

Centenarian: Epigenomic resilience to environmental challenges

**Healthy Life And Longevity: Centenarians In Italy And Israeli Lifestyle, Nutrition, Clinical, and Genetics
Museum of Natural History, Tel Aviv, Israel,
December 2nd, 2019**

Gil Atzmon, Ph.D, Einstein Faculty of Medicine and Genetics, USA and Faculty of Natural Sciences, University of Haifa, Israel.

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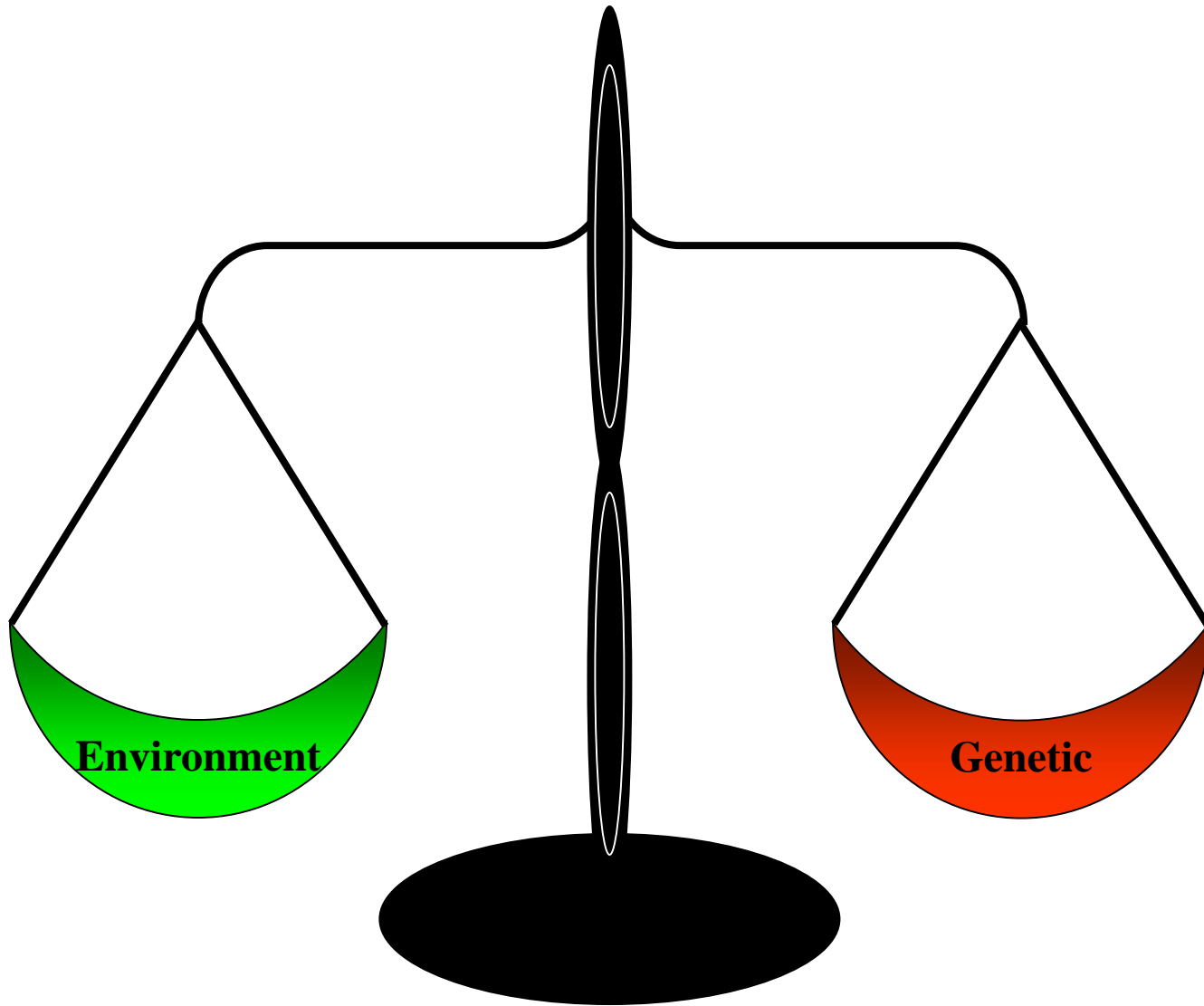


NATHAN SHOCK CENTERS
OF EXCELLENCE IN THE
BASIC BIOLOGY OF AGING

afar

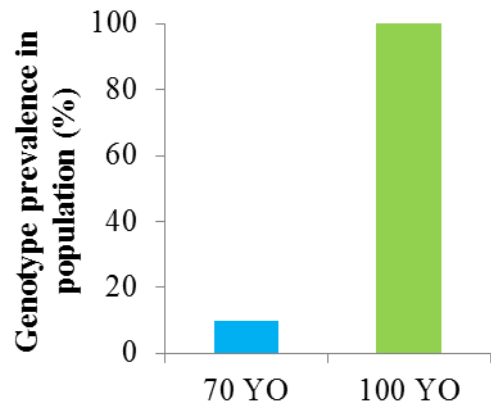
american federation for aging research



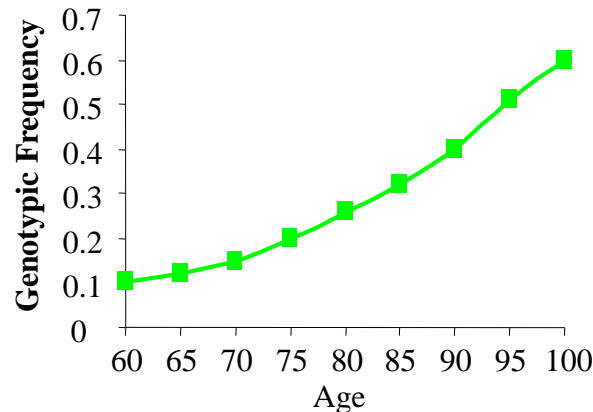


Candidate gene approach: Proven longevity associated genes

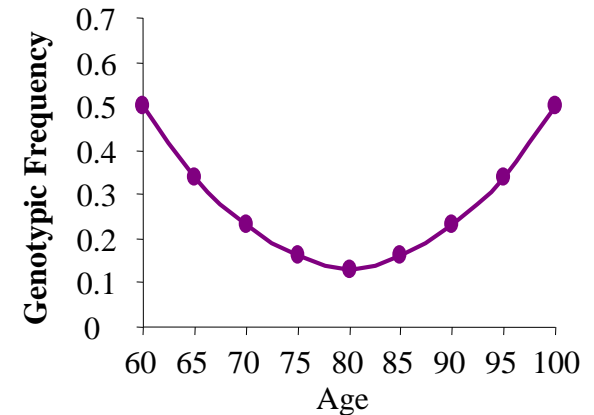
	C-C association	Trend	Buffering	Phenotype	Publication
CETP	X	X	X	X	JAMA 2003
APOC3	X	X		X	PLoS B. 2006
Adiponectin	X	X		X	J. Geron. 2008
TSH	X			X	JCEM 2009
MTP	X(-)	X(-)	X(-)	X(-)	J. Geron. 2012
d3GHR	X	X		X	Science Adv. 2017



