Extended Longevity
IRB 2021-2023.
The Longevinaut Study #1

THE SAFETY AND EFFECTIVENESS OF THE EXTENDED LONGEVITY PROTOCOL ON THE EPIGENETIC AGING RATE IN HEALTHY INDIVIDUALS

Protocol Number: TD-EL-001

IRB approval number: IRCM-2019-285

Conducted by
Quantum Functional Medicine of Carlsbad, California
Dr. Juergen Winkler, MD
Through the Institute of Regenerative and Cellular Medicine (IRCM) of Santa Monica, California, Executive Director Dr. Barbara Krutchkoff, PhD

The Safety and Effectiveness of The Extended Longevity Protocol on the Epigenetic Aging Rate in Healthy Individuals
By Steven M. Schorr

www.extendedlongevity.com
sms@extendedlongevity.com

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An Institutional Review Board (IRB) has been conducted by Dr. Juergen Winkler of Quantum Functional Medicine of Carlsbad, California, under the auspices of the Institute of Regenerative and Cellular Medicine (IRCM) of Santa Monica, California, sponsored by Extended Longevity, Inc. of Kula, Hawaii, in support of the Extended Longevity Protocol in a study to demonstrate the reversal of three primary biomarkers measuring the ten (10) determinant factors of aging.

The final report for Longevinaut Study #1 includes a cohort of 11 men and women ages 55–75 who have taken the Extended Longevity Protocol daily for up to one year.

Part 1. Introduction

This Institutional Review Board (IRB) report discusses the results of a year-long study involving a cohort of 11 individuals, ages 55–75, who underwent epigenome tests, telomere tests, and C-Reactive Protein (CRP) tests. The aim of the study was to investigate the relationship between the biomarkers of aging, the 10 determinant factors of aging, and the health and aging of the participants.

1. **Methods:**

The study was conducted at a research center, and all participants provided informed consent prior to enrolling in the study.

A. Epigenome tests were conducted using a DNA methylation array to assess the methylation status of specific genes.
B. Telomere tests were conducted using a quantitative polymerase chain reaction (qPCR) method to measure the length of telomeres, which are protective structures at the ends of chromosomes that shorten with age.
C. Hs-C-RP tests were conducted using a high-sensitivity assay to measure levels of this protein in the blood, which is a marker of inflammation.

All tests were conducted at baseline, after 6 months, and after one year.

2. **Process:**

The Extended Longevity Protocol is a set of 10 phytotherapeutic extract formulations that address the 10 determinant factors of aging. Each participant has taken baseline tests to measure their epigenome, their telomere length, and their inflammation via the Hs C-RP test.

The participants then commenced with the consumption of a standardized daily dose of 1 ml of each of the 10 phytotherapeutic extract formulations provided by Extended Longevity, Inc.

The participants were then administered a set of tests at baseline, 6 months, and 12 months of product consumption.

3. **Analysis:**

A thorough analysis of the Investigative Review Board (IRB) was conducted by Dr. Juergen Winkler of Quantum Functional Medicine of Carlsbad, California, under the auspices of the Institute of Regenerative and Cellular Medicine of Santa Monica, California, for the Longevity Study of 11 men and women aged 55–75 who have taken the Extended Longevity Protocol daily for one year.

The analysis showed that there has been significant success in decelerating the biomarkers of aging across the cohort. The data collected at the baseline, 6-month, and 12-month marks indicate a marked improvement in the epigenome, telomere length, and inflammation levels of the majority of the participants.

4. **Conclusion:**

The Extended Longevity Protocol has demonstrated the ability to address the key factors that contribute to aging, and the results of the study support this claim. The findings indicate that this protocol has the potential to significantly improve the overall health and longevity of individuals.

It is important to note that while the study results are encouraging, further research is necessary to fully understand the extent of the benefits and potential risks of the Extended Longevity Protocol. However, based on the collected and analyzed data, it is evident that the Extended Longevity Protocol has the potential to significantly improve the health and longevity of individuals who use it.

In conclusion, the Investigative Review Board conducted by Dr. Juergen Winkler of Quantum Functional Medicine of Carlsbad, California, under the auspices of the Institute of Regenerative and Cellular Medicine of Santa Monica, California, has produced significant findings regarding the effectiveness of the Extended Longevity Protocol in decelerating three biomarkers of aging. The study results are encouraging and indicate potential for improving the overall health and longevity of individuals who use this protocol. However, further research is necessary to fully understand the benefits and potential risks of the protocol.

Part 2. The Tests

1. **Elysium Health Index Epigenome Tests**

Epigenome testing, in particular the independent laboratory tests provided by Elysium Health Index Epigenome Test, was used to affirm and/or modify the initial research findings from the epigenome tests conducted by TruDiagnostic, Inc.

Epigenome testing is a type of genetic testing that examines how genes are regulated and expressed without altering the underlying DNA sequence. The epigenome refers to the chemical modifications of the DNA and its associated proteins that control gene expression. These modifications, such as DNA methylation, histone modifications, and non-coding RNA, can influence gene expression.

Elysium Health is a company that provides a DNA-based epigenetic health test that examines the methylation patterns in specific genes associated with aging. The test analyzes a person's epigenome to determine their "epigenetic age," which can be compared to their chronological age to assess the individual's risks relative to their biological age.

The epigenetic test provided by Elysium Health involves collecting a small sample of saliva and analyzing it for DNA methylation patterns. The test examines methylation patterns in specific genes associated with age-related processes. The test is analyzed using advanced DNA sequencing technologies to detect specific methylation patterns in genes associated with the rate of aging. The test evaluates methylation patterns across the genome, which are then compared to a database of known methylation patterns to determine the individual's age as it compares to the methylation patterns of people from various age groups. This database is statistically analyzed to draw a comparison of the relative ages of the individuals. For example, someone who is 50 years old would present a methylation pattern that would be different from that of a 60-year-old person and statistically different from that of a 70-year-old person. On average, if you are 70 years old but have the methylation pattern of a 54-year-old person, you are considered to be biologically 54 years old. Your chronological age remains consistent with the accumulation of years as defined by a standard calendar.

Overall, epigenome testing, including the test provided by Elysium Health, provides valuable insights into the potential risks of aging and age-related ailments and can help individuals make informed decisions about their health and lifestyle choices.

2. **TruDiagnostic Epigenome Tests**

Epigenome testing, in particular the independent laboratory test provided by www.trudiagnostic.com, is a type of genetic testing that examines chemical modifications to DNA and its associated proteins that regulate gene expression. These modifications, such as DNA methylation and histone modifications, can influence the activity of genes and are influenced by various environmental factors.

TruDiagnostic is a company that provides epigenetic testing services for individuals interested in learning more about their health and potential disease risk factors. The company's epigenetic testing analyzes DNA methylation patterns to evaluate an individual's risk for certain conditions, such as cancer, diabetes, and heart disease.

To perform the test, TruDiagnostic collects a sample of the individual's blood, which is then analyzed using advanced DNA sequencing technologies to detect specific methylation patterns in genes associated with various health conditions. The test evaluates methylation patterns across the genome, which are then compared to a database of known methylation patterns to determine the individual's age as it compares to the methylation patterns of people from various age groups. This database is statistically analyzed to compare the relative ages of the individuals. For example, someone who is 50 years old would present a methylation pattern that would be different from that of a 60-year-old person and statistically different from that of a 70-year-old person. On average, if you are 70 years old but have the methylation pattern of a 54-year-old person, you are considered to be biologically 54 years old. Your chronological age remains consistent with the accumulation of years as defined by a standard calendar.

The test results provided by TruDiagnostic include an individualized report that assesses the individual's age based on their epigenetic profile. The report provides their overall epigenetic age and an evaluation of their response to certain interventions.

Overall, epigenome testing, including the test provided by TruDiagnostic, offers valuable insights into an individual's ability to analyze epigenetic patterns and can provide a more complete understanding of an individual's overall rate of aging. Epigenome testing has the potential to revolutionize personalized medicine by providing a more comprehensive understanding of an individual's biological age, health risks, and potential treatment options.

3. **SpectraCell Telomere Tests**

Telomere testing, in particular the independent laboratory test provided by www.spectracell.com, is a type of genetic testing that measures the length of telomeres, the protective caps at the end of each chromosome. Telomeres are known to shorten with age and cellular stress, and their length has been linked to various health conditions, including cancer, heart disease, and aging. Telomeres are repetitive DNA sequences that protect the ends of chromosomes from damage and are associated with the aging process. As cells divide, telomeres gradually become shorter until they reach a critical length, leading to cell death or senescence.

SpectraCell is a company that provides a telomere analysis test, which measures the length of telomeres in an individual's white blood cells. The test examines the length of an individual's telomeres to assess their cellular aging and overall health status.

The telomere analysis test provided by SpectraCell involves collecting a small sample of blood and analyzing it for telomere length. The test measures the length of telomeres in white blood cells, which are indicative of the overall health of an individual's immune system.

The results of the telomere analysis test provided by SpectraCell are presented in a report that provides an individualized assessment of an individual's cellular aging. The report includes information on the individual's telomere length and a comparison of their telomere length to their chronological age.

Overall, telomere testing, including the test provided by SpectraCell, has the potential to revolutionize personalized medicine by providing a more comprehensive understanding of an individual's cellular aging. By measuring telomere length, individuals can take proactive steps to maintain or improve their health and prevent or manage age-related ailments.

4. **HS C-RP Tests**

Independent local laboratory testing was conducted and coordinated by Quantum Functional Medicine using Hs C-RP testing, which provides insight into the state of inflammation in the individual. C-reactive protein (C-RP) testing is a blood test that measures the level of C-reactive protein in the blood. C-RP is a protein produced by the liver in response to inflammation, and elevated levels of C-RP are often indicative of systemic inflammation in the body.

The Hs C-RP test provides valuable information on the state of inflammation in an individual's body. Elevated levels of C-RP have been linked to an increased risk of cardiovascular disease, diabetes, and certain cancers. By measuring C-RP levels, the test can help identify potential health risks associated with chronic inflammation.

The Hs C-RP test is a simple blood test that involves drawing a small amount of blood from the individual. The blood is then sent to a laboratory for analysis, and the results are usually available within a few days.

The results of the Hs C-RP test are presented as a numeric value, with higher values indicating increased inflammation in the body. The test can help healthcare providers identify potential health risks associated with chronic inflammation and develop appropriate treatment plans.

By measuring C-RP levels, the Hs C-RP test can help identify individuals who may benefit from lifestyle changes, such as exercise and healthy eating habits, to reduce inflammation in the body. The test can also help healthcare providers monitor the effectiveness of treatments for chronic inflammation, such as medications or dietary supplements.

Overall, Hs C-RP testing provides valuable insight into the state of inflammation in an individual's body. The test is a useful tool for identifying potential health risks associated with chronic inflammation and developing appropriate treatment plans to improve overall health and wellbeing.

Part 3. The Results

A. Epigenome Tests.

1. Epigenome Data Chart #1.

	Patient.ID	Test	X		EL.ID	Kit.ID	Female	Chron Age	PCHorvath1	PCHorvath2	PCHannum	PCPhenoAge	mAge_Hannum	PhenoAge	PCGrimAge	mAge_Hovarth	Elysium Age	Clock Average Baseline	(-) Age Reduction	% Reduction from Chron age	% Reduction from Clock Average
1	206693320008_R01C01	Baseline		9/7/65	KT1	7VJSK77	1	56.3	58.9	62.2	64.9	60.1	53.3	38.8	65.3	63.6		58.4	-2.1	-3.8%	
1	206693320008_R02C01	6 month		9/7/65	KT1	JPRUMDM	1	56.8	57.7	60.8	58.3	50.6	47.4	27.3	62.6	65.8		53.8	3.0	5.2%	5.5%
1	206693320008_R03C01	12 month		9/7/65	KT1	PL2K3VZ	1	57.3	58.7	61.3	59.4	53.7	47.5	29.4	63.4	62.9		54.5	2.7	4.8%	5.0%
1		12 month		9/7/65	KT1	ELYSIUM	1	57.3	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>	>>>>>>	>>>>>>	48		9.3	19.3%	15.88%
2	206693320008_R04C01	Baseline		5/13/58	RG1	XD2TRH4	0	63.6	63.0	66.9	69.2	65.9	58.1	54.6	76.3	82.0		67.0	-3.4	-5.4%	
2	206693320008_R05C01	6 month		5/13/58	RG1	MJSFPR6	0	64.1	65.4	69.7	70.5	68.6	60.2	52.8	76.0	86.9		68.8	-4.7	-7.3%	-6.8%
2	206693320008_R06C01	12 month		5/13/58	RG1	2ZWV3JM	0	64.6	66.2	70.0	69.4	68.2	59.9	53.7	76.2	83.4		68.4	-3.8	-5.9%	-5.5%
2		12 month		5/13/58	RG1	ELYSIUM	0	64.6	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	56		8.6	15.3%	12.82%
3	206699840068_R01C01	Baseline		3/24/53	JG1	MY9A4WF	1	69.2	67.9	65.9	70.6	59.1	61.5	47.4	78.3	73.0		65.5	3.8	5.4%	
3	206699840068_R02C01	6 month		3/24/53	JG1	DLQTP7F	1	69.7	67.2	64.6	67.2	55.8	58.4	46.9	77.6	71.0		63.6	6.1	8.8%	9.7%
3	D/O																				
4	206699840068_R03C01	Baseline		11/17/62	JW1	QBBYUVF	0	59.6	65.4	62.0	65.6	55.1	55.8	42.3	67.6	69.7		60.4	-0.9	-1.4%	
4	206699840068_R04C01	6 month		11/17/62	JW1	NMXX8R4	0	60.2	65.3	62.5	65.6	55.1	52.5	43.7	68.2	70.2		60.4	-0.2	-0.3%	-0.3%
4	206699840068_R04C01	12 month		11/17/62	JW1	C3V6QKB	0	61.0	68.7	63.9	65.4	58.8	54.5	43.6	69.0	70.1		61.7	-0.7	-1.2%	-1.2%
4		12 month		11/17/62	JW1	ELYSIUM	0	61.0	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	52		9.0	14.8%	14.58%
5	206699840068_R05C01	Baseline		1/19/48	CH1	2EP9ABZ	0	74.4	68.2	67.1	74.4	68.0	61.6	50.0	78.2	71.1		67.3	7.1	9.5%	
5	206699840068_R06C01	6 month		1/19/48	CH1	W45J2HQ	0	74.9	71.4	69.6	75.9	74.6	62.7	52.4	79.6	72.2		69.8	5.1	6.8%	7.3%
5	207269880150_R03C01	12 month		1/19/48	CH1	W45J2HQ	0	75.4	69.7	67.0	73.5	69.5	63.4	47.5	78.4	71.0		67.5	7.9	10.5%	11.7%
5		12 month		1/19/48	CH1	ELYSIUM	0	75.4	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	56		19.4	25.7%	28.7%
6	206699840068_R07C01	Baseline		4/1/54	RG2	HLEJ58L	0	68.2	61.0	57.3	66.3	56.2	61.7	37.7	72.7	67.9		60.1	8.1	11.9%	
6	206699840068_R08C01	6 month		4/1/54	RG2	PENRL36	0	68.7	62.5	59.0	67.9	60.4	60.7	46.0	74.3	72.3		62.9	5.8	8.5%	9.3%
6	206699840068_R08C01	12 month		4/1/54	RG2	PENRL36	0	69.2	62.3	56.3	66.2	58.1	60.3	42.4	72.7	69.5		61.0	8.2	11.9%	13.5%
6		12 month		4/1/54	RG2	ELYSIUM	0	69.2	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	47		22.2	32.1%	36.41%
7	207321570079_R07C01	Baseline		5/2/66	PG1	CYYZR5X	1	55.4	50.8	50.2	57.6	49.2	52.6	40.2	62.2	60.2		52.9	2.5	4.6%	
7	207321570079_R07C01	n/a		5/2/66	PG1	n/a	1	56.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a		n/a	n/a	n/a	
7	207321570079_R07C01	12 month		5/2/66	PG1	5J2BBUV	1	56.8	55	52.2	55.9	50.2	45.6	31.7	64.4	60.8		52.0	4.8	8.4%	9.2%
7		12 month		5/2/66	PG1	ELYSIUM	1	56.8	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	41		15.8	27.8%	29.79%
8	207331530046_R03C01	Baseline		11/10/58	AG1	YYVWHC9	1	62.8	58.3	56.8	63.1	55.5	61.0	54.9	69.4	82.6		62.7	0.1	0.1%	
8	207331530046_R04C01	6 month		11/10/58	AG1	TXVRVGX	1	63.3	70.4	71.5	74.3	72.2	52.0	44.4	71.0	69.7		65.7	-2.4	-3.8%	-3.6%
8	207331530046_R08C01	12 month		11/10/58	AG1	NYLSC3M	1	64.1	72.9	75.0	76.8	74.6	63.8	57.0	n/a	84.6		72.1	-8.0	-12.5%	-11.1%
8		12 month		11/10/58	AG1	ELYSIUM	1	64.1	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	n/a				
9	207331530046_R01C01	Baseline		8/27/57	MC1	N5LJFLC	0	64.1	59.6	58.1	67.2	64.9	54.8	44.1	75.1	65.7		61.2	2.9	4.5%	
9	207331530046_R02C01	6 month		8/27/57	MC1	EKS2LS8	0	64.6	58.3	56.8	63.1	55.5	51.9	38.8	72.4	64.5		57.7	6.9	16.30%	11.9%
9	D/O																				
10	207331530046_R07C01	Baseline		4/9/59	MM	44HBLWC	1	63.8	61.2	63.6	64.4	56.8	72.8	71.7	55.2	45.3		61.4	2.4	3.8%	
10	207331530029_R02C01	6 month		4/9/59	MM	TBMX7XZ	1	64.2	63.6	65.9	65.3	55.0	56.6	45.9	72.6	74.8		62.5	1.7	2.7%	2.8%
10	207331530046_R06C01	12 month		4/9/59	MM	3CBS9AV	1	64.8	48.0	50.0	54.1	44.7	43.4	30.0	n/a	61.7		47.4	17.4	26.8%	36.7%
10		12 month		4/9/59	MM	ELYSIUM	1	64.8	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	>>>>>>>	53		11.8	18.2%	19.22%
11	207331530046_R05C01	Baseline		7/8/47	DG	JRB7SSH	1	74.2	72.6	73.6	77.4	70.4	63.5	59.1	79.3	84.4		72.5	1.7	2.2%	
11	207331530046_R08C01	6 month		7/8/47	DG	NYLSC3M	1	74.8	75.2	75.6	75.2	6.9	63.8	57.0	n/a	84.6		62.6	12.2	16.3%	19.5%
11	D/O																				

