

Biomarkers -- Long list collected others over the years.

Johnny Adams

(949) 922-9786

JAdams@AgingInterventionFoundation.org

Last updated 11/19/2018. Constantly improved.

This list has been collected over the years. It's long, parts are not particularly well organized, and contains considerable duplication with the practical short list www.AgingIntervention.org/1_BiomarkerPersonalPracticalBasicList.pdf

Friendly disclaimer: It's not my intention to provide specific medical advice but rather to provide others with information to better understand their health. This is not medical advice including diagnosis and treatment. Always seek the advice of a trained health professional for medical advice, diagnosis or treatment.

Here's the latest list of biomarkers, health measures and comments I send to GRG once or twice a year. These could be used to evaluate the results of studies of treatments for age related decline.

Quoted members' comments were previously sent to GRG or are otherwise public. Authors may have revised them over time.

When implementing a therapy, it's very important to have the right biomedical measurements to know if it's safe, and how it's working. This is often overlooked in do-it-yourself experiments. Placebo, and how one "feels" are deceptive.

It's important that small trials be done under expert supervision, and that you don't spare necessary expense for items like experts, lab tests etc.

If you're trying to duplicate the results of an animal study in humans, usually good to include the same measures as the animal study.

Feedback Inhibition

Homeostasis is where a body's mechanisms go into action to achieve a stable, often preset state. When augmenting a substance (often "natural"), you may get a boost in biological measures, and feel great -- at first. You may even want to write a glowing testimonial about the product that's causing it. Then homeostasis begins and the body may compensate by reducing its own production, seeking to achieve the previously set level.

Eventually the body can become dependent, so if the external source is stopped you are now deficient, and dependent on the external source -- very possibly with feelings like weakness,

illness, emotional upset or depression, and other really bad things because you're now deficient. It takes a long time to get back to where you originally were – if ever.

A classic example of this is testosterone and other hormones.

If you wrote a testimonial about a product, try to get it removed and the current story about it posted.

There are comprehensive biomarker systems consisting of a great number of tests, and types of tests. Questions and problems can arise with increased complexity, like

- **The logistics of a large number of tests.**
- **Will the phlebotomy lab be able to handle it?**
- **What is the published – and real – error of the tests? (I've seen 50% error between replicates from an advanced state-of-the-art lab)**
 - o **Will you need to do replicates (2 or 3) to get more accuracy.**
- **Will the test still be available in the future?**
- **Do you get expert interpretation of the tests?**
 - o **Will interpretation, or the same interpretation, be available in the future?**
- **Will the test change in the future, making for difficult comparisons?**
- **Be prepared to have to deal with managing the data, perhaps yourself.**
 - o **Compare the practicality of sophisticated online systems**
- **Will data management systems be available in the future?**
 - o **Will costs increase, will the design change, how will that affect interpretation**

If you opt for complex testing, having simple lab tests done for ongoing comparison would probably be a good idea.

Note: Other info is in my personal folders – example Zymo, RayBiotech, Vital Signs etc ***

Biomarkers

Types – from James Kirkland presentation at IAGG/GSA conference 2017

Dosing and pharmacokinetics biomarkers

Pharmacodynamic biomarkers

Mechanism biomarkers

Surrogate endpoint biomarkers

Ones I believe most important – Safety and CBC, inflammation, DNA methylation, mental, and physiological.

Life Extension (LEF) blood tests – doctor's order not needed, probably not covered by insurance.

www.lifeextension.com/Vitamins-Supplements/Blood-Tests/Blood-Tests

1-800-678-8989

Others:

WellnessFX www.wellnessfx.com

LabsMD www.labsmd.com

Kiosk Labs www.koslabs.net

Walk In Lab NOTE: I had a problem clicking on this. You may have to type it in your browser.

www.walkinlab.com

Google around for others.

Main labs are Quest and LabCorp. They're similar, but not methods, reference ranges etc. are different and not exactly comparable, so suggest standardizing on LabCorp.

Age Management Blood Test Panel

www.lifeextension.com/INE801E

Some categories and a few details

SAFETY -- By far the most important.

Like liver, kidney, blood, lipids, cerebrovascular, and others.

Complete Blood Count With Differential

This is a basic test for any therapy

INFLAMMATION – an effect and cause of aging

Note: Chronic measures of inflammation are highly important.

As of 11/24/18 CRP, IL-6, TNF-alpha are beginning to be considered somewhat transient measures, and questions raised as to their validity as chronic measures.

Research is being conducted into whether measures like

CXCL9 (Chemokine (C-X-C motif) ligand 9) = MIG (Monokine induced by gamma interferon), TRAIL, IFNG (Interferon gamma), EOTAXIN, GROA and some others are better long term measures, and how they can be measured.

Stay tuned.

C-Reactive Protein (CRP) – has been considered the most useful and reliable measure of inflammation

Fibrinogen

RANTES (T-Cell Specific Protein)

IL-6 (Do IL-6 measurements in the morning as there's a trough in the morning, peak in the afternoon)

TNF-alpha

Other advanced

Haptoglobin

Also IL-10, IL-17, TNF tumor necrosis factor

Cystatin?

Top Level: Myriad RBM InflammationMAP

And do complete blood count and metabolic panel

Note: Myriad is state-of-the-art, but some of these can have high variations. Replicates are suggested.

www.myriadrbm.com/products-services/humanmap-services/inflammationmap

Others

www.myriadrbm.com/products-services/humanmap-services

Maybe www.agecurve.co.uk protein profile

Just found, **considering – checking whether the reports have exact values, Myriad InflammationMap has reference range as “<XX”**

Cytokine Panel LCCYT

www.lifeextension.com/Vitamins-Supplements/itemLCCYT/Cytokine-Panel-Blood-Test

DNA METHYLATION AGE / EPIGENETIC CLOCK

Zymo Research, Osiris Green, Steve Horvaths lab, Malav/Nova Southwestern, Cygenia, MD Anderson, Willard Freedman’s “Targeted DNA Methylation & Mitochondrial Heteroplasmy Core” at the University of Oklahoma Health Sciences Center

MENTAL / COGNITIVE

Note: Experts advise cognitive tests can be terribly misleading because practice effects will give a blizzard of false positive results.

Trailmaking B (and A)

* Be aware some of the B tests you can find to download (typically the numbers and letters are in a box) are missing number 13.

One expert with very good experience in it has advised that with loss of cognitive function we lose our ability to learn with practice.

Also, after an intervention one acquaintance had a pronounced improvement in Trailmaking B results. Upon retesting over a period of time (after no treatment) it went back, almost to baseline. Then within an hour after re-treatment a pronounced improvement in Trailmaking B – suggesting it had to do more with signaling than rebuilding neurons.

If any member would be interested in locating a version of the Trailmaking B test that varies the position of the numbers or letters – or a programming whiz would create an online version that places the numbers and letters in random positions – please proceed and keep us informed.

Reaction test and others -- Human Benchmark <https://www.humanbenchmark.com>

Useful: Biomarkers of Alzheimers, see Early Indicators of Alzheimer’s Disease www.maxwellbiosciences.com/articles/research/biomarkers-alzheimers-disease

MoCA – Montreal Cognitive Assessment.

Mini self MoCA www.mocatest.org/splash
MoCA app (professional) www.mocatest.org

CNS Vital Signs

I re-tested my own CNS Vital Signs. At first a couple measures were “Low Average” “Low”, and “Average”.

Then re-tested and all 3 were “Above average”.

Made me feel like I’m from Lake Wobegon.

Sounds like practice effect, or maybe only doing selected tests, perhaps with increased focus (I’d really rather not be mentally low), had an effect.

and even started to consider the Muse relaxation headband -- relaxation score and number of “birds” (a relaxation indicator) – definite training effect with this one

Mini-Mental Status Examination (MMSE), Adcog – standard tests to evaluate cognitive function. They’re free

Evoke EEG

Cambridge Cognition

=====

DigitSpan and related

The following are for your information only.

Rolf Martin, the designer of the DigitSpan page below, may be available for customization and data analysis.

You can contact Rolf at blueberrystudy@gmail.com

www.HealthspanStudy.com/HowAreYouToday

www.HealthspanStudy.com/MyDiary

www.HealthspanStudy.com/DietSurvey

New digit-span measurement page that can enable visitors to check the earliest cognitive changes at the very start of the 20-year pathway toward age-associated cognitive decline, MCI and Alzheimer's:

Digitspan Online Measurement

www.HealthspanStudy.com/digitspan

background on the central importance of digit-span data:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=wrap+blsa+digit+span>

Along with these measurement pages, web pages currently used for the 2002-2018 Wild Blueberry Health Study will also be available to participants in the Microbiome SIG.

