Interventional Trials Provider Sheet

TruDiagnostic™ The Epigenetic Company

Report: Immune (Intrinsic vs. Extrinsic Biological Age) | **Specific Outcome:** *Intrinsic* Epigenetic Age | **Patient Outcome:** > Chronological Age and as low as possible

Recommendations	Protocol from the Study	Summary	Citation of Study
Establish consistant and effective sleeping patterns	Total Sleep Time= 7.97 hrs & Sleep Regulated Index Score= 80.62	Irregular sleep patterns can increase risk of higher IEAA by 4.13 years compared to those with regulated sleep patterns. Establishing consistant and effective sleeping patterns by achieving an average TST of 7.97 hrs and SRI of 80.92 may **reduce epigenetic age by 2.48 years.**	Carskadon, M.A., et al. A pilot prospective study of sleep patterns and DNA methylation-characterized epigenetic aging in young adults. (2019)
Mediterranean Diet	MD (Mix of nutrients, anti-oxidants, and anti-inflammatory molecules as per UNESCO) implemented long-term (1+ years) among eldery (65+ years) to promote rejuventation.	Aging effects of MD are dependant on ethnicity, sex, genetics, and environmental background. Overall, there is epigenetic improvement noted by MD with **1.5 years reversed** but with needs of a "personalized approach".	Gensous,N. One-year Mediterranean diet promotes epigenetic rejuvenation with country- and sex-specific effects: a pilot study from the NU-AGE project (2020)
Vitamin D	4000 IU/day per Chen et al. 3000 IU/day per Fahy et al. A constant decrease of on average 3 nmol/L serum vitamin D for every 10 years of age.	Participants aged epigenetically slower compared to their chronological age when given a personalized dose of vitamin D supplementation **as well as modification of nutrition status, reversing epigenetic age by 1.3-years (Horvath).**	Vetter, V.M. et al. Vitamin D supplementation is associated with slower epigenetic aging (2022) **Strath, L.J., et al. Accelerated Epigenetic Aging Mediates the Association between Vitamin D Levels and Knee Pain in Community-Dwelling Individuals (2022)**
Vitamin B12 & Folic Acid	Long term implementation of folic acid (400 µg d–1) and vitamin B12 (500 µg d–1) supplementation in older adults (65–75 years of age)	400 mcg folic acid and 500 mcg vitamin B12 supplementation effectively decreases epigenetic aging in women with the MTHFR 677CC genotype, **potentially reducing epigenetic age by 2.7 years.** Higher doses of folate may be recommended in men to produce a higher biological effect as women.	Sae-Lee, C., et al. Dietary Intervention Modifies DNA Methylation Age Assessed by the Epigenetic Clock (2018)
rhGH, DHEA, Metformin	Use of rhGH (0.015 mg/kg), DHEA (50 mg), and metformin (500 mg) on middle aged men (ages 51-65), may reverse aspects of human aging while also taking 3000 IU vitamin D3 and 50 mg elemantal zinc daily.	Long-term use of 0.015mg/kg rhGH in combination with 50mg DHEA, 500mg metformin, 3000 IU vitamin D3, and 50mg elemental zinc can reverse aspects of human aging, **up to 6.48 years**, in middle aged men as noted in this study.	Fahy et al. Reversal of epigenetic aging and immunosenescent trends in humans (2019)
Low-fat, Mediterranean diet & Low-calorie diets with Physical Activity	Long term implementation (18 months) of diet with PA for individuals with high BMI (>30.2) and increased risk of IHF (10.7%) and NALFD (59%). The MED/LC diet consists of restricted carbohydrates intake (<40gr/day for 2 months with increased gradual intake for up to 80gr/ day) and high protein + fat intake. The low-fat diet consists of 30% of calories derived from fat, 10% of calories from saturated fat, and an intake of 300 mg of cholesterol per day.	Aerobic training may alter the DNA methylation status of blood cells while epigenetic modulations may be affected by MED/LC diet interventions due to ellagic acid (inflammatory agent).	Meir, A.Y et al. Effects of lifestyle interventions on epigenetic signatures of liver fat: Central randomized controlled trial (2021)
Mediterranean Diet & DASH	Specifics of MD & DASH not provided. Individuals ages 35+ were placed on either MD or DASH diets while food intake was recorded on a questionnaire consisting of 188 items.	Mediterranean diet delayed biological age **by 0.23 years** while the DASH diet delayed aging by **0.17 years** with increased adherance.	Esposito, Simona et al. Mediterranean diet and other dietary patterns in association with biological aging in the Moli-sani Study cohort (2022)
Physical Activity and Long term Diet	One of four arms (diet only, PA only, diet+PA, control) for post-menopausal women.	Increasing Physical Activity (PA) reduces EML (epigenetic mutation load) which is associated with decreased risk of cancer and mortality. Aging increases leptin resistance. As seen in this study, those who participated in the dietary intervention had reduced their DNAmGrimAA by **0.41 years** while those participating in the physical activity intervention had reduced DNAGrimAA by **0.03 years.**	Fiorito G. et al. DNA methylation-based biomarkers of aging were slowed down in a two-year diet and physical activity intervention trial: the DAMA study (2021)
Physical Functional Ability	Weight loss interventions combined with dietary counseling over 12 weeks for individuals ages 65+ with high BMI (>30 kg/m2).	Average weight loss was 4.6 kg noted in individuals aged 65+ with a BMI >30 kg/m2. An increased grip strength was significantly associated with **decreased epigenetic age of 0.30 years** (Hannum). Increased gait speed noted a **decreasing DNA methylation age of 0.02 years** (Hannum, Horvath, and PhenoAge). Increasing physical functional ability can effectively decrease biological age.	Petersen, C.L., et al. Weight management intervention identifies association of decreased DNA methylation age with improved functional age measures in older adults with obesity (2021)

