Written Testimony of Steve Horvath
Hearing on "The Fountain of Youth? The Quest for Aging Therapies"
House Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
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My name is Steve Horvath. I was a professor of Human Genetics and Biostatistics at the University of California, Los Angeles ("UCLA"). My research lies at the intersection of several fields including biogerontology, anti-aging clinical trials, epigenetic biomarkers of aging, epidemiology, systems biology, and comparative biology. With my UCLA colleagues, we published the first epigenetic clock for saliva, the first pan-tissue clock, and the first pan mammalian clock. I've recently joined Altos Labs, a biotechnology start-up focused on cellular health and rejuvenation.

I am testifying in my personal capacity as a scientist and researcher and am honored to speak to the members of this committee on the timely and important topic.

Epigenetic Clocks in Aging Studies

I am here today to speak to you about a new class of molecular aging biomarkers known as epigenetic clocks, which allow us to measure aging in all mammalian cells, tissues, organs.

Epigenetic aging clocks keep track of chemical modifications of the DNA molecules. An epigenetic clock is a biochemical test that can be used to measure the age of a cell. The test is based on DNA methylation levels, measuring the age-related changes to the methyl groups to one's DNA molecules in your genome.

"Epi-" means "above", and it relates to how epigenetics, or methylation, controls your gene expression. Building on work following the Human

Genome Project, we now understand that your DNA or genome alone is not your destiny. Epigenetics much more than genetics alone can drive change in your cells and tissues, and importantly it is believed that many of these epigenetic changes may be modifiable. Many researchers believe that emerging work in epigenetics may be critical for development of more personalized and effective medicines.

We now can reliably predict human age currently using a simple blood draw. By applying epigenetic clocks to DNA collected before and after a drug treatment, we're able to quickly determine if a drug is affecting the aging process. Using these epigenetic aging clocks, we and others have found interventions that greatly reverse the age of rodents. Some of these results are expected to matter for human health as well.

In 2019, we published results from a Phase 1 human clinical trial that demonstrated a notable first – that a treatment consisting of already approved drugs and supplements could reverse all established epigenetic clocks in healthy older men age 50 to 65. This work was sponsored by a start-up biotechnology company named Intervene Immune. A Phase 2 trial known as TRIIM-X is now ongoing in California in order to assess if this same treatment can be applied to older men & women age 40 to 80. The trial may also determine if it leads to functional improvements in older individuals, such as increased leg strength that will delay onset of frailty.

This ongoing work has provided a very helpful example or template for the longevity research community. When used along with standard clinical and physiological testing, epigenetic clocks could add a rigorous and practical approach for determining if a new longevity drug is safe & effective for use in healthy older individuals. Preventative medicine trials that previously took 5-7 years may now be completed in only 1-2, although tracking of longer-term health outcomes is critical as well.

The biotech industry is also now developing exciting new drugs targeting the biology of aging. As the data mature, there will be a need for a clear

regulatory framework for drug approval in healthy older individuals. In addition, looking at current classifications to ensure they are inclusive of these new therapies would be helpful.

My hope is that this Committee and others in government will recognize the recent biomedical breakthroughs including biomarkers of aging and modernize the approval process for new longevity treatments.

When we look back at past centuries to find the high rate of child mortality completely unacceptable: nearly 50 percent of babies born in the US in 1800 did not live past their fifth birthday. I predict that future generations will look back at our times and recoil in horror at the high mortality rate and our poor public health. Globally, over 100,000 people die each day due to age-related diseases. We don't have to accept this anymore.

We have an opportunity and arguably obligation to leverage recent biomedical breakthroughs to identify longevity interventions that may delay the onset of chronic diseases, and which may revolutionize the field of preventative medicine.

Thank you for your time and invitation to speak on this important topic.

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