<http://www.blueberrystudy.com>

~~~~~

Blueberry Mental Test – find out whether this is working?

[www.healthspanstudy.com/start/2017.htm](http://www.healthspanstudy.com/start/2017.htm)

[www.healthspanstudy.com/teaberrystudy/MHome2017.htm](http://www.healthspanstudy.com/teaberrystudy/MHome2017.htm)

[www.healthspanstudy.com/Hearing2017/index.htm](http://www.healthspanstudy.com/Hearing2017/index.htm)

Face Memory: [http://healthspanstudy.com/2018\\_Memory\\_for\\_Faces](http://healthspanstudy.com/2018_Memory_for_Faces)

This high-precision measurement will allow some and possibly most individuals to measure 2% changes, for better or worse, in their memory scores at 95% confidence within 2 or 3 months. Measurements generally take less than 2 minutes, giving us very high power per minute of measurement.

=====

A second memory measurement page worth considering is:

<http://www.memtrax.com>

California Stroop test

Stroop Color and Word Test

## IMMUNE

My circle of associates and I are seeking immune testing with interpretation from the Advanced sources below.

Note: Trying to be our own immunologist or relying on a physician who is not highly skilled in immunology can be a problem, in that we might miss something as basic as evaluating whether a pneumonia vaccination is needed.

If going to use the Stanford HIMC, then would becoming the patient of a Stanford immunologist be advised?

Advanced

We need comprehensive testing with expert interpretation, standard for our group.

**UCLA Immune Assessment Core is upgrading its panel to include more age related measures, starting with TEMRA, and naïve memory cells or naïve T cells.**

[www.pathology.ucla.edu/iac](http://www.pathology.ucla.edu/iac)

[www.pathology.ucla.edu/iac-services](http://www.pathology.ucla.edu/iac-services)

Stanford HIMC <http://iti.stanford.edu/himc.html>

Stanford Immunological Center

<http://iti.stanford.edu/human-systems-immunology-center.html>

Quantrex

National Jewish Labs [www.NJLabs.org](http://www.NJLabs.org)

A major initiative is underway to develop markers as a fee for service. Details later.

CD4/CD8 ratio

Senescent T cells

Produce naïve T cell (production)

Primary NK cells

T cells

B cells

neutrophil to lymphocyte ratio (NLR)

Individuals aged 18 to 50 years had significantly lower NLR ( $p=0.019$ ) and PLR ( $p<0.05$ ) than older individuals aged 51 to 85 years.

[www.omicsonline.org/open-access/reference-values-of-neutrophillymphocyte-ratio-plateletlymphocyte-ratio-and-mean-platelet-volume-in-healthy-adults-in-north-centra-.php?aid=68492](http://www.omicsonline.org/open-access/reference-values-of-neutrophillymphocyte-ratio-plateletlymphocyte-ratio-and-mean-platelet-volume-in-healthy-adults-in-north-centra-.php?aid=68492)

For cancer patients this study suggests that the survival advantage is in part due to having a low NLR.

[www.nature.com/articles/s41598-018-22425-3](http://www.nature.com/articles/s41598-018-22425-3)

Streptococcus pneumoniae Antibody IgG 23 Serotypes lab test

IgA, IgG, IgE, IgM

Lymphocyte subset panel 5-quest

CBC with adiff blood, comprehensive metabolic panel

These LEF/LabCorp are useful but not comprehensive.

LC096925 T-Lymphocyte Helper/Suppressor Profile (has CD4, CD8 and ratio)

[www.lifeextension.com/Vitamins-Supplements/itemLC096925/T-Lymphocyte-Helper-Suppressor-Profile-Blood-Test](http://www.lifeextension.com/Vitamins-Supplements/itemLC096925/T-Lymphocyte-Helper-Suppressor-Profile-Blood-Test)

LC505016 Natural Killer Cell Surface Antigen (CD3-CD56+ Marker Analysis)

[www.lifeextension.com/Vitamins-Supplements/itemLC505016/Natural-Killer-Cell-Surface-Antigen-CD3-CD56-Marker-Analysis-Blood-Test](http://www.lifeextension.com/Vitamins-Supplements/itemLC505016/Natural-Killer-Cell-Surface-Antigen-CD3-CD56-Marker-Analysis-Blood-Test)

What else?

### **SELF ADMINISTERED HEALTH EVALUATIONS**

Normally we don't like subjective measures, but how we feel (even placebo) can be useful – or may even be the most important. *“If it's placebo – I'll take it!”*

Medical Outcomes Study Questionnaire Short Form 36

Health Survey (SF-36)

[https://www.brandeis.edu/roybal/docs/SF-36\\_website\\_PDF.pdf](https://www.brandeis.edu/roybal/docs/SF-36_website_PDF.pdf)

[https://www.rand.org/health/surveys\\_tools/mos/36-item-short-form.html](https://www.rand.org/health/surveys_tools/mos/36-item-short-form.html)

Credit to Rolf Martin for these [healthspanstudies@gmail.com](mailto:healthspanstudies@gmail.com)

Do it yourself

Daily

Quality of Life            rate from -10 to +10

Overall health

Peacefulness

Sharpness

Energy

Mood

Sleep quality

Aches and pains

Score (total of the above, or apply weights to each according to what's important to you)

### Weekly

List anything new, like observations, changes to routine, exercise, foods, medicines, supplements etc this week

WOMAC Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Can be repurposed as a measure of pain and inflammation.

<https://en.wikipedia.org/wiki/WOMAC>

[www.womac.org](http://www.womac.org)

These are simple, really good.

Contact Rolf Martin at [healthspanstudies@gmail.com](mailto:healthspanstudies@gmail.com) to be included in his study.

[www.healthspanstudy.com/homepage/decisionspeed/HowAreYouToday.htm](http://www.healthspanstudy.com/homepage/decisionspeed/HowAreYouToday.htm)

[www.paulrichterscicore.org/BBS/dietsurvey/dietpg1.htm](http://www.paulrichterscicore.org/BBS/dietsurvey/dietpg1.htm)

[www.healthspanstudy.com/teaberrystudy/mydiary.htm](http://www.healthspanstudy.com/teaberrystudy/mydiary.htm)

## **GENERAL MARKERS OF CELLULAR SENESENCE OR AGING**

P16 -- The cyclin- dependent kinase inhibitor CDKN2A, commonly referred to as p16INK4a or p16. Blood and skin biopsy

## **PHYSIOLOGICAL**

Basic

- Body weight
- Temperature
- Blood pressure
- Body Mass Index
- Heart rate variability
- Grip strength
- Sit in chair -- number of times can stand up and sit down
- Number of push ups can do
- Walking speed

How much ground you can cover in a minute, 6 minutes

The next is a measure of stamina. Consistency from test to test is important. This may be individualized depending on one's available equipment, whether a track is available, and inclination.

Examples

- Time walking as fast as possible until you *\*really\** want to stop  
(somewhat subjective, but useful and fairly accurate)

and/or

- Time on a treadmill at a fast speed and incline until you *\*really\** want to stop



- Running on treadmill with 4% incline at 5 mph, how long until have to grab rails
- Can stand on one leg > 20 sec(?) / How long can stand on one leg.
- Reaction time [www.humanbenchmark.com/tests/reactiontime](http://www.humanbenchmark.com/tests/reactiontime)

Optional, Worth considering

- Variability of blood cells (and mortality)
- Visual contrast sensitivity (eyes and olfactors are extension of the brain)
- FEV1 -- forced air velocity, although this takes a long time to change. (takes long time bef you can see changes)
- Is this energy production?-->Resting Metabolic Rate [www.bodyspec.com/what-is-rmr](http://www.bodyspec.com/what-is-rmr)
- VO2 max testing [www.bodyspec.com/what-is-vo2](http://www.bodyspec.com/what-is-vo2)
- lean body mass, total body fat, visceral adipose tissue, and bone density  
DEXA scan [www.bodyspec.com/what-is-dxa](http://www.bodyspec.com/what-is-dxa) (takes 2 yr bef you can see changes)

Various other assessment batteries are available

H-Scan

InSilico Medicine [www.aging.ai](http://www.aging.ai) Is this ready for prime time?

### SENESCENT CELL MEASUREMENT

Top level researchers at UCSD have developed a test to determine the differential expression of a panel of senescence associated genes in human PBMCs (peripheral blood mononuclear cells) before and after administering senolytic drugs.

As of Oct 2018 our group is using this in a senolytics small study.

Here's a selection of LabCorp tests (available through Life Extension) for a relatively simple and low cost measurement of before and after senolytics results collected by our senior scientist friend Bryant Villaponteau.

| Description                  | Tests For         |
|------------------------------|-------------------|
| C-Reactive Protein (CRP)     | Inflammation      |
| Carbohydrate antigen 19.9    | Aberrant Cells    |
| Carcinoembryonic antigen     | Aberrant Cells    |
| Fasting Glucose              | Energy Metabolism |
| Hemoglobin A1C               | Glycation         |
| Interleukin 6 (IL6)          | Inflammation      |
| Insulin-Like Growth Factor 1 | Growth & Repair   |
| Insulin                      | Energy Metabolism |

C-Reactive Protein (CRP)

<https://www.lifeextension.com/Vitamins-Supplements/itemLC120766/C-Reactive-Protein-CRP-Cardiac-Blood-Test>

Carbohydrate antigen 19.9

[www.lifeextension.com/Vitamins-Supplements/itemLC002261/Carbohydrate-Antigen-199-Blood-Test](http://www.lifeextension.com/Vitamins-Supplements/itemLC002261/Carbohydrate-Antigen-199-Blood-Test)

Carcinoembryonic antigen

[www.lifeextension.com/Vitamins-Supplements/itemLC002139/Carcinoembryonic-Antigen-CEA-Blood-Test](http://www.lifeextension.com/Vitamins-Supplements/itemLC002139/Carcinoembryonic-Antigen-CEA-Blood-Test)

Tumor Necrosis Factor-alpha

[www.lifeextension.com/Vitamins-Supplements/itemLC140673/Tumor-Necrosis-Factor-Blood-Test](http://www.lifeextension.com/Vitamins-Supplements/itemLC140673/Tumor-Necrosis-Factor-Blood-Test)

Hemoglobin A1C (HbA1C)

<https://www.lifeextension.com/Vitamins-Supplements/itemLC001453/Hemoglobin-A1C-HbA1C-Blood-Test>

Fasting Glucose AND Insulin (combined in one test)

<https://www.lifeextension.com/Vitamins-Supplements/itemLC302186/Fasting-Glucose-and-Insulin-Blood-Test>

Interleukin 6 (IL6) AND Y Insulin-Like Growth Factor 1 (combined in one test)

<https://www.lifeextension.com/Vitamins-Supplements/itemLC375046/IL-6-IGF-1-Blood-Test>

## **ENERGY PRODUCTION. BIOLOGICAL**

- Zymo ATP test??
- Sit in chair -- number of times can stand up and sit down
- Resting Metabolic Rate [www.bodyspec.com/what-is-rmr](http://www.bodyspec.com/what-is-rmr)
- Actions like: How many times a person can lift about a 15 lb weight from the floor to above their head with arms extended (in a somewhat circular motion)
- Indirect calorimetry
- The Urinary Metabolic Profile, US BioTek
- Mitochondrial energy assay

## **HORMONES**

hGH

Testosterone

Free T4

Cortisol

TSH

Prolactin

FSH

Leutenizing Hormone

ACTH, Plasma

IGF I, Lc/Ms

    Z Score (Male

Others?

LEF/LabCorp Male/Female panels can be useful

[http://www.lifeextension.com/Search#q=male%20panel&sort=relevancy&f:hierarchicalcategory=\[Products\]](http://www.lifeextension.com/Search#q=male%20panel&sort=relevancy&f:hierarchicalcategory=[Products])

[http://www.lifeextension.com/Search#q=female%20panel&sort=relevancy&f:hierarchicalcategory=\[Products\]](http://www.lifeextension.com/Search#q=female%20panel&sort=relevancy&f:hierarchicalcategory=[Products])

## **MICROBIOME**

uBiome

Zymo?

Mapmygut?

AmericanGut [www.americangut.org](http://www.americangut.org)

Others to be determined

## **TELOMERES**

[www.LifeLength.com](http://www.LifeLength.com)

Worth considering, less extensive [www.TeloYears.com](http://www.TeloYears.com)

-----  
-----

### **Day of the Week to do lab draws**

This developed after conversation with my long time MD friend, recently retired head of pathology and lab.