Average Chronological Age	64.0
Average Epigenome Baseline	61.0
Tru Average deceleration- 1 year	52.2
Elysium Average deceleration - 1 ye	50.0

Average age deceleration Chron to Elysium	14.0
Average age deceleration Baseline to Elysium=	11.0
Percent Reduction Chron to Elysium	-21.9%
Percent Reduction Baseline to Elysium	-18.1%

2. Epigenome Testing Analysis

The Longevinaut Study #1 began in September 2021. The original cohort included 11 people ages 55 to 74. There were six (6) women and five (5) men enrolled in the study. The study was planned for gathering test data over a 12-month duration.

a. Baseline TruDiagnostic Epigenome Tests

Baseline testing of the epigenome was conducted by an independent laboratory, TruDiagnostic Labs, for each cohort participant. The baseline epigenome results were typically not identical to the chronological age of the participant. As indicated in the chart above (Chart #1).

- Of the total starting cohort, 8 participants decelerated from their chronological age, and 3 participants aged normally.

b. 6-Month TruDiagnostic Epigenome Tests

6-month testing of the epigenome was conducted by independent laboratory TruDiagnostic Labs for each cohort participant. After 6 months, an epigenome test was given to all 11 participants in the cohort.

- Of the total cohort of 11 who consumed the Extended Longevity Protocol for 6 months, 7 participants were below age and 3 participants were above their chronological age. Data for one of the cohort's 6-month tests was unavailable.

c. 12-Month TruDiagnostic Epigenome Tests

12-month testing of the epigenome was conducted by independent laboratory TruDiagnostic Labs for each cohort participant. Epigenome tests were given to all eight of the remaining cohorts. Three of the cohort participants had dropped out of the original study for personal reasons.

- Of the total remaining cohort of 8 who consumed the Extended Longevity Protocol for 12 months, 5 participants were below their chronological age and 3 were above. Data for one of the cohort's 12-month tests was unavailable.
- Of those 7 participants with ages below their chronological age, the average reduced age was -8.83 years, with the most reduced chronological age of -12.2 years and the least at 1.7 years.

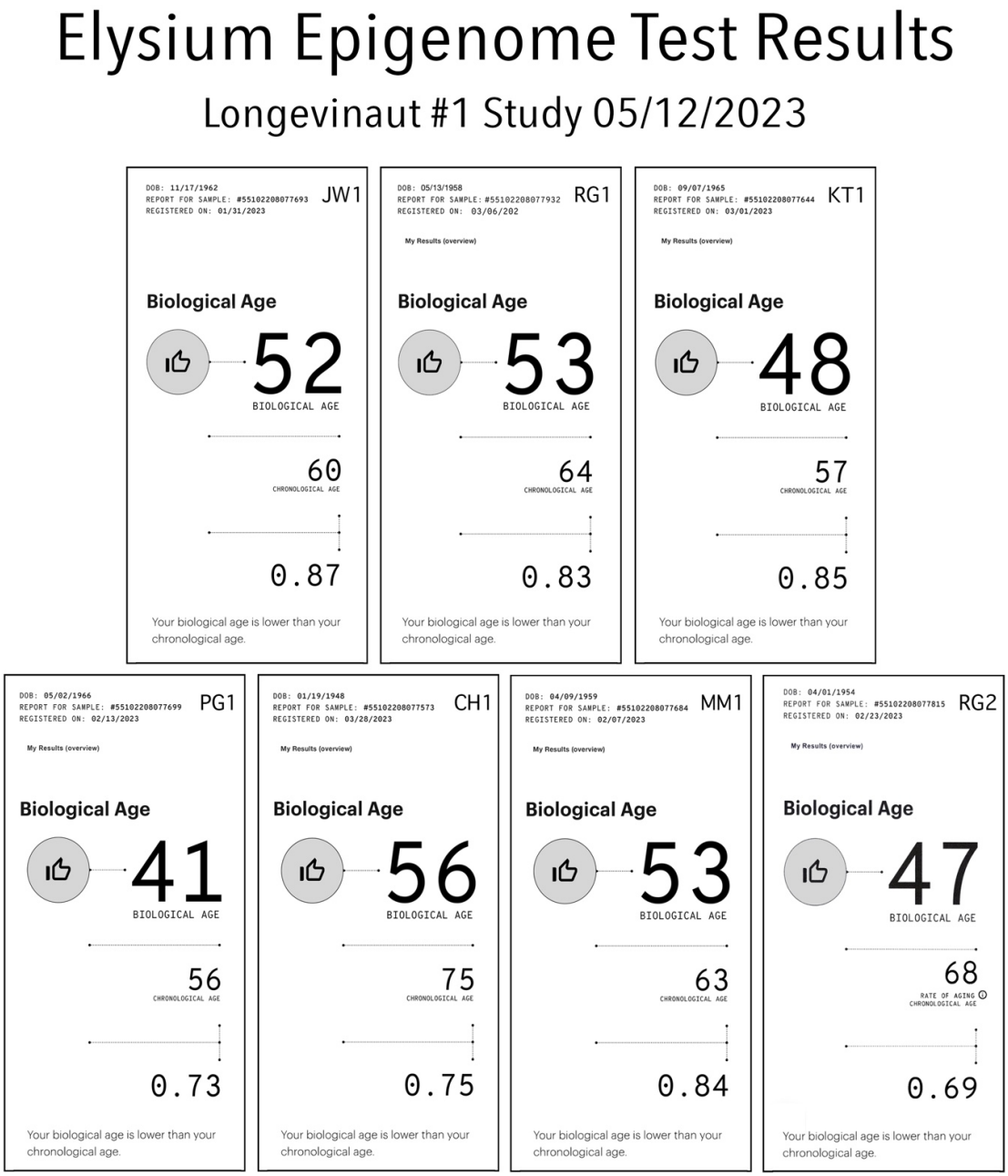
d. 12-Month Elysium Epigenome Testing

12-month additional testing of the epigenome was conducted by an independent laboratory, ElysiumHealth.com/index-labs, for each cohort participant. Epigenome tests were given to all eight of the remaining cohorts. Three of the cohort participants had dropped out of the original study for personal reasons.

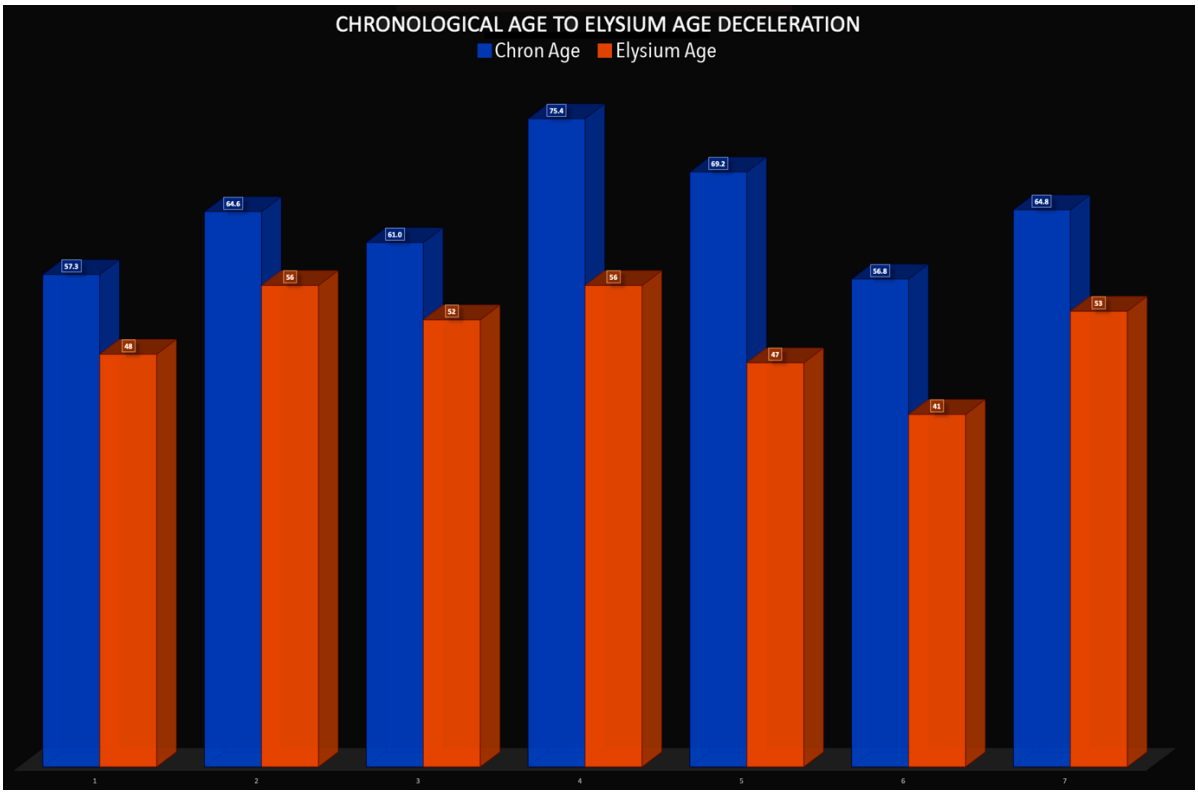
- Of the total cohort of 8 who consumed the Extended Longevity Protocol for 12 months, 7 participants were below their chronological age and 0 were above. Data for one of the cohort's 12-month Elysium tests was unavailable.
- Of those 7 participants with ages below their chronological age, the average reduced age was -13.73 years, with a maximum reduction of -22.2 years from their chronological age and a minimum reduction of -8.6 years.

