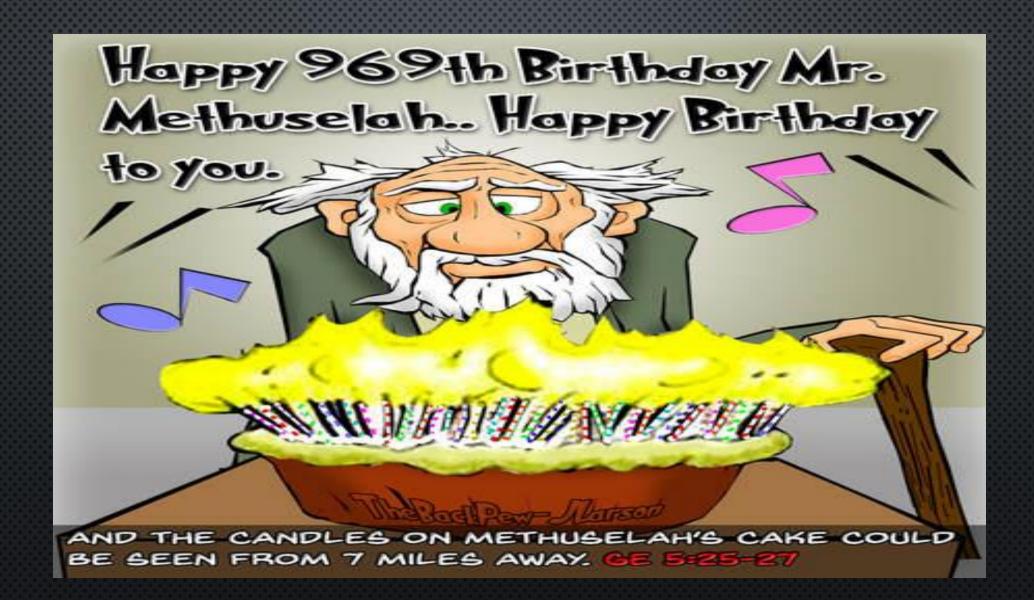
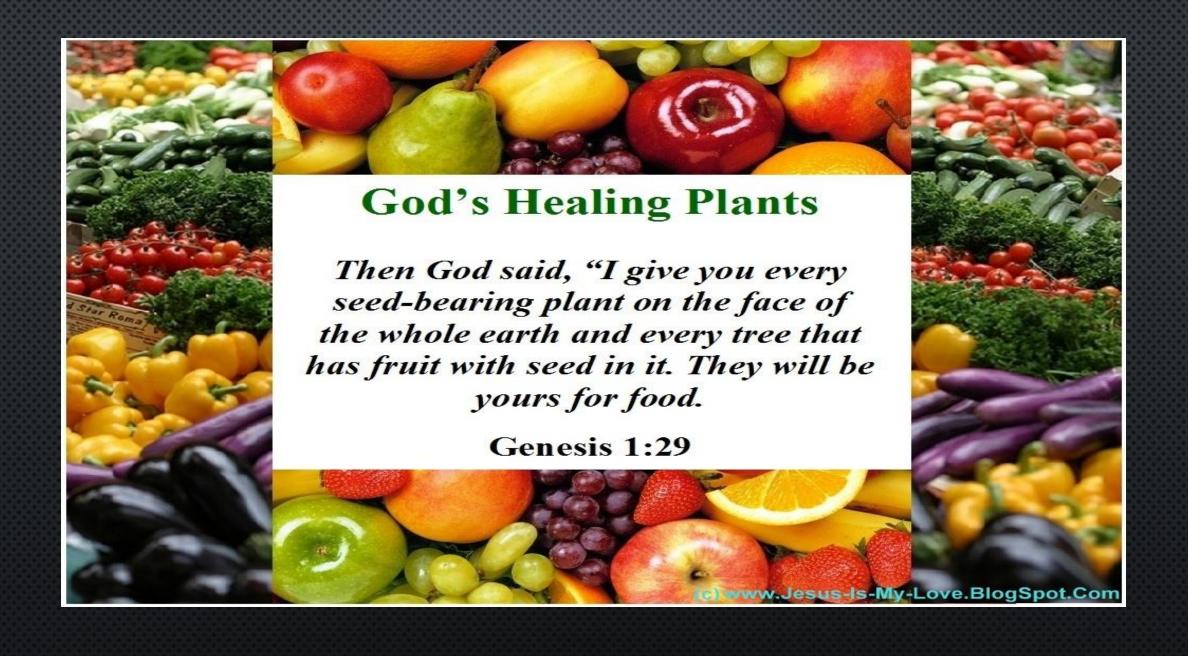
CARDIAC LONGEVITY: PLANNING FOR 100 YEARS

JOEL KAHN, MD, FACC
KAHN CENTER FOR CARDIAC LONGEVITY
BINGHAM FARMS, MI
CLINICAL PROFESSOR, WAYNE STATE UNIVERSETY



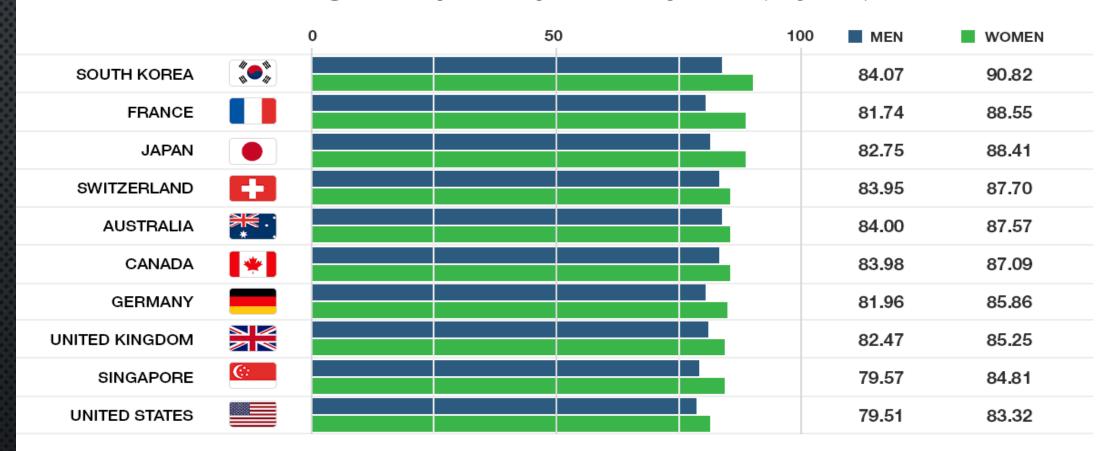
The Long Lives of Antediluvians

	Age	Birth	Death
>Adam \	930	0	930 AC*
- Seth	912	130 AC	1042 AC
-> Enos	905	235 AC	1140 AC
Cainan	910	325 AC	1235 AC
Mahalaleel	895	395 AC	1290 AC
> Jared	962	460 AC	1422 AC
> Enoch	365	622 AC	Missing
- Methuselah	969	687 AC	1656 AC
> Lamech	777	874 AC	1651 AC
Noah	950	1056 AC	2006 AC ter Creation



Projected US Life Expectancy Compared With Other Rich Nations

Average life expectancy at birth by 2030 (in years)



Source: Statista chart: 8286

JEANNE CALMENT 122 YEARS OLD



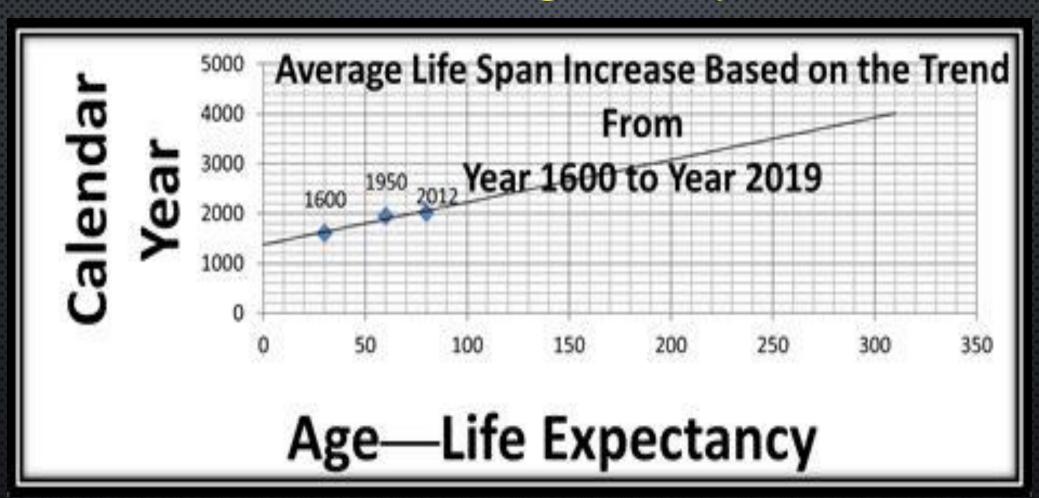


I only have one wrinkle and I'm sitting on it.