I do lab tests on Tuesday mornings (or Wed if cannot do Tues)

Later in the week it's possible the blood will be sitting around over the weekend or lab techs may not be as attentive.

Not Monday because I usually take Sunday completely off and rest, so hormones etc may not be representative of normal – and lab techs are coming off a weekend.

### **Time of day**

Mornings, 8:30-9:30

-----

When you get an unexpected lab measurement, repeat it.

Sometimes it's wrong.

-----

We want parameters that don't have daily/weekly/monthly/yearly fluctuation

That show changes over a short period of time (like 3 month)

Do tests at the same time of day

-----

### **Lab Tests -- no MD order required**

Life Extension Foundation blood tests

You do not need doctor or prescription -- order through them. It's done at LabCorp.

They send requisition and list of LabCorp locations near you

They often have sales

[www.lifeextension.com/Vitamins-Supplements/Blood-Tests/Blood-Tests](http://www.lifeextension.com/Vitamins-Supplements/Blood-Tests/Blood-Tests)

800-678-8989

WellnessFX [www.wellnessfx.com](http://www.wellnessfx.com)

LabsMD [www.labsmd.com](http://www.labsmd.com)

Kiosk Labs [www.koslabs.net](http://www.koslabs.net)

Walk In Lab NOTE: I had a problem clicking on this. You may have to type it in your browser.

[www.walkinlab.com](http://www.walkinlab.com)

----

**Life Extension**

[www.lifeextension.com/Vitamins-Supplements/Blood-Tests/Blood-Tests](http://www.lifeextension.com/Vitamins-Supplements/Blood-Tests/Blood-Tests)

**1-800-678-8989**

**View test results**

**Log in, top right click on my name, click Account Options**

**In middle under My Account Options Click Lab Testing, click View Results**

**BASICS**

CBC LC381822 \$35

Includes IL-6, ?????

--

Inflammation IL-6/IGF-1

?Incl w/CBC LC381822 ????

Separate LC375046 \$135

C-Reactive Protein (CRP), cardiac

?Incl w/CBC LC381822 ?????

Separate LC120766 \$42

Fibrinogen LC001610 \$31

--

Immune CD4/CD8 LC096925 \$138.75

LC505016 \$138.75

-----

For immune:

These LEF/LabCorp are useful but not comprehensive.

LC096925 T-Lymphocyte Helper/Suppressor Profile

LC505016 Natural Killer Cell Surface Antigen (CD3-CD56+ Marker Analysis)

Hemoglobin, Glycosylated (HbA1C) LC001453

Cystatin -- measure of kidney, also inflammation LC121251

Also in inflammation page. Do not double order.

Ferritin LC0045980

Cytokine Panel, serum LCCYT

Complement C3, serum LC006452

C-Reactive Protein (CRP), cardiac LC120766

ESR(Erythrocyte Sedimentation Rate, S-Westergren LC005215

IL-6/IGF-1 LC375046

Fibrinogen LC001610

Haptoglobin Special order

Cystatin -- measure of kidney, also inflammation LC121251

Also in Chem CBC Lipid page. Do not double order.

Interleukin 6 (IL-6) individual test LC140916

Coagulation /Thrombotic Risk Panel LC329552

Thyroid Panel LC100018

Creatine Kinase (CK), total , serum LC001362

Homocysteine, plasma LC706994

Vitamin D LC081950  
Autoimmune Disease Screen LC100041  
Natural Killer Cell Surface Antigen(CD3-CD56+) LC505016  
T-Lymphocyte Helper/Suppressor Profile LC096925  
Includes -CD4/CD8 ratio

-----  
Hormones  
Male panel LC322582

-----  
Over the counter urine, saliva tests at drug stores, internet like  
glucose  
ketone

others only available w/physician prescription

Labs don't want to be liable for self diagnosis – they could get sued.

Be aware of potential negative consequences of self-diagnosis and independent action

**ZZZZZZZZZZ**

-----  
**PhysioAge physical exam and monitoring system**

[www.physioage.com](http://www.physioage.com)

-----  
???Like a caterpillar 80 then 4X, then  
Drop ones w less than 10% chg bec we don't believe we have any sign info  
Then do the differences and rank in terms of decreasing change order -- inflammation  
biomarkers -- ie ones that changed the most on top  
Then ones remaining w/b increasing -- rank those in incr order

-----  
**Useful papers on biomarkers**

<http://www.pnas.org/content/112/30/E4104>

biological age calculation – relies on standardization at age 26

[www.pnas.org/content/pnas/suppl/2015/07/01/1506264112.DCSupplemental/pnas.1506264112.sapp.pdf](http://www.pnas.org/content/pnas/suppl/2015/07/01/1506264112.DCSupplemental/pnas.1506264112.sapp.pdf)

<https://academic.oup.com/biomedgerontology/article/68/6/667/873700>

[www.ncbi.nlm.nih.gov/pubmed/16318865](http://www.ncbi.nlm.nih.gov/pubmed/16318865)

-----  
**Urinary 8-oxo-7,8-dihydroguanosine as a Potential Biomarker of Aging.**

Simple urine test could measure how much our body has aged

<https://www.sciencedaily.com/releases/2018/02/180227090733.htm>

<https://www.frontiersin.org/articles/10.3389/fnagi.2018.00034/full>

-----  
“Ultimate” Organ / Human on a chip

I have lots of info on this -- folder

E:\1\_1\_1\_AIF\EngineeredTissuesForTesting

<https://wyss.harvard.edu/technology/human-organs-on-chips>

[http://www.livescience.com/58640-organ-on-chip-liver-fda.html?utm\\_source=lst-newsletter&utm\\_medium=email&utm\\_campaign=20170412-lst](http://www.livescience.com/58640-organ-on-chip-liver-fda.html?utm_source=lst-newsletter&utm_medium=email&utm_campaign=20170412-lst)

-----  
FOR OUR PLASMA EXCHANGE STUDY SEE

PlasmaExchangeBiomarkerComparison\_X.xlsx

SAFETY, ALL STUDIES

C:\Users\user\Desktop\Biomarkers\theranos\_lab\_form.pdf

-----  
**Blueberry Study Measurements**

[www.healthspanstudy.com/start/2017.htm](http://www.healthspanstudy.com/start/2017.htm)

[www.healthspanstudy.com/teaberrystudy/MHome2017.htm](http://www.healthspanstudy.com/teaberrystudy/MHome2017.htm)

[www.healthspanstudy.com/Hearing2017/index.htm](http://www.healthspanstudy.com/Hearing2017/index.htm)

-----  
**Zymo Research**

[www.zymoresearch.com/services/dna-methylation-analysis](http://www.zymoresearch.com/services/dna-methylation-analysis)

[www.zymoresearch.com/services/epigenetic-aging-clock](http://www.zymoresearch.com/services/epigenetic-aging-clock)

<https://www.mydnage.com/services>

Also see [www.myDNAge.com](http://www.myDNAge.com)

<http://www.zymoresearch.com/epigenetics/dna-methylation/bisulfite-conversion/ez-dna-methylation-lightning-kit>

Public

[www.mydnage.com](http://www.mydnage.com)

Larry (Xi-Yu) Jia MD interview on Kathy Ireland WorldWide

<https://zymoresearch.wistia.com/medias/ergzy0ajdg>

//////////

**DNA METHYLATION SERVICE PROVIDERS**

**Zymo is above**

Steve Horvath at UCLA. Fine option for some studies.

**Osiris Green** has been praised in articles  
Cost is \$65 + \$7.83 shipping = \$72.83  
+/- 5 yr. accuracy. Range probably not acceptable.

Cygenia

[www.cygenia.com/?q=en/epigenetic-services/biological-age](http://www.cygenia.com/?q=en/epigenetic-services/biological-age)

3 CpG sites, +/- 5 yr. accuracy. Range probably not acceptable. They're in Germany.

MD Anderson

World class. Not sure whether they provide a kit, or only data analysis services.

[www.mdanderson.org/research/research-resources/core-facilities/dna-methylation-analysis-core.html](http://www.mdanderson.org/research/research-resources/core-facilities/dna-methylation-analysis-core.html)

**Willard Freedman runs a “Targeted DNA Methylation & Mitochondrial Heteroplasmy Core”** at the University of Oklahoma Health Sciences Center which has specific expertise quite different from Horvath's

They do provide “core services”. Of particular interest is the shore-shelf and intragenic regions as they may relate to phenotypic changes with age.

[Willard-Freeman@ouhsc.edu](mailto:Willard-Freeman@ouhsc.edu)

<http://aging.ouhsc.edu/Cores/TargetedDNAMethylationMitochondrialHeteroplasmyCore.aspx>

Malav/Nova – 10/23/2017 Looks outstanding. See email in DNAmethylation folder

////////// END DNA METHYLATION SERVICE PROVIDERS

-----

**Myriad RBM**

Human InflammationMAP

[www.myriadrbm.com/products-services/humanmap-services/inflammationmap](http://www.myriadrbm.com/products-services/humanmap-services/inflammationmap)

Others

[www.myriadrbm.com/products-services/humanmap-services](http://www.myriadrbm.com/products-services/humanmap-services)

Human DiscoveryMAP

Human ExplorerMAP

Human OncologyMAP

HumanMAP

Human CardiovascularMAP

Human AngiogenesisMAP

Human InflammationMAP

Human ImmunoMAP

Human NeuroMAP

Human MetabolicMAP

Human KidneyMAP

Human CytokineMAP A

Human CytokineMAP B

-----  
**SomaLogic**

→ [www.somallogic.com/Products-Services/SOMAScan](http://www.somallogic.com/Products-Services/SOMAScan)

[www.somallogic.com/Products-Services/SOMAScan](http://www.somallogic.com/Products-Services/SOMAScan)

[www.somallogic.com/resources/somamer-reagent-characterization-data](http://www.somallogic.com/resources/somamer-reagent-characterization-data)

**ebook Choose the Right Protein Biomarker Discovery Tool**

<http://info.somallogic.com/choosing-the-right-protein-biomarker-discovery-tool>

[www.somallogic.com/wp-content/uploads/2016/09/SomaLogic-Inflammation-Panel-I-Report-Template.pdf](http://www.somallogic.com/wp-content/uploads/2016/09/SomaLogic-Inflammation-Panel-I-Report-Template.pdf)

<http://www.somallogic.com/somallogic/media/Assets/PDFs/SSM-002-Rev-2-SOMAScan-Technical-White-Paper-3-7-15.pdf>

[www.somallogic.com](http://www.somallogic.com)

-----  
**Home**

23andMe : \$149

Ubiome: \$100

Veritas Genomics full sequence : \$999

Dnafit: \$129

Standard Lipid and other blood tests: \$200

Enox2 oncoblot cancer test: \$800

----  
The COR system under development will allow daily testing, tracking and customized recommendations on key biomarkers at home to quickly see what works.

Planned measures: Cholesterol (HDL, LDL, Total), Fasting Blood Glucose, Inflammation (Fibrinogen), and Triglycerides.

Surely more will be added in the future.

Indiegogo fundraiser page has details:

[www.indiegogo.com/projects/cor-the-gold-standard-health-tracker-fitness#](http://www.indiegogo.com/projects/cor-the-gold-standard-health-tracker-fitness#)

Fundraiser is closed.

Updates on development and testing:

[www.indiegogo.com/projects/cor-the-gold-standard-health-tracker-fitness#/updates/all](http://www.indiegogo.com/projects/cor-the-gold-standard-health-tracker-fitness#/updates/all)

For example, January 2018 offers a story about how an early adopter benefitted from quickly knowing Red Yeast Rice supplements worked, and another's LDL condition improved after the systems Beta Glucan statin recommendation.



December 2017 has sections that will resonate with many of us,  
like **We all react differently to foods**  
and especially **Live a long full life.**

Excerpt from November

### **Health Experiments**

With EVT units in hand and algorithms working for Total Cholesterol, Triglycerides, HDL, LDL and Glucose, we have begun sampling our blood daily to see what foods move and don't move our analytes. No one has ever tied blood samples so closely to the daily decisions we make in our health. Now we are starting to see what that looks like so we can put it to the best possible use for your health. (continues). . .

It has other videos – see the thumbnails under the video window.

Bob Messerschmidt the founder and architect has a lot of background in this. Others are highly experienced.

Web site [www.knowyourcor.com](http://www.knowyourcor.com)

You can sign up for their newsletter at the bottom.