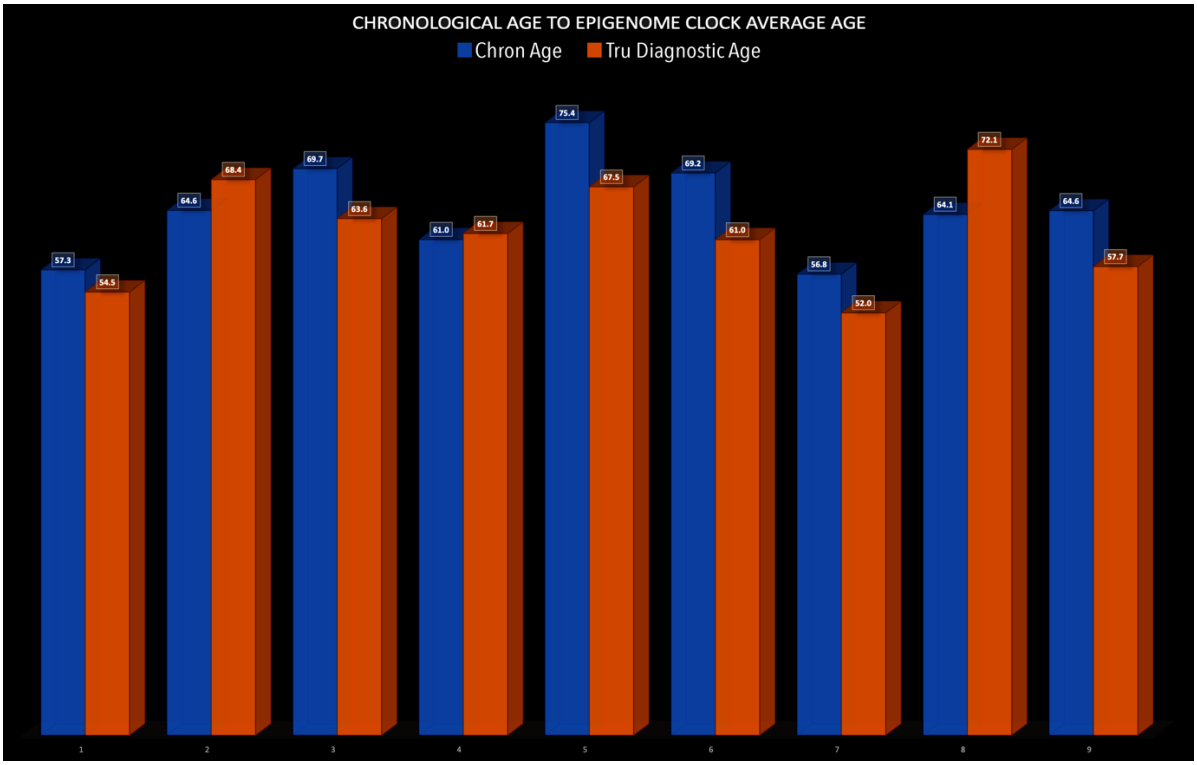
3. Elysium Epigenome Test Results

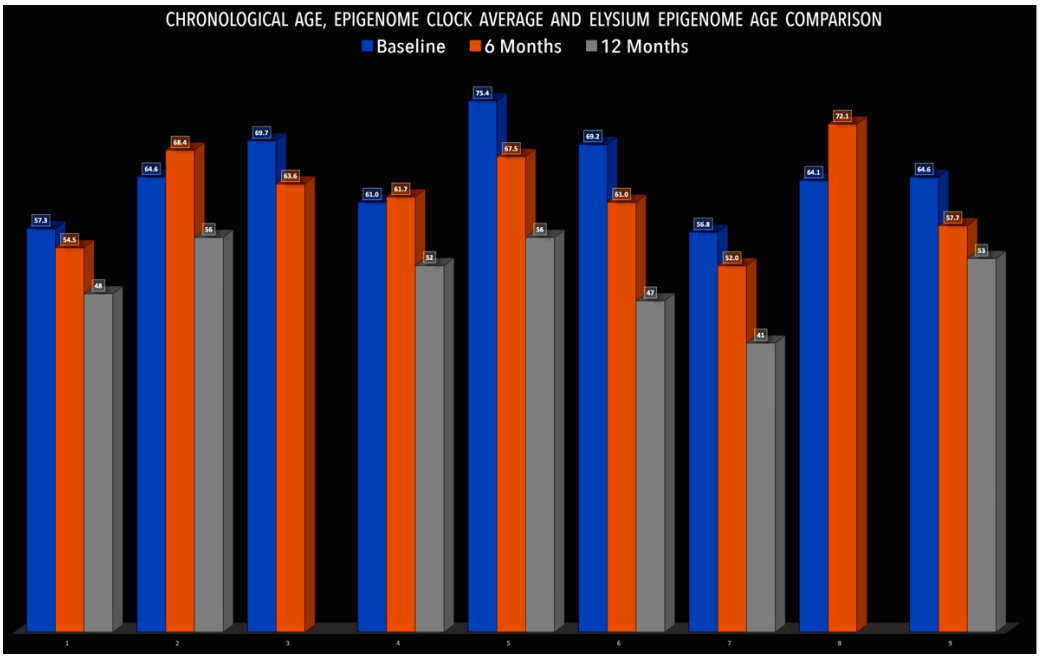
Average age deceleration Chron to Elysium	14.0
Average age deceleration Baseline to Elysium=	11.0
Percent Reduction Chron to Elysium	-21.9%
Percent Reduction Baseline to Elysium	-18.1%



4. Visualizing the Epigenome Test Results







B. Telomere Tests Age Reversal Results

1. Data Chart #2

EXTENDED LONGEVITY Telomere Test Cohort of Eleven 9/2021 through 1/2023

	Test Subject	Date	Baseline Telomere	6 MO in BP	1 yr	Percent +-	Age differential
1	RG a.63 M	9.2.21	8,010	8,220	8,680	7.72%	35 to 20
2	KT a.56 F	8.30.21	10,600	n/a	10,380	-2.12%	Hyper telomere
~~3~~	JG a F. DO	9.9.21	8,930	8,730	N/A	-2.29%	20 to 22
4	HC a.73	9.14.21	8,260	8,070	8,090	-2.10%	30 to 35
5	JW a. 58 M	9.14.21	7,010	8,250	7,390	5.14%	65 to 55
~~6~~	DG a.74 F DO	11.4.21	8,850	N/A	N/A	N/A	25
7	MC a.64 M	10.5.21	6,270	6,970	n/a	10.04%	75 to 65
8	AG a.63 F	10.26.21	7,680	8,020	8,430	8.90%	50 to 20
9	PG a.55 F	11.08.21	8,930	8,370	9,230	3.25%	30 to 20
10	MM a.63 F	1.11.22	7,800	8,140	8,820	11.56%	60 to 20
11	RG a.68 M	11.15.21	7,300	8,900	8,190	10.87%	60 to 30

7 positive gains average	8.21%
2 negitive loss average	-2.11%
2 drop outs	

2. Telomere Testing and Analysis

In the Longevinaut study, the Extended Longevity Protocol was administered to a cohort of 11 individuals, and their telomere lengths were measured at baseline, 6 months, and 12 months.

The results of the study showed varying degrees of telomere elongation among the participants. For example, subject 2 (KT) had hyper-long telomeres at baseline and showed a decrease in telomere length at the 6-month mark. Subjects 3 (GJ) and 6 (DG) did not have a 1-year measurement, so it is unclear how the treatment affected their telomere length.

However, for the other 8 subjects, there was an overall trend of telomere elongation over the course of the study, ranging from a 2% increase (subject 4, HC) to a 12% increase (subject 10, MM). In general, the results showed that the Extended Longevity Protocol had a positive effect on the telomere length of the majority of the subjects. 78% of the cohort increased their telomere length.

Overall, the results of the Longevinaut study suggest that the Extended Longevity Protocol may have a positive effect on telomere length, which is an important marker of cellular aging and overall health.

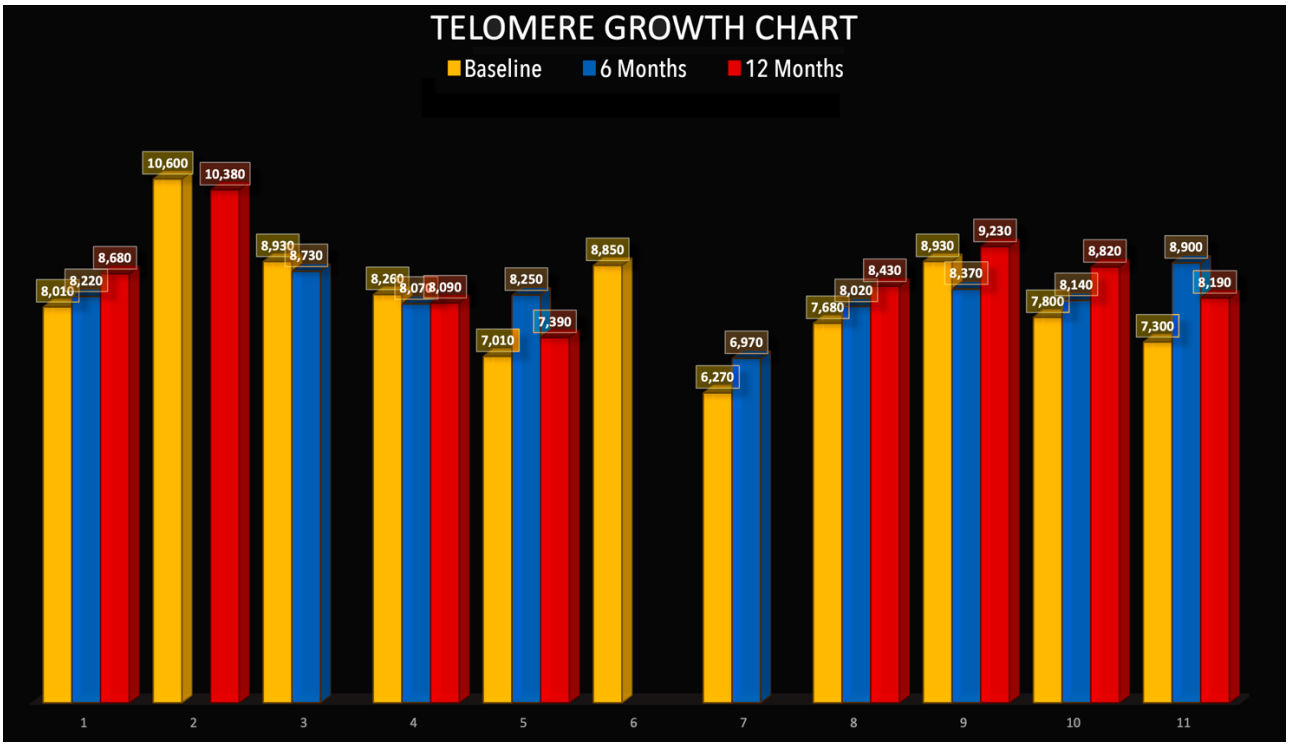
The percentage of age reduction and the relative number of years reversed.

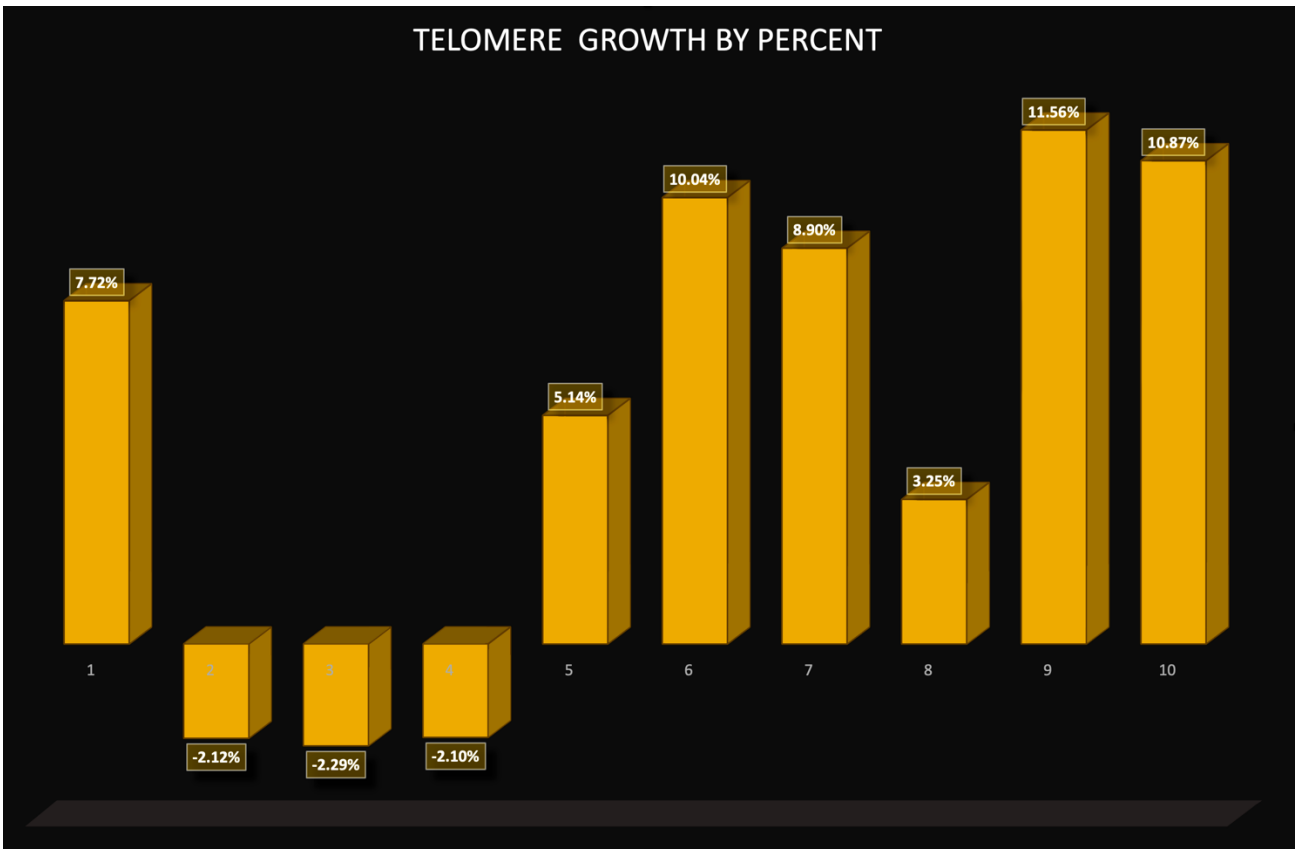
Based on the data, the Extended Longevity Protocol resulted in a decrease in the biological age of 78% of the participants. Specifically, the following participants showed a decrease in biological age:

- RG 63 M: 7.30% decrease in biological age, equivalent to 15 years reversed.
- KT 56 F: 2.12% increase in biological age, equivalent to 5 years of aging or more.
- HC 73 M: 2% increase in biological age, equivalent to 5 years of aging+.
- JW 58 M: 5% decrease in biological age, equivalent to 10 years reversed.
- AG 63 F: 8.80% decrease in biological age, equivalent to 30 years reversed.
- PG 55 F: 3.25% decrease in biological age, equivalent to 10 years reversed.
- MM 63 F: 12% decrease in biological age, equivalent to 40 years reversed.
- RG2 68 M: 10.80% decrease in biological age, equivalent to 30 years reversed.
- MC 64 M: 10.04% decrease in biological age, equivalent to 30 years reversed.

It's important to note that not all participants showed a decrease in biological age, and some showed no change or even an increase in biological age. However, the cases where there was a decrease in biological age suggest that the Extended Longevity Protocol may have potential for promoting healthy aging and potentially reversing some of the effects of aging.

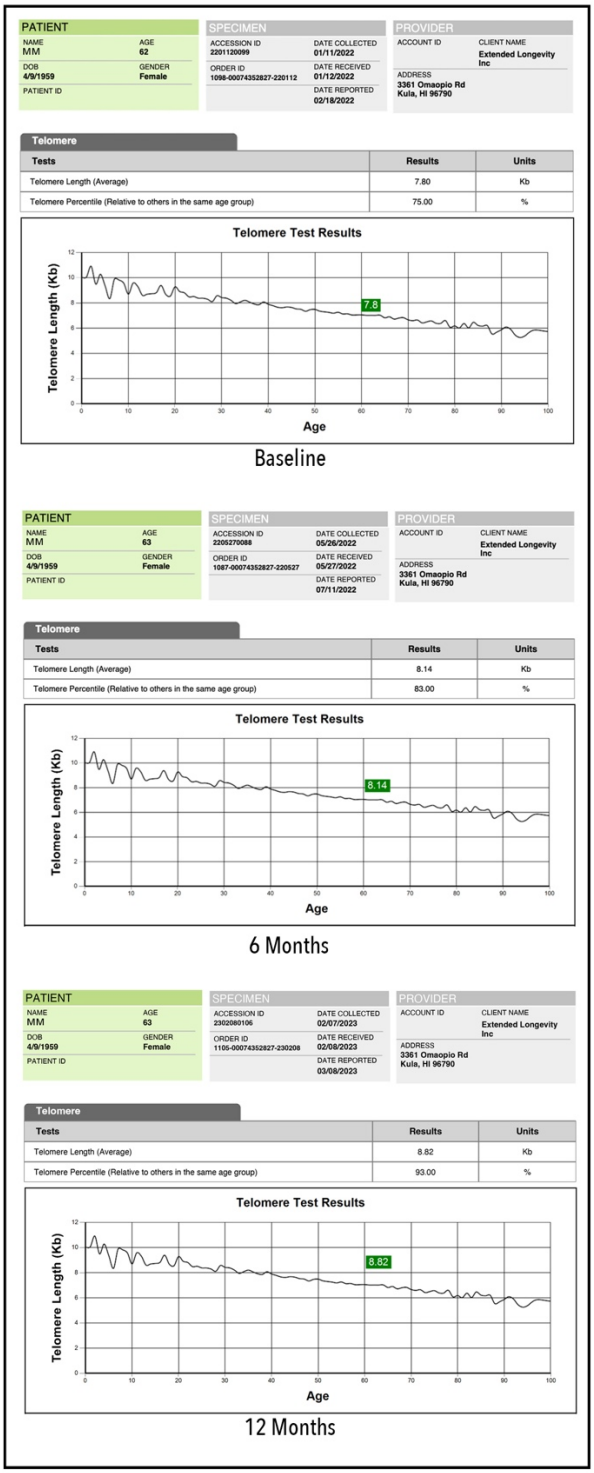
3. Visualizing the Telomere Test Results





4. Telomere Test Chart Examples

Participant #1 (Baseline, 6 mo. & 12 mo.)