Case Control analysis



Trend analysis

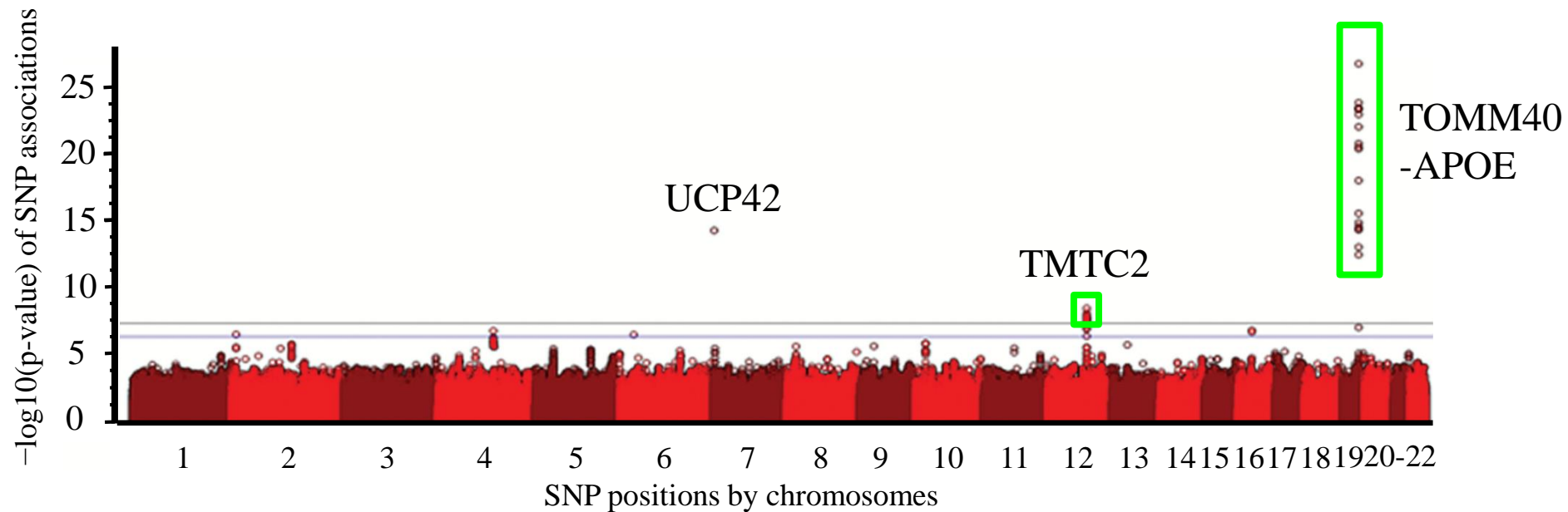


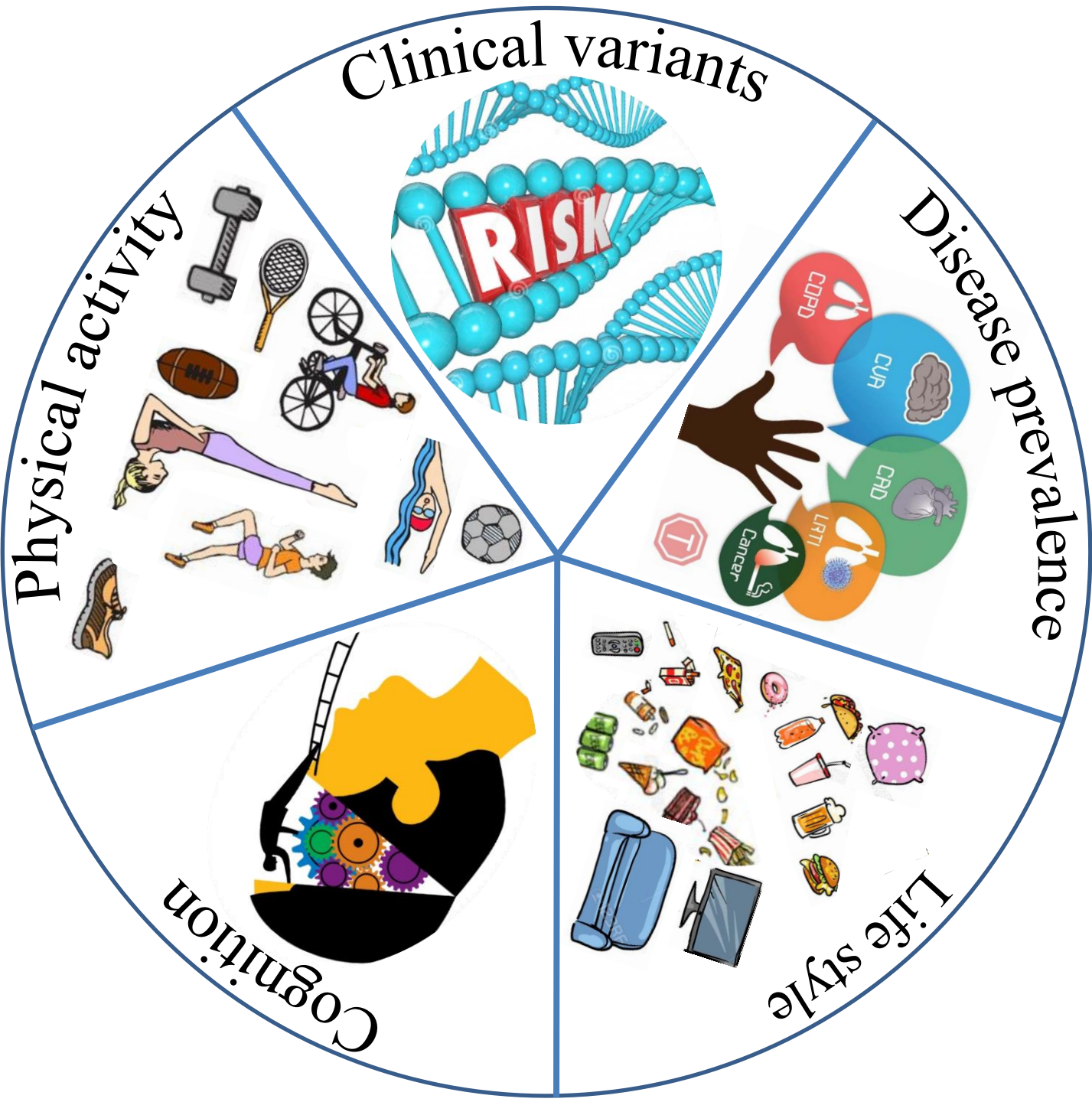
Buffering analysis

Longevity associated genes effect

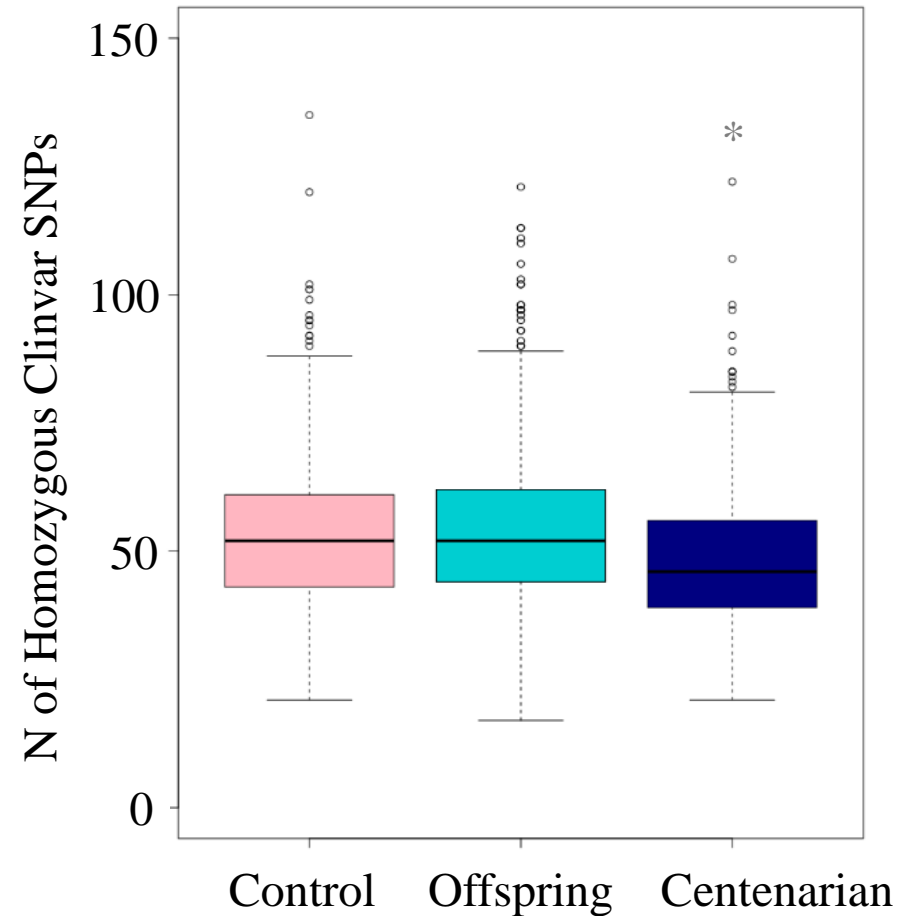
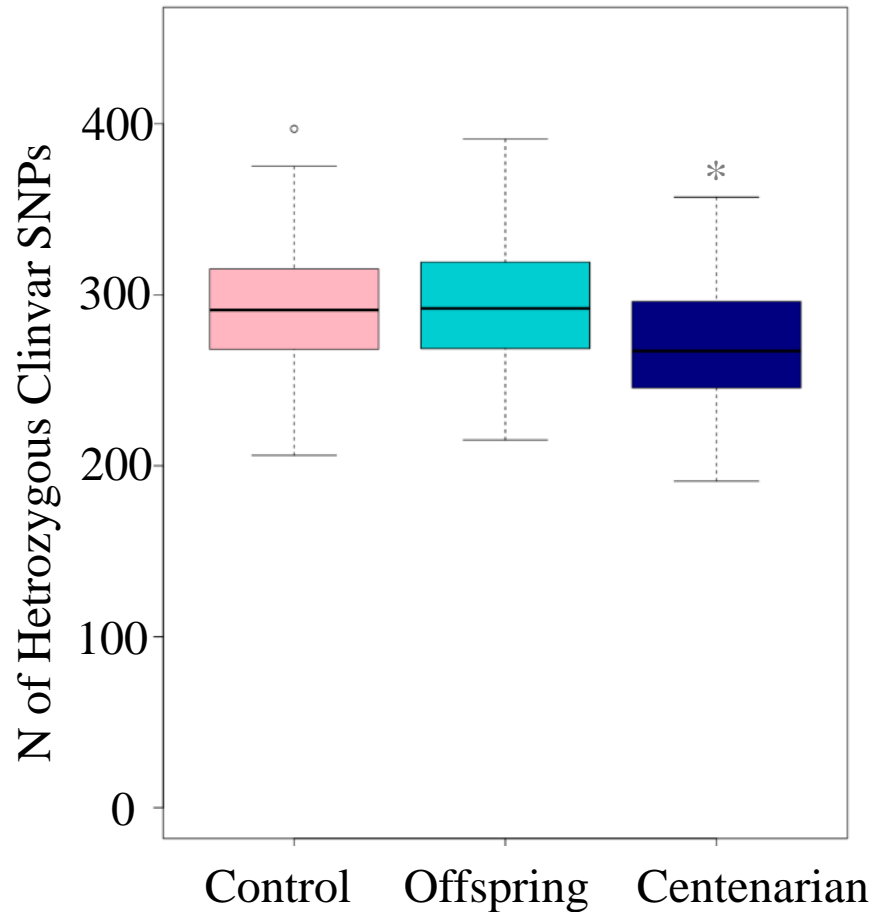
Gene polymorphism	Delay age associated disease
CETP	CVD and cerebrovascular events, Hypertension, Cognition and Alzheimer Disease
APOC3	CVD, Pre-diabetes and Hypertension
Adiponectin	Not determined
TSH	Not determined
MTP (-)	Triglyceride, VLDL and Chylomicron
d3GHR	Diabetes, Cancer

Manhattan plot displaying the meta-analysis of four extreme longevity cohort GWAS