----

-----

RayBiotech (under evaluation as of 5/4/2017)

[http://www.raybiotech.com/index.php?dispatch=feature\\_search.view](http://www.raybiotech.com/index.php?dispatch=feature_search.view)

<http://www.raybiotech.com/high-density-quantitative-biomarker-array-services.html#200-Human-Biomarkers>

Useful for measuring plasma/cord blood results

200/440/660 Human Biomarker Testing Service

Send us your samples and we will use the Human Cytokine Array Q4000 to quantitatively detect 200/440/660 human inflammatory factors, growth factors, chemokines, receptors, and cytokines in a single experiment.

From notes

need a minimum of 5 test samples, each 500 microliters and they will do the assay for a fee.

So quantitation of 200 biomarkers will cost \$478 x5.

Covers a lot of cytokines....we are on a fishing expedition.

If it delivered quantitation at a pico gram level and did indeed have a single digit CV then I would consider 2 rounds (one before (treatment) and one after 4 treatments )with the 660 biomarkers.

-----

Young.AI

[www.young.ai](http://www.young.ai)

Alex Zhavoronkov

Young.AI is an AI-empowered platform integrating multiple predictors of your age.

Use it to manage your health, track changes over time and optimize your lifestyle.

Take control of your health and aging rate.

The science behind Young.AI [www.ncbi.nlm.nih.gov/pubmed/27191382](http://www.ncbi.nlm.nih.gov/pubmed/27191382)

-----  
@Greg Tranah

Aging biomarkers were a topic presented by Greg Tranah at a Health Extension Salon presentation. Greg is accomplished and human oriented, a UCSF professor and works for Sutter Health

<http://www.cpmc.org/professionals/research/programs/science/tranah.html>

- Energy production is the biggest predictor of longevity
- Circadian rhythm  
(I recall he talked about when people go to bed is a predictor)  
Activity rhythms and dementia
- IL-6 (IL6)
- FEV1 -- forced air velocity
- Walking speed
- Grip strength
- Sit in chair -- number of times can stand up and sit down
- Variability of blood cells (and mortality)
- Visual contrast sensitivity (eyes and olfactors are extension of the brain)
- Can stand on one leg > 20 sec(?)  
How long can stand on one leg?

-----  
**HRV – Heart Rate Variability**

Polar strap

Software:

SelfLoops HRV

EliteHRV software – cell phone, download from Android PlayStore or iPhone App Store

-----  
Simple, common sense:

- 1) Someone once commented that an experienced geriatrician can watch a patient walk down a hall and gauge their health
- 2) A friend remarked that over his career a Midwestern doctor asked his patients “How are you?”. The ones with a more positive reply tended to live longer and in better health.

-----  
For elderly frail people.

Frailty Index 34

Interesting, but predicts mortality rather than biological age(based on serum biomarkers)

Not useful for our monitoring rejuvenation therapy.

Simple version

<https://consultgeri.org/try-this/general-assessment/issue-34.pdf>

Paper with more comprehensive test

[www.har-journal.com/wp-content/uploads/2015/04/HAR01-3172.pdf](http://www.har-journal.com/wp-content/uploads/2015/04/HAR01-3172.pdf)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2776593>

Researchers from Tulane University Health Sciences Center had a nice paper that they called “quantitative measures” of frailty, but it was also a questionnaire.

-----

#### Resting Metabolic Rate

Simple, non-invasive test that measures your caloric expenditures, which declines with aging. One RMR test is \$75 and two are \$140. RMR changes with exercise, but the test is done with you resting supine in a comfortable chair. It is done before you do VO2 max testing (below).

[www.bodyspec.com/what-is-rmr](http://www.bodyspec.com/what-is-rmr)

-----

DEXA scan which measures

**lean body mass, total body fat, visceral adipose tissue, and bone density.**

A single scan is \$45, a two scan package is \$85, and a 4 scan package is only \$170.

[www.bodyspec.com/what-is-dxa](http://www.bodyspec.com/what-is-dxa)

-----

VO2 Max testing – This is done on a treadmill and measures your VO2 max while running. This is a very useful test for competitive athletes. VO2 max declines as a function of age, so this is a good test to see if our “anti-aging” intervention has reversed the mitochondrial dysfunction that occurs as a function of aging.

[www.bodyspec.com/what-is-vo2](http://www.bodyspec.com/what-is-vo2)

-----

Thomas Perls has a biomarker panel

<https://longlifefamilystudy.wustl.edu/LLFS/Home.html>

[www.livescience.com/57409-aging-biomarker-signature-blood-test.html](http://www.livescience.com/57409-aging-biomarker-signature-blood-test.html)

[www.newser.com/story/236561/a-blood-test-predicts-how-well-youre-going-to-age.html?utm\\_source=part&utm\\_medium=foxnews&utm\\_campaign=rss\\_health\\_syn](http://www.newser.com/story/236561/a-blood-test-predicts-how-well-youre-going-to-age.html?utm_source=part&utm_medium=foxnews&utm_campaign=rss_health_syn)

-----

**12/3/2016 @Bill recommended**

**Age and Sex Distributions of Age-Related Biomarker Values in Healthy Older Adults from the Long Life Family Study**

Of 38 measured biomarkers, 34 were significantly correlated with age.

<https://www.ncbi.nlm.nih.gov/pubmed/27783390>

<http://onlinelibrary.wiley.com/doi/10.1111/jgs.14522/abstract;jsessionid=9A7B2D0E8F370CA0EED9D35A7259F556.f04t01>

Preview

[http://onlinelibrary.wiley.com/doi/10.1111/jgs.14522/epdf?r3\\_referer=wol&tracking\\_action=preview\\_click&show\\_checkout=1&purchase\\_referrer=onlinelibrary.wiley.com&purchase\\_site\\_license=LICENSE\\_DENIED\\_NO\\_CUSTOMER](http://onlinelibrary.wiley.com/doi/10.1111/jgs.14522/epdf?r3_referer=wol&tracking_action=preview_click&show_checkout=1&purchase_referrer=onlinelibrary.wiley.com&purchase_site_license=LICENSE_DENIED_NO_CUSTOMER)

-----  
@From Bill

Applied Proteomics Inc.

. . . Applied Proteomics with quantitation of over 300,000 peptide/protein biomarkers . . . you know, every peptide digest ( I call the debris field) . . . especially with the phosphoralation etc post translational medications. . . . but it is not out yet. Imagine quantifying the debris from all the slowly turning over or nonrenewable proteins. . . . using pattern recognition it would very likely be predictive of chronological age.

<http://www.appliedproteomics.com/proteomics/>

<http://www.bioagetest.com>

-----  
MARK-AGE biomarkers of ageing

<http://www.sciencedirect.com/science/article/pii/S0047637415000317>

-----  
AgeCurve  
protein profile

[www.agecurve.co.uk](http://www.agecurve.co.uk)

-----  
Age predictor using deep neural network trained on hundreds of thousands anonymized human blood tests. Enter your own data.

Created by InSilico Medicine and InVitro.

[www.aging.ai](http://www.aging.ai)

-----  
Wyss-Coray/Stanford/Alkahest trial

<https://clinicaltrials.gov/ct2/show/NCT02256306>

From clinicaltrials page:

Secondary Outcome Measures:

- Change on the 13-item ADAS-Cog [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]
- Change on the Trail-Making Test [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]  
[http://doa.alaska.gov/dmv/akol/pdfs/uiowa\\_trailmaking.pdf](http://doa.alaska.gov/dmv/akol/pdfs/uiowa_trailmaking.pdf)
- Change on the Clinical Dementia Rating scale Sum of Boxes (CDR-SB) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]  
[http://www.dementia-assessment.com.au/global/cdr\\_scale.pdf](http://www.dementia-assessment.com.au/global/cdr_scale.pdf)
- Change on the Functional Activities Questionnaire (FAQ) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

- Change on the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]
- Change on the Geriatric Depression Scale [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]
- Change on the Neuropsychiatric Inventory Questionnaire (NPI-Q) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

-----

Measures from Korean study: Clinical Trial to Evaluate the Potential Efficacy and Safety of Human Umbilical Cord Blood and Plasma

\* see this study for when tests were done/intervals and other details

<https://clinicaltrials.gov/ct2/show/NCT02418013?term=cord+blood&rank=37>

Also saved in

E:\\_1\_1\_1\_AIF\1\_1\_1\_1\_1\_PlasmaTransferAndExchange\UmbilicalCordAndWuyi\TrialToEvalUmbilicalCordBloodAndPlasma

From clinicaltrials page:

**PRIMARY**

Changes in scores of Short Physical Performance Battery (SPPB)

**SECONDARY**

Hand grip strength

SF\_36(The Short Form (36) Health Survey) as a measure of improvement in the quality of life [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]

Biomarkers for oxidative stress and inflammation as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]

The test is scheduled to be conducted at the day of transplantation (2nd visit) and at 1 week (3rd visit), 1 month (4th visit), 6 months (5th visit) after the treatments. Changes in biomarkers such as CRP, IL-1,6, IL-10, LIF, D-dimer, fibrinogen, TNF- $\alpha$ , CBC with differential, malondialdehyde, 4-hydroxynonenal will be assessed. After normality test on the average difference, either unpaired t-test or wilcoxon rank sum test will be conducted for statistical analysis.

**Biomarkers for immune response**

Eotaxin, FGF-2, Flt-3 Ligand, Fractalkine, G-CSF, GM-CSF, GRO, IFN $\alpha$ 2, IFN $\gamma$ , IL-1a, IL-1b, IL-1ra, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12(p40), IL-12(p70), IL-13, IL-15, IL-17, IP-10, MCP-1, MCP-3, MDC, MIP-1a, MIP-1b, PDGF-AA, PDGF-AB/BB, RANTES, sCD40L, sIL-2Ra, TGF $\alpha$ , TNF $\alpha$ , TNF $\beta$ , VEGF

Adrenal cortical hormone levels as a measure of efficacy for anti-aging effects [ Time Frame: Up to 6 months after transplantation ] [ Designated as safety issue: No ]

Telomere length as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]

Body composition as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]

Aging-related genetic and epigenetic markers as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]  
aging-related genetic markers (e.g ELOVL2. ) compared to baseline

mitochondria DNA copy number as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]  
Mitochondria DNA copy number of participants will be compared among the treatment groups.

Aging-related growth factors(GDF11, GDF15, Myostatin) as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]

DNA damage extent (8-hydroxyguanine level) as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]  
The investigators will assess changes of 8-hydroxyguanine in white blood compared to baseline which will be measured at the day of transplantation.

Changes in scores of Short Physical Performance Battery (SPPB) as a measure of efficacy for anti-aging effects [ Time Frame: 6 months period after transplantation ] [ Designated as safety issue: No ]

-----  
3D Face Scan (Reveals Biological Age Better Than A Blood Profile)

see How Old Are You 3D Face Scan Reveals Biological Age Better Than A Blood Profile.html  
Source: Chen W, Qian W, Wu G, et al. Three-dimensional human facial morphologies as robust aging markers. Cell Research. 2015.

Link to the article:

<http://www.medicaldaily.com/how-old-are-you-3d-face-scan-reveals-biological-age-better-blood-profile-327806>