PATIENT
NAME MM | AGE 62
DOB 4/9/1959 | GENDER Female
PATIENT ID

SPECIMEN
ACCESSION ID 2201120099 | DATE COLLECTED 01/11/2022
ORDER ID 1098-00074352827-220112 | DATE RECEIVED 01/12/2022
DATE REPORTED 02/18/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	7.80	Kb
Telomere Percentile (Relative to others in the same age group)	75.00	%

Baseline

PATIENT
NAME MM | AGE 63
DOB 4/9/1959 | GENDER Female
PATIENT ID

SPECIMEN
ACCESSION ID 2205270088 | DATE COLLECTED 05/26/2022
ORDER ID 1087-00074352827-220527 | DATE RECEIVED 05/27/2022
DATE REPORTED 07/11/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.14	Kb
Telomere Percentile (Relative to others in the same age group)	83.00	%

6 Months

PATIENT
NAME MM | AGE 63
DOB 4/9/1959 | GENDER Female
PATIENT ID

SPECIMEN
ACCESSION ID 2302080106 | DATE COLLECTED 02/07/2023
ORDER ID 1105-00074352827-230208 | DATE RECEIVED 02/08/2023
DATE REPORTED 03/08/2023

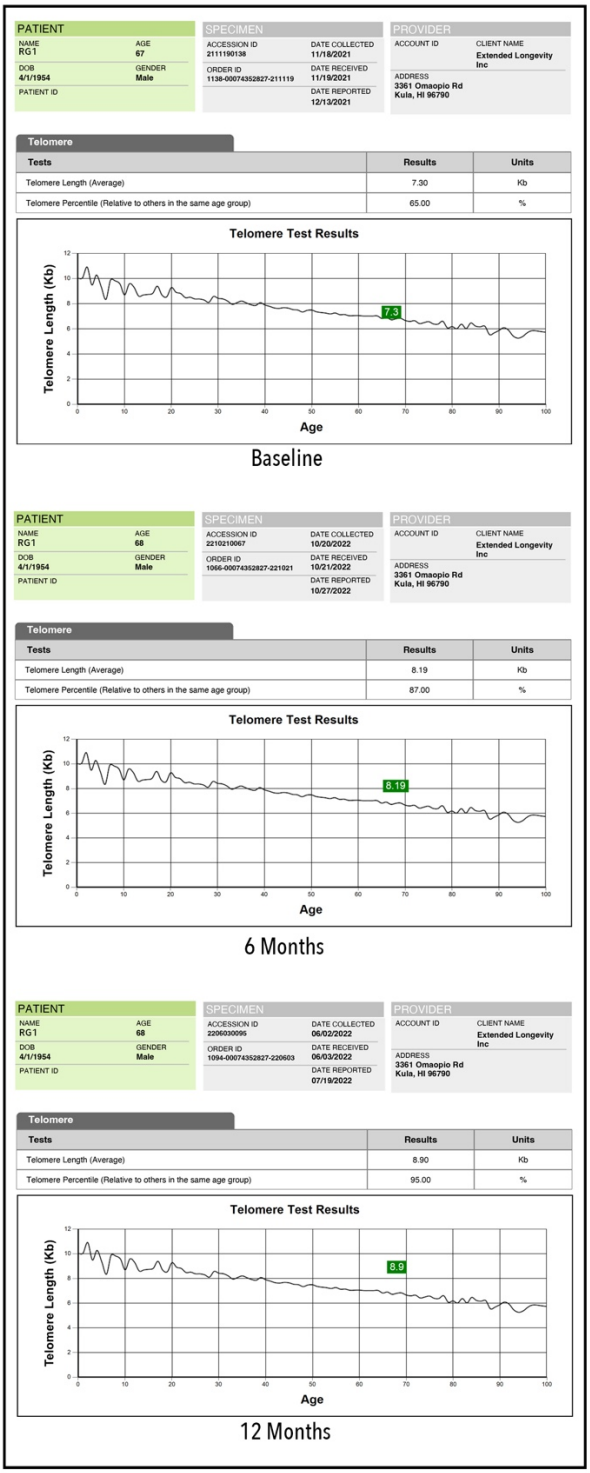
PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.82	Kb
Telomere Percentile (Relative to others in the same age group)	93.00	%

12 Months

Participant #2 (Baseline, 6 mo. & 12 mo.)



PATIENT
NAME RG1 | AGE 67
DOB 4/1/1954 | GENDER Male
PATIENT ID

SPECIMEN
ACCESSION ID 2111190138 | DATE COLLECTED 11/18/2021
ORDER ID 1138-00074352827-211119 | DATE RECEIVED 11/19/2021
DATE REPORTED 12/13/2021

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	7.30	Kb
Telomere Percentile (Relative to others in the same age group)	65.00	%

Baseline

PATIENT
NAME RG1 | AGE 68
DOB 4/1/1954 | GENDER Male
PATIENT ID

SPECIMEN
ACCESSION ID 2210210067 | DATE COLLECTED 10/20/2022
ORDER ID 1066-00074352827-221021 | DATE RECEIVED 10/21/2022
DATE REPORTED 10/27/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.19	Kb
Telomere Percentile (Relative to others in the same age group)	87.00	%

6 Months

PATIENT
NAME RG1 | AGE 68
DOB 4/1/1954 | GENDER Male
PATIENT ID

SPECIMEN
ACCESSION ID 2206030095 | DATE COLLECTED 06/02/2022
ORDER ID 1094-00074352827-220603 | DATE RECEIVED 06/03/2022
DATE REPORTED 07/19/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

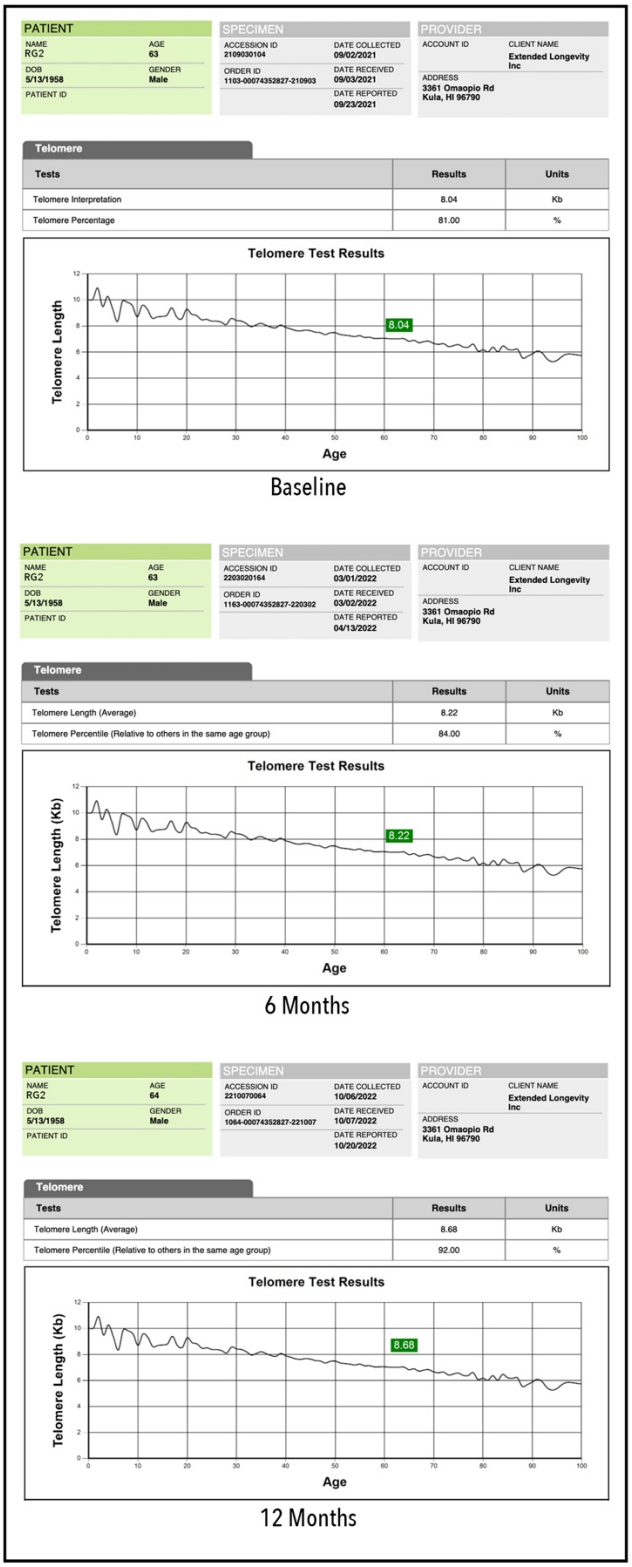
Telomere

Tests	Results	Units
Telomere Length (Average)	8.90	Kb
Telomere Percentile (Relative to others in the same age group)	95.00	%

12 Months

Participant #3 (Baseline, 6 mo. & 12 mo.)

Participant #4 (Baseline, 6 mo. & 12 mo.)



PATIENT
NAME RG2 | AGE 63
DOB 5/13/1958 | GENDER Male
PATIENT ID

SPECIMEN
ACCESSION ID 2109030104 | DATE COLLECTED 09/02/2021
ORDER ID 1103-00074352827-210903 | DATE RECEIVED 09/03/2021
DATE REPORTED 09/23/2021

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Interpretation	8.04	Kb
Telomere Percentage	81.00	%

Telomere Test Results

Telomere Length

Age

8.04

Baseline

PATIENT
NAME RG2 | AGE 63
DOB 5/13/1958 | GENDER Male
PATIENT ID

SPECIMEN
ACCESSION ID 2203020164 | DATE COLLECTED 03/01/2022
ORDER ID 1163-00074352827-220302 | DATE RECEIVED 03/02/2022
DATE REPORTED 04/13/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.22	Kb
Telomere Percentile (Relative to others in the same age group)	84.00	%

Telomere Test Results

Telomere Length (Kb)

Age

8.22

6 Months

PATIENT
NAME RG2 | AGE 64
DOB 5/13/1958 | GENDER Male
PATIENT ID

SPECIMEN
ACCESSION ID 2210070064 | DATE COLLECTED 10/06/2022
ORDER ID 1064-00074352827-221007 | DATE RECEIVED 10/07/2022
DATE REPORTED 10/20/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.68	Kb
Telomere Percentile (Relative to others in the same age group)	92.00	%

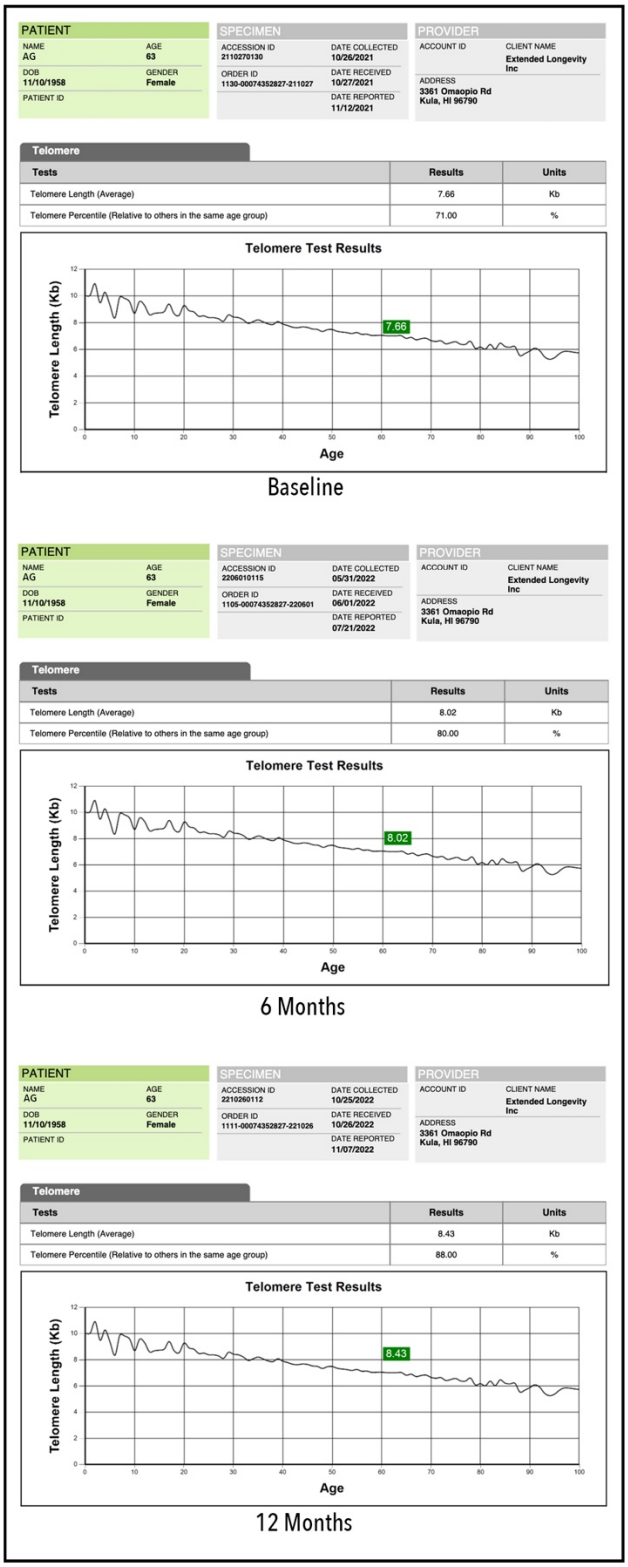
Telomere Test Results

Telomere Length (Kb)

Age

8.68

12 Months



PATIENT
NAME AG | AGE 63
DOB 11/10/1958 | GENDER Female
PATIENT ID

SPECIMEN
ACCESSION ID 2110270130 | DATE COLLECTED 10/26/2021
ORDER ID 1130-00074352827-211027 | DATE RECEIVED 10/27/2021
DATE REPORTED 11/12/2021

