




FOXO

THE FUTURE OF THE
LONGEVITY INDUSTRY



By Jon R. Sabes, CEO
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the future of life insurance

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a breakthrough discovery



Jon Sabes, CEO

“Our business was founded to evolve the status quo of the longevity industry.”

For centuries, predicting human lifespan has been the province of the longevity insurance industry—life insurance, annuities, and pensions. Little did anyone know that lifespan prediction, and longevity underwriting by extension, could be transformed by the science of epigenetics.

In September 2015, I became aware of the work of Dr. Steve Horvath, a world-renowned geneticist and biostatistician at the University of California, Los Angeles (UCLA), who had discovered new methods of measuring biological aging using the science of epigenetics. Upon learning of Dr. Horvath’s groundbreaking work, I identified that his lifespan predictive epigenetic technology could be applied to the global longevity insurance industry to improve mortality underwriting and risk classification.

Several years later, after working with Dr. Horvath, he reported developing a new scientific method to predict human lifespan by identifying epigenetic markers for individuals who lived longer and died sooner¹—essentially laying the foundation for a next-generation lifespan underwriting tool. In April 2017, our company exclusively licensed Dr. Horvath’s DNA Methylation Mortality Prediction (M-Panel) technology and began building a next-generation longevity company focused on commercializing epigenetic science into the actuarial and underwriting tools used by the global longevity industry.

Our foundational interest in applying epigenetic science into longevity underwriting stems from Dr. Horvath’s work and the discovery of the “epigenetic clock” in 2013. The relationship between individual risk of all-cause mortality and biological aging (as measured and defined by an epigenetic clock versus other measures) has proven to be significant and unmistakable.

a breakthrough discovery

Since the discovery of the epigenetic clock, we have witnessed a continued development of new clocks with EEAA, PhenoAge, GrimAge, and GrandAge. Given the continual exponential advances of technology, we have every reason to believe that the predictive power of these clocks will only continue to improve.

Early in our journey to apply epigenetic clock technology to the longevity insurance industry, we also discovered an overwhelming amount of scientific literature documenting the correlation of epigenetic science to numerous health and wellness conditions assessed in traditional longevity underwriting. In fact, thousands of peer-reviewed, epigenome-wide association studies (“EWAS”) have been published documenting the correlation of epigenetic markers to a wide swath of human health and wellness conditions. For example, tobacco use has been proven to leave an unequivocal epigenetic mark along the epigenome. And to our surprise, the longevity industry suffered from an inability to precisely measure tobacco use. This knowledge led us to discover that epigenetic science could effectively measure many risk assessment factors used in traditional underwriting and risk classification better than the current methods. Moreover, we knew that epigenetic science would introduce new predictive lifespan measures, such as the epigenetic clock, to improve the predictive models used to power the industry.

Accordingly, FOXO was created to discover and develop epigenetic science into a pivotal solution for the global longevity insurance industry. With expertise in the areas of molecular biology, machine learning, laboratory testing, and longevity underwriting, our team is committed to reimagining the future of longevity underwriting and supporting the growth of longevity markets with a next-generation underwriting protocol that utilizes the full benefits of scientific innovation and insight.

We invite you to read on and discover how our company is applying the cutting-edge technology of epigenetics and evolving the longevity industry into its future self.

the science behind our technology

The science behind our technology is based on the rapidly evolving discipline of molecular biology and the field of epigenetics. Our technology identifies and evaluates biomarkers occurring along the epigenome that are predictive of current states of health and wellness. And while genetics and epigenetics may sound similar, they are vastly different. Understanding the basic difference between these two distinct branches of biology is key to appreciating the power of innovation and the application of molecular technology to the longevity insurance industry.

GENETICS

Genetics is the study of human DNA, or the genome. Our genome consists of over three billion base pairs of code (consisting of Adenine (A), Guanine (G), Thymine (T) and Cytosine (C)) that contain the instructions for our physical biology. Our genetic code is inherited from our parents, and the arrangement of the base pairs plays an important role in who we become. Our genetic code is permanent and remains fixed throughout our lifetime.

In 2003, scientists sequenced the human genome at a cost of \$2.7 billion. Today, a human genome can be sequenced for less than \$1,000²—resulting in a vast expansion of the field of science and research known as molecular biology. While we still don't comprehend all aspects of human biology, studying the human genome has led to the understanding that our genetic sequence does not explain the whole of our biology; and for a more complete picture, one must also consider the workings of the epigenome to understand why some genes are expressed and others are not.

EPIGENETICS

Epigenetics studies how our genes are expressed by looking at what is happening on-top-of, or around, the epigenome. The prefix “epi-” means on-top-of, and epigenetics studies how biochemical markers (such as “methylation”) cause our DNA to express, turning on or off genes that result in changes to cellular function. In stark contrast to our genetic code, our epigenome changes dramatically in response to aging, behavior, and environmental factors, making it a dynamic aspect of our biology. Measuring epigenetic changes is relatively simple; thus, behaviors such as smoking that leave biochemical markers are able to be captured and quantified. Epigenetics explains a great deal of why our behaviors influence our individual health and wellness profiles that impact disease, aging, and healthspan.

