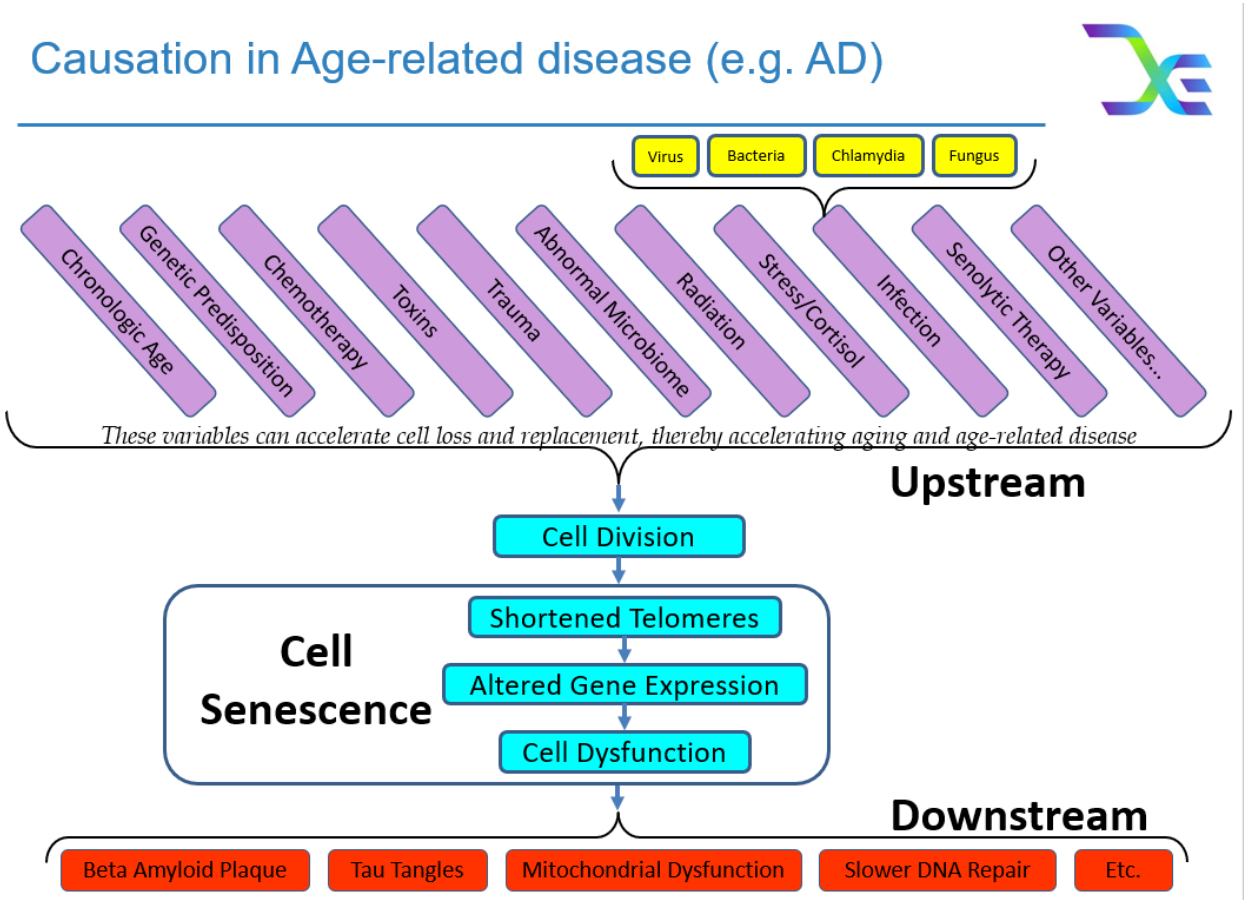
One result of this keen desire to ensure health is that we avoid discussions, meetings, conferences, and presentations that focus on longevity or age reversal. With prejudice to none, our goal is not longevity, but health; our goal is not age reversal, but the cure of the diseases of aging. Our concerns are not cosmetic, but more lie with more a fundamental issue.

We intend to create healthier lives by curing and preventing age-related disease, starting with Alzheimer's disease.

How Alzheimer's works

Why do we get Alzheimer's or any other dementia? And why do some of us get it so early, while others do not? What causes Alzheimer's and other dementias?

Alzheimer's occurs when the neurons of the brain become dysfunctional and are lost. The neurons, however, depend upon the health and function of the surrounding glial cells, cells that take care of the metabolic and physiological needs of those critical neurons. In some sense, the neurons are merely the "innocent bystanders" as the glial cells fail. In all of the various types of Alzheimer's dementia (sporadic, familial, etc.) and indeed in all of the age-related dementias (Lewy Body, Frontotemporal, Parkinson's, etc.) it is the glial cells that are the single common denominator. The glial cells fail as, having divided repeatedly over your lifetime, their telomeres shorten, and their pattern of gene expression becomes abnormal, insufficient, and pathological. The process is remarkably complex and affects a myriad of processes – including beta amyloid and tau tangles – but the fact that telomere shortening is always central to the pathology is what allows us to target telomeres in our goal of curing and preventing Alzheimer's and other age-related dementias.



Yet we know that a number of variables seem to play a role in the onset of Alzheimer's disease. One person shows symptoms at age 50, another at age 80. One person, with a history of head injuries (e.g., football players), or a history of infections, or a history of chemotherapy,

comes down with a dementia far earlier than another person. Not only does age itself play a role, but so do our genes (e.g., a double ApoE4 allele), and your life-long medical history. Why do so many things appear to play a role in our risk of dementia? The reason is that these are variables that accelerate glial cell loss and replacement, thereby accelerating aging and age-related disease. The result is dementia. Upstream, we have all the various risk factors – each of which determines the rate at which our glial cells divide and age – and downstream we have all the classic findings of dementia – including beta amyloid plaques, tau tangles, and a host of other findings.

The one oddball, perhaps, is vascular dementia, but even here we find that there are cells that show the same process of telomere shortening and cell failure. In the case of vascular dementia, the problem lies not with the glial cells, but the cells that line the blood vessels of the brain: the vascular endothelial cells. While the cells are different – glial or endothelial cells – the outcome is the same: the cells divide, telomeres shorten, gene expression changes, the cells cease to work normally, and the result is the failure and death of neurons. More importantly, the result is the loss of those we love.

In all cases, however, whatever the type of dementia, the key is that we can prevent or cure such dementias not by dealing with the dozens of risk factors that lie upstream, nor by trying to repair the dozens of findings that lie downstream, but by intervening in a single, critical point: the telomere.