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	7.66	Kb
Telomere Percentile (Relative to others in the same age group)	71.00	%

Telomere Test Results

Telomere Length (Kb)

Age

7.66

Baseline

PATIENT
NAME AG | AGE 63
DOB 11/10/1958 | GENDER Female
PATIENT ID

SPECIMEN
ACCESSION ID 2206010115 | DATE COLLECTED 05/31/2022
ORDER ID 1105-00074352827-220601 | DATE RECEIVED 06/01/2022
DATE REPORTED 07/21/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.02	Kb
Telomere Percentile (Relative to others in the same age group)	80.00	%

Telomere Test Results

Telomere Length (Kb)

Age

8.02

6 Months

PATIENT
NAME AG | AGE 63
DOB 11/10/1958 | GENDER Female
PATIENT ID

SPECIMEN
ACCESSION ID 2210260112 | DATE COLLECTED 10/25/2022
ORDER ID 1111-00074352827-221026 | DATE RECEIVED 10/26/2022
DATE REPORTED 11/07/2022

PROVIDER
ACCOUNT ID | CLIENT NAME Extended Longevity Inc
ADDRESS 3361 Omaopio Rd Kula, HI 96790

Telomere

Tests	Results	Units
Telomere Length (Average)	8.43	Kb
Telomere Percentile (Relative to others in the same age group)	88.00	%

Telomere Test Results

Telomere Length (Kb)

Age

8.43

12 Months

C. Hs C- Reactive Protein Tests

1. Hs C-RP Data Chart #3

	EXTENDED LONGEVITY Hs C-RP Test Cohort of 11 through 1/2022					
	Test Subject	Date	Baseline	6 MO	1 yr	Percent +- of Inflammation
1	RG a.63 M	9.2.21	n/a	1.41	5.15	-265.25%
2	KT a.56 F	8.30.21	n/a	0.6	0.49	18.33%
~~3~~	JG a F. DO	9.9.21	n/a	n/a	D/O	
4	HC a.73	9.14.21	n/a	2.05	0.31	84.88%
5	JW a. 58 M	9.14.21	n/a	2.13	0.75	64.79%
~~6~~	DG a.74 F DC	11.4.21	n/a	n/a	D/O	
7	MC a.64 M	10.5.21	n/a	2.15	D/O	
8	AG a.63 F	10.26.21	n/a	0.44	0.18	59.09%
9	PG a.55 F	11.08.21	n/a	11.17	2.04	81.74%
#	MM a.63 F	1.11.22	n/a	0.51	0.39	23.53%
#	RG a.68 M	11.15.21	n/a	0.36	0.5	-38.89%

2. HS C-RP Test Analysis

a. Baseline HS C-RP Tests

Initial baseline testing of the Hs C-RP inflammation marker was not conducted by the local independent laboratory for each cohort participant. This was a procedural misunderstanding, as indicated in the chart above (Chart #3).

b. 6-Month Hs C-RP Tests

6-month testing of the Hs C-RP and inflammation markers was conducted by a local independent laboratory for each cohort participant. As indicated in the chart above (Chart #3). After 6 months, the Hs C-RP test was given to all 8 of the participating cohorts.

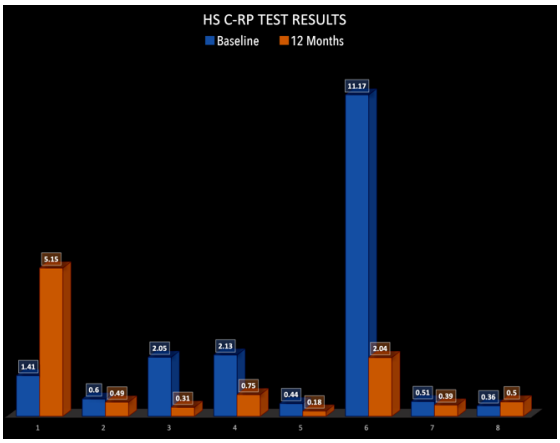
- Of the total cohort of 8 who consumed the Extended Longevity Protocol for 6 months, a baseline Hs C-RP was established.
- 4 of the cohort had Hs C-RP test results that are considered optimum (under 1).
- 4 of the cohort had Hs C-RP test results that were above optimum.

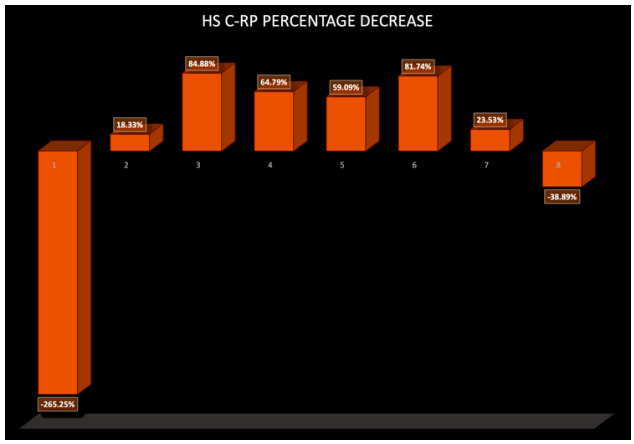
c. 12-Month Hs C-RP Tests

12-month testing of the Hs C-RP was conducted by independent labs for each cohort participant. The C-RP tests were given to all eight of the remaining cohorts.

- Of the total cohort of 8 who consumed the Extended Longevity Protocol for 12 months, 6 participants reduced their Hs C-RP inflammation marker and 2 increased their Hs C-RP marker.
- Of the six cohort participants who decreased their Hs C-RP inflammation, the average decrease was 55.39%, with the most decrease at 84.88% and the least decrease at 18.33%.
- Of the two cohort participants who increased their Hs C-RP inflammation, the average increase was 152.07%.
- It may be noteworthy to mention that one of the increasing participants had an exacerbated medical condition, which caused their inflammation to spike to 5.15 from a 6-month reading of 1.4. Also, the second cohort had an increase from 0.36 to 0.5, well within optimum tolerances.

d. Visualizing the Hs C-RP Test Results





D. **Discussion**

Scientific evidence is herein presented to support the conclusion that the Extended Longevity Protocol can affect a significant reversal of the biomarkers of aging for a small but important age-represented cohort. Through a managed study of up to 11 people ages 55–75 (half male and half female), a compelling picture emerges that demonstrates excellent results utilizing the Extended Longevity Protocol.

1. Three Definitive Biomarker Tests

Of the 7 Elysium Epigenome tests received at the end of the study, 100% had decelerated the Epigenome aging biomarker. (One additional test was pending as of the writing of this report). The cohort participants decelerated an average of 13.16 years or 22.5% from Baseline age at the beginning of the study, with the results as high as 22.2 years or 36.31% and as low as 8.6 years or 12.82%

Overall, based on the TruDiagnostic epigenome tests, the cohort reduced this biomarker of aging by an average of 14 years from chronological age and 11 years from baseline epigenome tests. This occurred to 77% of the cohort, a significant majority of the cohort participants, who decelerated 8.88% with a high of 36.4%, or 17.4 years of age deceleration, and a low of -11.1%, or +8 years of age acceleration, on the TruDiagnostic testing protocol.

Based on the telomere tests, 77.8% of the cohort reduced this biomarker of aging by an average of 8.2% from chronological age, with a high of 11.56%. The significance of this statistical gain is that 11.56% on the telomere chart signifies an age deceleration of 40 years, from 60 to 20.

With regard to the Hs C-RP test, an important marker for inflammation used as a standard of care in the medical industry, 75% of the cohort experienced a reduction of their inflammation after 12 months, with an average reduction of 55.4% for the 6 participants testing positive.

These results are very encouraging and indicate a breakthrough in the reversal of the biomarkers of aging and the benefits of health and wellbeing that this may engender.

Part 4: The Products Tested

The Extended Longevity Protocol, as described on the website www.extendedlongevity.com, is a set of 10 phytotherapeutic extract formulations designed to address the 10 determinant factors of aging.

The 10 determinant factors of aging include: the pineal clock, thymic involution, blood signaling, telomere length, senolytics, inflammation, stem cell exhaustion, cellular metabolic efficiency, the epigenome clock, and extracellular matrix stiffening.

A. Introduction:

The use of phytotherapeutic extract formulations in the Extended Longevity Protocol is significant as they are natural plant-based extracts that are rich in phytochemicals, antioxidants, and other bioactive compounds. These extracts have been traditionally used for medicinal purposes and have been shown to possess anti-aging and disease-fighting properties.

The 10 phytotherapeutic extract formulations in the Extended Longevity Protocol include ingredients such as curcumin, resveratrol, green tea extract, quercetin, and grape seed extract, among others. These ingredients have been extensively studied for their health benefits, and their inclusion in the Extended Longevity Protocol demonstrates a thoughtful and evidence-based approach to addressing the 10 determinant factors of aging.

The significance of the Extended Longevity Protocol lies in its ability to target multiple factors of aging simultaneously. By addressing oxidative stress, inflammation, mitochondrial dysfunction, DNA damage, epigenetic alterations, stem cell depletion, cellular senescence, telomere attrition, protein homeostasis, and nutrient sensing, the protocol offers a comprehensive approach to promoting longevity and preventing age-related diseases.

Additionally, the use of phytotherapeutic extract formulations is a non-invasive and natural approach to anti-aging, which may be particularly appealing to individuals who are looking for natural alternatives to traditional pharmaceutical interventions.

In conclusion, the Extended Longevity Protocol offers a significant and comprehensive approach to addressing the 10 determinant factors of aging through the use of the 10 phytotherapeutic extract formulations. The natural and evidence-based approach to anti-aging offered by this protocol may have significant implications for promoting longevity and preventing age-related diseases. Bottom of Form

B. The Extract Formulations

The formulations include: ***Pinetonal, Thyvolve, Blucosig, Telogenic, Sentophagy, Inflasove, Stemgenis, CMEnhance, Epiverse, and Elastage ECM***.

The 10 phytotherapeutic extract formulations included in the Extended Longevity Protocol and how they work to address their designated aspect of the aging process:

1. ***Pinetonal*** is a Formulation of six (6) plant species known to increase melatonin, pineol, zinc, and selenium, including phytotherapeutic extracts of ***Pistacia vera, Scutellaria baicalensis, Passiflora incarnata, Panax quinquefolius, Elitaria cardamomum, and Cinnamomum verum***. The Pineal, Hypothalmic, Pituitary, and Superchiasmatic Nucleolus (SCN) axis is the master time clock and

coordinates the body's circadian rhythm and the time-cycled release of melatonin and other critical hormones and neurotransmitters. "Resting" of the pineal gland function by supplementation of melatonin rejuvenates the pineal. As we age, we produce less and less melatonin. When the pineal gland's aging clock breaks down, it signals other parts of the body that it is time to age.

2. ***Thyvolve***: Designed for regenerating the thymus gland and reversing the age-dependent process of thymus involution It consists of six (6) phytotherapeutic extracts, including ***Selaginella involvens, Pinus sylvestris (Pollen), Curcuma longa, Zingiber officinale, Elitaria cardamomum, and Cinnamomum verum***. From the age of thirty, our thymus gland, which is responsible for producing immune-resistant T-cells, begins to involute, and by the age of 65, most of the thymus has been replaced by adipose fat, with consequent loss of immune function, immune depletion, and T-cell diminution.

3. ***Blucosig***: The formula is designed for blood signaling and transcription adjustment for aging reversal or rejuvenation via blood signaling to all cells. It contains phytotherapeutic extracts of ***Caulophyllum thalictroides, Trigonella foenum-graecum, Panax quinquefolius, Scutellaria baicalensis, and Curcuma longa***. Through experimentation with heterochronic parabiosis, in which a young and old mouse are surgically connected to share a common blood circulation, it was discovered that there were age-related signaling molecules circulating in the blood that told all of the body's 100 trillion cells to age. It was also discovered that this process can be reversed.

4. ***Telogenic***: phytotherapeutic extract of three (3) synergistic herbal analogs, including ***Astragalus membranaceus, Centella asiatica, and Salix alba.*** They are telomerase-creating natural plant extracts that stop the degradation of telomeres and rebuild them, reversing cell loss from telomere attrition. Located at the ends of chromosomes, telomeres protect chromosome ends. When we are born, our telomeres are at their longest. With every cell division throughout the course of our lives, our telomeres lose a bit of their DNA. With age and exposure to various sources of oxidative stress, telomeres gradually shorten until the cell cannot replicate. This process acts as an aging clock, counting down the remaining life of the cell.

5. ***Sentophagy***: Phytotherapeutic extraction of five (5) plant species known to induce autophagy and mitophagy, including ***Taraxacum officinale, Camellia senensis, Berberis vulgarus, Curcuma longa, and Cinnamomum verum***. Evidence shows the contribution of cellular senescence to age-related tissue dysfunction. Eliminating senescent cells resolves age-related disorders, which may increase lifespan. Because of a senescent-associated secretory phenotype (SASP), senescent cells are capable of coordinating distinct non-cell systemic responses that disrupt tissue homeostasis.

6. ***Inflasove*** is formulated to reduce systemic inflammation, which is a root cause of aging (called "inflammatory aging"). It contains phytotherapeutic extracts of ***Curcuma longa, Boswellia sacra, Salix alba, Camellia sinensis, and Cinnamomum verum***. Inflammation is a defense response of our body to hazardous stimuli. Chronic inflammation, caused by low-grade persistent inflammation, leads to tissue degeneration and is a contributor to various age-related diseases and natural processes in aging tissue. One of the major changes that occur during aging is the disregulation of the immune response, leading to a chronic systemic inflammatory state.

7. ***Stemgenis*** is formulated to regenerate active stem cells from the age-dependent condition called "stem cell exhaustion" and reverse it. It contains phytotherapeutic extracts of ***Garcinia indica, Astragalus membracanus, and Cinnamomum verum.*** The decrease in the renewal of stem cells leads to age-related disorders. "Stem Cell Exhaustion" is a consequence of DNA damage, senescence, and other factors. Stem cells can reveal ways that tissues interact during aging and possibly redirect

the fate of aging tissues. Stem cell exhaustion is a key component in the onset of age-related functional decline in every aspect of the human body.

8. ***CMEnhance*** is formulated to support cellular metabolic efficiency by increasing resveratrol, sirtuins, NAD, and NMN and contains phytotherapeutic extracts of ***Polygonum cuspidatum, Petroselinum crispum, Scutellaria baicalensis, Tabebuia avellanedae, Curcuma longa, and Cinnamomum verum***. When oxidative stress is minimized, cellular metabolic efficiency (CME) is achieved, increasing the efficiency of the cell mitochondria's ATP energy-producing reaction. High antioxidant levels combined with bioavailability are the keys to establishing CME, increasing energy, and reducing metabolic oxidative stress at the cellular level. This will also have the effect of reducing inflammation and slowing down the aging process.