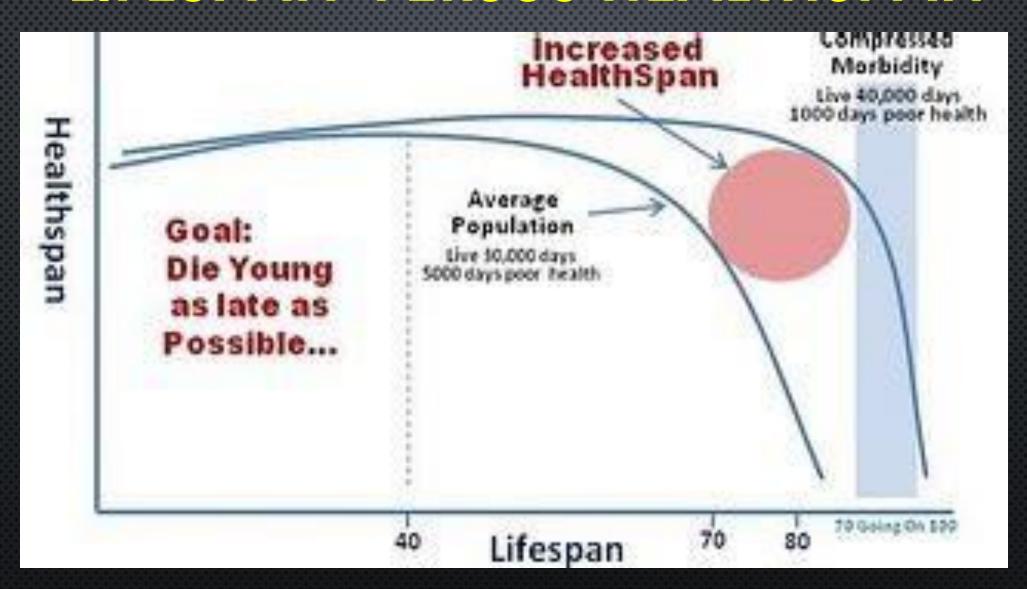
— Jeanne Calment —

AZ QUOTES

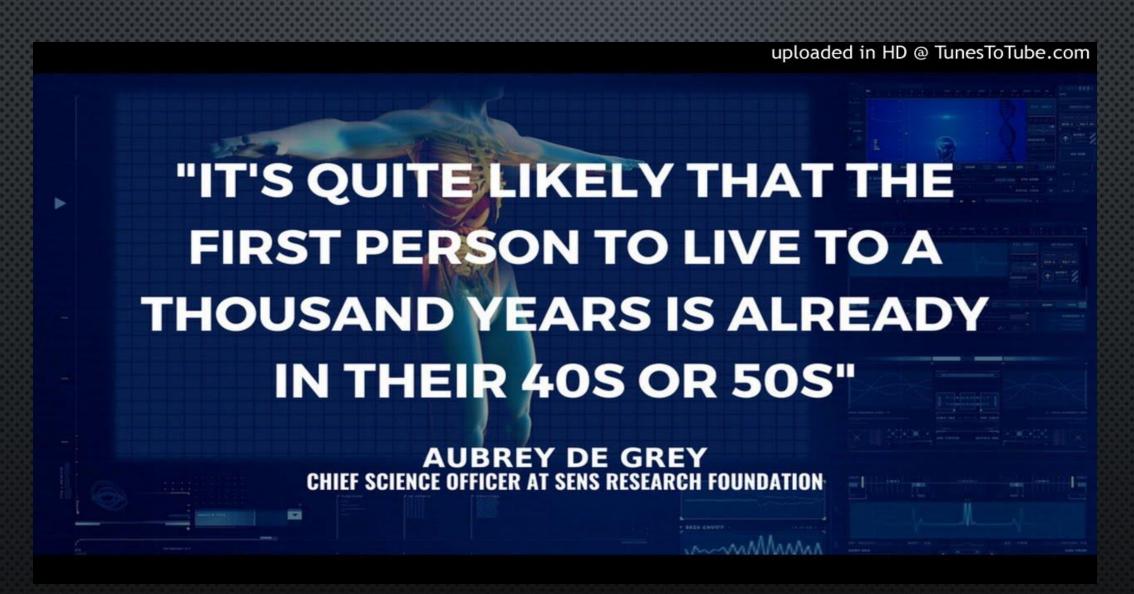
HOW LONG CAN WE LIVE? WANT TO LIVE?



LIFESPAN VERSUS HEALTHSPAN

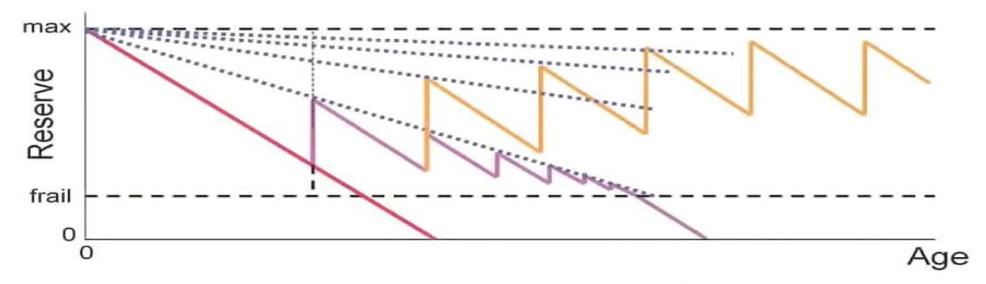


LIVE 10 MORE HEALTHY YEARS....



LONGEVITY ESCAPE VELOCITY



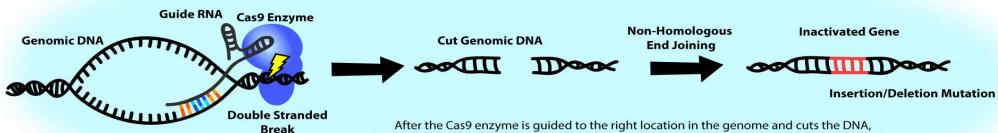


Fixing half the damage, then 3/4, then 7/8, ...

- (a) outpaces the so-far-unfixable damage, and
- (b) maintains healthspan indefinitely.

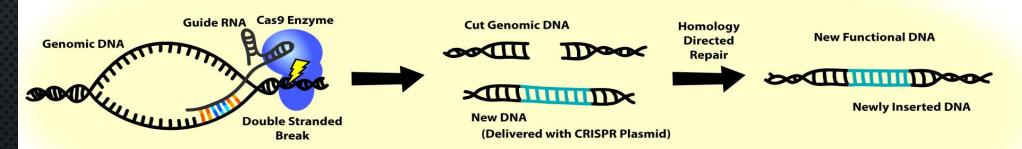
THE FUTURE IS NEAR AND BRIGHT

Gene Silencing with CRISPR



the cell's natural repair mechanisms take over. The cut is fixed by non-homologous end joining. This process is error-prone and does not perfectly replace the cut DNA, often resulting in an insertion or deletion mutation which silences the gene.

Gene Insertion with CRISPR



To insert a gene, the new gene is added into the original CRISPR plasmid. It is designed to line up perfectly with the cut DNA strands, so the cell uses a different technique, homology directed repair, to incorporate a new stretch of DNA into the genome.

By 2030, CRISPR has the potential to cure these 13 diseases.





https://www.synthego.com/blog/crispr-cure-diseases?utm_campaign=Blog&utm_medium=email&_hsenc=p2ANqtz-9TY2

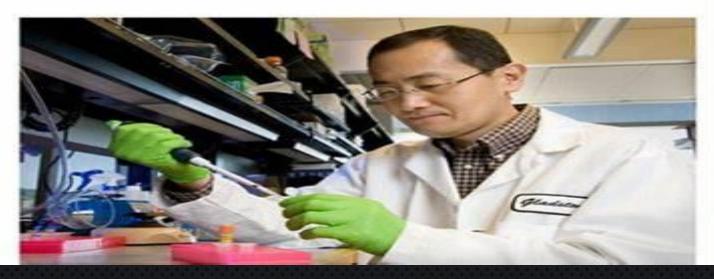
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DUCHENNE MUSCULAR DYSTROPHY SICKLE CELL DISEASE **BETA THALASSEMIA HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION ALZHEIMER'S DISEASE HUNTINGTON'S DISEASE AUTISM SPECTRUM DISORDER RETINITIS PIGMENTOSA** SPECIFIC (BIALLELIC RPE65 MUTATION-ASSOCIATED) RETINAL **DYSTROPHY** LEBER CONGENITAL AMAUROSIS LUNG AND ESOPHAGEAL CANCERS **B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA CERVICAL CANCER**