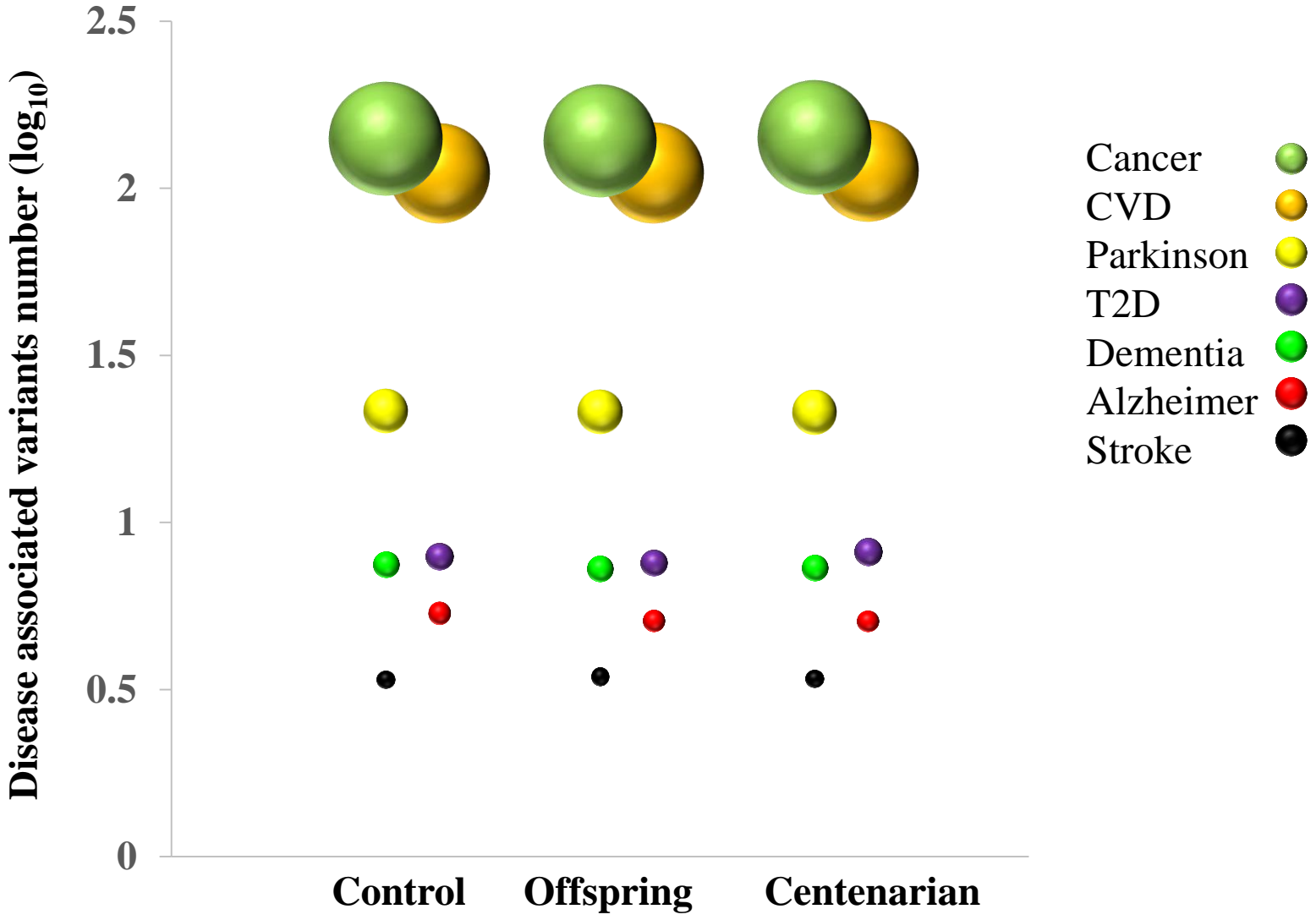


Comparison of median values of ClinVar SNPs between offspring, control and centenarians

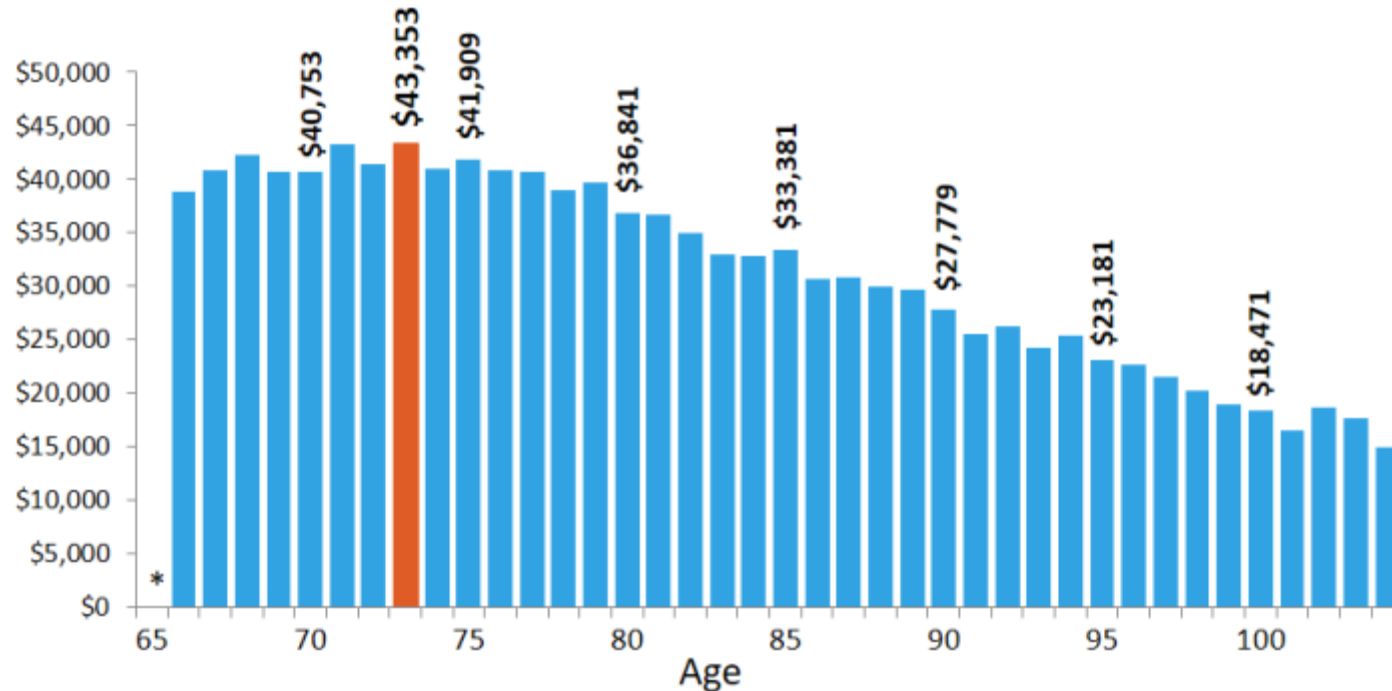


*p<0.01

Comparison of median values of disease associated SNPs between offspring, control and centenarians



Monthly health care expenditures within 1 year of death



Number of decedents	Ages 66-69: 0.1 million	Ages 70-74: 0.2 million	Ages 75-79: 0.2 million	Ages 80-84: 0.2 million	Ages 85-89: 0.3 million	Ages 90-94: 0.2 million	Ages 95-99: <0.1 million	Ages 100+: <0.1 million
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SOURCE: Kaiser Family Foundation, "Medicare Spending at the End of Life: A Snapshot of Beneficiaries Who Died in 2014 and the Cost of Their Care," July 2016.



