Lifestyle/Diets, Epigenomic Reprogramming and Longevity of SDAs

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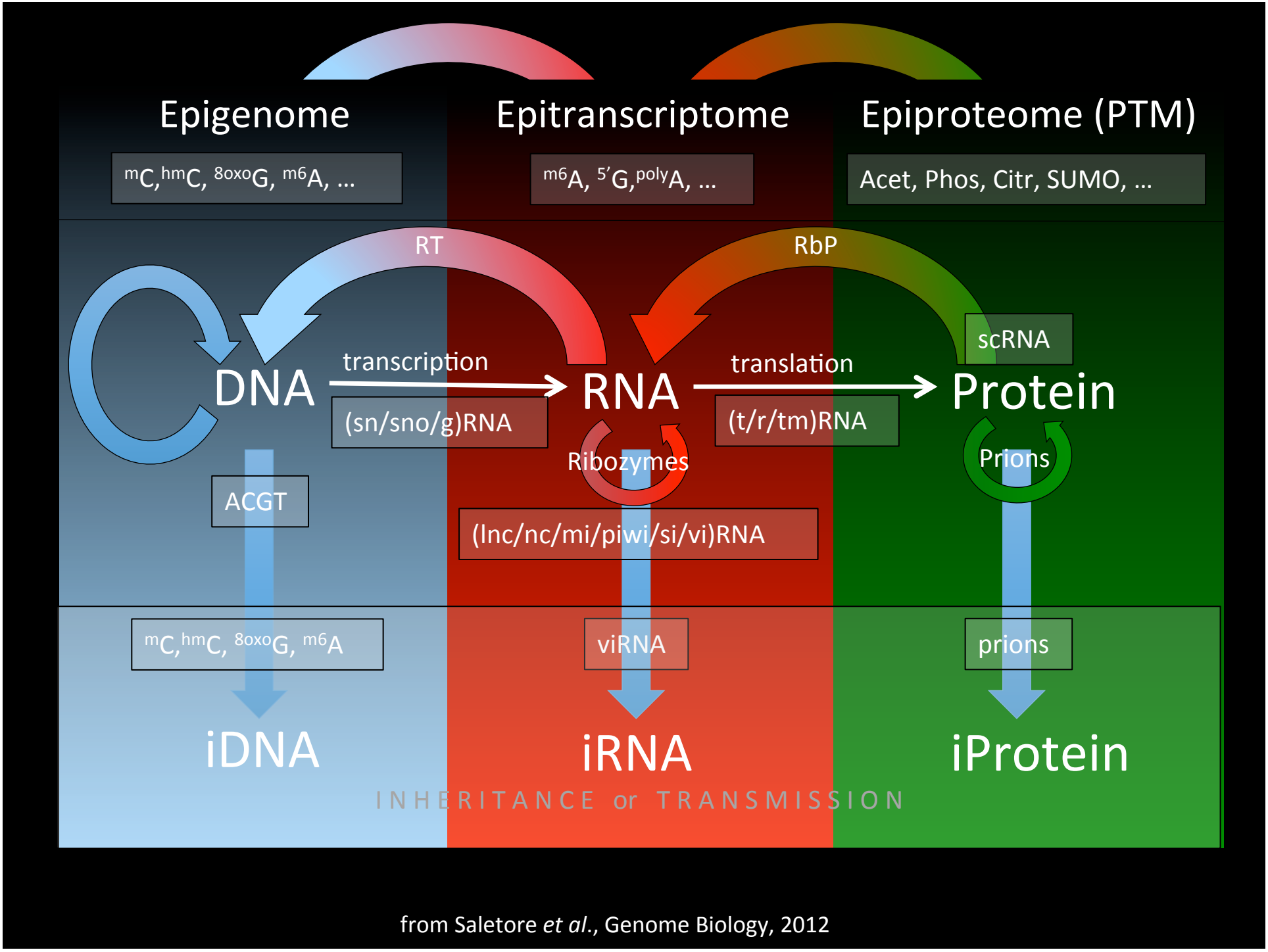