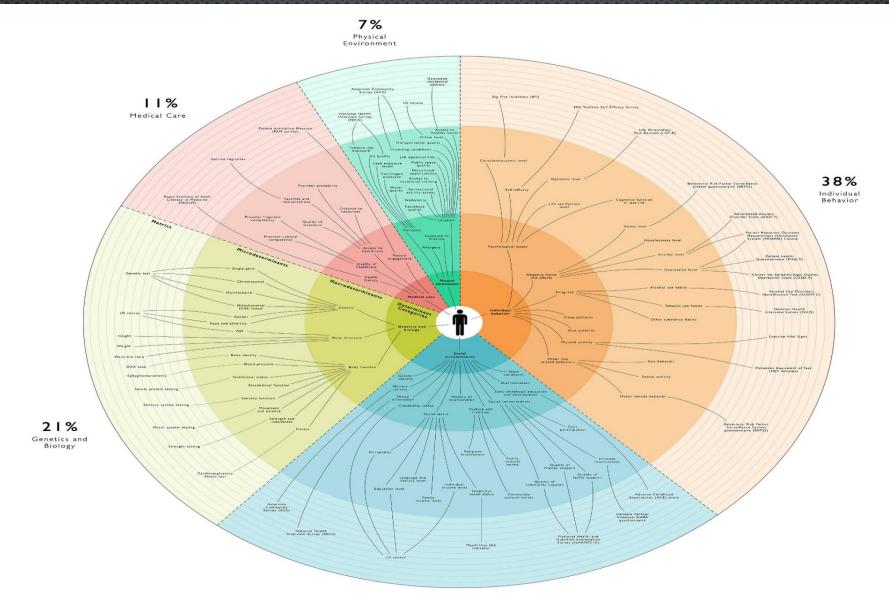
YAMANAKA FACTORS

Shinya Yamanaka Wins 2012 Nobel Prize in Medicine

Gladstone and UCSF Scientist Recognized for Stem Cell Discovery

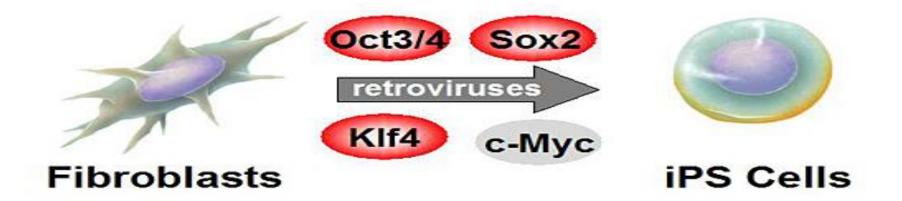


DETERMINANTS OF HEALTH: GENETIC 21%





Induced Pluripotent Stem (iPS) Cells



Mouse iPS cells reported in 2006 Human iPS cells reported in 2007

GENES AND LONGEVITY OF LIFESPAN

- AGING IS A COMPLEX PROCESS INDICATED BY LOW ENERGY LEVELS, DECLINED PHYSIOLOGICAL ACTIVITY, STRESS INDUCED LOSS OF HOMEOSTASIS LEADING TO THE RISK OF DISEASES AND MORTALITY. SEVERAL ENVIRONMENTAL AND PHYSIOLOGICAL FACTORS CONTRIBUTE TO THE AGING PROCESS. HOWEVER, ABOUT 40% HUMAN LIFE EXPECTANCY IS INHERITED AMONG GENERATIONS, MANY LIFESPAN ASSOCIATED GENES, GENETIC MECHANISMS AND PATHWAYS HAVE BEEN DEMONSTRATED DURING LAST DECADES.
- INT J MOL SCI. 2022 FEB; 23(3): 1499.

BE THE CEO OF YOUR OWN HEALTH

"You Are The CEO
Of Your Own
LIFE
start making executive
decisions Today!"

Stephen Luke

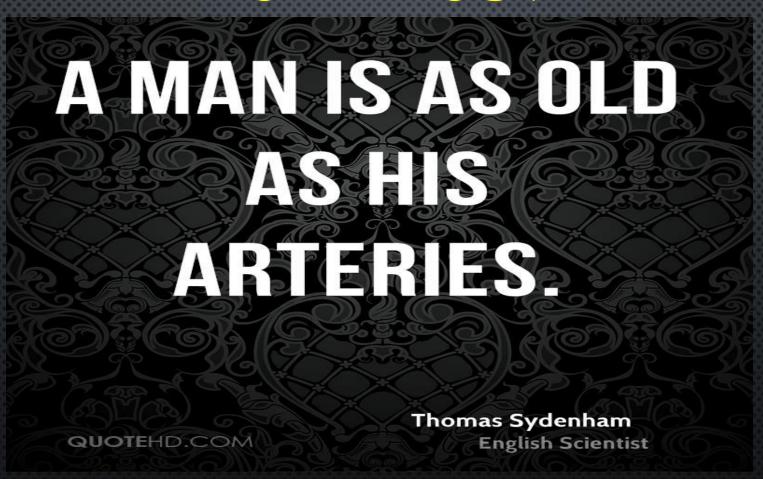
DON'T DIET OF HEART DISEASE: KNOW YOUR ARTERIAL AGE



EVERY 40 SECONDS

someone in the US has a heart attack.

THOMAS SYDENHAM, MD 1624-1689



CAROTID INTIMAL MEDIAL THICKNESS ULTRASOUND: CIMT

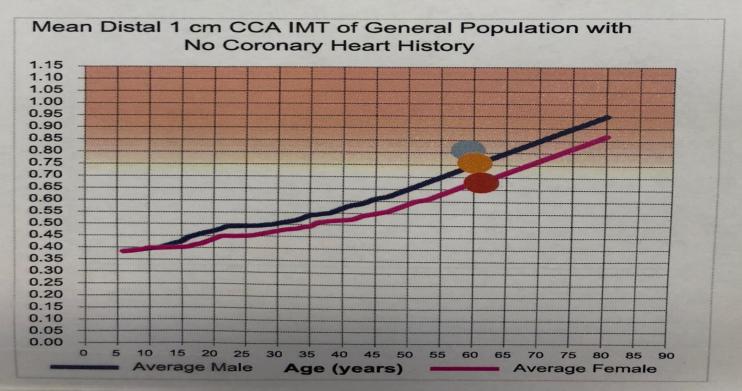
Carotid Intima Media Thickness (CIMT)

- Direct in vivo measurement of thickness of carotid artery wall by B-mode ultrasound
- Vessel wall thickness correlates with status of atherosclerosis and CV events
- Atherosclerosis is a systemic disorder
 - Atherosclerosis in the carotid artery is predictive of disease in other vascular beds



CIMT ARTERIAL AGE

	Current and Previous CIMT Measurements					
	Date	Age	Arterial Age	CIMT	Percentile	
	Aug 2018	61	52	0.677	35th	
0	Aug 2017	60	60	0.756	52nd	
0	Dec 2016	59	65	0.806	67th	



CORONARY ARTERY CALCIUM SCORE: CT

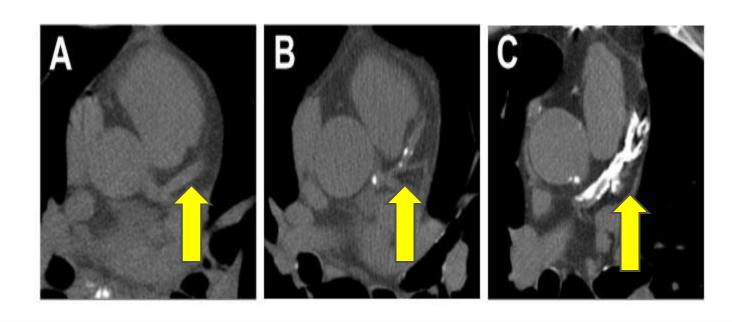
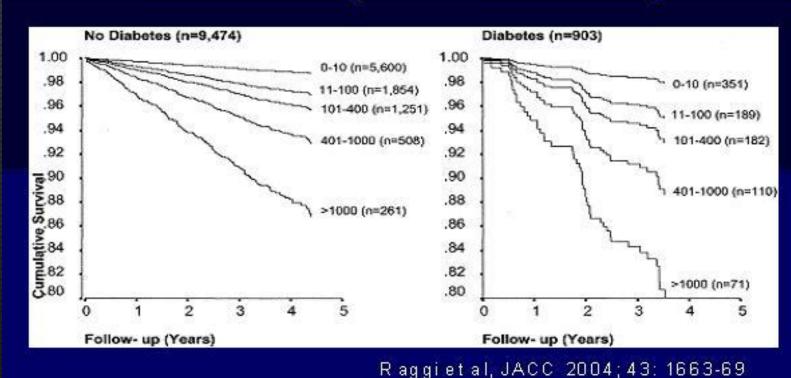


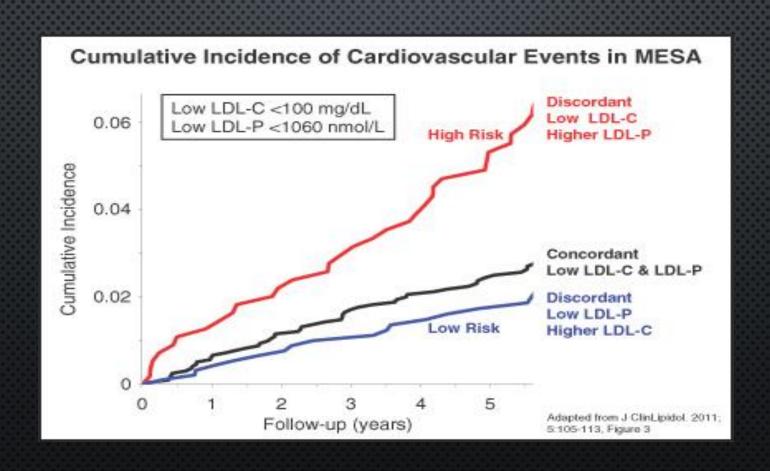
Figure 1 - Images illustrating the coronary artery calcium score of three patients with increasing calcification grades in the territory of the anterior descending artery: A. no calcification; B. mild calcification; C. severe calcification.