9. ***Epiverse***: epigenetic reversing (DNAm, cytosine methylation) synergistic herbal formulation of six (6) plant species Included are phytotherapeutic extracts of ***Berberis vulgaris, Pinus sylvestris (Pollen), Lepidium meyenii, Taraxacum officinale, Elitaria cardamomum, and Cinnamomum verum***. Epigenetics refers to the modification of our DNA, RNA, or protein, which can change and regulate these molecules without altering the primary sequence. Our genetics, lifestyle, the food we eat, and the environment we live in affect these modifications and therefore affect how our genes behave. Epigenetics can explain how external factors cause modifications to our DNA and its structures, which result in gene regulation.

10. ***Elastage ECM*** is formulated to stimulate the growth of elastin and strengthen the flexibility of the extracellular matrix. Elastic fibers, composed of an elastin core (90%) surrounded by fibrillin-rich microfibrils (10%), endow tissues with critical mechanical properties such as resilience, flexibility, and elasticity. This formulation contains ***Paeonia lactiflora***, ***Antheum graveolens***, ***Camellia seneisis***, ***Vitiis vineferia***, ***Curcuma longa, and Cinnamomum vera.*** Aging results from the accumulation of intra-intermolecular crosslinks between molecules with slow turnovers, such as collagen and elastin. The extracellular matrix is mostly comprised of collagen and elastin. Both proteins are first formed at birth and decrease with time. Any damage that does occur with age and disease is essentially irreparable. The decrease in elastin, in turn, increases collagen content and ECM stiffness. This causes age-related diseases such as hypertension and atherosclerosis. The decrease in elastin content puts an upper limit on the functioning of the cardiovascular and pulmonary systems, and this limit is estimated to be about 100–120 years.

    Overall, the 10 phytotherapeutic extract formulations included in the Extended Longevity Protocol work together to address the 10 determinant factors of aging. By targeting multiple aspects of aging simultaneously, the protocol offers a comprehensive approach to promoting longevity and preventing age-related diseases. The Extended Longevity Protocol anti-aging intervention shows a slowing down of the aging process and a reduction in the risk of age-related diseases. Reducing the burden of age-related diseases on healthcare systems and improving the overall health of the population will require a multifaceted approach that addresses social determinants of health, promotes healthy lifestyles, and supports access to healthcare for all individuals.

Part 5: Conclusion

Through organized clinical testing, the Extended Longevity Protocol anti-aging intervention conclusively demonstrates a slowing down and reversal of the aging process and, consequently, a reduced risk of age-related diseases. Reducing the burden of age-related diseases on healthcare systems and improving the overall health of the population will require an approach that addresses social determinants of health.

The results of the Institutional Review Board (IRB) demonstrated a significant aging deceleration, where 77% of the cohort decelerated 15–22% for those who took the Extended Longevity Protocol for a one-year period. This is a great success and provides hope for the aging population to improve their quality of life and potentially reduce their risk of age-related diseases.

Of the seven (7) Elysium epigenome tests received at the end of the study, 100% had decelerated the epigenome aging biomarker. The cohort participants decelerated an average of 13.16 years, or 22.5%, from baseline age at the beginning of the study, with results as high as 22.2 years, or 36.31%, and as low as 8.6 years, or 12.82%. Based on the trudiagnostic epigenome tests, the cohort reduced this biomarker of aging by an average of 14 years from chronological age and 11 years from baseline epigenome tests. This occurred in 77% of the cohort, a significant majority of the cohort participants, decelerating 8.88% with a high of 36.4%, or 17.4 years of age deceleration, and a low of -11.1%, or +8 years of age acceleration, based on the Trudiagnostic testing protocol.

In the telomere tests, 77.8% of the cohort reduced this biomarker of aging by an average of 8.2% from chronological age, with a high of 11.56%. What is significant about this statistical gain of 11.56% on the telomere chart is that it signifies an age deceleration of 40 years, from 60 to 20 years old. **In the Hs C-RP test**, an important marker for inflammation used as a standard of care in the medical industry, **75%** of the cohort experienced a reduction of their inflammation after 12 months, with an average reduction of 55.4% for the 6 participants testing positive.

These results are very encouraging and indicate a breakthrough in the reversal of the biomarkers of aging and the benefits of health and wellbeing that this may engender. The use of natural and evidence-based phytotherapeutic extract formulations to address the 10 determinant factors of aging in the Extended Longevity Protocol is a promising approach to promoting healthy aging. The consistent and significant aging deceleration seen in this study is a testament to the effectiveness of this approach. While it is important to remain cautious and continue to study the complex biology of aging, these results provide valuable insights into potential interventions for promoting longevity and healthy aging. The benefits of slowing down the aging process and reducing the risk of age-related diseases could have significant implications for the overall health of the aging population. It is important to note that further research is necessary to fully understand the benefits and potential risks of the Extended Longevity Protocol. However, the success seen in this IRB study provides hope for the potential of natural and evidence-based interventions to improve the quality of life for aging individuals.

In conclusion, the Investigative Review Board conducted by Dr. Juergen Winkler of Quantum Functional Medicine of Carlsbad, California, under the auspices of the Institute of Regenerative and Cellular Medicine of Santa Monica, California, has produced significant findings regarding the effectiveness of the Extended Longevity Protocol in decelerating the biomarkers of aging. The study results are encouraging and indicate potential for improving the overall health and longevity of individuals who use this protocol. However, further research is necessary to fully understand the benefits and potential risks of the protocol.

Appendix I – Product Details

The 10 phytotherapeutic extract formulations presented address various aspects of aging, including cellular metabolic efficiency, epigenetic regulation, mitochondrial function, inflammation, oxidative stress, and extracellular matrix regeneration. By addressing these factors, the extracts may help to mitigate the effects of aging and promote overall health and longevity.

Clinical research data supports the potential benefits of many of these extracts. For example, studies have shown that resveratrol (a component of CMEnhance) may have anti-aging effects and improve metabolic function, while curcumin has potent anti-inflammatory and antioxidant properties. Berberine (a component of Epiverse) has been shown to improve glucose metabolism and reduce cardiovascular risk factors, and polyphenols may have neuroprotective and anti-cancer effects as well.

While the use of all 10 extracts may not guarantee an extended lifespan beyond the upper limits of current human longevity, it is possible that their combined effects may help to slow down the aging process and promote healthy aging. However, further research is needed to fully understand the potential benefits and limitations of these extracts and their effects on lifespan.

Considering the 10 phytotherapeutic extracts presented in Extended Longevity, it is hypothesized that the use of all 10 extracts can lead to an extended human lifespan by addressing the 10 determinant factors of aging. The extracts are Pinetonal, Thyvolve, Blucosig, Telogenic, Sentophagy, Inflasolve, Stemegenis, CMEnhance, Epiverse, and Elastage ECM. Clinical research data supports the potential benefits of each of these extracts, including the enhancement of cellular metabolic efficiency, the reversal of epigenetic aging, and the regeneration of the extracellular matrix, among others. By addressing these factors, it is possible to slow down the aging process and extend the lifespan of all human beings.

Telogenic, Sentophagy, and Inflasolve work together to support healthy cellular metabolism, reduce inflammation, and maintain healthy blood sugar levels, which are all important factors in promoting longevity. Pinetonal, Thyvolve, and Blucosig target cellular health and immune system function, helping to protect against age-related diseases and increase resistance to stress. Stemegenis and CMEnhance support cellular energy production and metabolic efficiency, which can promote vitality and reduce the effects of oxidative stress. Epiverse and Elastage ECM target epigenetic modifications and the extracellular matrix, respectively, which can help reduce the effects of aging on the body's tissues and organs.

The combination of these 10 formulations can work together to provide a comprehensive approach to addressing the aging process, promoting healthy cellular function, supporting immune system function, maintaining metabolic efficiency, and protecting against the effects of oxidative stress and tissue damage. By addressing these various factors in a holistic manner, the use of these formulations can potentially lead to an extension of a healthy lifespan and an improvement in overall health and well-being as we age.

It is important to note that while the use of these formulations can provide support for healthy aging, lifestyle factors such as a healthy diet, regular exercise, and stress management are also important for promoting longevity and overall health.

1. **Pinetonal** targets the pineal gland, hypothalamus, and suprachiasmatic nucleus, which are responsible for managing the circadian rhythms of the day-night cycle. By promoting the efficient production of melatonin, an important signaling molecule, the body is better able to regulate sleep and wake cycles, as well as other biological processes that are influenced by circadian rhythms.

   The pineal gland is a unique organ that synthesizes melatonin as the signaling molecule of the natural photoperiodic environment and as a potent neuronal protective antioxidant. A functional pineal gland is necessary for preserving optimal human health.

   Melatonin, along with its metabolites, has been known to significantly reduce the oxidative stress burden of aging cells or cells exposed to toxins. Known as the sleep hormone, melatonin also has antioxidant, anti-inflammatory, anti-apoptotic, and many other crucial properties. In mammals, this multitasking indolamine is synthesized in the pineal gland in a circadian manner in response to the photoperiodic information received via the retino-hypothalamic pathway. It is directly released into the bloodstream, where it is distributed to all tissues. The pineal gland regulates the cyclic production of the hormones in our body by producing melatonin, and as we age, it produces less and less.

   The disappearance of the nocturnal peak of melatonin is a specific sign that the organism is aging and, with it, the deterioration of the hormonal control of our essential functions. It is necessary to reverse this trend to maintain melatonin production, helping to recover and maintain the pineal gland in the state in which it was during youth (between 15 and 20 years of age). The nocturnal peak of melatonin is produced by the pineal gland between one and three a.m. Since the pineal gland produces melatonin only at night, giving your body melatonin at night protects and rests the pineal gland. Therefore, the pineal gland can regenerate and maintain itself in a youthful state, producing molecules that regulate the entire hormonal neuroendocrine system, resulting in the normalization of immunological, metabolic, and endocrine functions, thus slowing down and potentially reversing aging.

   i. ***Pistacia vera,*** is a rich source of natural plant-based melatonin. 3 mg of melatonin can be found in 18 pistachio nuts.

   ii. ***Scutellaria baicalensis,*** inhibited the aggregation of neuronal amyloidogenic proteins, inducing the dissolution of amyloid deposits. It stimulates brain tissue regeneration by inducing the differentiation of neuronal precursor cells.

   iii. ***Passiflora incarnata,*** has antioxidant, antiparkinsonian, and memory-enhancing activities. It contains multiple bioactive metabolites such as flavonoids (like chrysin) that show CNS depressant activity, amino acids (like GABA), and harmala alkaloids (reversible monoamine oxidase-A inhibitors).

   iv. ***Panax quinquefolius,*** significantly extended life span and extended life span via modulation of multiple longevity assurance genes, including genes involved in insulin signaling and stress response pathways.

   v. ***Elitaria cardamomum***, the highest source of plant-based zinc, may be effective against a variety of bacterial strains that contribute to fungal infections.

   vi. ***Cinnamomum verum,*** activates the insulin signaling pathway, the anti-oxidative pathway, and serotonin signaling for its lifespan-prolonging effect.

2. **Thyvolve** supports the regeneration of the thymus gland, which is responsible for the production of T-cells, critical components of the immune system. By enhancing the function of the thymus gland, Thyvolve helps to improve immune function and increase resistance to disease.

   The deterioration of the immune system with progressive aging is believed to contribute to morbidity and mortality in elderly humans due to the increased incidence of infection, autoimmunity, and cancer. Dysregulation of T-cell function is thought to play a critical role in these processes.

   One of the consequences of an aging immune system is the process termed thymic involution, where the thymus undergoes a progressive reduction in size due to profound changes in its anatomy associated with the loss of thymic epithelial cells and a decrease in thymopoiesis. This decline in the output of newly developed T cells results in diminished numbers of circulating naive T cells and impaired cell-mediated immunity. Several theories have been proposed to explain this 'thymic menopause," including the possible loss of thymic progenitors or epithelial cells, a diminished capacity to rearrange T-cell receptor genes, and alterations in the production of growth factors and hormones.

   As the primary site of T cell development, the thymus plays a key role in the generation of a strong yet self-tolerant adaptive immune response, which is essential in the face of a potential threat from pathogens. The thymus undergoes rapid degeneration following involution as part of the aging process. The thymus is capable of regenerating and restoring its function to some degree. Potential mechanisms for this endogenous thymic regeneration include keratinocyte growth factor (KGF) signaling and a more recently described pathway in which innate lymphoid cells produce interleukin-22 (IL-22) in response to the loss of double-positive thymocytes and upregulation of IL-23 by dendritic cells. Endogenous repair is unable to fully restore the thymus, particularly in the elderly population, and this paves the way for the need for exogenous strategies to help regenerate or even replace thymic function. Thymic decline also occurs as an inevitable chronic process in which the thymus gland undergoes involution with age. Thymic involution differs from aging in other organs in that it cannot be reversed.

   i. ***Selaginella involves***, stimulates, and regenerates the thymus.

   ii. ***Pinus sylvestris (Pollen)***, a source high in natural growth hormone

   iii. ***Curcuma longa, is*** known to be a powerful antioxidant.

   iv. ***Zingiber officinale,*** supports T-cell development.

   v. ***Elitaria cardamomum***, cardamom, is a source of zinc.

   vi. ***Cinnamomum verum***, Known to be a powerful antioxidant

3. **Blucosig** is formulated to support blood signaling and transcription adjustment, which may lead to aging reversal or rejuvenation via blood signaling to all cells. Blucosig is a synergistic herbal analog formulation of five plant extracts, including ***Caulophyllum thalictroides, Panax quinquefolius, Scutellaria baicalensis, Trigonellum foenum, and Curcuma longa.***

Blucosig is an herbal analog to the underlying research that identified two key determinants as the causal factors for aging in blood signaling: TGF-1, which activates ALK5/pSmad 2, 3, and goes up with age, and oxytocin (OT), which activates MAPK and diminishes with age. Blucosig helps to mitigate the negative effects of age-related blood signaling by promoting the activation of MAPK and reducing the activation of ALK5/pSmad 2, 3.

Heterochronic parabiosis research, which involves surgically connecting a young and old animal to share a common blood circulation, has identified a few morphogenic pathways that account for most of the phenotypes of aging. Blucosig's herbal analogs of synthetic molecular structures may be utilized in the rejuvenation of multiple old organs and represent significant progress in reversing human tissue aging.

Overall, the potential benefits of this phytotherapeutic extract formulation are to promote healthy aging through the regulation of age-related blood signaling. The underlying research and analog herbal compounds in Blucosig offer a promising approach to promoting healthy aging through the modulation of blood signaling pathways.

i. ***Caulophyllum thalictroides***, or blue cohosh, is a known oxytocin synergist with a long history of use in traditional herbal medicine. Panax quinquefolius ginseng extract demonstrated inhibition of the expression of TGF1, Smad2, and 3.

ii. ***Trigonellum foenum,*** is known to have hypocholesterolemic, antilipidemic, antioxidant, hepatoprotective, anti-inflammatory, antibacterial, antifungal, antiulcer, antilithigenic, anticarcinogenic, and other miscellaneous medicinal effects.

iii. ***Scutellaria baicalensis,*** decreases expression of TGF- isoforms, TGF- receptors, and SMADs. The herb effectively inhibited basal and TGF-1-induced cancer cell proliferation.

iv. ***Panax quinquefolius,*** significantly extended life span and extended life span via modulation of multiple longevity assurance genes, including genes involved in insulin signaling and stress response pathways.

v. ***Curcuma longa,*** increases the ability of human epidermal keratinocytes to differentiate during replicative senescence. It has anti-inflammatory and antioxidant properties and can mitigate the symptoms of aging.