Centenarian and their Offspring are healthier

Aging Cell (2017) 16, pp644-651

doi: 10.1111/acel.12591

Impact of early personal-history characteristics on the Pace of Aging: implications for clinical trials of therapies to slow aging and extend healthspan

Daniel W. Belsky,^{1,2,3} Avshalom Caspi,⁴ Harvey J. Cohen,^{1,3} William E. Kraus,¹ Sarah Richie Poulton⁵ and Terrie E. Moffitt^{1,5,6,7}

Journal of the American Geriatrics Society

Clinical Phenotype of Families with Longevity

Gil Atzmon, PhD,¹ Clyde Schechter, MD,¹ William Greiner, RN,² Deborah Davidson, MBA,³ Gad Rennert, MD, PhD,⁴

Journal of Gerontology: MEDICAL SCIENCES
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Translational Article

Special Issue on Extreme Longevity

Health Span Approximates Life Span Among Many Supercentenarians: Compression of Morbidity at the Approximate Limit of Life Span

Stacy L. Andersen,¹ Paola Sebastiani,² Daniel A. Dworkin,³ Lori Feldman,⁴ and Thomas T. Perls¹

Journal of Gerontology: MEDICAL SCIENCES
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Comprehensive Health Status Assessment of Centenarians: Results From the 1999 Large Health Survey of Veteran Enrollees

I. Selim,^{1,2,4} Grace Fincke,^{1,4} Dan R. Berlowitz,^{1,4} Donald R. Miller,^{1,4} Shirley X. Qiu,^{1,4} Cong,¹ William Rogers,^{1,5} Bernardo J. Selim,⁴ Xinhua S. Ren,^{1,4} Lewis E. Kazis^{1,4}

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Autopsy reports in extreme longevity

M. Motta^{A,*}, E. Bennati^A, M. Vacante^A, G. Stanta^B, E. Cardillo^A, M. Malaguarnera^A, L. Giarelli^{B,1}

^ADepartment of Neuroscience Sciences, University of Catania, Concatteda Hospital, Via Medina, 820, I-95126 Catania, Italy

^BDepartment of Anatomy, Department of Clinical, Morphological and Technological Sciences, University of Trieste, Cattinara Hospital, Strada di Fiume, 447, I-34139 Trieste, Italy

Compression of Morbidity and Exceptional Longevity

Khadija Ismail, MS^{1,*}, Lisa Nussbaum, MPH^{2,*}, Paola Sebastiani, PhD², Stacy Andersen, PhD³, Thomas Perls, MD, MPH³, Nir Barzilai, MD¹, and Sofiya Milman, MD, MS¹

¹Department of Medicine, Division of Endocrinology and Institute for Aging Research, Albert Einstein College of Medicine, Bronx, NY 10461

²Department of Biostatistics, Boston University School of Public Health, Boston, MA 02118

³Geriatrics Section, Department of Medicine, Boston University School of Medicine and Boston Medical Center, Boston, MA 02118

Prevalence of Chronic Illness in Community-Dwelling, Predominantly Male U.S. Veteran Centenarians

Raya Eljadel Kheibek, MD, MPH,^{1,*} Ali Fokar, MPH,² Nawar Shara, PhD,³ Leakie K. Bell-Wilson, RN,⁴ Hans J. Moore, MD,^{5,6} Edwin Olsen, MD, JD,^{7,*} Marc R. Blackman, MD,^{8,9} and Maria D. Llorente, MD¹⁰

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Exceptional Parental Longevity Associated with Reduced Risk of Alzheimer's Disease and Memory Decline

James Hirsch, M.D.,^{1,2,3,4} Mindy J. Katz, P.P.H.,^{1,2,4} Culling Wang, M.B.B.S.,^{1,2,4} Nir Barzilai, M.D.,^{1,4,5} and Thomas T. Perls, M.D.,^{1,4,5}

Favorable Glucose Tolerance and Lower Prevalence of Metabolic Syndrome in Offspring without Diabetes Mellitus of Centenarian Siblings: The Leiden Longevity Study

Wouter J. van Tilburg, MD, PhD,^{1,*} Anton J. M. de Craen, PhD,^{2,*} and Albertine M. Zwaan, PhD,^{3,*}

Research Article

Members of Long-Lived Families Healthier than Peers? Evidence from the Framingham Heart Study

Offspring of Centenarian are healthier

Centenarian Offspring: Start Healthier and Live Longer

Emily R. Adams, BA¹, Vikki G. Nolan, MPH¹, Stacy L. Andersen, BS¹, Thomas T. Perls, MD, MPH¹, and Dellara F. Terry, MD, MPH¹

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Health Consequences of Familial Longevity Influence Among the Chinese Elderly

Yi Zeng,^{1,2} Huashuai Chen,^{1,2} Xiaoming Shi,¹ Zhaoxue Yin,¹ Ze Yang,⁴ Jun Gu,² and Dan Blazer³

Does the longevity of one's parents predict the health of their offspring?

P. Gueresi^{A,*}, R. Miglio^B, D. Monti^B, D. Mari^{C,D}, P. Sansoni^E, C. Caruso^F, E. Bonafede^G, L. Bucchi^H, G. Sgarbi^I, R. Ostan^J, M.G. Palmas^K, E. Pini^L, M. Scurti^M, C. Franceschi^N

Inflammation, But Not Telomere Length, Predicts Successful Ageing at Extreme Old Age: A Longitudinal Study of Semi-supercentenarians

Yasumichi Arai^{A,1}, Carmen M. Martin-Ruiz^{B,1}, Michiyo Takayama^C, Yukiko Abe^A, Toru Takebayashi^D, Shigeo Koyasu^E, Makoto Suematsu^{A,C}, Nobuyoshi Hirose^{A,C}, Thomas von Zglinicki^{B,A,C}

Low Inflammation in Centenarian Siblings: a comparison with their offspring

Jacob K Pedersen^{A,*}, Axel Skytthe^B, Matt McGue^{A,B}, Lawrence S Honig^{C,D,E}, Claus Wischmann^{F,G,H,I}, Thomas BL Kirkwood^J, Giuseppe Passarino^K, P Eline Slagboom^{M,N}, James W Vaupel^O, and Kaare Christensen^P



Exceptional Longevity and life style

Table 1. Mean Maximum Body Mass Index (BMI) and Prevalence of Overweight and Obesity During Lifetime in People with Exceptional Longevity and the National Health and Nutrition Examination Survey (NHANES) I Population

BMI, kg/m ²	Men			Women		
	With Exceptional Longevity (n = 90)	NHANES I (n = 5,254)	P-Value	With Exceptional Longevity (n = 249)	NHANES I (n = 7,924)	P-Value
Maximum, mean ± standard deviation	25.4 ± 2.8	25.6 ± 4.0	.63	25.0 ± 3.5	24.9 ± 5.4	.90
< 25.0, %	52.2	45.0	.19	56.2	58.8	.33
≥ 25.0, %	47.8	55.0	.31	43.8	41.2	.71
25.0–29.9 (overweight), %	43.3	42.9	.89	34.2	25.0	.001
≥ 30.0 (obese), %	4.5	12.1	.03	9.6	16.2	.006