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Report: Immune (Intrinsic vs. Extrinsic Biological Age) | **Specific Outcome:** *Extrinsic* Epigenetic Age | **Patient Outcome:** > Chronological Age and as low as possible

Recommendations	Protocol from the Study	Summary	Citation of Study
Vitamin D	4000 IU/day per Chen et al. 3000 IU/day per Fahy et al. A constant decrease of on average 3 nmol/L serum vitamin D for every 10 years of age.	Participants aged epigenetically slower compared to their chronological age when given a personalized dose of vitamin D supplementation **as well as modification of nutrition status, reversing epigenetic age by 1.3-years (Horvath).**	Vetter, V.M. et al. Vitamin D supplementation is associated with slower epigenetic aging (2022) **Strath, L.J., et al. Accelerated Epigenetic Aging Mediates the Association between Vitamin D Levels and Knee Pain in Community-Dwelling Individuals (2022)**
rhGH, DHEA, Metformin	Use of rhGH (0.015 mg/kg), DHEA (50 mg), and metformin (500 mg) on middle aged men (ages 51-65), may reverse aspects of human aging while also taking 3000 IU vitamin D3 and 50 mg elemantal zinc daily.	Long-term use of 0.015mg/kg rhGH in combination with 50mg DHEA, 500mg metformin, 3000 IU vitamin D3, and 50mg elemental zinc can reverse aspects of human aging, **up to 6.48 years**, in middle aged men as noted in this study.	Fahy et al. Reversal of epigenetic aging and immunosenescent trends in humans (2019)

Report: Rate of Aging | **Specific Outcome:** DunedinPACE | **Patient Outcome:** > 1 and as low as possible

Recommendations	Protocol from the Study	Summary	Citation of Study
Caloric Restriction	25% Caloric Restriction (intake 25% below individual's baseline level) long term (2 years) in healthy adults (men ages 21-50 years, premenopausal women ages 21-47 years) with BMI (22-27.9 kg/m^2)	Reducing caloric intake by 25% long-term can potentially slow down aging and prevent multiple chronic diseases in healthy individuals with a BMI of 22-27.9 kg/m^2. Pace of Aging is reduced by **0.41 years per 1 chronological year** and GrimAge DNA methylation is moderately delayed by **0.17 years after 1 year of caloric restriction.**	Waziry R. et al. Effect of Long-Term Caloric Restriction on DNA Methylation Measures of Biological Aging in Healthy Adults: CALERIE™ Trial Analysis (2021)
Vitamin D	4000 IU/day per Chen et al. 3000 IU/day per Fahy et al. A constant decrease of on average 3 nmol/L serum vitamin D for every 10 years of age.	Participants aged epigenetically slower compared to their chronological age when given a personalized dose of vitamin D supplementation **as well as modification of nutrition status, reversing epigenetic age by 1.3-years (Horvath).**	Vetter, V.M. et al. Vitamin D supplementation is associated with slower epigenetic aging (2022) **Strath, L.J., et al. Accelerated Epigenetic Aging Mediates the Association between Vitamin D Levels and Knee Pain in Community-Dwelling Individuals (2022)**

Report: Telomere | **Specific Outcome:** Predicted Telomere Age | **Patient Outcome:** < Chronological Age

Recommendations	Protocol from the Study	Summary	Citation of Study
Telomere	Long-term implementation of Vitamin D supplementation in individuals ages 60-85 years old.	Participants who went from deficiency at baseline to sufficiency at the end of treatment had reduced epigenetic age by nearly **0.25 years (Horvath)** and **0.11 longer rLTL (telomere length).**	**Conway, J. Vitamin D Supplements Linked to Slower Epigenetic Aging (2022)** **Vetter, V.M et al. Epigenetic Clock and Leukocyte Telomere Length Are Associated with Vitamin D Status but not with Functional Assessments and Frailty in the Berlin Aging Study II (2020)**

TruDiagnostic™ is a U.S. based epigenetic testing and research company. We use a multi-omic approach to help health care providers and their patients understand and benefit from the information found in the fluid epigenome. Our primary focus is DNA Methylation, offering a variety of algorithms and lab services for those who want the most accurate and insightful longevity analysis from a CLIA-certified and HIPAA-compliant lab.

With our test, you can finally track Aging; ***the number one risk factor for most chronic diseases and death.*** Using our advanced epigenetic age testing algorithms, we are able to objectively quantify age and the effects of medical interventions intended to reduce accelerated aging and the subsequent links to disease and health.

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