[http://biometrics.cse.msu.edu/Publications/Face/HanOttoJain\\_AgeEstimationFaceImages\\_HumansMachinePerformance\\_ICB13.pdf](http://biometrics.cse.msu.edu/Publications/Face/HanOttoJain_AgeEstimationFaceImages_HumansMachinePerformance_ICB13.pdf)

<http://www.sciencedirect.com/science/article/pii/S1877050915001908>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4256302/>  
-----

H-SCAN

1. Auditory reaction time
2. Highest audible pitch
3. Vibrotactile sensitivity
4. Visual reaction time
5. Muscle movement speed
6. Lung: forced vital capacity
7. Lung: forced expiratory volume, 1 sec

8. Decision reaction time
9. Decision movement speed
10. Short Term Memory
11. Alternate button tapping
12. Visual accommodation

<http://ultimatecare.com/testhscan.htm>

<http://archive.aged.org/default.asp?page=SmallMeasuringAgeIssue9>

Elliott Small, GRG member is distributor and working on the next generation.

\*\*\*\*\*

### **DNA DAMAGE**

CONSIDERING 8-hydroxyguanine

<https://www.cellbiolabs.com/8-ohg-rna-damage-elisa> \$419

[www.cellbiolabs.com/8-ohg-rna-damage-elisa](http://www.cellbiolabs.com/8-ohg-rna-damage-elisa)

\*\*\*\*\*

### **MENTAL MEASURES START #####**

Note: Experts advise cognitive tests can be terribly misleading because practice effects will give a blizzard of false positive results.

Trailmaking B (and A)

\* Be aware some of the B tests you can find to download (typically the numbers and letters are in a box) are missing number 13.

One expert with very good experience in it has advised that with loss of cognitive function we lose our ability to learn with practice.

Also, after an intervention he had a pronounced improvement in Trailmaking B results. Upon retesting over a period of time (after no treatment) it worsened. Then within an hour after re-treatment a pronounced improvement in Trailmaking B – suggesting it had to do more with signaling than rebuilding neurons.

If any member would be interested in locating a version of the test that varies the position of the numbers or letters – or a programming whiz would be interested creating an online one that places the numbers and letters in different positions – please proceed and keep us informed.

Reaction test and others -- Human Benchmark <https://www.humanbenchmark.com>

### **CNS Vital Signs**

<http://www.cnsvs.com>

Measures basic brain functions:

composite memory

verbal memory

visual memory

executive function

processing speed  
psychomotor speed  
reaction time  
complex attention  
cognitive flexibility  
simple visual attention  
motor speed

### **Trailmaking B (and A)**

See

E:\1\_1\_1\_AIF\1\_1\_1\_1\_1\_BiomarkersOfAgingAndHealthMeasures\1\_TrailMakingTest  
Test B because it takes the longest

**NOTE: IN SOME YOU MAY FIND AND DOWNLOAD, THE LAST NUMBER IN TEST B -- #13 IS MISSING This is confusing**

This one is OK (download powerpoint)

**[TRAILS A & B forms - Me.umn.edu](http://www.me.umn.edu)**

**<http://www.me.umn.edu/~wkdurfee/projects/driving/docs/TrailMaking.ppt>**

MoCA – Montreal Cognitive Assessment.

Mini self MoCA [www.mocatest.org/splash](http://www.mocatest.org/splash)

MoCA app (professional) [www.mocatest.org](http://www.mocatest.org)

Mini-Mental Status Examination (MMSE)

overwhelmingly found in literature for cognition, memory, thinking  
has Alzheimer's Dis. Assessment Scale, Cognitive subscale (ADAS-Cog)

Cambridge Cognition

[www.cambridgecognition.com](http://www.cambridgecognition.com)

Human Benchmark

Note – at first it gives a message that it's "not a secure site". I went ahead and think it's probably OK, can explain if you like.

But if you don't want to go to the site, it's mental tests

Number Memory -- Remember the longest number you can.

Reaction Time -- Test your visual reflexes.

Verbal Memory -- Keep as many words in short term memory as possible.

Visual Memory -- Remember an increasingly large board of squares.

<https://www.humanbenchmark.com>

@Jim Watson:

SF12 or SF36 – standardized reportable quality of life scores.

Several cognitive tests avail online -- MMSE, Adcog – standard tests to evaluate cognitive function – they're free

@Richard suggested



Beta 2-microglobulin  
CCL11  
GDF-8 (myostatin)  
Haptoglobin  
MCP-1/CCL2  
DECREASE  
GDF-11 (Eotaxin)  
IGF-1  
Oxytocin  
Teleomerase  
MENTAL  
Folstein  
MMSE  
Trail making  
fingernail growth

@Bill  
BLSA  
MMSE  
Trail making

Wyss-Coray plasma transfer

<https://clinicaltrials.gov/ct2/show/NCT02256306>

(Primary = safety)

Secondary Outcome Measures:

Change on the 13-item ADAS-Cog [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change on the Trail-Making Test [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change on the Clinical Dementia Rating scale Sum of Boxes (CDR-SB) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change on the Functional Activities Questionnaire (FAQ) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change on the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change on the Geriatric Depression Scale [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change on the Neuropsychiatric Inventory Questionnaire (NPI-Q) [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Other Outcome Measures:

Change in functional connectivity in the default mode network as assessed by resting state functional MRI [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

Change in plasma biomarkers associated with AD Differential effect of therapy on above outcomes as a function of ApoE genotype [ Time Frame: 18 weeks ] [ Designated as safety issue: No ]

-----  
CNS Vital Signs  
<http://www.cnsvs.com>

Steve Perry used it in the GDF11 experiment  
E:\\_1\_1\_1\_AIF\\_1\_1\_1\_1\_1\_PlasmaTransferAndExchange\GDF11\_StevePerry  
Mental – this and probably others  
2014-04-14 - CNS Vital Signs Report.pdf  
-----

Reaction tests(?)

PEBL Test Battery  
<http://pebl.sourceforge.net/battery.html>  
[http://pebl.sourceforge.net/wiki/index.php?title=PEBL\\_Test\\_Battery](http://pebl.sourceforge.net/wiki/index.php?title=PEBL_Test_Battery)

Luminosity.com(?)

-----  
@Bill's computerized test (press button in response to sound, reaction time?)  
GRG member's computerized test (press button in response to sound, reaction time?)

Early Alzheimers detection  
[http://www.alz.org/national/documents/checklist\\_10signs.pdf](http://www.alz.org/national/documents/checklist_10signs.pdf)

-----  
#####

GRG thread:

Auditory P300 are obtained from signal averaging of scalp-recorded potentials. Visual P300 has also been described. I suppose tactile P300 would also be possible. We observed an increase in P300 latency in Alzheimer's disease patients relative to controls (see below). However, more striking than the increase in latency was the deterioration of the morphology of the P300. Whereas the P300 was clearly distinguishable in cognitively intact younger and older patients, it deteriorated significantly and was very difficult or impossible to identify in many patient's with Alzheimer's disease.

@Sheldon  
GRG Member

J Gerontol. 1989 Nov;44(6):M195-200.  
Longitudinal P300 latency changes in Alzheimer's disease.  
Ball SS1, Marsh JT, Schubarth G, Brown WS, Strandburg R.  
Author information

Abstract

A longitudinal study of the changes in latency of the P300 (P3) wave of the auditory event-related brain potential was undertaken in a group of 18 thoroughly screened and diagnosed

possible and probable Alzheimer's disease (pAD) patients and 15 normal controls. On initial recording, P3 latency was significantly prolonged in the pAD group by more than 1.5 standard deviations (40 msec) beyond the normal group. Over the course of the next 3 years, the rate of increase in P3 latency was significantly greater for the patient group than for the controls. The rate of change in P3 latency may reflect accelerated senescence in Alzheimer's disease. Development of the auditory P300 as a marker of neurobiological processes in aging and dementia is discussed.  
PMID: 2809106

@On Fri, May 8, 2015 at 5:00 AM, Stanley Primmer <[stanley\\_primmer@hotmail.com](mailto:stanley_primmer@hotmail.com)> wrote:  
On Fri, May 8, 2015 at 5:00 AM, GRG Member wrote:

-----

Please see the abstract below that briefly describes a method used to measure the permeability and breakdown of the blood-brain barrier (BBB). I have also attached an article by Eric Braverman and Kenneth Blum that describes a study of P300 latency as a measure of brain effectiveness. As I recall, the P300 method involves attaching multiple electrical sensors to a subject's scalp. A sharp sound is emitted, and the time between the sound and its reception by the sensors is the latency period. Their graph in Fig. 2 shows a clear correlation with increasing age and increasing latency. Dr. Braverman told me that this methodology doesn't work with a subject who is deaf. However, Sheldon, you probably have better information on the subject due to your direct experience. The following are some Pubmed links to other articles coauthored by Braverman and Blum on P300.

<http://www.ncbi.nlm.nih.gov/pubmed/25251414>

<http://www.ncbi.nlm.nih.gov/pubmed/23526928>

<http://www.ncbi.nlm.nih.gov/pubmed/14521274>

@Stan Primmer

Neuron. 2015 Jan 21;85(2):296-302. doi: 10.1016/j.neuron.2014.12.032.

Blood-brain barrier breakdown in the aging human hippocampus.

Montagne A1, Barnes SR2, Sweeney MD1, Halliday MR1, Sagare AP1, Zhao Z1, Toga AW3, Jacobs RE2, Liu CY4, Amezcua L5, Harrington MG6, Chui HC5, Law M7, Zlokovic BV8.

Abstract

The blood-brain barrier (BBB) limits entry of blood-derived products, pathogens, and cells into the brain that is essential for normal neuronal functioning and information processing. Post-mortem tissue analysis indicates BBB damage in Alzheimer's disease (AD). The timing of BBB breakdown remains, however, elusive. Using an advanced dynamic contrast-enhanced MRI protocol with high spatial and temporal resolutions to quantify regional BBB permeability in the living human brain, we show an age-dependent BBB breakdown in the hippocampus, a region

critical for learning and memory that is affected early in AD. The BBB breakdown in the hippocampus and its CA1 and dentate gyrus subdivisions worsened with mild cognitive impairment that correlated with injury to BBB-associated pericytes, as shown by the cerebrospinal fluid analysis. Our data suggest that BBB breakdown is an early event in the aging human brain that begins in the hippocampus and may contribute to cognitive impairment.

**@From:** [grg-bounces@lists.ucla.edu](mailto:grg-bounces@lists.ucla.edu) [<mailto:grg-bounces@lists.ucla.edu>] **On Behalf Of**  
Sheldon Ball

**From:** [grg-bounces@lists.ucla.edu](mailto:grg-bounces@lists.ucla.edu) [<mailto:grg-bounces@lists.ucla.edu>] **On Behalf Of** GRG  
Member

**Sent:** Wednesday, May 06, 2015 11:38 PM

**@To:** Dr. Harold Katcher; Gerontology Research Group

**To:** GRG Member; Gerontology Research Group

**Subject:** Re: [GRG] Translational Science

@Sheldon Ball

GRG Member

I am interested in what you find out. Objective markers of CNS changes with age will be useful for assessing anti-aging interventions.

A brief overview of age-associated changes in the central nervous system may be found at [http://www.anvita.info/wiki/Age\\_Associated\\_Changes\\_In\\_The\\_Cns](http://www.anvita.info/wiki/Age_Associated_Changes_In_The_Cns).