43.8 vs. 41.2
p=NS

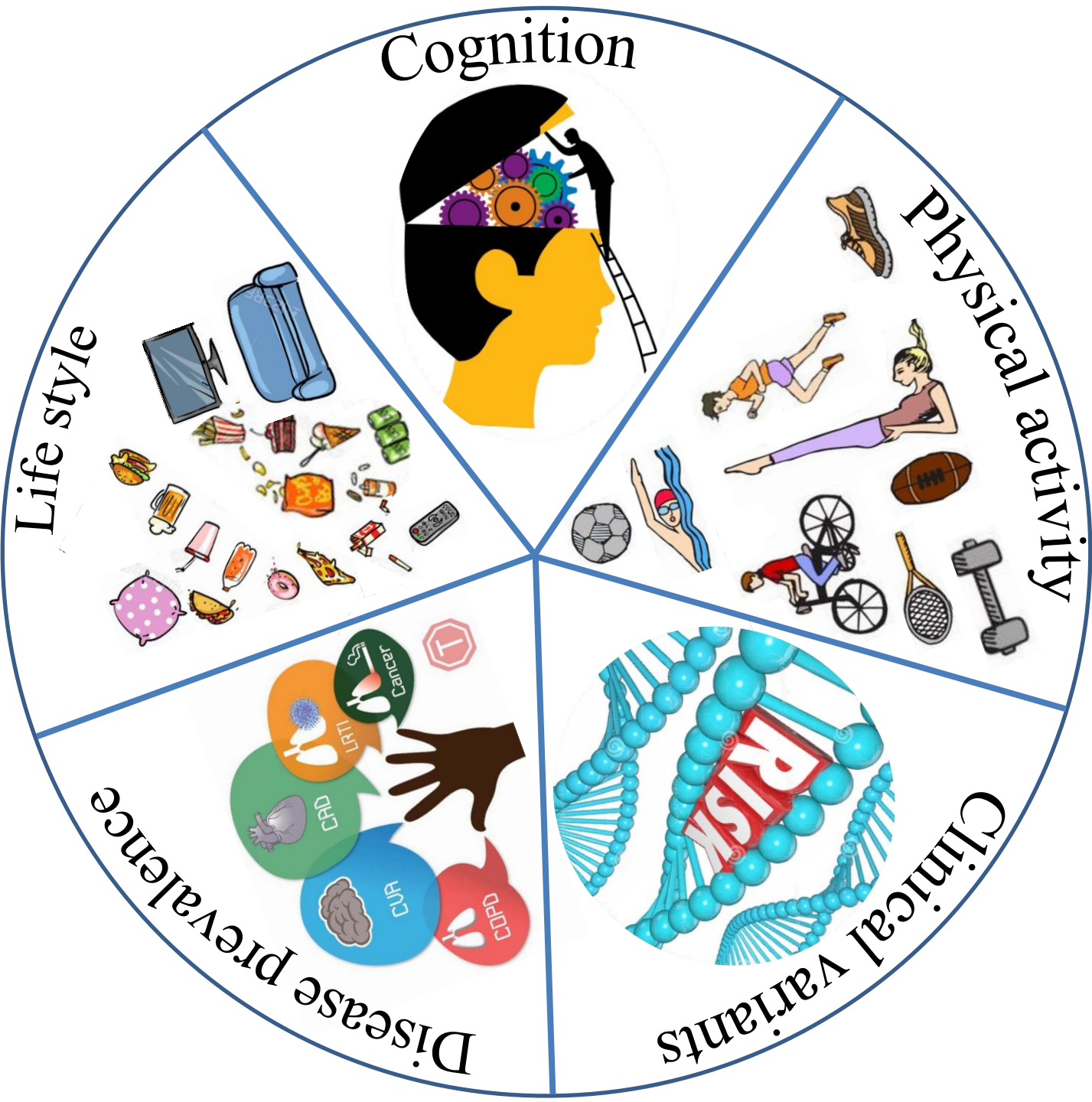
Exceptional Longevity and life style, con.

Table 2. Lifestyle Factors in Ashkenazi Centenarians and National Health and Nutrition Examination Survey (NHANES) I Population

Lifestyle Factor	Men			Women		
	Exceptional Longevity (n = 90) (%)	NHANES I (n = 1,497) (%)	P-Value*	Exceptional Longevity (n = 356) (%)	NHANES I (n = 1,667) (%)	P-Value*
Smoked \geq 100 cigarettes during life	59.6	74.5	.003	29.9	26.2	.25
Consumed alcohol daily	23.9	22.4	.77	12.1	11.3	.80
Reported regular moderate physical activity	43.1	57.2	.07	47.0	44.1	.76
Reported low-calorie diet	20.8	21.1	.32	27.3	27.1	.14
Reporting low-fat diet	29.1	41.1	.17	35.4	38.5	.22
Reporting low-salt diet	32.1	34.3	.80	30.5	30.1	.67

* Derived from Student *t*-test or chi-square test.

- Smoke and drink the same as 70 years younger control
- Doesn't exercise
- No special diet
- Almost half, are either obese or overweight



Cognitive function and longevity

www.impactaging.com

AGING, May 2012, Vol. 4. No 5

Research Paper

Positive attitude towards life and emotional expression as personality phenotypes for centenarians

Kaori Kato^{1,2}, Richard Zweig¹, Nir Barzilai³, and Gil Atzmon³

www.impactaging.com

AGING, March 2013, Vol. 5 No 3

Research Paper

Personality, self-rated health, and cognition in centenarians: Do personality and self-rated health relate to cognitive function in advanced age?

Kaori Kato¹, Richard Zweig¹, Clyde B. Schechter², Joe Verghese^{3,4}, Nir Barzilai^{4,5}, and Gil Atzmon^{4,5}

Aging & Mental Health, 2015

Positive attitude toward life, emotional expression, self-rated health, and depressive symptoms among centenarians and near-centenarians

Kaori Kato^{a*}, Richard Zweig^b, Clyde B. Schechter^c, Nir Barzilai^d and Gil Atzmon^{d,e}