OUR MISSION

The same technology that is transforming healthcare with precision-based diagnostics and therapeutic medicines promises to change the future of longevity underwriting. Our mission is to lead discovery, development, and integration of this technology into a next-generation underwriting protocol for the global longevity insurance industry. Our research is focused on developing a broad portfolio of epigenetic biomarkers that supports and replaces the traditional underwriting protocols. From a simple saliva sample, we are able to determine the traditional underwriting health factors insurance companies have long sought to measure with greater accuracy and precision. Over time, we hope to provide unprecedented insights into health, wellness, disease, and aging—resulting in innovative new opportunities for the development of products that improve consumer health.

our technology

Our technology is inspired by the work of UCLA geneticist and biostatistician, Dr. Steve Horvath who in 2013 published the landmark paper, “The Epigenetic Clock,” which demonstrated that epigenetics can be used to estimate biological aging. In late 2016, our Chief Science Officer, Dr. Brian Chen, along with Dr. Horvath and an international coalition of scientists reported that epigenetics could be used to “predict all-cause mortality above and beyond chronological age and traditional risk factors” with a new clock called the DNA Methylation Mortality Predictor.³ The development of the DNA Methylation Mortality Predictor was derived from a meta-analysis study involving a cohort of more than 13,000 individuals who were followed for decades and included more than 2,700 mortality events.

“Our technology is based on the new and rapidly evolving science of epigenetics that identifies and evaluates molecular biomarkers of health and wellness occurring along the epigenome.”

Our technology team, led by Dr. Brian Chen, seeks to discover, develop, and commercialize unique patterns of methylation occurring along the epigenome in order to understand and assess individual health and wellness. In a sense, we are reverse engineering patterns of methylation along the epigenome that correlate not only to mortality, but to specific measurements of human health and wellness. We refer to the identification of patterns of methylation as “epigenetic biomarkers.”

The process of identifying epigenetic biomarkers is achieved by applying advanced supervised machine learning and artificial intelligence technologies to create predictive models that correlate epigenetic profiles with states of health, wellness, disease, and aging.

insurtech and underwriting

OUR RESEARCH

The process of identifying epigenetic biomarkers is achieved by applying advanced supervised machine learning and artificial intelligence technologies to create predictive models that correlate epigenetic profiles with states of health, wellness, disease, and aging. We believe epigenetic biomarkers can replicate traditional assessments of health and wellness and are currently developing epigenetic biomarkers that target specific age-related diseases such as cancer, cardiovascular disease, diabetes, and neurological disorders. In addition to our efforts to identify epigenetic biomarkers, we are also advancing other programs that will expand the use of epigenetics in the development of a more comprehensive understanding of disease and healthspan.

The DNA Methylation Mortality Predictor could “predict all-cause mortality above and beyond chronological age and traditional risk factors.”

Our specific challenge has been to take the myriad existing EWAS and translate them into effective epigenetic biomarkers that can integrate into a longevity underwriting protocol. In 2019, we initiated and completed the FOXO Pilot Study to establish the baseline efficacy for the use of epigenetic biomarkers for life insurance underwriting.

This study was a self-designed parallel underwriting of 1,295 individuals whose health was analyzed using research laboratories to measure fifty-two clinical chemistries from blood, urine, plasma and saliva. In addition, individuals were screened for tobacco/alcohol/drugs of abuse, as well as underwritten for risk classification by a leading facultative underwriting group. As one of the most ambitious studies of its kind, the FOXO Pilot Study demonstrated that epigenetic biomarkers could be identified in both blood and saliva for traditional underwriting health and wellness factors.

AN EVOLUTION UNDERWAY

Insurtech transformation of longevity underwriting and risk classification with new advanced biological technologies is inevitable. Traditional paramedical collection of blood and urine will soon be a relic of the past, as the invasiveness (deep venous puncture for a drawing of blood); inconvenience (difficulty scheduling in-person visits); and slow pace (often taking six to eight weeks from start to finish) of underwriting will soon look medieval.

Consider: Although tobacco exposure was documented to be lethal by the mid-1960s, the actuarial tables that distinguished between smokers and non-smokers were not even developed until the 1980s.^{6,7} Today, 19% of the American population uses tobacco, and smoking remains a leading cause of preventable death in America.⁸ The advent of new technologies in the scientific field of epigenetics provides an excellent example of the ability to improve underwriting precision from the current method of cotinine biomarker measurement from urine. The short half-life of cotinine in the blood stream has created a game of cat-and-mouse, wherein non-smokers pick up the tab of smokers. The idea of accepting “smoking amnesia” as an approved industry practice will soon be considered repugnant. The tables are turning, and soon consumers and insurers will not tolerate anything less than precise measurements of individual health and wellness conditions, such as tobacco exposure.

Insurtech innovation is turning from unconventional data sources such as credit scores to precise molecular measures of individual health and wellness. New molecular technologies can not only help better determine an insurance applicant’s risk class, but also improve customer engagement and incentivize better health outcomes, while keeping premiums affordable and offering innovative forms of coverage.

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FOOTNOTES AND CITATIONS

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