Slowed central processing and reaction time may be amenable to measurement.

Back in the late 1980s I was enthused about reports of P300 changes with age and with Alzheimer's disease. This seemed like an objective measure of a neural signal originating from deep brain structures. I sought out and worked Jim Marsh at UCLA on auditory P300 changes in Alzheimer's disease patients. The results were difficult to interpret and the long-term usefulness in question. I still wonder if the method could be improved to obtain more meaningful results.

**END MENTAL MEASURES #####**

\*\*\*\*\*

\*\*\*\*\*

**START of Measure energy objectively**, rather than when subject says they “feel they have more energy”

\*\*\* Seems like it's interrelated with other measures

@Bill V

How many times a person can lift about a 15 lb weight from the floor to above their head with arms extended (in a somewhat circular motion)

Measure output

Exercise cycle output --

1.

10-15 warmup – lk at calorie output, revs/min, pulse rate  
After about 10-15 min “magic” happens – blood flow incr, it’s easier to put out  
2a.

Then you go up to 85% max heart rate f/that age  
Crank up exercise bike, see how long you can maintain  
2b.

Maintain work output – 60 watts, 200 calories

Adj load so comfortable w/heart rate at 85%

Aft warmup does (f/example the 70 rev/min) give you a lower or higher heart rate?

Do you have to work harder or is it easier?

@Penny Dacks

Indirect calorimetry is a great option - I'm not an expert on the tools available to humans but I believe that sports medicine will have some useful tools.

Another option is digital biomarkers of activity, quantifying function in real-life. FitBit is one obvious example. A more sophisticated and in-depth option is offered by OrcaTech, developed by Jeffrey Kaye at OHSU. It's an unobtrusive home-monitoring system that records a wide variety of signals like gait, physical activity in the home, when and how much time is spent on phone & computer, etc. Kaye is developing it for a variety of uses including an alternative read-out of activities of daily living and cognitive status - presumably it could be quite useful as a read-out of fatigue and energy-use as well. He has quite a few papers on pubmed about the technology. That said, I have to admit that I haven't looked at whether available for individual consumer purchase rather than researchers.

<http://www.ohsu.edu/xd/research/centers-institutes/orcatech/index.cfm>

@Kingsley Morse’s suggestions for measuring energy level

1.) A pedometer can measure how far one walks each day, which takes energy.

2.) The Urinary Metabolic Profile offered by  
US BioTek

<https://www.usbiotek.com/Downloads/information/OAQRG.pdf>

3.) Search Google's indices with key words  
like

mitochondria energy assay

Assay: Measurement of Mitochondrial Function

<http://www.genengnews.com/gen-articles/assay-measurement-of-mitochondrial-function/2259/>

@Harold Katcher

feeling like 'you have more energy' is not a measurement of energy but of mood - a feeling of energy lack is a constant complaint of depressives.

“Secondary” measures of energy

1. grip strength

2. endurance

older -- – Adapt to younger people?

<http://physical-therapy.advanceweb.com/Article/Endurance-Testing-and-Training-in-the-Frail-Elderly.aspx>

younger -- number of pushups or curls

-----

Misc:

Gibbs free energy

The amount of ATP, FADH<sub>2</sub>, NADH and NADPH

Measure the efficiency of mitochondria you'd want to find out how many ATPs are produced per molecule of glucose taken in - assuming that intake of sugar is the same (or is it, as there is an age-dependent insulin resistance?) you'd find that less total ATP is produced in aging cells which are less efficient --so there would be a lesser ATP content.

I believe that ATP content is pretty easy to measure using a luciferin-luciferase reaction.

I'd guess that even single-cell amounts could be measured using a scintillation counter.

END of Measure energy objectively

\*\*\*\*\*

@Thomas Coote from GRG message

. . . very good correlation between glomerular filtration rate and age in humans. So I would expect undesirable metabolic products such as urea/uric acid and creatine to be cleared less efficiently with age. I will have blood analysed before and after, so any change in these should be apparent.

@Harold Katcher from GRG message

Hello Thomas et al,

All of those markers are informative of various conditions that increases with aging. As we learned - the results of simple, routine tests like CBCs and blood sugar etc. could be used in an algorithm to predict age with a fair degree of accuracy. Of course, who knows how a complete replacement of plasma by strangers' plasma would effect the normal results and how long it would take this perturbation to calm down with respect to blood proteins (depends on the half-lives of proteins and perhaps other factors in the bloodstream). And that's not to mention the new proteins the body may make in response to the procedure itself? So what else are markers of aging? We know that the Horvath methods of dealing with different kinds of tissues and assessing the state of DNA methylation of a number of sites (and not too many - those sites vary by tissue of course) is has a correlation coefficient of 0.96 - so I'd start with that - Horvath is willing to do the assays for a heck of a lot less than those hundreds of largely irrelevant and proving nothing blood markers. That's one thing - and what about functional testing - like with the rats (have older folks swim in water mazes - no I think not, but there are other tests). The Horvath test on peripheral blood monocytes would be inappropriate I think - because several lines of evidence lead me to believe that hematopoietic stem cells are rejuvenated very late compared to other stem cells as evidence exists (though disputed do you remember Amy Wagers and Shane Mayack and the retraction of articles from Nature and Blood?) that these cells are not rejuvenated by serum factors but by juxtacrine interactions with bone stromal cells. So maybe a liver biopsy - could be done with a long needle? Skin of course is an 'obvious' place to start as well if exploring - structural changes you'd expect if there were real rejuvenation would be revealed by punch biopsies.

\*\*\*\*\*

Cell senescence biomarkers  
Human Cellular Senescence PCR Array

[http://www.sabiosciences.com/rt\\_pcr\\_product/HTML/PAHS-050Z.html](http://www.sabiosciences.com/rt_pcr_product/HTML/PAHS-050Z.html)

See CellSenescenceBiomarkers folder

Also E:\\_1\_1\_1\_AIF\1\_1\_1\_1\_1\_PlasmaTransferAndExchange\Kipro

-----  
Short Physical Performance Battery (SPPB) as a measure of efficacy for anti-aging effects  
[http://www.ndorms.ox.ac.uk/prove/documents/assessors/outcomeMeasures/SPPB\\_Protocol.pdf](http://www.ndorms.ox.ac.uk/prove/documents/assessors/outcomeMeasures/SPPB_Protocol.pdf)  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2845214/>

-----  
Measures from Steve Perry's GDF11 experiment  
E:\\_1\_1\_1\_AIF\1\_1\_1\_1\_1\_PlasmaTransferAndExchange\GDF11\_StevePerry

Mental  
2014-04-14 - CNS Vital Signs Report.pdf

-----  
@From Dr. Joseph Dhahbi  
Circulating small noncoding RNAs as biomarkers of aging.  
[http://www.academia.edu/6566043/Circulating\\_small\\_noncoding\\_RNAs\\_as\\_biomarkers\\_of\\_aging](http://www.academia.edu/6566043/Circulating_small_noncoding_RNAs_as_biomarkers_of_aging)

-----  
<http://www.genomebiology.com/2015/16/1/185>  
Conclusions  
We identify a novel and statistically robust multi-tissue RNA signature of human healthy ageing that can act as a diagnostic of future health, using only a peripheral blood sample. This RNA signature has great potential to assist research aimed at finding treatments for and/or management of AD and other ageing-related conditions.

-----  
Transcriptome – useful, but not sure whether or when tests will be available  
<http://sage.buckinstitute.org/age-its-all-in-your-blood/>  
<http://www.nature.com/ncomms/2015/151022/ncomms9570/pdf/ncomms9570.pdf>  
<https://gerontologyresearchgroup.wordpress.com/2015/12/02/there-must-be-something-substantially-different-in-young-blood-compared-to-old/>

-----  
Biomarker/medical measurement Q&A from

Liz Parrish Reddit "Ask me anything" session 10/11/15

[https://www.reddit.com/r/Futurology/comments/3ocsb/ama\\_my\\_name\\_is\\_liz\\_parrish\\_ceo\\_of\\_bioviva\\_the/](https://www.reddit.com/r/Futurology/comments/3ocsb/ama_my_name_is_liz_parrish_ceo_of_bioviva_the/)

Q: Attendee asked about criteria / measurements / biomarkers

LizParrishBioViva: We are using both visual biomarkers, MRI and a panel of blood and tissue testing including work on telomere length with Spectracell and Life Length and epigenetic testing.

Q: Do you directly measure how much the telomeres have been lengthened?

LizParrishBioViva: Yes

jansen1975: They are looking at % short telomeres as well as changes to average telomere length using TAT and QTRAP assays.

Q: What age markers did BioViva note before treatment on the above patient?

LizParrishBioViva: We blood and tissue samples and they will be analyzed for all available biomarkers

-----

Quantification of biological aging in young adults

See <http://www.pnas.org/content/112/30/E4104.full>

<http://www.pnas.org/content/suppl/2015/07/01/1506264112.DCSupplemental/pnas.1506264112.sapp.pdf>

Saved to SupplementalMethodsToQuantificationOfBiologicalAgingInYoungAdults.pdf

Starting with

Biomarkers measuring results

Numerous blood measures: starts at "Pace of Aging"

Glycated hemoglobin, forced expiratory volume in one second (FEV1) and others (it continues)

Physical Limitations

Cognitive Testing

Retinal Imaging

Self Rated Health

Later

“Measuring diminished physical capacity at age 38 years.” Physical Functioning, Physical Limitations, Cognitive Testing, Retinal Imaging

Later Self Rated Aging, Facial Aging

-----

@Bill's nitric oxide (FeNO) and oximeter as measure of aging intervention

-----

SAFETY, ADVERSE EVENTS



From Young Plasma Transfusions for Progressive Supranuclear Palsy

<https://www.clinicaltrials.gov/ct2/show/NCT02460731?term=Young+Plasma+Transfusions+for+Progressive+Supranuclear+Palsy&rank=1>

Drug limiting toxicity (DLT), defined as:

- 1) any Grade 3 or higher adverse event (AE) per National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) for which there is reasonable possibility that salsalate caused the event,
- 2) any Grade 2 AE in the CTCAE system organ class of nervous system disorders that is considered clinically significant and for which there is reasonable possibility that salsalate caused the event, or
- 3) any Grade 2 or higher treatment-related adverse events during administration that do not resolve promptly with supportive treatment

-----

<https://www.luminexcorp.com/clinical/ruo-products/>

-----

@Early email from Harold Katcher

\*\*\* THIS MAY HAVE CHANGED OVER TIME \*\*\*

GRG Member, sent to GRG email discussion forum

\*\*\* in 2014 so may have been updated

For plasma transfer

Blood tests

Cytokines and antibodies (some may not be feasible the first 8 are required, 11 is highly preferred as are 11 – 15.

1. CRP
2. TNF-alpha
3. TGF-beta
4. IL-10
5. IL-6
6. IL-1
7. Soluble TNF-receptor (type I)
8. Soluble TNF-receptor (type II)