from Saletore *et al.*, Genome Biology, 2012

ENCODE: Encyclopedia of DNA Elements

An integrated encyclopedia of DNA elements in the human genome

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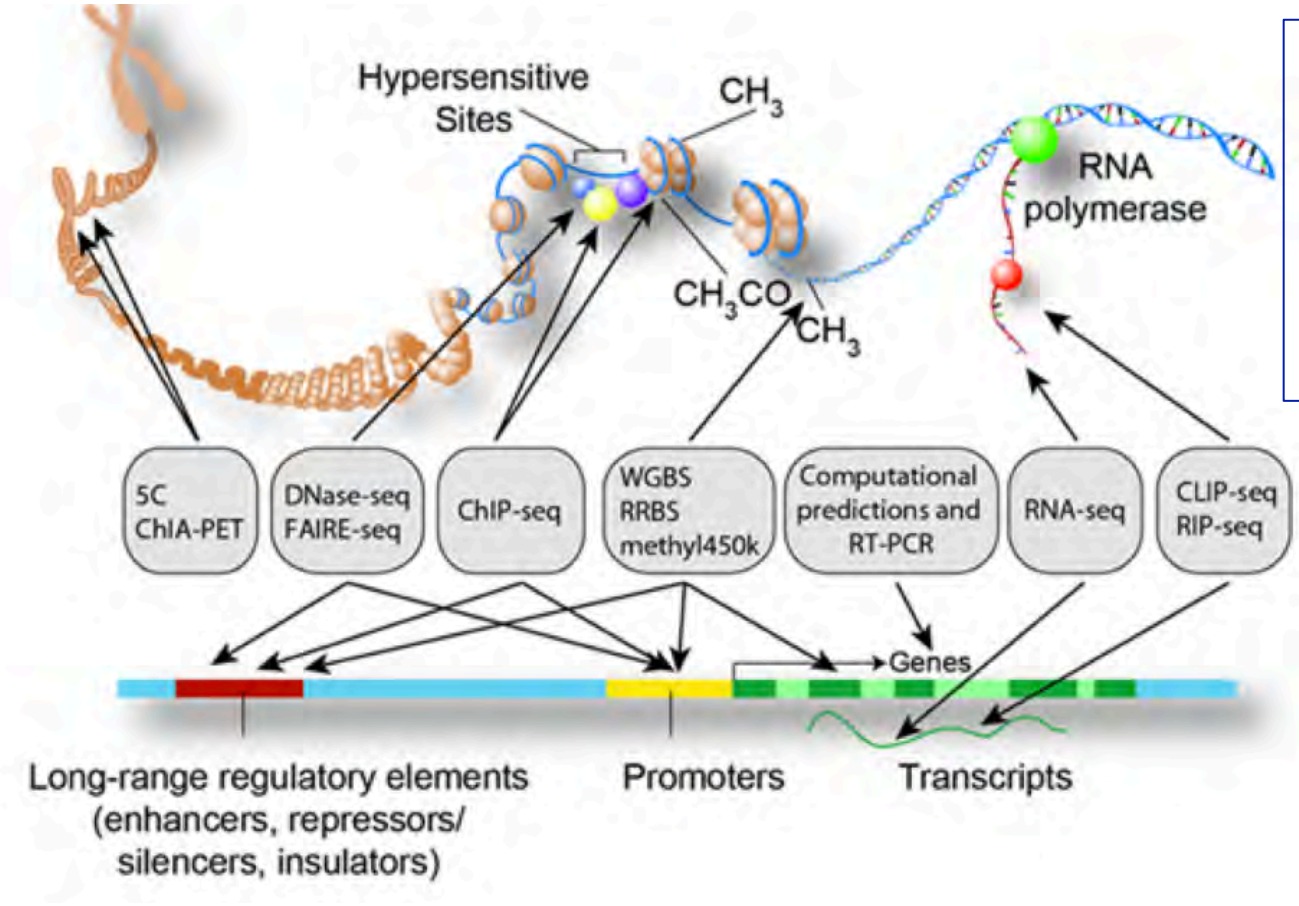

- 5C ChIA-PET: Chromatin Interaction Analysis by Paired-End Tag Sequencing
- FAIRE: Formaldehyde-Assisted Isolation of Regulatory Elements
- CLIP: Cross-linking immunoprecipitation

The ENCODE Project Consortium, Nature, 2012

Image credits: Darryl Leja & Michael Pazin (NHGRI), Ian Dunham (EBI)

"To build a comprehensive parts list of functional elements in the human genome, including elements that act at the protein and RNA levels, and regulatory elements that control cells and circumstances in which a gene is active".

Genomics, Epigenetics & Epigenomics

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- Genomics/Genetics vs. Epigenetics vs. Epigenomics

- Epigenetics is the study of changes in gene function that are mitotically and/or meiotically heritable and that do not entail a change in DNA sequence, i.e., **no change on DNA sequence.**

- Epigenomics is the genome-wide study of epigenetic elements and it deals with genomic maps of stable yet reprogrammable nuclear changes that control gene expression, **but not involved in DNA sequence alteration**.