CACS MATTERS

Coronary Artery Calcium Imaging predicts All Cause Mortality: Observational study



ADVANCED LABS: LDL-PARTICLE NUMBER



ADVANCED LABS: LIPOPROTEIN(A)

- ↑ Macrophage IL-8 expression
- ↑ Monocyte cytokine release
 - **★** EC binding
 - ↑ Upregulation of adhesion molecules
 - ↑ SMC proliferation
 - ↑ Proteoglycan matrix binding
 - ↑ Foam/cell formation
 - ↑ Necrotic core formatiom
 - ↑ Lesion calcification

Pro-inflammatory

↑ Oxidized Phosopholipids

OxPL

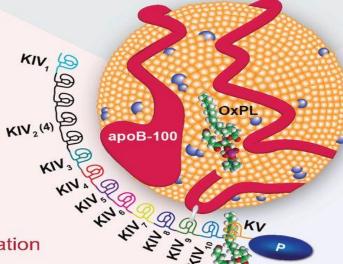
- ↑ Monocyte chemotaxis/transmigration
 - Carries MCP-1

- **↑** EC PAI-1 expression

Prothrombotic

- ↑ TFPI activity
- ↑ Platelet responsiveness

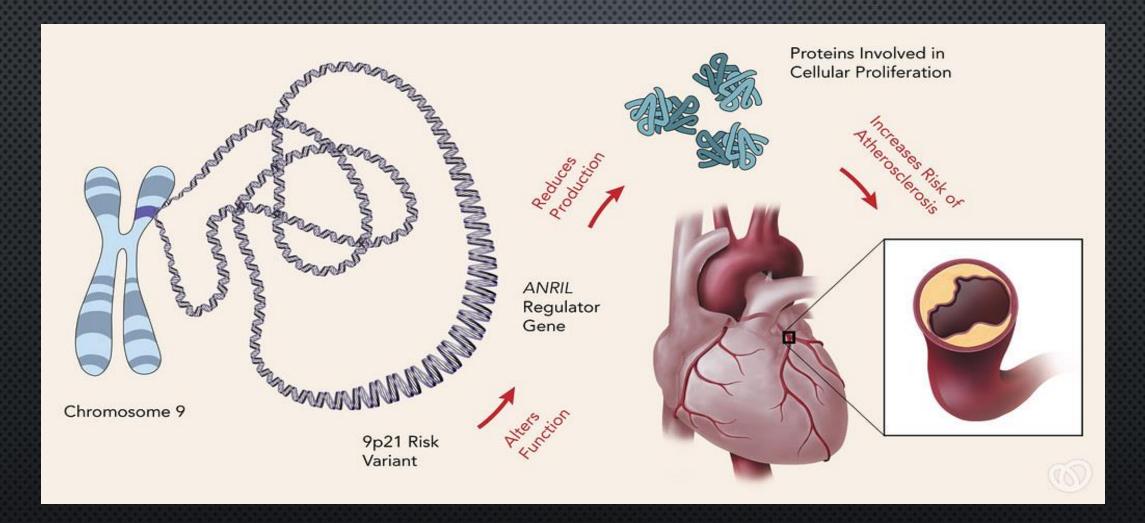
Proatherogenic

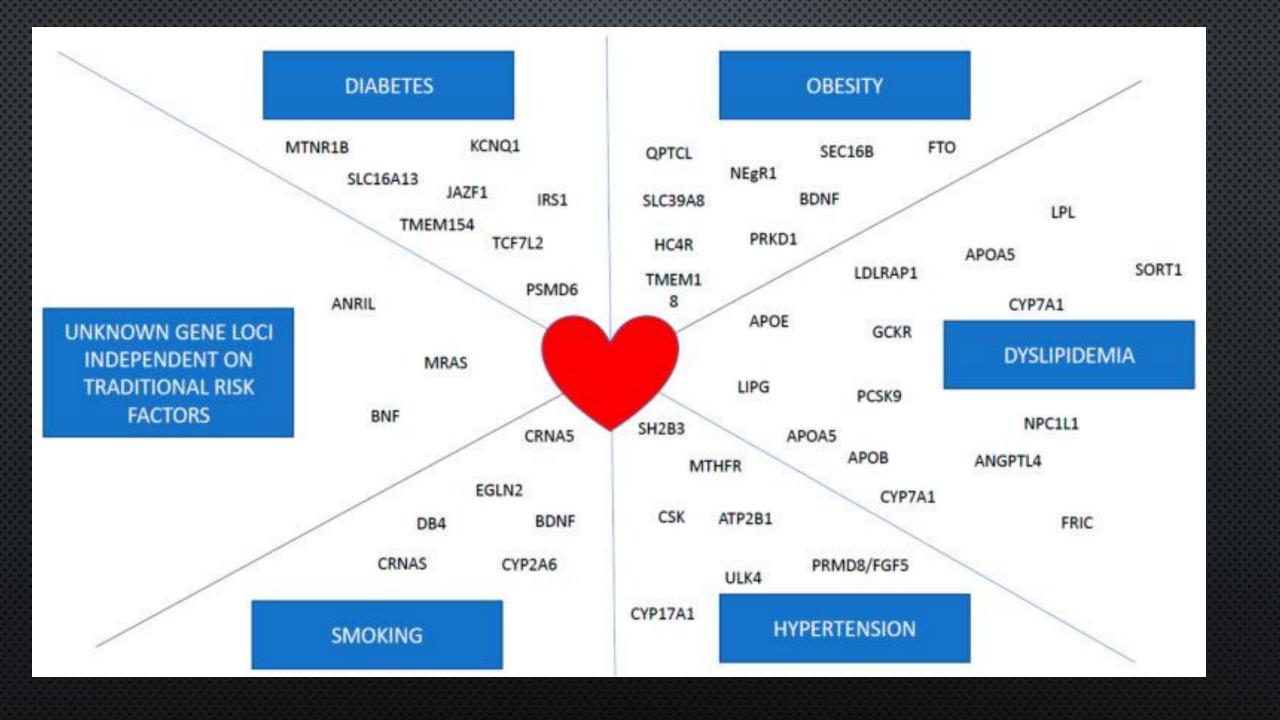


INTEGRATIVE PRIORITIZATION OF CAUSAL GENES FOR CORONARY ARTERY DISEASE

- WE IDENTIFIED 162 UNIQUE CANDIDATE CAUSAL CAD GENES
- WHEN THEIR CAUSAL EFFECT WAS RANKED, THE TOP CANDIDATE CAUSAL CAD GENES WERE CDKN2B (ASSOCIATED WITH THE 9P21.3 RISK LOCUS) AND PHACTR1; BOTH EXERTING THEIR CAUSAL EFFECT IN THE ARTERIAL WALL.
- CIRCULATIONGENOMIC AND PRECISION MEDICINE VOLUME 15, ISSUE 1, FEBRUARY 2022; PAGE E003365

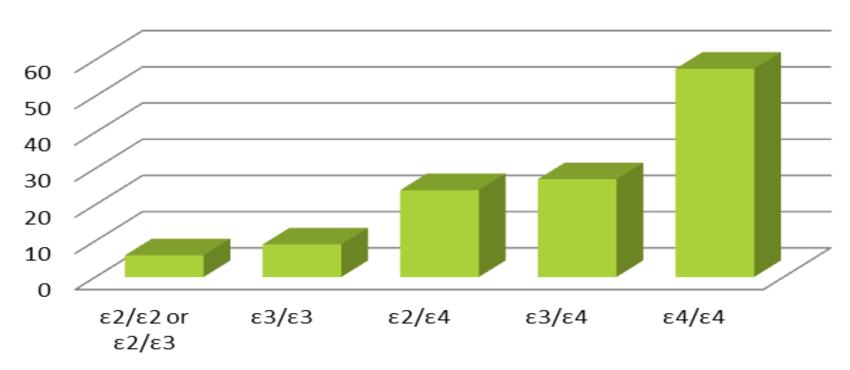
LABS: 9P21 GENE





LABS: APOE4

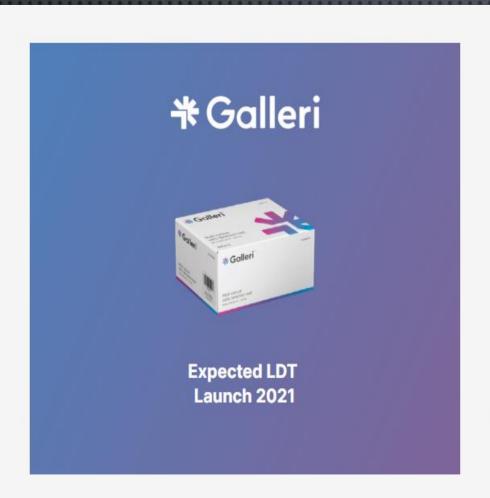




HEAVY METALS BLOOD DRAW

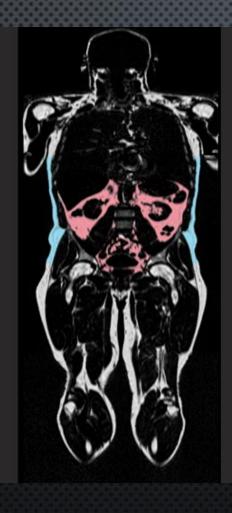


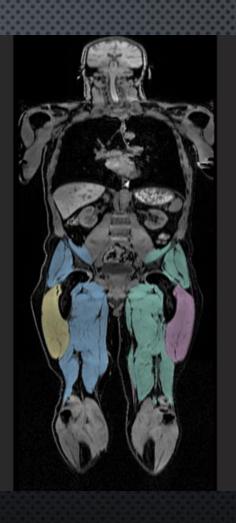
NEW CANCER SCREENING BLOOD PANEL: GALLERI



