ETERNLFX EVALUATION RESULTS

In 2020 Combilytics Corp embarked on a process to evaluate our natural senolytic product EternLFX. The product is designed to clear senescent or "zombie" cells, finding a simple test to measure an effect was the first priority.

Introduction

Cellular senescence entails essentially irreversible replicative arrest, apoptosis resistance, and frequently acquisition of a pro-inflammatory, tissue-destructive senescence-associated secretory phenotype (SASP). Senescent cells accumulate in various tissues with aging and at sites of pathogenesis in many chronic diseases and conditions. The SASP can contribute to senescence-related inflammation, metabolic dysregulation, stem cell dysfunction, aging phenotypes, chronic diseases, geriatric syndromes, and loss of resilience. Delaying senescent cell accumulation or reducing senescent cell burden is associated with delay, prevention, or alleviation of multiple senescence-associated conditions.

Senescent cells are spread throughout the body. In clinical trials more than one type of test is used to understand the clearance of senescent cells by senolytics. Many of these tests are invasive and require tissue biopsies and frequent blood draws. To date there is no single test that can evaluate how many senescent cells are cleared or are currently present in the body.

What is known, from two Phase 1 human trials [1, 2], is that when senescent cells are cleared (by senolytics) the body responds in a self-healing manner. This appears to be due to the reduction in SASP (senescence associated secretory phenotype). SASP is secreted by senescent cells and has a predominantly negative effect on people over 35. SASP is made up of over 500 secretions, some of which are known to cause; cell remodeling, recruitment of nearby healthy cells to become senescent, interference with cellular communication, cause inflammation and initiate other harmful processes.

These harmful processes have a profound effect as we age.

Methods and Materials Tests

As we searched for tests that measure biological age it was decided to use DNAm (epigenetic DNA methylation) testing from www.trudiagnostic.com to see if EternLFX could move any of these age markers back in time.

What markers could help to understand the effect of EternLFX on the human body?

1) IntrinsicAge – this is related to DNA methylation.
2) Extrinsic Age – this is a measure of immunosenescence.
3) Telomere length – longer telomeres are considered an indicator of a lower biological age.
4) DunedinPoAm – this is a pace of aging marker.

Evaluation Protocol

Once a test methodology was established, a protocol to evaluate EternLFX was designed. This protocol is a 7-month evaluation process that requires a beginning DNAm test and an ending DNAm test.

Using senolytics to clear senescent cells is typically done in an on-off cycled protocol. Taking senolytics every day is not required nor desirable. The dose required to be an effective senolytic is quite high and the buildup of senescent cells is initially slow, as a result the on-off cycle of very high dose natural senolytic compounds is considered the safest and most effective way to clear the slow buildup of these immortal senescent cells.

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Over a 7-month period the evaluator would take EternLFX according to the same instructions provided to all customers. www.combilytics.com/instructions The dose is based on body weight.

The evaluation protocol is:

- Beginning DNAm test
- 1 month on
    - 2 months off
- 1 month on
    - 2 months off
- 1 final month for a 7 month total evaluation period.
- End DNAm test

Results

Results from 4 evaluators.

1) 71 year-old male
    a. Intrinsic Age (years) – before 58.6 > after 44.5 = 14 year improvement
    b. Extrinsic Age (years) – before 49.3 > after 34.4 = 15 year improvement
    c. Telomere (length, age) – 6.78Kb, 80.7 > after 7.13Kb, 42.9 = 37.8 year improvement
2) 65 year-old female
    a. Intrinsic Age (years) - before 61.4 > after 56.06 = 5.34 year improvement
    b. Extrinsic Age (years) - before 47.4 > after 52.00 = 4.8 year regression
    c. Telomere (length, age) – not currently available
3) 67 year-old male
    a. Intrinsic Age (years) – before 66.86 > after 65.56 = 1.3 year improvement
    b. Extrinsic Age (years) - before 65.4 > after 55.31 = 10.9 year improvement
    c. Telomere (length, age) – 6.76Kb, 67.7 > after 6.78Kb, 65.9 = 1.8 year improvement
4) 58 year-old female
    a. Intrinsic Age (years) – before 59.2 > after 54.6 = 4.6 year improvement
    b. Other results not currently available

Discussion

While these results show a positive change in several age-related markers. Further studies are planned.

To participating in one of our studies, please contact steve@combilytics.com you must be in the US or Canada to participate.

References

1) Justice JN, Nambiar AM, Tchkonia T, et al. Senolytics in idiopathic pulmonary fibrosis: Results from a first-in-human, open-label, pilot study. *EBioMedicine*. 2019;40:554-563. doi:10.1016/j.ebiom.2018.12.052 https://pubmed.ncbi.nlm.nih.gov/30616998/

2) Hickson LJ, Langhi Prata LGP, Bobart SA, et al. Senolytics decrease senescent cells in humans: Preliminary report from a clinical trial of Dasatinib plus Quercetin in individuals with diabetic kidney disease [published correction appears in EBioMedicine. 2020 Feb;52:102595]. *EBioMedicine*. 2019;47:446-456. doi:10.1016/j.ebiom.2019.08.069 https://pubmed.ncbi.nlm.nih.gov/31542391/