9. Autoantibodies/ - against a variety of factors (RF, ANA, anti-thyroid Ab)
10. Immune complexes
11. BNP (brain natriuretic protein)
12. granulocyte colony-stimulating factor (G-CSF)
13. CCL-11 ('eotaxin')
14. MIG (monokine induced by gamma interferon)
15. macrophage colony-stimulating factor (M-CSF)
16. Exosomes RNA content (if only – would require 'deep sequencing')

Lymphocytes

1. FACS for distribution of b-cells, t-cells (CD-3, CD-28) CD4+, CD25+, CD8+ CD28+

2. P16INK4a expression in T - cells

#### Metabolism

1. Insulin and glucose
2. IGF-1
3. Lipids and apolipoproteins (apo A1, apoB, apoC, apoE)
4. Testosterone (free)
5. Hemoglobin concentration
6. DHEA
7. Free T3
8. Sedimentation rate

Other factors (cellular factors also in the blood (or liver, skin – we need an earlier marker than HSC rejuvenation)

1. Telomerase
2. Telomere length
3. MMP-9
4. miRNA expression profiling (qPCR)

#### Safety labs

1. CBC
2. LFT's
3. BUN and creatinine

#### Functional Testing

1. Cognitive ability/memory testing (computerized?)
2. Physical strength, Up and Go
3. Presbyopia
4. FEV
5. Age-specific quality of life scale

Senescent Symptoms to be photographed (with a ruler alongside)

1. Balding patterns
2. Age spots
3. Senile fold (earlobe)

plasma exchange

grip strength, total blood hemoglobin, TUG tests (time of up and go)- and maybe some psychological tests where the aged score appreciably worse than younger people

@From 4/4/2015 message

No single determinant in the blood,  
there are age dependent changes in TNF receptors (type II),  
hemoglobin concentrations,

hematocrit etc..

There is the very well known increase in inflammatory cytokines, and the increase in CCL-11 (which Villeda showed caused cognition deficits and a down-turn in neurogenesis, as did aging itself, which caused a concomitant increase CCL-11 "eotaxin" concentration).

Re. using human subjects - changes in age phenotype will become visible over time to other humans.

Tests of speed of perception, tests of short-term memory.

No need to confine to blood tests.

Tests of skin thickness and structure are possible with the relatively non-invasive 'punch' skin biopsies.

Consider computer generated parameters

Such signs as hairline recession are not apparent in animals but are in men.

Age spots - the appearance and disappearance of which are not taken into account would be a good indicator of physiological age, certainly their disappearance would be very strong evidence - are measures not possible in animals..

“Best would be”

Change in epigenetic marks - such as DNA cytosine methylations- which Horvath showed to be an accurate indicator of chronological age - and see whether these patterns change to be more like that of a younger organisms.

And also of importance would be to isolate stem cells and check the ratios of age-related gene's transcription rates.

If ratio of a specific DNA/chromatin repair enzymes to specific inflammatory cytokine transcription is at certain level we can probably tell what life-stage the organism is in.

Best indicators of age are physical appearance and function - and those are the parameters to be measured to establish that rejuvenation has occurred.

Monitor multiple concurrently

Since except possibly for epigenetic changes in DNA that are age-predictive and perhaps tissue and age specific transcriptional profiles (including miRNAs) there are no age-biomarkers (though both the epigenetic marking of cells and transcriptional profiles would both contribute to discerning an effect.

Perhaps better approach is to see the effect on the diseases of aging - particularly on the underlying processes of atheroma growth,

heart performance and

tests of mental agility and physical performance as well

Luminosity-like test could be given to determine visual and other processing speeds - test of memory are easy to perform.

Also other common markers of aging (like balding – may seem trivial but a reversal would be impressive)

disappearing age spots (photographed) would also contribute to a narrative of rejuvenation.

The changes are likely to take weeks (and reason to suppose even longer for the immune system),

but we could see if such underlying causes of aging diseases such as

presence of senescent cells,

chronic low-grade inflammation with simple blood tests.

Skin biopsies could demonstrate changes in

skin thickness and composition - properties known to change with aging.

-----

See email for poster:

METHYLATION Fwd introduction to Willard Freeman Oklahoma.msg

Willard Freedman [Willard-Freedman@ouhsc.edu](mailto:Willard-Freedman@ouhsc.edu)

Willard Freedman runs a “Targeted DNA Methylation & Mitochondrial Heteroplasmy Core” at the University of Oklahoma Health Sciences Center which has specific expertise quite different from Horvath’s

They do provide “core services”. Of particular interest is the shore-shelf and intragenic regions as they may relate to phenotypic changes with age.

<http://aging.ouhsc.edu/Cores/TargetedDNAMethylationMitochondrialHeteroplasmyCore.aspx>

<http://aging.ouhsc.edu/Cores/TargetedDNAMethylationMitochondrialHeteroplasmyCore/BisulfiteOligonucleotideCaptureSequencing.aspx>

<http://aging.ouhsc.edu/Cores/TargetedDNAMethylationMitochondrialHeteroplasmyCore/AbsoluteDNACopyNumberAnalysis.aspx>

More

<http://ouhsc.edu/search.aspx?q=Targeted%20DNA%20Methylation%20&%20Mitochondrial%20Heteroplasmy%20Core>

See this folder

TargetedAnalysesOfDNAMethylationAndMitochondrialHeteroplasmy.pdf

-----

DNA methylation

1/21/2017

CYGENIA

<http://www.cygenia.com/?q=en/epigenetic-services/biological-age>

1/8/2017

<https://www.osirisgreen.com/>

Methylation Biomarker of Aging Assessment as a Service to the Public

<https://www.fightaging.org/archives/2017/01/an-interview-with-neil-cope-at-osiris-green-offering-dna-methylation-biomarker-of-aging-assessment-as-a-service-to-the-public/>

**Zymo Research**  
SEE ABOVE

1/7/16 spoke w/epigenetic specialist Chris x259.

DIY -- Bisulfite Conversion kits

Horvath probably using kits like theirs, and next gen sequencing to look at

They have service to do that.

Email [services@zymoresearch.com](mailto:services@zymoresearch.com)

phone 949-679-1190.

<http://www.zymoresearch.com/services/dna-methylation-analysis>

See Sample Data tab

Says "Services are customizable and can be combined to suit your needs!"

Maxi-Seq <http://www.zymoresearch.com/services/inquiry>

Keith Booher [kbooher@zymoresearch.com](mailto:kbooher@zymoresearch.com)

--

DNA methylation per Steve Horvath -- This has been questioned by one or two experts I have spoken with.

on science exchange

<https://www.scienceexchange.com/search/?query=DNA%20methylation>

Need age standardization, not just raw data. They should be aware of the Horvath age index correlated with chronological age.

came up from google search "steve horvath methylation testing"

<https://www.scienceexchange.com/services/methylation-analysis>

<http://www.epigentek.com/services/dna-methylation-analysis/bisulfite-sequencing/?gclid=CNWk38vsk8oCFZFfgodybALFw>

-----

Horvath methylation age

<http://www.genomebiology.com/2013/14/10/R115>

<https://labs.genetics.ucla.edu/horvath/htdocs/dnamage/>

----

@Steve Horvath

<http://www.pnas.org/content/early/2014/10/10/1412759111>

Obesity accelerates epigenetic aging of human liver

Abstract

Because of the dearth of biomarkers of aging, it has been difficult to test the hypothesis that obesity increases tissue age. Here we use a novel epigenetic biomarker of aging (referred to as an

“epigenetic clock”) to study the relationship between high body mass index (BMI) and the DNA methylation ages of human blood, liver, muscle, and adipose tissue. A significant correlation between BMI and epigenetic age acceleration could only be observed for liver ( $r = 0.42$ ,  $P = 6.8 \times 10^{-4}$  in dataset 1 and  $r = 0.42$ ,  $P = 1.2 \times 10^{-4}$  in dataset 2). On average, epigenetic age increased by 3.3 y for each 10 BMI units. The detected age acceleration in liver is not associated with the Nonalcoholic Fatty Liver Disease Activity Score or any of its component traits after adjustment for BMI. The 279 genes that are underexpressed in older liver samples are highly enriched ( $1.2 \times 10^{-9}$ ) with nuclear mitochondrial genes that play a role in oxidative phosphorylation and electron transport. The epigenetic age acceleration, which is not reversible in the short term after rapid weight loss induced by bariatric surgery, may play a role in liver-related comorbidities of obesity, such as insulin resistance and liver cancer.

Citation.

Steve Horvath, Wiebke Erhart, Mario Brosch, Ole Ammerpohl, Witigo von Schönfels, Markus Ahrens, Nils Heits, Jordana T. Bell, Pei-Chien Tsai, Tim D. Spector, Panos Deloukas, Reiner Siebert, Bence Sipos, Thomas Becker, Christoph Röcken, Clemens Schafmayer, and Jochen Hampe

**Obesity accelerates epigenetic aging of human liver**

PNAS 2014 : 1412759111v1-201412759.

DNA methylation age is associated with mortality in a longitudinal Danish twin study

<http://onlinelibrary.wiley.com/enhanced/doi/10.1111/ace.12421/>

-----  
H-SCAN

1. Auditory reaction time
2. Highest audible pitch
3. Vibrotactile sensitivity
4. Visual reaction time
5. Muscle movement speed
6. Lung: forced vital capacity
7. Lung: forced expiratory volume, 1 sec
8. Decision reaction time
9. Decision movement speed
10. Short Term Memory
11. Alternate button tapping
12. Visual accommodation

<http://ultimatecare.com/testhscan.htm>

<http://archive.agedmed.org/default.asp?page=SmallMeasuringAgeIssue9>

Elliott Small, GRG member is distributor and working on the next generation.

-----  
Implanted chip communicates with mobile phone for precise, real-time medical measurements – and measuring the effects of drugs and aging interventions.

A chip implanted under the skin allows for precise, real-time medical monitoring  
<http://www.kurzweilai.net/a-chip-implanted-under-the-skin-allows-for-precise-real-time-medical-monitoring>

A chip placed under the skin for more precise medicine  
<http://actu.epfl.ch/news/a-chip-placed-under-the-skin-for-more-precise-medi/>

-----  
Software Turns Smartphones into Tools for Medical Research  
[http://www.biosciencetechnology.com/news/2015/07/software-turns-smartphones-tools-medical-research-0?et\\_cid=4698151&et\\_rid=608568146&location=top](http://www.biosciencetechnology.com/news/2015/07/software-turns-smartphones-tools-medical-research-0?et_cid=4698151&et_rid=608568146&location=top)  
Saved to this folder: Software Turns Smartphones into Tools for Medical Research.html

Over the counter urine, saliva tests at drug stores, internet

glucose  
keytone

others only available w/physician prescription

Labs don't want to be liable for self diagnosis -- could sue them.

-----  
Be aware of consequences of self-diagnosis and independent action  
-----

Responses to request for aging biomarkers and health measures sent to the GRG email discussion forum and a few others collected:

We want parameters that don't have daily/weekly/monthly/yearly fluctuation

-----  
Theranos labs  
<https://www.theranos.com/test-menu>

Recent controversy  
<http://fortune.com/2015/10/31/theranos-timeline/>  
They updated their web page  
<https://www.theranos.com/>

<http://labtestsonline.org/>  