1	Required Blood Draws
43%	Positive Predictive Value (modeled)
44%	Sensitivity for All Cancers (Stages 1-3)
50 +	Cancers Detected
93%	Tissue of Origin Accuracy
>99%	Specificity

TOTAL BODY MRI NON-CONTRAST





BRAIN VOLUME QUANTIFICATION



HOME SLEEP STUDIES FOR APNEA



LIFESTYLE AND LONGEVITY

- RESEARCHERS FROM THE HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH CONDUCTED A MASSIVE STUDY OF THE IMPACT OF HEALTH HABITS ON LIFE EXPECTANCY, USING DATA FROM THE WELL-KNOWN NURSES' HEALTH STUDY (NHS) AND THE HEALTH PROFESSIONALS FOLLOW-UP STUDY (HPFS).
- THE NHS INCLUDED OVER 78,000 WOMEN AND FOLLOWED THEM FROM 1980 TO 2014. THE HPFS INCLUDED OVER 40,000 MEN AND FOLLOWED THEM FROM 1986 TO 2014.
- THIS IS OVER 120,000 PARTICIPANTS, 34 YEARS OF DATA FOR WOMEN, AND 28 YEARS OF DATA FOR MEN.
- CIRCULATION VOLUME 138, ISSUE 4, 24 JULY 2018; PAGES 345-355

LIFESTYLE AND LONGEVITY HEALTHY LIFESTYLE AT AGE 50 ADDS 12-14 YRS

- EAT A HEALTHY DIET
- EXERCISE 30 MINUTES OR MORE A DAY
- MAINTAIN A HEALTHY WEIGHT, SPECIFICALLY, A HEALTHY BODY MASS INDEX)
- Don't drink too much alcohol, which means no more than one 5 oz glass of wine a day for women, and two for men
- Never smoke

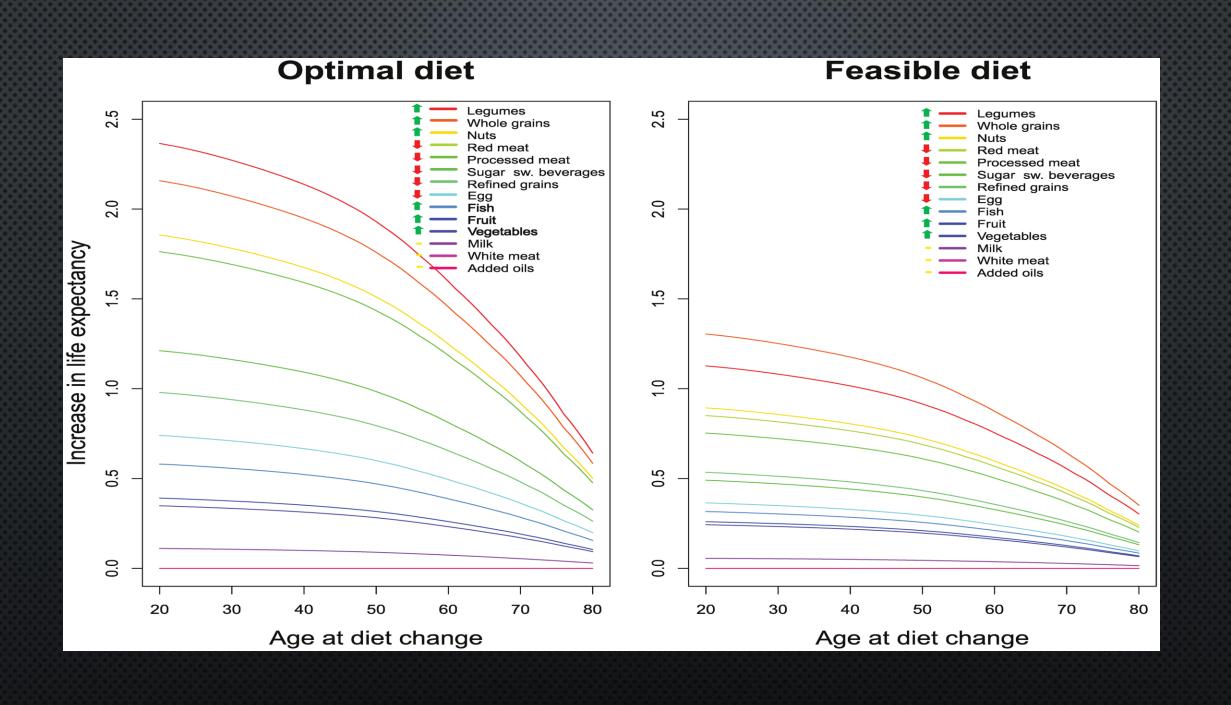
THREE TOP FOODS FOR LIFE EXPECTANCY



CELEBRATING 20 YEARS
OF COLLABORATION AND INNOVATION

ESTIMATING IMPACT OF FOOD CHOICES ON LIFE EXPECTANCY: A MODELING STUDY

- THE LARGEST GAINS WOULD BE MADE BY EATING MORE: LEGUMES (FEMALES: 2.2, MALES: 2.5)
- WHOLE GRAINS (FEMALES: 2.0, MALES: 2.3)
- NUTS (FEMALES: 1.7 MALES: 2.0)
- LESS RED MEAT (FEMALES: 1.6 MALES: 1.9) AND LESS PROCESSED MEAT FEMALES: 1.6 MALES: 1.9



BLUE ZONES



The Blue Zone

Where are people living the longest?

The top 5 countries by average life expectancy



The Blue Zone contains the highest concentrations of people

who are active past the age of 100.





FAMILY FIRST

Invest time with family & add up to 6 years to your life.

WINE @ FIVE

Enjoy a glass of wine with

good friends each day.



80% RULE

Eat mindfully & stop when 80% full.



MOVE NATURALLY

Find ways to move more! You'll burn calories without thinking about it.



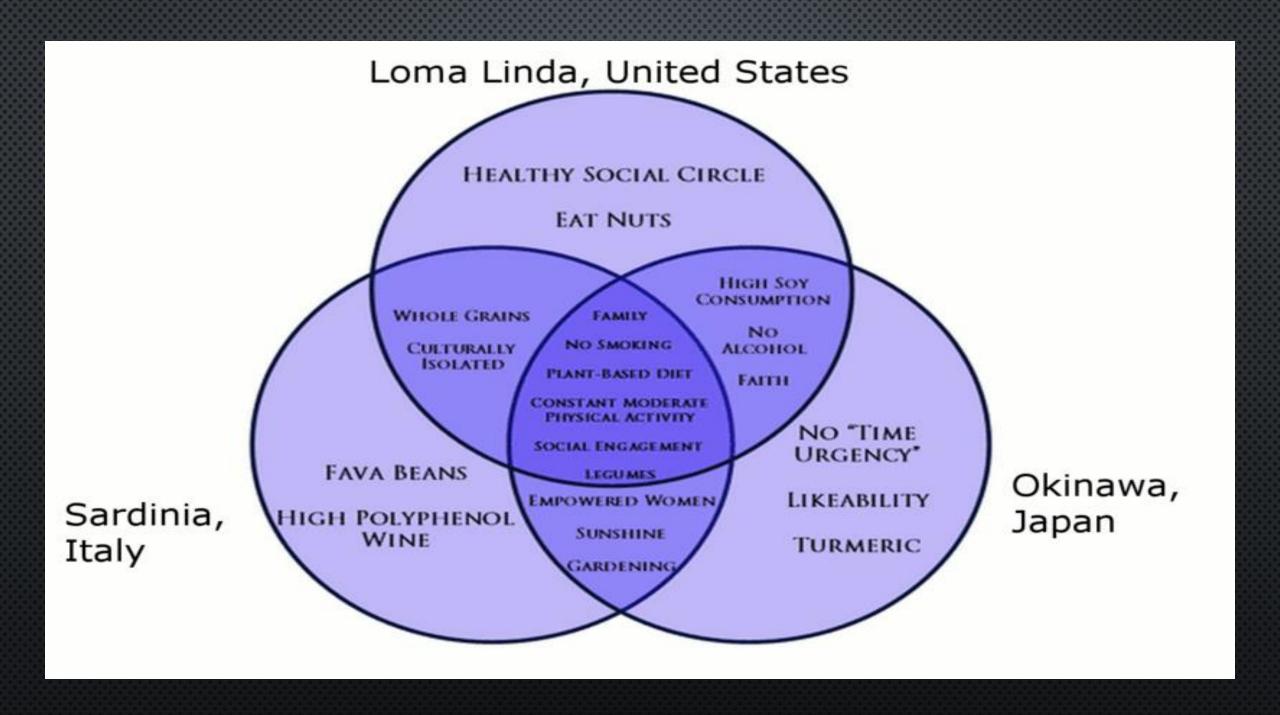
who support positive behaviors.

POWER 9®

Live longer by applying these principles from the people who have lived longest!