4. **Telogenic** Formula is designed to increase the length of telomeres and contains extracts of ***Astragalus membranaceus, Centella asiatica, and Salix alba.*** This formula is a synergistic herbal analog providing support for telomere rejuvenation.

Telomeres are the protective caps found at the ends of your chromosomes that protect our genetic information during cellular division. For our bodies to heal and function properly, cells must divide to produce new cells to replace old, worn-out cells. Telomeres allow our cells to divide without damaging or scrambling the cells' genetic information. Telomeres are like the plastic tips on shoelaces, as they keep the chromosome ends from tangling and fraying. When we are born, our telomeres are at their longest. With every cell division throughout the course of our lives, our telomeres lose a bit of their DNA. With age and accumulated exposures to various sources of oxidative stress throughout our lifetimes, telomeres gradually shorten until the cell cannot replicate.

This shortening process acts as an aging clock, counting down the remaining life of the cell. At a certain point, chromosomes in the cell reach a critical length and can no longer be replicated. When this occurs, the cell enters a state of growth arrest known as "cellular senescence," which is the equivalent of aging. Cellular senescence is a primary driver of the aging process, which links cellular damage with the larger, anatomical effects of aging. Senescent cells do not directly cause aging but instead have a cumulative effect leading to larger, more visible consequences of tissue breakdown and, over time, the signs and symptoms of old age (sagging, wrinkled skin, decreased muscle mass, weakened immunity, etc.). This mechanism explains how microscopic changes to our trillions of cells slowly manifest in the gradual, almost invisible process of aging. Senescent cells differ from their younger counterparts. Cells that contain chromosomes with telomeres approaching a critically short length undergo changes that result in further damage to the organism. Whereas young cells secrete proteins that maintain healthy, functioning tissue, cells approaching senescence begin to secrete inflammatory cytokines that break down these proteins.

Telomeres play a crucial role in cellular division and the aging process. As we age and accumulate oxidative stress, telomeres gradually shorten until the cell can no longer replicate. This shortening process acts as an aging clock, counting down the remaining life of the cell. When telomeres reach a critically short length, chromosomes in the cell can no longer be replicated, leading to cellular senescence and tissue breakdown.

Telogenic Phytotherapeutic Extract Formulation promotes healthy aging through the regulation of telomere length. By supporting telomere rejuvenation, Telogenic offers a promising approach to promoting healthy aging and reducing the negative effects of cellular senescence.

The study titled "Willow Bark Extract Increases Lifespan and Stress Resistance in Caenorhabditis elegans and Saccharomyces cerevisiae" was conducted by researchers at Concordia University in Canada. The study investigated the effects of a Salix alba extract on the lifespan and stress resistance of two different types of cells: Caenorhabditis elegans (a type of roundworm) and Saccharomyces cerevisiae (a type of yeast). The researchers found that the extract increased the lifespan of both types of cells, with the greatest effect seen in the yeast cells. Specifically, the extract increased the lifespan of the yeast cells by up to 475%. In addition to increasing lifespan, the extract also improved the stress resistance of the yeast cells. The researchers found that the extract increased the yeast cells' resistance to oxidative stress, a type of cellular damage that can contribute to aging and age-related diseases. The extract also increased the yeast cells' resistance to heat stress, another type of stress that can damage cells. Overall, this study provides evidence that a Salix alba extract may have potential for promoting cellular health and longevity by increasing lifespan and improving stress resistance.

The study, titled "Willow bark extract increases telomerase activity in human preadipocytes," was conducted by researchers at the University of Pavia in Italy. The study investigated the effects of a Salix alba extract on telomerase activity, which is an enzyme that plays a key role in maintaining telomere length and preventing cellular aging. The researchers found that the extract increased telomerase activity in human preadipocytes (precursor cells to fat cells) in a dose-dependent manner, meaning that higher doses of the extract resulted in greater increases in telomerase activity. In addition to increasing telomerase activity, the extract also promoted telomere elongation in the preadipocytes. Telomere elongation is a marker of healthy aging, as shortened telomeres are associated with cellular aging and age-related diseases. Overall, this study provides evidence that Salix alba extract increases telomerase activity and promotes telomere elongation. While more research is needed to fully understand the effects of Salix alba on telomere health, this study suggests that it may have promising applications for promoting healthy aging.

i. ***Astragalus membranaceus,*** has been shown in studies to increase telomerase activity and telomere length in cultured human cells. Studies on Centella asiatica and Salix alba have shown potential for telomere rejuvenation. A study published in the journal Aging Research Reviews in 2018 examined the effects of a compound called cycloastragenol, which is found in Astragalus membranaceus, on telomere length in human cells. The study found that cycloastragenol could promote telomere elongation and reduce the negative effects of cellular senescence. One of the most promising compounds for telomere rejuvenation is telomerase, an enzyme that helps to maintain telomere length. In one study, researchers at the University of California, Los Angeles (UCLA) found that a telomerase activator called TA-65 could increase telomere length in human cells. The study found that participants who took TA-65 for 12 months had a significant increase in telomere length compared to those in a control group.

ii. ***Centella asiatica,*** A study published in the Journal of Ethnopharmacology in 2013 found that a water extract of Centella asiatica had a protective effect on telomere length in cultured human cells exposed to oxidative stress. Another study published in the journal Evidence-Based Complementary and Alternative Medicine in 2013 found that an extract of Centella asiatica had a protective effect on telomere length in mice with induced oxidative stress.

iii. ***Salix alba***, One study, published in the journal Phytotherapy Research in 2014, investigated the effects of a Salix alba extract on telomerase activity in human cells. The study found that the extract increased telomerase activity and promoted telomere elongation, suggesting that Salix alba may have potential for promoting healthy aging. Another study, published in the journal Evidence-Based Complementary and Alternative Medicine in 2018, investigated the effects of a Salix alba extract on cellular lifespan in yeast cells. The study found that the extract increased the lifespan of the yeast cells and improved their resistance to oxidative stress, suggesting that Salix alba may have potential for promoting cellular health and longevity. While more research is needed to fully understand the effects of Salix alba on telomere health and cellular lifespan, these studies suggest that the plant extract may have potential for promoting healthy aging.

5. **Sentophagy** is a senolytic formula that contains six plant species—***Taraxacum officinale, Camellia senensis, Berberis vulgarus, Petroselinum crispum, Curcuma longa, and Cinnamomum verum***—that induce autophagy and mitophagy. Autophagy and mitophagy are important cellular processes that clear damaged or dysfunctional organelles and proteins. These processes are crucial for cellular homeostasis and longevity.

Cellular senescence is a state of permanent cell cycle arrest induced by cellular stresses. During the aging process, senescent cells (SCs) accumulate in tissues, contributing to the development of various age-related diseases. SCs produce proinflammatory molecules known as the senescence-associated secretory phenotype (SASP), which can cause tissue damage and impair tissue repair capacity.

Sentophagy supports senolytic cellular functions, increasing the efficiency of autophagy and mitophagy. Autophagy is a fundamental biological process that removes damaged organelles, and disordered autophagy is involved in various diseases. Autophagy is activated in response to adverse environmental conditions, such as the deprivation of nutrients, hypoxia, pathogen infection, radiation, and oxidative stress, as a survival mechanism. Autophagy plays a role in cellular homeostasis, development, and longevity, and it contributes to whole-body rejuvenation. Sentophagy's formula is a synergistic herbal analog that provides senolytic cellular support, increasing the efficiency of autophagy and mitophagy.

i. ***Berberis vulgaris***, also known as barberry, is a plant commonly used in traditional medicine. Research has shown that the plant contains several bioactive compounds, including berberine, which has senolytic properties. In a study published in the journal Aging Cell in 2020, researchers found that berberine was effective in eliminating senescent cells in vitro and in vivo. The study also demonstrated that berberine improved various age-related phenotypes, such as physical function and tissue health, in mouse models.

ii. ***Petroselinum crispum***, also known as parsley, is an herb commonly used in cooking. Recent research has shown that parsley contains several bioactive compounds with potential senolytic properties. In a study published in the journal BMC Complementary Medicine and Therapies in 2020, researchers found that parsley extract was effective in eliminating senescent cells in vitro. The study also demonstrated that parsley extract improved various age-related phenotypes, such as oxidative stress and inflammation, in cell cultures.

iii. ***Taraxacum officinale***, also known as dandelion, has been found to have senolytic properties, meaning it can selectively induce the death of senescent cells. In a study published in the journal Oncotarget in 2016, a dandelion root extract was shown to induce senescence-associated cell death in human fibroblasts, which are cells that make up the connective tissue in the body. The study concluded that dandelion root extract has potential as a natural senolytic agent for the prevention and treatment of age-related diseases.

iv. ***Camellia sinensis***, also known as green tea, has been extensively studied for its health benefits, including its anti-aging effects. In a study published in the journal Nutrients in 2018, green tea catechins were found to have senolytic properties and were shown to selectively induce apoptosis (programmed cell death) in senescent cells. The study concluded that green tea catechins have potential as a natural senolytic agent for the prevention and treatment of age-related diseases.

v. ***Curcuma longa***, also known as turmeric, has been found to have a wide range of health benefits, including anti-inflammatory and antioxidant effects. In a study published in the journal BioMed Research International in 2014, curcumin, the active compound in turmeric, was shown to induce apoptosis in senescent cells, indicating its potential as a senolytic agent. The study also found that curcumin reduced the number of senescent cells in the liver and kidneys of aged rats.

vi. ***Cinnamomum verum***, also known as cinnamon, has been studied for its potential health benefits, including its anti-inflammatory and antioxidant effects. In a study published in the journal PLOS ONE in 2015, cinnamon extract was shown to have senolytic properties and was able to selectively induce apoptosis in senescent cells. The study also found that cinnamon extract improved the health span of aged mice by reducing the number of senescent cells in various tissues.

6. **Inflasolve** is a synergistic herbal analog formula comprising five (5) plant species: ***Curcuma longa, Boswellia sacra, Salix alba, Camellia sinensis, and Cinnamomum verum***. This formula is designed to address inflammaging, a chronic low-grade inflammation that accelerates the aging process and age-related diseases.

Chronic inflammation is known to be a key factor in aging, and inflammaging can be triggered by a variety of factors, including oxidative stress, cellular damage, and genetic predisposition. Inflasolve has been designed to address this issue by providing a range of compounds that have been shown to

possess anti-inflammatory and antioxidant properties, which can help reduce the impact of chronic inflammation on the body.

The research literature suggests that the ingredients in Inflasolve have anti-inflammatory, antioxidant, and anti-aging properties. Curcuma longa, for example, is a powerful anti-inflammatory agent that has been used for centuries in traditional medicine to treat a range of conditions. Silybum marianum, Scutellaria baicalensis, and Acacia catechu have also been shown to possess anti-inflammatory and antioxidant properties, while quercetin has been shown to have anti-inflammatory and anti-aging effects.

Research studies have demonstrated the anti-inflammatory and pain-relieving properties of the plant extracts present in Inflasolve. Curcumin, the active ingredient in Curcuma longa, has been found to have antioxidant, antiseptic, antifungal, and anti-inflammatory properties. One study by Yang et al. showed that the water solubility of curcumin can be increased by using heat, resulting in a 12-fold increase in bioavailability. Boswellia sacra has been shown to have anti-inflammatory properties and can reduce inflammation in the body by inhibiting the production of pro-inflammatory cytokines. A study by Siddiqui et al. found that an extract of Boswellia sacra was effective in reducing inflammation in a rat model of arthritis. Salix alba has been found to have anti-inflammatory properties due to its content of salicin, a compound that is converted to salicylic acid in the body and has anti-inflammatory effects. Camellia sinensis, or green tea extract, contains polyphenols that have anti-inflammatory effects and have been found to reduce inflammation in animal studies. Cinnamomum verum, or true cinnamon extract, has been found to have anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines. In summary, Inflasolve's combination of plant extracts provides anti-inflammatory and pain-relieving effects, making it a potential treatment option for various conditions associated with inflammation.

Inflasolve provides a synergistic anti-inflammatory effect that can help reduce the chronic inflammation that contributes to aging and age-related diseases. While some of the individual extracts have been studied more extensively than others, the research supports the use of these extracts for their anti-inflammatory and anti-aging properties.

i. ***Curcuma longa,*** contains curcumin, an active ingredient with antioxidant, antiseptic, antifungal, and anti-inflammatory properties. It is known for its ability to reduce inflammation and relieve pain.

ii. ***Boswellia sacra,*** is another extract found in Inflasolve. It contains boswellic acids, which have been shown to have anti-inflammatory properties and may help reduce the symptoms of osteoarthritis.

iii. ***Salix alba,*** is an extract that has been shown to reduce pain and inflammation. It contains salicin, a compound that is similar to aspirin and can help alleviate pain.

iv. ***Camellia sinensis,*** is another extract found in Inflasolve. It is known for its anti-inflammatory and antioxidant properties, and it may also have neuroprotective effects.

v. ***Cinnamomum verum,*** is an extract that has been shown to have anti-inflammatory, antioxidant, and antimicrobial properties. It may help lower blood sugar levels and reduce inflammation associated with metabolic disorders.

7. **Stemgenis** is designed to address stem cell exhaustion, which occurs when stem cells lose their ability to divide as we age. This can lead to age-related disorders. Stemgenis contains phytotherapeutic extracts of ***Garcinia indica, Astragalus membranaceus, and Cinnamomum verum***, which work synergistically to provide regenerative support for stem cell functionality. Stem cells are precursor biological cells that can self-renew and differentiate into multiple mature cells. There are two major categories of stem cells: embryonic stem cells and adult stem cells. Metabolic signaling and signals from the microbiome also affect stem cells. Stem cell exhaustion is a result of DNA damage, senescence, and other factors. Stem cells have the potential to reveal ways that tissues interact during aging and redirect the fate of aging tissues. Stem cell regenerative capacity persists throughout life, but the biochemical cues regulating organ stem cells change with age in ways that preclude productive regenerative responses. Experimental recalibration of specific biochemical cues can rescue the effective regenerative capacity of old stem cells, demonstrating that old stem cells can maintain old organs.

   Overall, the Stemgenis formula is designed to address the issue of stem cell exhaustion that occurs with aging by promoting the proliferation and differentiation of stem cells. The phytotherapeutic extracts in this formula have been chosen for their ability to protect against age-related diseases, modulate the immune system, and promote cellular regeneration. By promoting the health and function of stem cells, the Stemgenis formula may help slow the aging process and improve overall health and vitality.

   i. **Garcinia indica**, Also known as kokum, this fruit has been traditionally used in Ayurvedic medicine to treat a variety of conditions, including inflammation, wound healing, and infections. Recent research has shown that extracts of Garcinia indica have antioxidant and anti-inflammatory effects, as well as the ability to improve insulin sensitivity and protect against age-related cognitive decline. It also has the potential to promote the proliferation and differentiation of stem cells.

   ii. ***Astragalus membranaceus***, This root has been used in traditional Chinese medicine for centuries to enhance vitality and promote longevity. It has been found to have a variety of health benefits, including antioxidant and anti-inflammatory effects, immune system modulation, and protection against age-related diseases such as cardiovascular disease and neurodegeneration. It has also been shown to increase telomerase activity and promote the proliferation and differentiation of stem cells.

   iii. ***Cinnamomum verum***, Also known as Ceylon cinnamon, this spice has been shown to have a variety of health benefits, including anti-inflammatory and antioxidant effects, as well as the ability to improve insulin sensitivity and lower blood sugar levels. It has also been found to enhance neuroprotection and cognitive function. Cinnamon has also been shown to stimulate the proliferation and differentiation of stem cells.