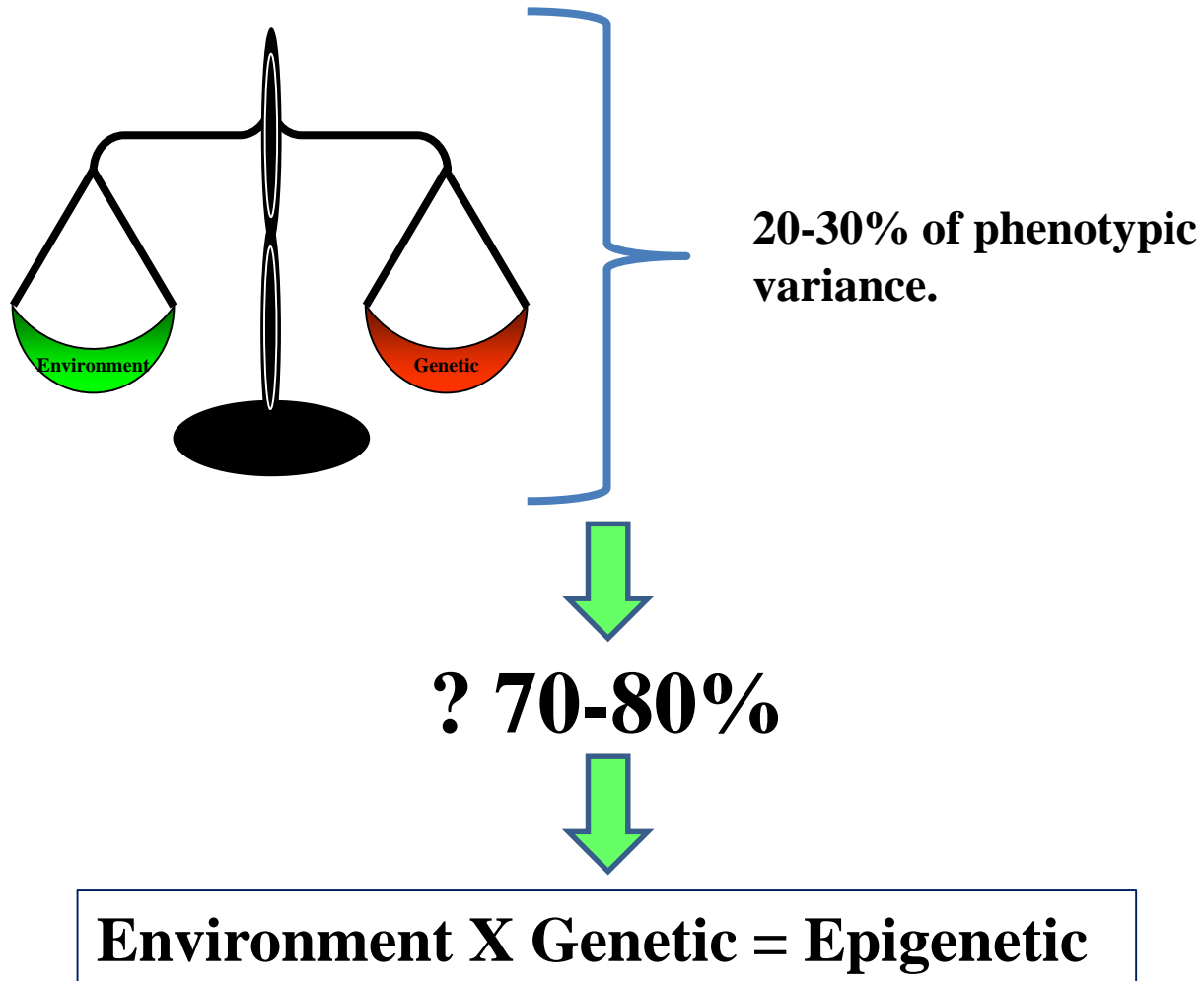
- **Personality as well as self-rated health may play important roles in cognitive function in advanced age.**
- **Centenarians in both self- and informant-report groups tended to be optimistic, easygoing, and outgoing and to consider laughter as an important part of their life**
- **Positive attitudes/affect and favorable personality in conjunction with self-rated health may play an important role in mental health outcomes in advanced age.**

Longevity Summary

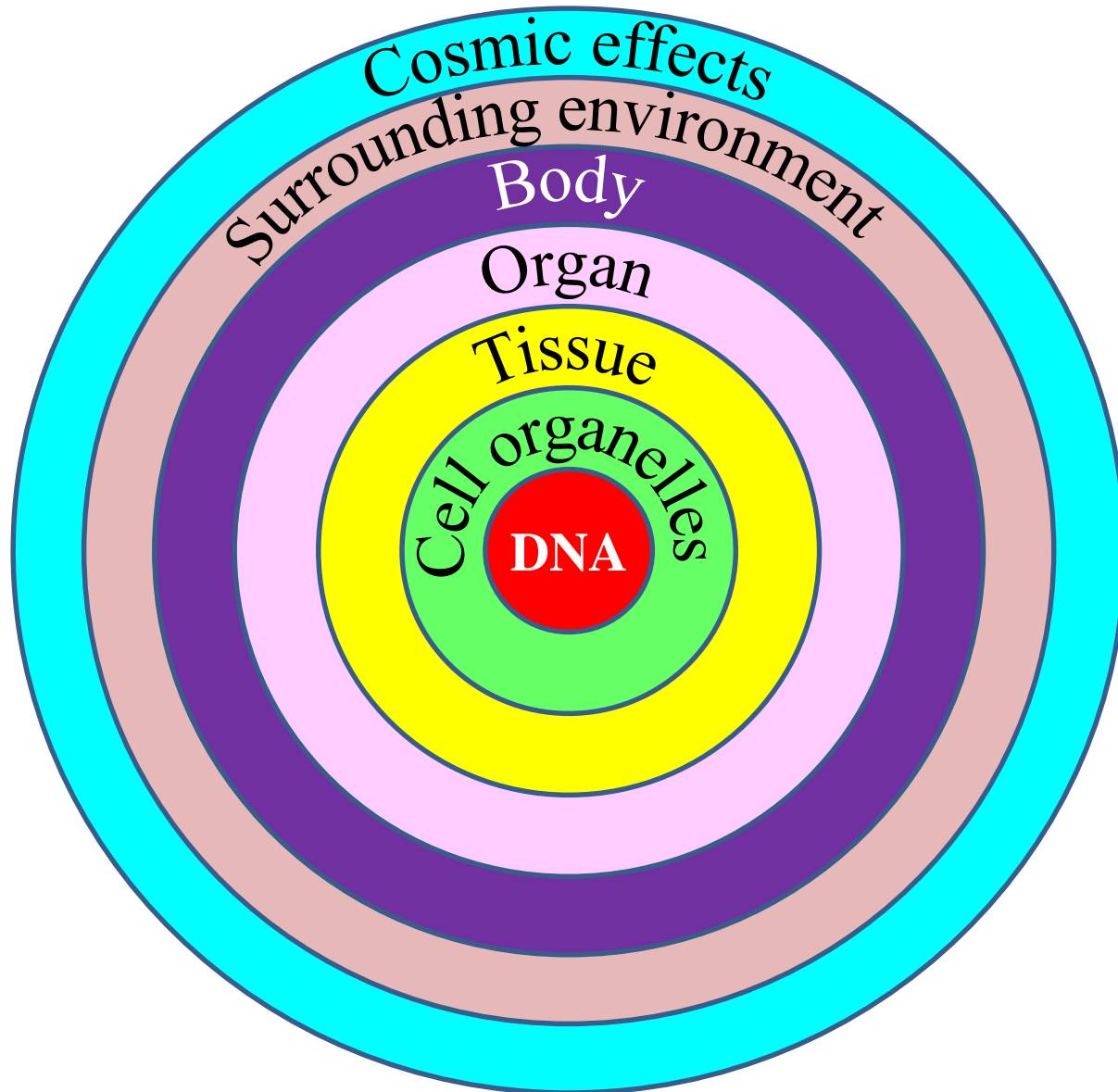
	Centenarian	Control
Disease Prevalence	+	+
Life Style	+	+
Physical Activity	+	+
Spiritually	+	
Cognition	+	+
Appearance	+	+