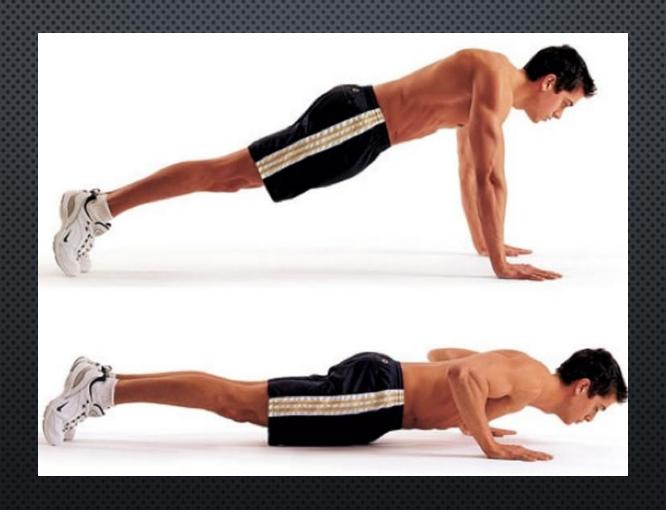
Belong to a faithbased community, & attend services 4 times a month to add 4-14 years to your lifespan.



LEGUMES: THE MOST IMPORTANT DIETARY PREDICTOR OF SURVIVAL IN OLDER PEOPLE OF DIFFERENT ETHNICITIES

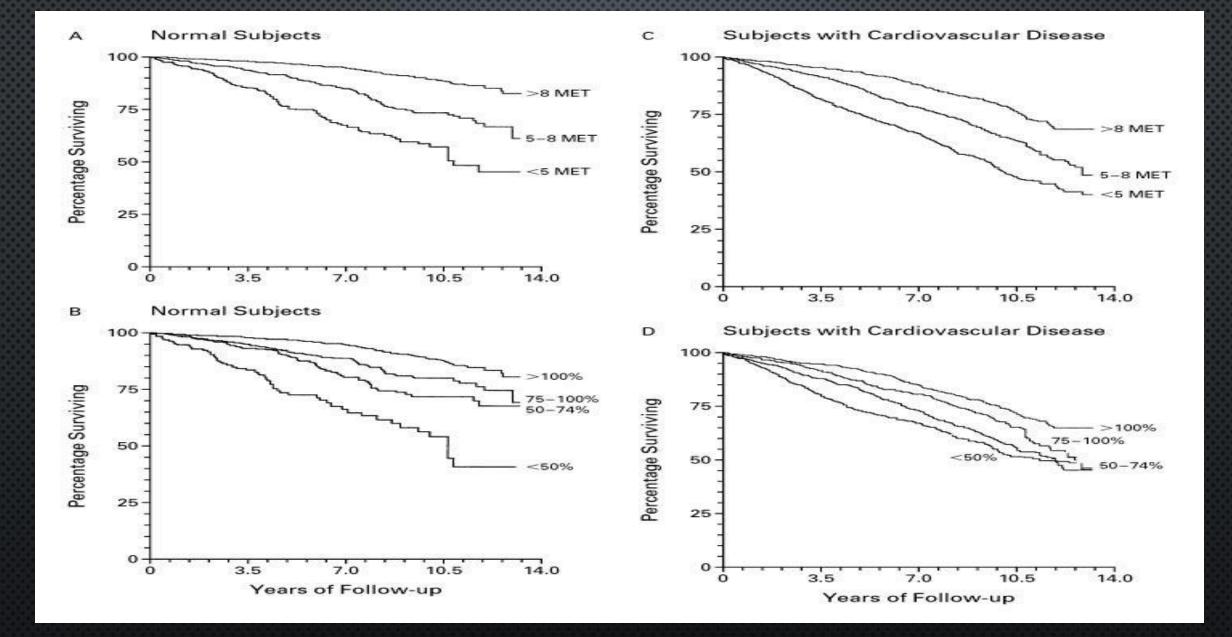
- TO IDENTIFY PROTECTIVE DIETARY PREDICTORS AMONGST LONG-LIVED ELDERLY PEOPLE, THE "FOOD HABITS IN LATER LIFE STUDY WAS UNDERTAKEN AMONG FIVE COHORTS IN JAPAN, SWEDEN, GREECE AND AUSTRALIA.
- THERE WERE 785 PARTICIPANTS AGED 70 AND OVER THAT WERE FOLLOWED UP TO SEVEN YEARS.
- THE LEGUME FOOD GROUP SHOWED 7-8% REDUCTION IN MORTALITY HAZARD RATIO FOR EVERY 20G INCREASE IN DAILY INTAKE WITH OR WITHOUT CONTROLLING FOR ETHNICITY
- ASIA PAC J CLIN NUTR 2004;13(2):217-20.

SIMPLE FITNESS TESTS AND LONGEVITY



EXERCISE CAPACITY AND MORTALITY AMONG MEN REFERRED FOR EXERCISE TESTING (TREADMILL)

- WE STUDIED A TOTAL OF 6213 CONSECUTIVE MEN REFERRED FOR TREADMILL EXERCISE TESTING FOR CLINICAL REASONS DURING A MEAN 6.2 YEARS OF FOLLOW-UP.
- THE PEAK EXERCISE CAPACITY MEASURED IN METABOLIC EQUIVALENTS (MET) WAS THE STRONGEST PREDICTOR OF THE RISK OF DEATH AMONG BOTH NORMAL SUBJECTS AND THOSE WITH CARDIOVASCULAR DISEASE.
- N Engl J Med 2002; 346:793-801



PUSHUP CAPACITY AND HEART EVENTS

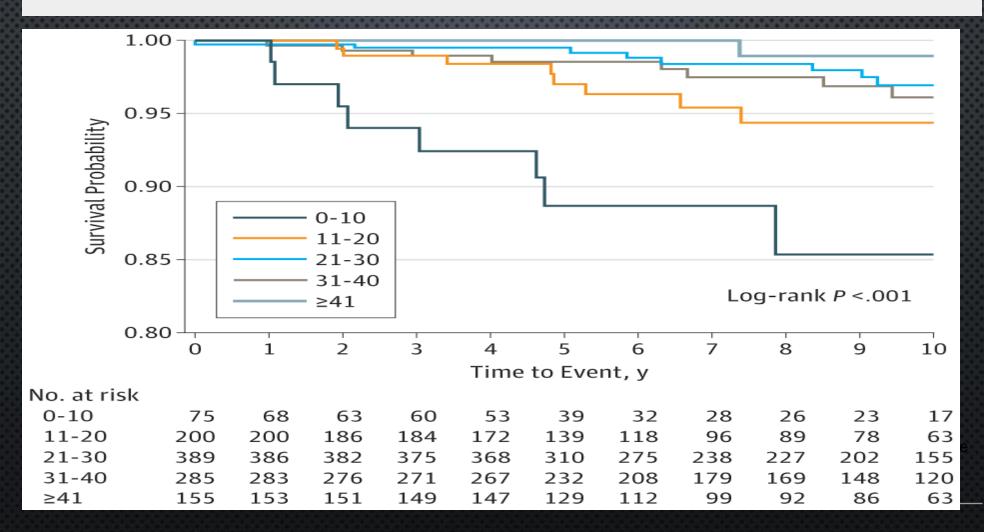


ASSOCIATION BETWEEN PUSH-UP EXERCISE CAPACITY AND FUTURE CARDIOVASCULAR EVENTS AMONG ACTIVE ADULT MEN

- THIS STUDY OF 1104 OCCUPATIONALLY ACTIVE ADULT MEN FOUND A SIGNIFICANT NEGATIVE ASSOCIATION BETWEEN BASELINE PUSH-UP CAPACITY AND INCIDENT CARDIOVASCULAR DISEASE RISK ACROSS 10 YEARS OF FOLLOW-UP.
- PARTICIPANTS ABLE TO COMPLETE MORE THAN 40 PUSH-UPS WERE ASSOCIATED WITH A SIGNIFICANT REDUCTION IN INCIDENT CARDIOVASCULAR DISEASE EVENT RISK COMPARED WITH THOSE COMPLETING FEWER THAN 10 PUSH-UPS.
- PUSH-UP CAPACITY IS A NO-COST, FAST, AND SIMPLE MEASURE THAT MAY BE A USEFUL AND OBJECTIVE CLINICAL ASSESSMENT TOOL FOR EVALUATING FUNCTIONAL CAPACITY AND CARDIOVASCULAR DISEASE RISK.
- JAMA NETW OPEN. 2019 FEB; 2(2): E188341

From: Association Between Push-up Exercise Capacity and Future Cardiovascular Events Among Active Adult Men

JAMA Netw Open. 2019;2(2):e188341. doi:10.1001/jamanetworkopen.2018.8341



Date of download: 4/10/2022

HOW FAST CAN YOU CLIMB 4 FLIGHTS OF STAIRS? IT MAY REVEAL YOUR HEART HEALTH

- RESEARCHERS SAY HOW QUICKLY A PERSON CAN WALK UP FOUR FLIGHTS OF STAIRS MAY BE AN INDICATOR OF THEIR HEART HEALTH.
- Participants who climbed the stairs in less than 40 to 45 seconds achieved more than 9 to 10 METs.
- THEY ALSO SAY THERE ARE OTHER TASKS, SUCH AS CARRYING A BAG OF GROCERIES TO A CAR, THAT CAN BE USED AS A PRELIMINARY GAUGE OF HEART HEALTH.
- HTTPS://WWW.HEALTHLINE.COM/HEALTH-NEWS/HOW-FAST-CAN-YOU-CLIMB-4-FLIGHTS-OF-STAIRS-IT-MAY-REVEAL-YOUR-HEART-HEALTH

v O₂max

A 3-MINUTE TEST OF CARDIORESPIRATORY FITNESS 30 SQUATS IN 45 SECONDS

We recruited a convenient sample of 40 adults between 18 and 64 years from the general U.S. population. Participants completed 30 squats in 45 seconds, paced by a metronome.