8. **CMEnhance** is designed to support cellular metabolic efficiency (CME), which increases the efficiency of the cell mitochondria's ATP energy production, leading to increased energy, health, and well-being. The formula contains phytotherapeutic extracts of ***Polygonum cuspidatum, Scutellaria baicalensis, Tabebuia avellanedae, Curcuma longa, and Cinnamomum verum***. These extracts act as antioxidants that neutralize the radical oxygen species responsible for oxidative stress within the cell, allowing CME to occur. High antioxidant levels and high bioavailability are essential for

achieving CME, which also reduces inflammation, slows down cell apoptosis, and slows down the aging process. The formula works by passing through the cellular and mitochondrial membranes to facilitate the neutralization of ROS, the by-product of the cell's energy creation reaction, and increase the efficiency of ATP production.

Research studies support the benefits of these plant extracts in enhancing cellular metabolic efficiency, which can lead to increased ATP production and improved energy levels. For example, a study published in the Journal of Medicinal Food found that baicalin from Scutellaria baicalensis improved mitochondrial function and energy production in cells. Another study published in the Journal of Agricultural and Food Chemistry found that cinnamon extract increased ATP production in cells. These and other studies provide evidence for the efficacy of the CMEnhance formula in enhancing cellular metabolic efficiency and supporting overall health and well-being.

i. ***Polygonum cuspidatum***, Also known as Japanese Knotweed, Polygonum cuspidatum is a rich source of resveratrol, which has been shown to activate sirtuin enzymes and improve mitochondrial function. Sirtuin enzymes are involved in regulating metabolism and cellular stress responses, and their activation has been linked to improved cellular metabolic efficiency.

ii. ***Scutellaria baicalensis,*** contains flavonoids such as baicalin, which has antioxidant and anti-inflammatory properties. Baicalin has been shown to protect against mitochondrial dysfunction and improve cellular energy production.

iii. ***Tabebuia avellanedae***, also known as Pau d'arco, has been shown to have anti-inflammatory and antioxidant properties. It contains compounds such as lapachol and beta-lapachone, which have been shown to enhance mitochondrial function and improve ATP production.

iv. ***Curcuma longa***, also known as turmeric, contains the active ingredient curcumin, which has been shown to have antioxidant and anti-inflammatory properties. Curcumin has been shown to improve mitochondrial function and ATP production.

v. ***Cinnamomum verum***, also known as true cinnamon, contains compounds such as cinnamaldehyde and eugenol, which have antioxidant and anti-inflammatory properties. These compounds have been shown to improve mitochondrial function and increase ATP production.

9. **Epiverse** Included are phytotherapeutic extracts of ***Berberis vulgaris, Pinus sylvestris (Pollen), Lepidium meyenii, Taraxacum officinale, Elitaria cardamomum, and Cinnamomum verum***. This formula is an herbal analog to HGH, DHEA, and Metformin (with Vitamin D3 and Zinc) that was elucidated in the TRIIM study, whose research was published in September 2019 and was the first demonstration of epigenetic clock reversal by an exogenous biochemical therapy. An Overview of Epigenetics Epigenetics is the study of heritable, nonencoded genetic changes that turn genes on or off. Epigenetic modifications can modulate gene expression and/or alter cellular signaling pathways, which may affect individual susceptibility to various diseases. Epigenetics plays crucial biological roles in processes as diverse as development, learning, metabolism, and the progression of diseases such as cancer. Epigenetics refers to the modification of our DNA, RNA, or protein, which can change and regulate these molecules without altering the primary sequence. Our genetics, lifestyle, the food we eat, and the environment we live in affect these modifications and therefore affect how our genes behave. Epigenetics can explain how external factors cause modifications to our DNA and its structures, which result in gene regulation. DNA methylation, the most abundant and best-studied

epigenetic modification, is now recognized as a reliable indicator of biological age. Epiverse contains the following extracts: Berberis vulgaris, source of Berberine, an analog to Metformin, an anti-diabetic Pinus sylvestris (Pollen), a source high in natural growth hormone Lepidium meyenii, Maca, a natural source of DHEA Taraxacum officinale, or dandelion, is a source high in vitamin D. Elitaria cardamomum, cardamom, is a source of zinc. Cinnamomum verum. Known to be a powerful antioxidant.

i. **Berberis vulgaris**, also known as barberry, is a shrub native to Europe and Asia. Berberine, an alkaloid present in Berberis vulgaris, has been shown to have anti-inflammatory, anti-diabetic, and anti-aging effects. A study published in the Journal of Clinical Endocrinology and Metabolism in 2012 found that berberine could improve glucose metabolism and insulin sensitivity in patients with metabolic syndrome. Another study published in the Journal of Applied Physiology in 2015 showed that berberine supplementation could improve exercise performance and mitochondrial function in mice.

ii. ***Pinus sylvestris***, also known as Scots pine, is a species of pine tree found throughout Europe and Asia. Pollen from Pinus sylvestris is a natural source of growth hormone, which has been shown to have anti-aging effects. A study published in the Journal of Clinical Endocrinology and Metabolism in 1992 found that growth hormone replacement therapy improved body composition, bone density, and lipid metabolism in elderly men.

iii. **Lepidium meyenii**, commonly known as maca, is a root vegetable native to the Andes mountains of Peru. Maca has been traditionally used for its fertility-enhancing and aphrodisiac properties. A study published in the Journal of Ethnopharmacology in 2016 found that maca extract could improve cognitive function and reduce oxidative stress in rats.

iv. ***Taraxacum officinale***, also known as dandelion, is a common weed found throughout the world. Dandelion is a rich source of vitamins and minerals, including vitamin D. A study published in the Journal of Agricultural and Food Chemistry in 2012 found that dandelion extracts had potent antioxidant activity.

v. **Elitaria cardamomum**, commonly known as cardamom, is a spice native to India and Southeast Asia. Cardamom is a rich source of zinc, which has been shown to have anti-inflammatory and immune-boosting effects. A study published in the Journal of Nutrition in 2009 found that zinc supplementation could reduce markers of oxidative stress and inflammation in elderly women.

vi. ***Cinnamomum verum***, also known as true cinnamon, is a spice native to Sri Lanka. Cinnamon has been shown to have anti-inflammatory, antioxidant, and anti-aging effects. A study published in the Journal of Medicinal Food in 2011 found that cinnamon supplementation could improve glucose metabolism and lipid profiles in patients with type 2 diabetes.

10. **Elastage ECM** is a phytotherapeutic extract formulation designed to address extracellular matrix (ECM) stiffness, which is one of the determinants of aging. The formula contains six extracts: ***Paeonia lactiflora, Antheum graveolens, Camellia sinensis, Vitiis vineferia, Curcuma longa, and Cinnamomum vera***. The primary function of Elastage ECM is to stimulate elastin growth and improve the flexibility of the ECM, which includes collagen and elastin. The ECM's stiffness is a result of cross-linking between proteins, which reduces their functionality and can lead to the development of age-related diseases such as hypertension and atherosclerosis.

Elastin is a stable protein that makes up the majority of the ECM's elastic fibers, along with fibrillin-rich microfibrils. However, elastin content decreases with age, causing collagen to become more predominant and increasing ECM stiffness. Elastin degradation products can also cause inflammation and activate receptors for advanced glycation end products (AGE). The decrease in elastin content also puts a limit on the cardiovascular and pulmonary systems' functioning. The formula's six extracts have been shown to improve the flexibility of the ECM, potentially improving the functioning of the cardiovascular and pulmonary systems and reducing the risk of age-related diseases.

The combination of elastogenic herbal extracts in Elastage ECM may help to enhance the regeneration of the extracellular matrix by stimulating the production of elastin, reducing inflammation and oxidative stress, and protecting against UV-induced damage.

A study by Fedintsev and Moskalev (2020) suggests that non-enzymatic modifications of long-lived macromolecules, such as glycation and carbonylation, are a missing hallmark of aging. Enhancing ECM regeneration may help reduce these modifications and thereby extend longevity. The authors suggest that strategies to reduce these modifications could potentially extend lifespans. One such strategy could be the enhancement of ECM regeneration, as the extracellular matrix is a major site of non-enzymatic modifications due to its long-lived proteins. Furthermore, the study by Fedintsev and Moskalev (2020) highlights the importance of maintaining the balance between ECM components, such as collagen and elastin, in order to prevent age-related diseases such as atherosclerosis and hypertension. By enhancing ECM regeneration and promoting the growth of elastin, Elastage ECM may help to maintain this balance and prevent age-related diseases, ultimately contributing to extending longevity.

i. ***Paeonia lactiflora***, Also known as peony, this herb has been used in traditional medicine for its anti-inflammatory and antioxidant properties. Studies have shown that peony extract can help increase the production of collagen, elastin, and hyaluronic acid, which are all important components of the ECM. Peony extract may also help to reduce inflammation and oxidative stress in the skin, which can contribute to the breakdown of the ECM.

ii. ***Antheum graveolens***, Also known as dill, this herb is rich in antioxidants and has been shown to have anti-inflammatory properties. Dill extract has been found to help protect against UV-induced damage to the skin, which can contribute to the breakdown of the ECM. Dill extract may also help stimulate the production of collagen and elastin, which are important for maintaining the elasticity and strength of the ECM.

iii. ***Camellia senenis***, Also known as green tea, this herb is rich in antioxidants and has been shown to have anti-inflammatory and anti-carcinogenic properties. Green tea extract has been found to help protect against UV-induced damage to the skin and may also help stimulate the production of collagen and elastin, which are important for maintaining the elasticity and strength of the ECM.

iv. ***Vitiis vineferia***, Also known as grape seed extract, this herb is rich in antioxidants and has been shown to have anti-inflammatory and anti-carcinogenic properties. Grape seed extract has been found to help protect against UV-induced damage to the skin and may also help stimulate the production of collagen and elastin, which are important for maintaining the elasticity and strength of the ECM.

v. ***Curcuma longa***, Also known as turmeric, this herb is rich in antioxidants and has been shown to have anti-inflammatory and anti-carcinogenic properties. Turmeric extract has been

found to help protect against UV-induced damage to the skin and may also help stimulate the production of collagen and elastin, which are important for maintaining the elasticity and strength of the ECM.

vi. ***Cinnamomum vera***, Also known as cinnamon, this herb is rich in antioxidants and has been shown to have anti-inflammatory and anti-microbial properties. Cinnamon extract may help improve circulation and oxygenation of the skin, which can contribute to the regeneration of the ECM. Cinnamon extract may also help stimulate the production of collagen and elastin, which are important for maintaining the elasticity and strength of the ECM.

Appendix II - Research Data Bibliography

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4. Cinnamomum verum: "Cinnamon extract improves fasting blood glucose and glycosylated hemoglobin level in Chinese patients with type 2 diabetes" published in Nutrition Research in 2012.
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46. Paeonia lactiflora: The root extract of Paeonia lactiflora has been shown to have anti-inflammatory effects and can protect against oxidative stress, which can contribute to the degradation of the ECM. (Reference: Lee et al., 2017)
47. Anethum graveolens: Anethum graveolens has been shown to have anti-inflammatory and anti-oxidative properties, which can protect against ECM degradation. (Reference: Chauhan et al., 2019)
48. Camellia sinensis: The polyphenols found in Camellia sinensis have been shown to have anti-inflammatory and anti-oxidative effects, and can protect against ECM degradation. (Reference: Chen et al., 2016)
49. Vitis vinifera: The polyphenols found in Vitis vinifera have been shown to have anti-inflammatory and anti-oxidative effects, and can protect against ECM degradation. (Reference: Tito et al., 2018)
50. Curcuma longa: Curcumin, the active compound in Curcuma longa, has been shown to have anti-inflammatory and anti-oxidative properties, and can protect against ECM degradation. (Reference: Aggarwal et al., 2013)
51. Cinnamomum verum: Cinnamomum verum has been shown to have anti-inflammatory and anti-oxidative effects, and can protect against ECM degradation. (Reference: Kumar et al., 2015)
    - Fedintsev, A. and Moskalev, A. Stochastic non-enzymatic modification of long-lived macromolecules – A missing hallmark of aging, Ageing Research Reviews (2020). https://doi.org/10.1016/j.arr.2020.101097
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54. Camellia sinensis: Green tea extract, derived from Camellia sinensis, has been found to have anti-aging effects by promoting collagen synthesis and reducing inflammation (Katiyar et al., 2011).
55. Vitis vinifera: Resveratrol, a compound found in Vitis vinifera, has been shown to have anti-aging effects by promoting ECM synthesis and reducing oxidative stress (Baur and Sinclair, 2006).
56. Curcuma longa: Curcumin, the active component in Curcuma longa, has been found to have anti-aging effects by promoting ECM synthesis and reducing inflammation (Liao et al., 2019).

Appendix III – Support Documentation

INSTITUTE OF REGENERATIVE AND CELLULAR MEDICINE
INSTITUTIONAL REVIEW BOARD

May 25, 2021

Dr. Juergen Winkler, MD
5814 Van Allen Way
Carlsbad, CA 92008

Dear Dr. Winkler,

On May 12, 2021, the IRCM IRB approved the following protocol:

> THE SAFETY AND EFFECTIVENESS OF THE EXTENDED LONGEVITY PROTOCOL ON THE EPIGENETIC AGINGRATE IN HEALTHY INDIVIDUALS
> Protocol Number: TD-EL-001
> IRB approval number: IRCM-2019-285

Attached are the stamped approved version of the protocol and the approved consent form. Please contact us to schedule a continuing review on, or prior to, Dec. 8, 2021.

Please sign and return the attached investigator's agreement.

Please keep in mind that IRB approval does not constitute exemption from applicable local, state or federal regulations or requirements, and is not a substitute for any required pre-market approval.

We look forward to working with you as your study progresses.

Sincerely,

James P. Faber
Secretary, IRCM IRB
HHS/OHRP IRB00009500

The Safety and Effectiveness of the Extended Longevity Protocol on the Epigenetic AgingRate in Healthy Individuals

TABLE OF CONTENTS

The Longevinaut Study#1: The Safety and Effectiveness of the Extended Longevity Protocol on the Epigenetic Aging Rate in Healthy Individuals

Aim
The purpose of this study is to quantifiably determine if the Extended Longevity Protocol has a significant clinical effect on epigenetic age. Through the epigenetic age test we hope to see an impact on the epigenetic age within one year.

Rationale
Despite considerable effort, successful treatment of reversing one's biological age has deemed to be a difficult therapeutic challenge. There is evidence that the Extended Longevity Protocol is a safe and effective treatment option to improve clinical care of healthy individual's biological age.

Studies have shown that the Extended Longevity Protocol decelerates aging and the risk of age-related diseases.