LabCorp and Quest

#####

From notes

Wagers used SomaLogic ....they have 1126 protein biomarkers. ....but you need to fill their array.....minimum cost is \$32,000 per run of 32 test samples.

Again lots of interleukines. They claim to have 70 biomarkers of ageing but when I quizzed on whether they determined this with people of widely separate ages.....they had not

#####

SomaLogic.com

<http://www.somallogic.com/somallogic/media/Assets/PDFs/SSM-002-Rev-2-SOMAscan-Technical-White-Paper-3-7-15.pdf>

See SSM-002-Rev-2-SOMAscan-Technical-White-Paper-3-7-15.pdf

Renamed in this folder

2014SomaScanWhitePaper\_SSM-002-Rev-2-SOMAscan-Technical-White-Paper-3-7-15.pdf

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0026332>

<http://meridianvalleylab.com/>

Hormones dropdown: <http://meridianvalleylab.com/about-hormone-testing#>

HealthTell

New company HealthTell has Immunosignature™ Technology

High-density Peptide Array Platform

<http://www.healthtell.com/science/>

<http://www.healthtell.com/product-platform/>

<http://www.healthtell.com/>

-----

@James P. Watson MD and Vinci Giuliano

HRV

-----

@Florence Comite MD

HbA1C, if 5 or less correlates with longevity.

And HDL, an older biomarker, if at the higher end of range, also correlates with longevity.

There are others however most are variable and should be judged in the context of many other factors, family history, genomics, sleep, nutrition, exercise, other metabolomics.

-----

Per neuro-endocrinologist with patient experience and high credentials

Q: Usually what hormone assays?

Which lab test company do you use for hormone assays?

A: Labcorp or Quest



Are there hormone assay panels you would suggest?

Assay all pituitary hormones

don't usually anterior oxy and vasopresin

prolactin

leutinizing hormone

FSH

growth hormone

IGF-1

thyroid stim hormone

ACTH (adrenocorticotropic hormone)

-----

@Thomas Coote

GRG Member

PHYSICAL: 1) Muscle strength 2) Short Physical Performance Battery

CHEMICAL: 1) Serum albumin 2) IL-6 3) Urea 4) Eotaxin (my idea)

MENTAL/COGNITIVE: 1) MMSE

PROTEOMIC: 1) Plasma transferrin

GENETIC: 1) miRNA expression by QrPCR (several candidates).

. . . obviously ease of analysis and cost of analysis would have to be considered.

A couple I have rejected are Systolic BP and CRP as they are quite variable and may change due to non-age related circumstances.

-----

@Bill

GRG Member

Theranos panel

[https://www.theranos.com/test-menu?ref=for\\_providers](https://www.theranos.com/test-menu?ref=for_providers)

grip strength

Inflammation markers

IL-6, IL-10, IL-17, TNF tumor necrosis factor

Glucose tolerance?

IGF11

-----

@John

GRG Member

Lipofuscin accumulation (can this be tested?)

in neurons

- Weight

- Resting blood pressure

- FEV1

- max grip strength each hand

- number of push ups in 60 seconds

- number of chin ups in 60 seconds

-----  
@Sven Bulterijs – HAS

GRG Member -- HAS

Hallmarks of Aging Score

<https://www.youtube.com/watch?v=nn41Kpa2iXk&noredirect=1>

-----  
@David Cross

GRG Member

Additional Biomarkers of Aging for consideration:

--Pulmonary function ('Pulmonary Age')--via Spirometry

--Arterial Stiffness--via Sphygmocor

--Measure of cognitive function--'CNS Vital Signs' is one option

--Are there measures of Stem Cell health & functionality (e.g., total #s, regenerative capacity, mobilization, etc.) that can be used as a tangible Biomarker of Aging?

--Telomere Length: Maria Blasco's Life Length lab measures (in PBMCs) not only median telomere length but also the % of 'critically-short' telomeres, which is actually the more important measure, as per Harley, Greider, et.al., it takes only one critically-short telomere to throw a cell into senescence.

--Immune measure: The UCLA Clinical Immunology Laboratory at the Geffen School of Medicine (Tony Butch/Najib Aziz) performs a "Flow T-cell subset Analysis" which measures the % of senescent CD8+/CD28- T-cells, which per Harley/Andrews/Blasco is considered a very important "biomarker of immune aging."

The research of Rita B. Effros (UCLA) over many years demonstrates that CD28 T-cell senescence is a major factor in immunosenescence, which is of course critical to aging, and "inflammaging," including the finding that senescent CD28- T-cells secrete and increase the circulation of the pro-inflammatory cytokine TNF-alpha (Effros 2011, 2013). Her research plus that of several others demonstrates that the % of CD28- T-cells contributes to a number of age-related degenerative diseases, including rheumatoid arthritis

(Weyand & Gorozny 2014), "early atherosclerotic damage in rheumatoid arthritis patients" (Gerli, et.al. 2004), and "increased cardiovascular risk in diabetes mellitus" (Giubilato, et.al. 2011), among others.

-----  
Josh Mittleldorf blog:

Luigi Fontana has experience in biomarkers

I suggest you contact Luigi Fontana at Wash U in St Louis for this. He has lots of experience with age markers in humans.

lfontana@dom.wustl.edu

-----  
Vince Giuliano

Resting heart rate

avg one hour before going to sleep and waking  
smartwatch

<http://www.anti-agingfirewalls.com/2015/01/17/digital-health-health-and-fitness-wearables-part-2-looking-for-practical-stress-biomarkers/>

@Vince

[www.Mybasis.com](http://www.Mybasis.com)

transfer data to smartphone

go another step

-----  
@Jim Watson said this re Quercetin and Dasatinib. Otherwise applies?

Before everyone goes out and buys Quercetin and Dasatinib, it would be wise to conduct an IRB-approved trial for these two agents with specific age-related phenotypes as primary endpoints.

This could include one or more of the following conditions:

1. Presbyopia (pesbyopia?)- This could easily be measured with eye exams by a "blinded examiner" (no pun intended) - age-related visual changes can be measured by diopter changes
2. Prebycusis - This could also be easily measured with hearing tests. Age-related hearing loss is manifested by a characteristic high frequency conduction hearing loss
3. Decline in LVEF - This could easily be measured with echocardiography
4. Vascular reactivity - This could easily be measured with nitroprusside-induced changes in BP and arterial waveforms on A-line

This could also be done with flow-mediated dilation (FMD)

5. Skin aging - this could easily be measured with a skin biopsy - this could be done with beta-galactosidase staining and p16 staining

6. Muscle aging - this could easily be measured with a muscle biopsy - this could be done with beta-galactosidase staining and p16 staining

7. Liver aging - this could easily be measured with a liver biopsy with beta-galactosidase staining and p16 staining

I think it is time to do this under an IRB.

-----  
@Paul Wakfer

GRG Member

. . . the lab animal to human conversion factor relative to metabolic rate differences. For mice this computes to about 7.3, so the human equivalent dose would only be  $3500/7.3 = 480$  mg for a 70 kg human. This is an easily available dose and about what I and Kitty have been getting proportionate to our weights (62 and 50 kg respectively) for well over a decade now.

-----  
@J Pedro Magalhaes  
GRG Member

developed the Digital Ageing Atlas, a new portal of age-related changes at different biological levels that might be useful for your purposes:

<http://ageing-map.org/>

For gene expression biomarkers please see:

<http://www.ncbi.nlm.nih.gov/pubmed/19189975?dopt=Abstract>

-----  
Another member or resource (I don't recall)

Problems if can't stand on one leg > 20 sec.

Is how long can a person can stand on one leg an indicator?

-----  
Wound healing. How to test in humans?

-----  
MRI

view/measure brain calcification and other

-----  
Evaluate with an electron microscope?

-----  
The study, which has been published in Nature Communications, used certain types of blood cells and brain tissue to examine the age-associated changes in gene expression.

<http://sage.buckinstitute.org/age-its-all-in-your-blood/>

-----  
Experimental Gerontology 41 (2006) 1243–1246

Mini Review

Recent results: Biomarkers of aging

Tom Johnson

@See TomJohnsonPaperExcellent.pdf in this folder

////////////////////////////////////  
////////////////////////////////////  
////////////////////////////////////

Old:

Responders to the thread

Greg Tranah <http://www.cpmc.org/professionals/research/programs/science/tranah.html>

Steve Horvath <http://www.biostat.ucla.edu/Directory/Shorvath>

Thomas Coote

J Pedro Magalhaes <http://www.liv.ac.uk/integrative-biology/staff/joao-de-magalhaes/>  
Daniel Wuttke <https://www.linkedin.com/pub/daniel-wuttke/28/531/3a9>  
Florence Comite <http://www.comitemd.com/meet-our-team/dr-florence-comite/>

-----  
**J Pedro Magalhaes**

**Sent:** Saturday, October 11, 2014 6:01 AM

**To:** Gerontology Research Group

**Subject:** Re: [GRG] Biomarkers of aging....suggestions?

we have recently developed the Digital Ageing Atlas, a new portal of age-related changes at different biological levels that might be useful for your purposes:

<http://ageing-map.org/>

<http://www.ncbi.nlm.nih.gov/pubmed/25232097?dopt=Abstract>

Obviously not all aging related changes would be suitable biomarkers, but this should give you some ideas.

For gene expression biomarkers please see:

<http://www.ncbi.nlm.nih.gov/pubmed/19189975?dopt=Abstract>

as mentioned in the GRG list, there's also a number of epigenetic markers (by Steve Horvath, etc.)

**Florence Comite**

**Sent:** Saturday, October 11, 2014 7:34 AM

**To:** Gerontology Research Group

**Subject:** Re: [GRG] Biomarkers of aging....suggestions?

Hi,

I would suggest HbA1C, if 5 or less correlates with longevity.

And HDL, an older biomarker, if at the higher end of range, also correlates with longevity.

There are others however most are variable and should be judged in the context of many other factors, family history, genomics, sleep, nutrition, exercise, other metabolomics.

Best,

Florence

Gavrilov and Gavrilova

**Predictors of Exceptional Longevity: Effects of Early-Life Childhood Conditions, Midlife Environment and Parental Characteristics**

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4318523/>

////////////////////////////////////

ORIG WORD DOC

\*\*\* See James P Watson's \*\*\*

HRV

1 of 3

To those below, from Johnny Adams

Everyone on this email has expertise in aging biomarkers.

Maybe you can exchange info.

Forwarded below is an email I thought might interest Greg and Steve. It's a post from the Gerontology Research Group discussion list. I'm co-admin. Let me know if you would like me to sign you up. If you decide it's not for you, you can be removed at any time.

Steve Horvath has been pioneering the use of DNA methylation as a biomarker of aging. (My description surely is inadequate and he can provide a web reference and/or better explain)

Recently Greg gave an excellent presentation, much of which was on aging biomarkers.

Greg Tranah <http://www.cpmc.org/professionals/research/programs/science/tranah.html>

Steve Horvath <http://www.biostat.ucla.edu/Directory/Shorvath>

Thomas Coote

J Pedro Magalhaes <http://www.liv.ac.uk/integrative-biology/staff/joao-de-magalhaes/>

Daniel Wuttke <https://www.linkedin.com/pub/daniel-wuttke/28/531/3a9>

Florence Comite <http://www.comitemd.com/meet-our-team/dr-florence-comite/>