Results

Of the 40 participants, there were 18 men and 22 women. Mean age was 31.2 years (SD = 9.9). We found that the best predictors were HR features P1/height and $(P2-P3)/age^3$.

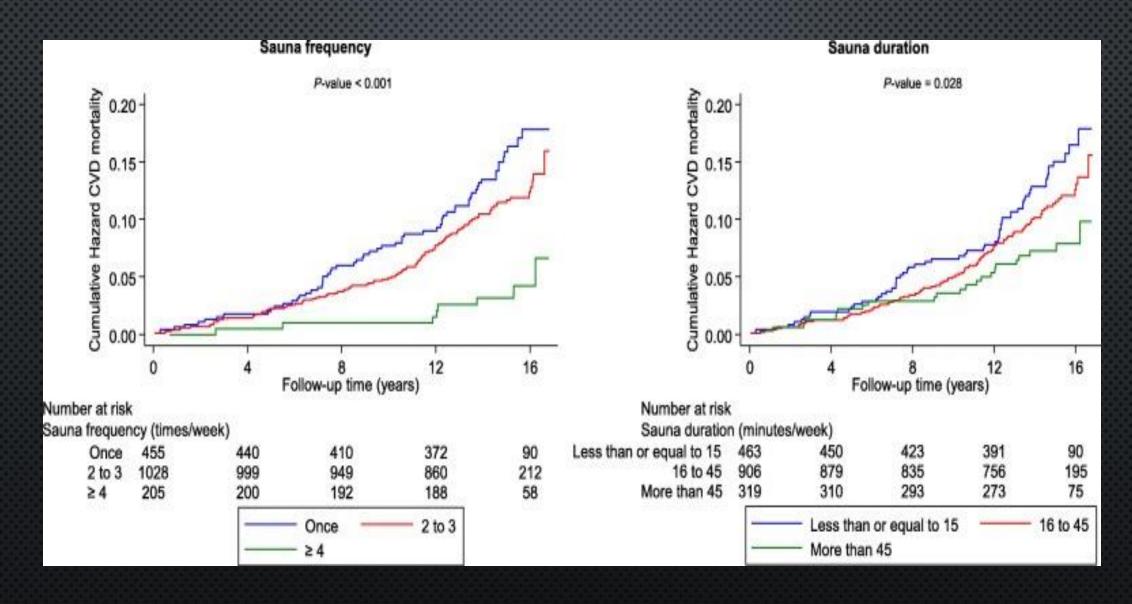
Conclusions

The study provided strong evidence for the validity of the squat test in the clinical setting.

BONUS LONGEVITY HABITS: SAUNA

- SAUNA BATHING IS ASSOCIATED WITH REDUCED CARDIOVASCULAR MORTALITY AND IMPROVES RISK PREDICTION IN MEN AND WOMEN: A PROSPECTIVE COHORT STUDY
- "HIGHER FREQUENCY AND DURATION OF SAUNA BATHING ARE EACH STRONGLY, INVERSELY, AND INDEPENDENTLY ASSOCIATED WITH FATAL CVD EVENTS IN MIDDLE-AGED TO ELDERLY MALES AND FEMALES. THE FREQUENCY OF SAUNA BATHING IMPROVES THE PREDICTION OF THE LONG-TERM RISK FOR CVD MORTALITY"
- BMC MED 2018 NOV 29;16(1):219

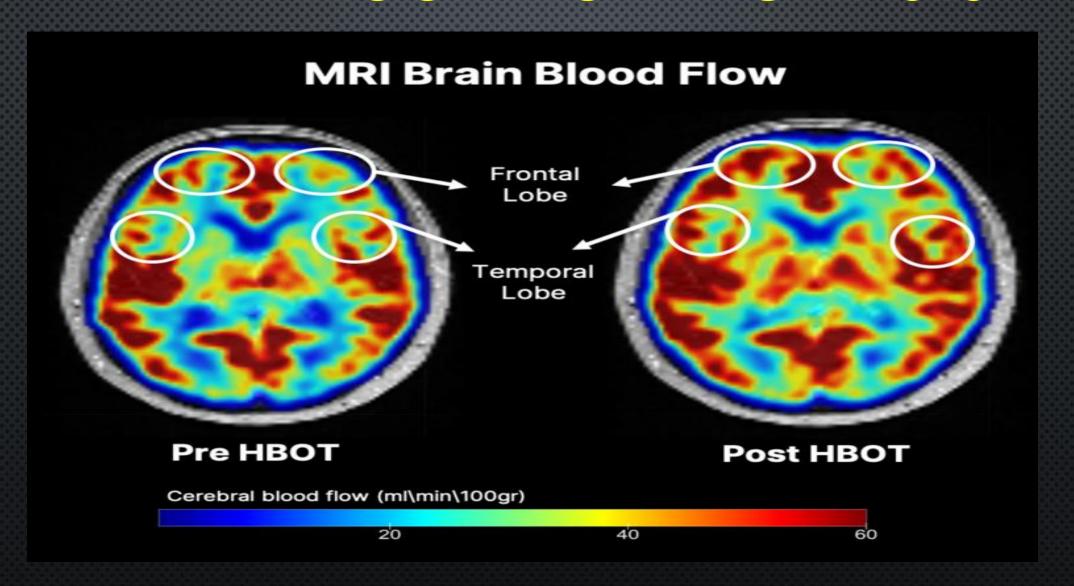
SAUNA AND CVD MORTALITY



HYPERBARIC OXYGEN THERAPY HBOT



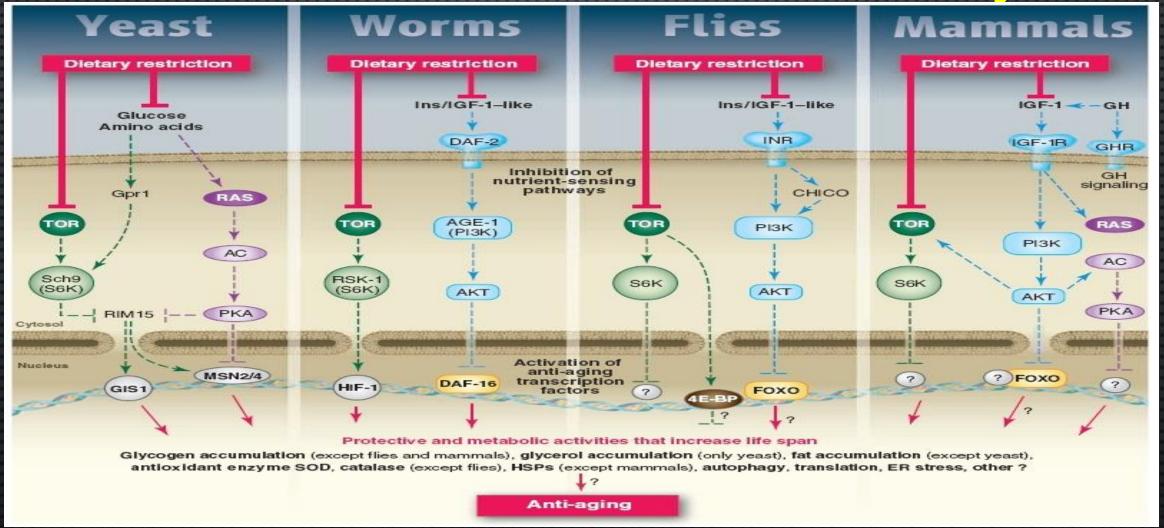
BRAIN BLOOD FLOW INCREASES



EAT LESS SOMETIMES



Eat Less:Conserved Cellular Pathways



Fasting Options

Research has suggested that different versions of fasting diets, such as reducing caloric intake on certain days or at certain times, not only can help with weight loss, but also can extend longevity in animals and improve health in humans. Here are some different approaches under study:.

The Daniel Fast

A 21-day partial fast based on the Old Testament fasts recorded in Daniel 1 and Daniel 10. A vegan diet, with no additives, preservatives, sweeteners, caffeine, alcohol, white flour or processed foods. Can be modified to include some animal products.

Fasting-Mimicking Diet (FMD)

Reduced caloric intake for five consecutive days, done once a month for patients who are obese or have multiple disease risk factors, every three to four months for others. Starts at 1,100 calories the first day and about 750 calories each of the next four days, before returning to normal eating. Food choices are high in unsaturated fats and low in sugars and protein.

Alternate-Day Fasting (ADF)

No food or reduced calories on "fast" days, alternating with "feast" days, on which food is consumed as desired.

5 and 2 Regimen

Five days of eating as desired, with two consecutive or nonconsecutive "fast" days with minimal caloric intake: 500 calories for women, 600 for men.

Early Time-Restricted Feeding (ETRF)

Last meal is eaten by midafternoon with no food again until breakfast the next morning.

THE WALL STREET JOURNAL.