Centenarians are resilience to environmental effects

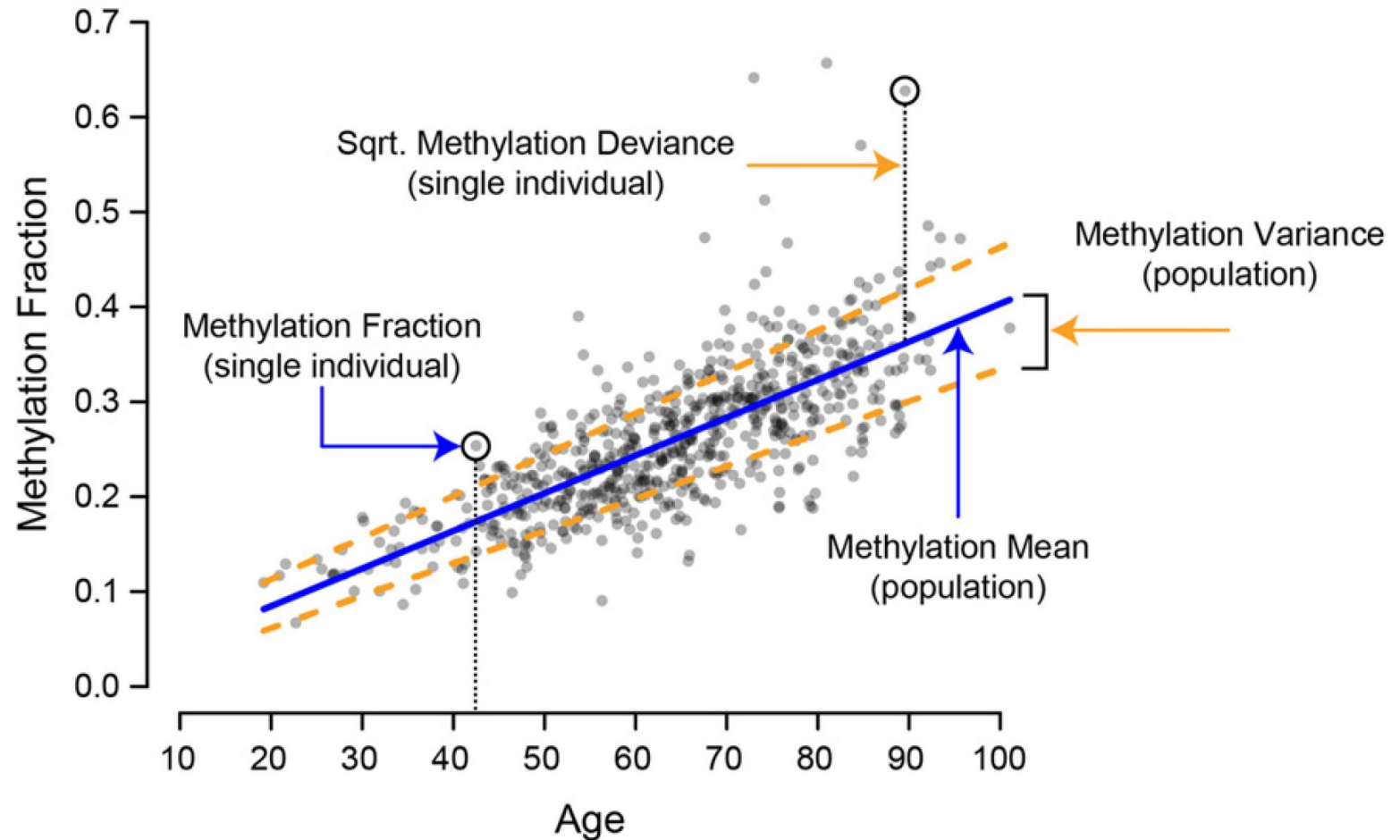
Environment vs. Genetics



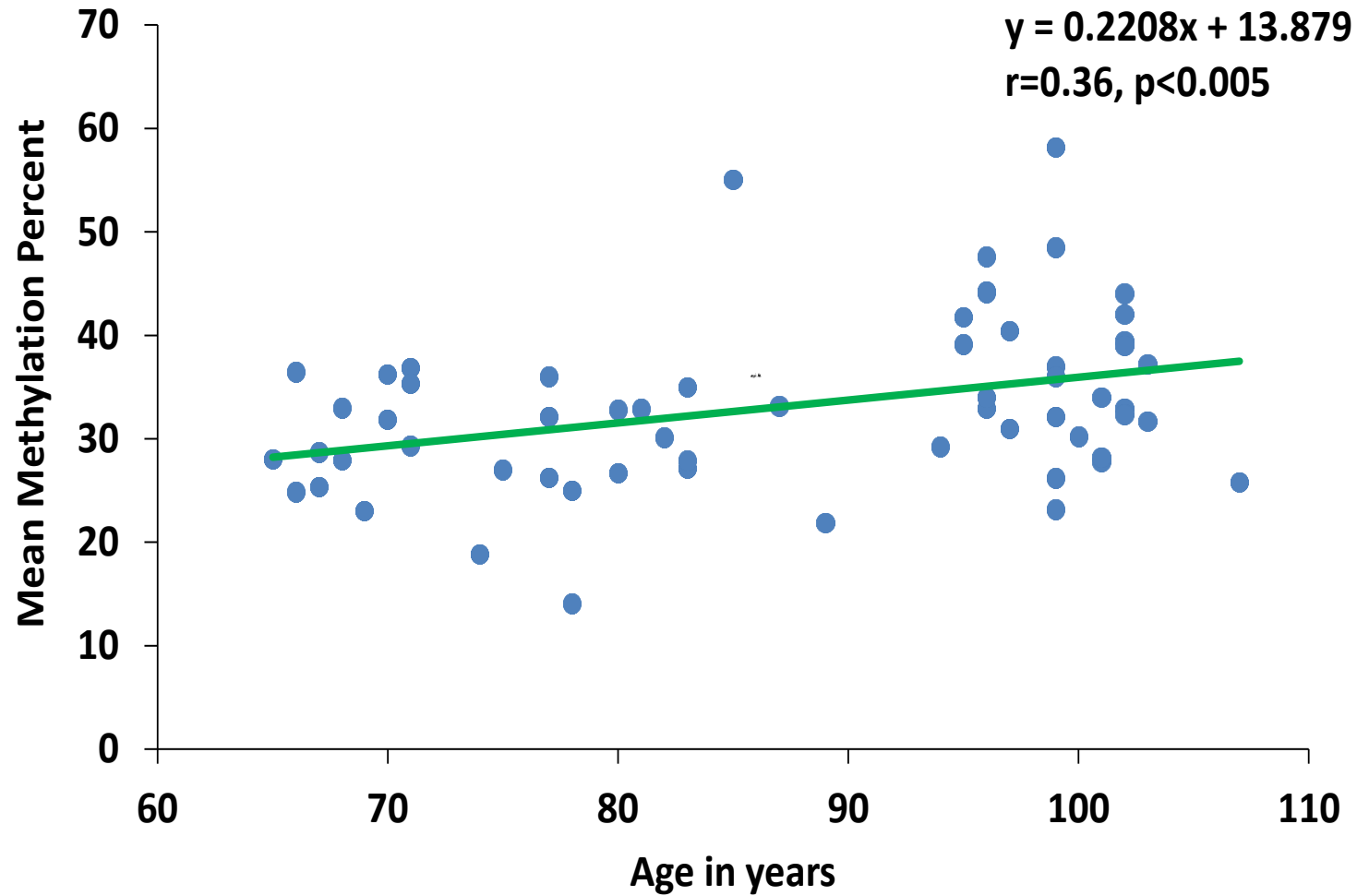
DNA-Environment interaction



Methylation with age



Methylation with age con.



Conclusion:

Epigenetic may play a crucial role in the way we all aged especially in healthy cognitive long life demonstrated by centenarian.

Few suggestions





*Have A
year of
healthy*

Living