Fasting Mimicking Diets

Dr. Valter Longo pioneered the research that characterized these nutrient-sensing pathways

- He demonstrated that the IGF-1, mTOR and PKA pathways are critical for promoting aging
- Elevation of these nutrient-sensing pathways accelerates aging processes



Low levels of IGF-1 are associated with the longest living human populations (centenarians)

Category	Weight Loss	Lean Body Mass Protection	Cholesterol Reduction	Fasting Blood Glucose	Rejuvenation & Regeneration	Food
Calorie Restriction	✓		✓	✓		✓
Intermittent Fasting	//		✓	//		
Time-Restricted Feeding	✓		✓	✓		✓
Periodic Fasting	√ ✓	✓	✓	///	///	
Fasting Mimicking Diet	111	√ √	✓	///	111	✓

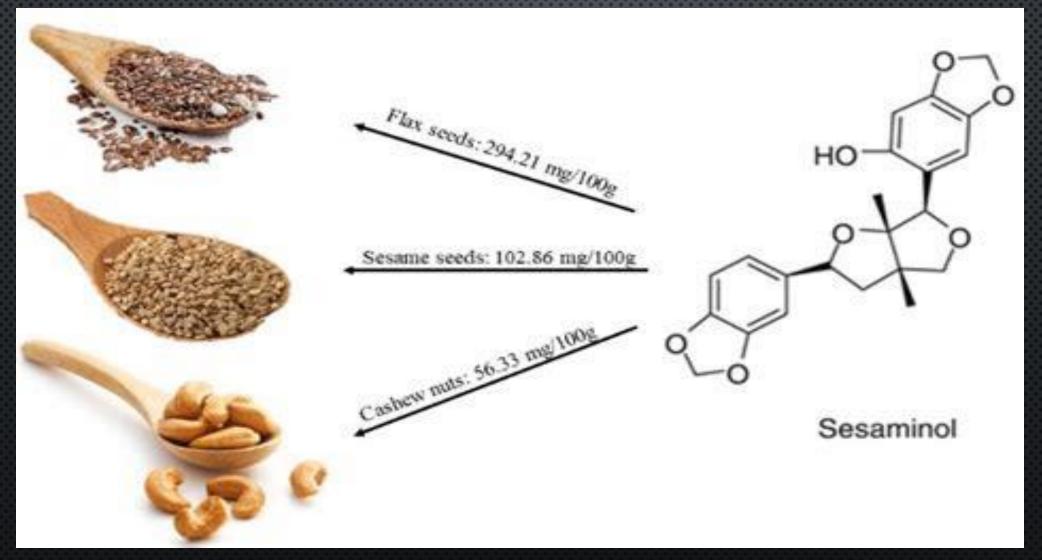
PROLON: THE FMD



EAT LIGNAN RICH FOODS

- LIGNANS ARE <u>POLYPHENOLIC COMPOUNDS</u> FOUND IN PLANTS.
- LIGNAN <u>PRECURSORS</u> ARE FOUND IN A WIDE VARIETY OF PLANT-BASED FOODS, INCLUDING SEEDS, <u>WHOLE</u> <u>GRAINS</u>, <u>LEGUMES</u>, FRUIT, AND VEGETABLES.
- FLAXSEEDS ARE THE RICHEST DIETARY SOURCE OF LIGNAN PRECURSORS.

TOP THREE SOURCES OF LIGNANS IN FOOD



LIGNAN INTAKE AND RISK OF CORONARY HEART DISEASE

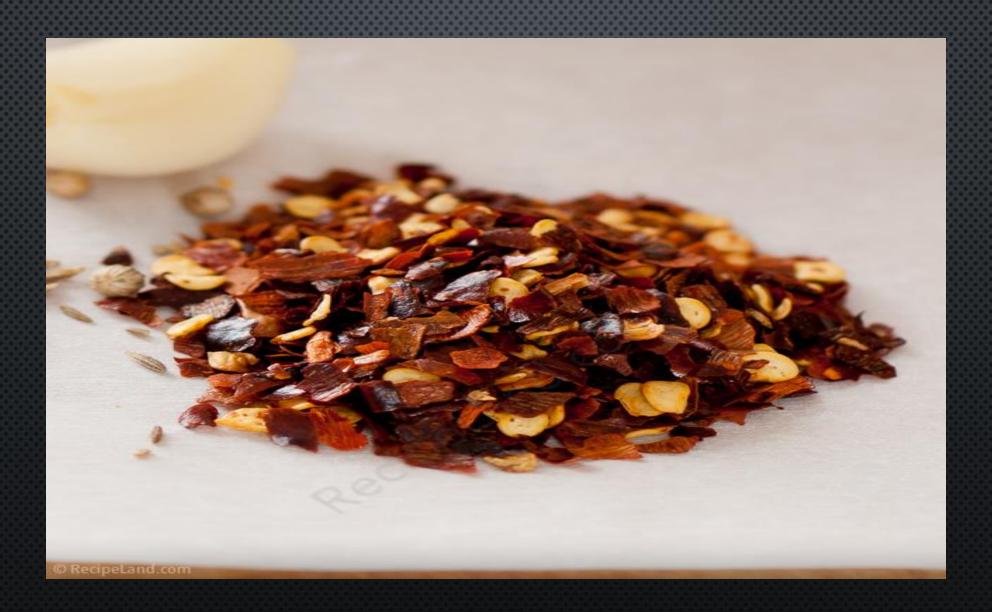
- WE PROSPECTIVELY FOLLOWED 214,108 MEN AND WOMEN IN 3 COHORTS WHO DID NOT HAVE CARDIOVASCULAR DISEASE OR CANCER AT BASELINE. DIET WAS REPEATEDLY ASSESSED USING A VALIDATED FOOD FREQUENCY QUESTIONNAIRE EVERY 2-4 YEARS SINCE BASELINE
- INCREASED LONG-TERM INTAKE OF LIGNANS WAS ASSOCIATED WITH A SIGNIFICANTLY LOWER RISK OF TOTAL CHD IN BOTH MEN AND WOMEN. POSSIBLE SYNERGISTIC EFFECTS MAY EXIST BETWEEN LIGNAN AND FIBER INTAKE IN RELATION TO CHD RISK REDUCTION, POSSIBLY THROUGH ENHANCING THE PRODUCTION OF ENTEROLIGNANS.
- J AM COLL CARDIOL 2021 Aug 17;78(7):666-678

THE ASSOCIATION OF HOT RED CHILI PEPPER CONSUMPTION AND MORTALITY: A LARGE POPULATION-BASED COHORT STUDY

- THE FREQUENCY OF HOT RED CHILI PEPPER CONSUMPTION WAS MEASURED IN 16,179 PARTICIPANTS AT LEAST 18 YEARS OF AGE.

 TOTAL AND CAUSE-SPECIFIC MORTALITY WERE THE MAIN OUTCOME MEASURES OVER 19 YEARS OF FOLLOW-UP.
- HOT RED CHILI PEPPERS WAS ASSOCIATED WITH A 13% REDUCTION IN THE INSTANTANEOUS HAZARD OF DEATH.
- , THE CONSUMPTION OF HOT RED CHILI PEPPER WAS ASSOCIATED WITH REDUCED MORTALITY. HOT RED CHILI PEPPERS MAY BE A BENEFICIAL COMPONENT OF THE DIET.

SPICE IT UP



VITAMINS? COQ10 AND SELENIUM

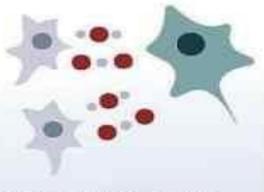
- RESEARCHERS FROM SWEDEN CONDUCTED A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY THAT INCLUDED 443 HEALTHY ADULTS BETWEEN 70 AND 88 YEARS OLD. THE PARTICIPANTS RECEIVED EITHER A PLACEBO OR A COMBINATION OF 200 MG A DAY OF COQ10 AND 200 MCG A DAY OF SELENIUM TABLETS.
- DURING AN EXTENSIVE FOLLOW UP TIME OF 5.2 YEARS, 12.6% OF THE PLACEBO RECIPIENTS HAD DIED OF CARDIOVASCULAR DISEASE, COMPARED TO ONLY 5.9% IN THE SUPPLEMENT GROUP, WHICH IS AN IMPRESSIVE AND SIGNIFICANT DIFFERENCE.
- INT J CARDIOL. 2013;167(5):1860-6

SENESCENCE AND SENESCENT CELLS: SENOLYTICS

WHY ARE SENESCENT CELLS HARMFUL?



SENESCENT CELLS
PRODUCE MOLECULES
THAT
DISTURB FUNCTION OF
NEIGHBOURING CELLS



SENESCENT CELLS CAN EVEN MISGUIDE THEIR NEIGHBOURS TO BECOME CANCER CELLS

SENOLYTICS: UNDER HUMAN STUDY CURRENTLY

Senolytics

Senolytic Cocktail of:

- 1) Dasatinib
- 2) Quercetin
- 3) Fisetin

Selective removal of senescent cells - Age-related accumulation of senescent cells contributes to atherosclerosis, aging of the eye (cataracts, AMD), osteoporosis, skin and brain aging, Kirkland and colleagues at Mayo Clinic show that senescent cells are selectively eliminated by "senolytic" drugs.



RX FOR LONGEVITY?

- METFORMIN (TAME STUDY)
- RAPAMYCIN
- DASATINAB AND QUERCETIN

AVAILABLE AND INTRIGUING

- GLY-NAC (GLYCINE AND NAC)
- SPERMIDINE (WHEAT GERM)
- QUERCETIN AND FISETIN
- GINGER COMPOUNDS
- NAD+ BOOSTERS (NR, NMN)

LIVE LONG ENOUGH TO LIVE FOREVER?

THE SCIENCE
BEHIND RADICAL LIFE EXTENSION

FANTASTIC VOYAGE

TO LIVE FOREVER

RAY KURZWEIL

TERRY GROSSMAN
M.D.