- Transcriptomics: genome-wide/global study of mRNAs

DNA methylation, a small step of the DNA modification, but a giant step in the epigenommic reprogramming

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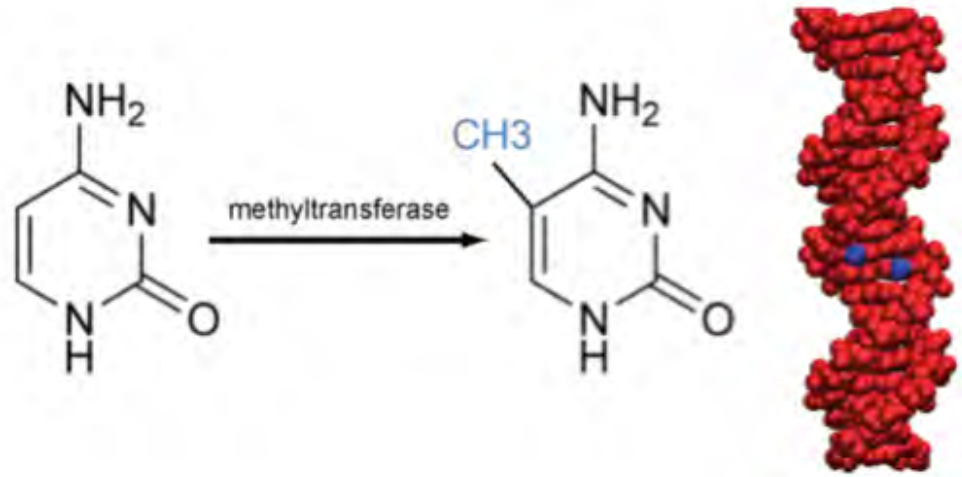

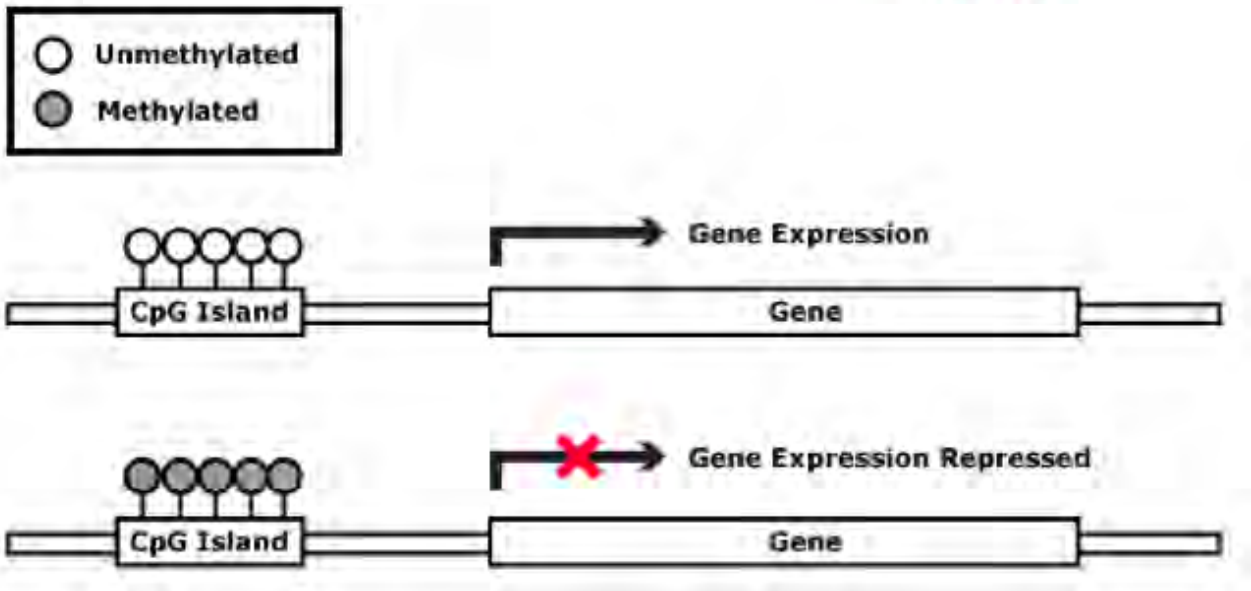

DNA methylome and human aging
Model Predictions: Multi-tissue Support

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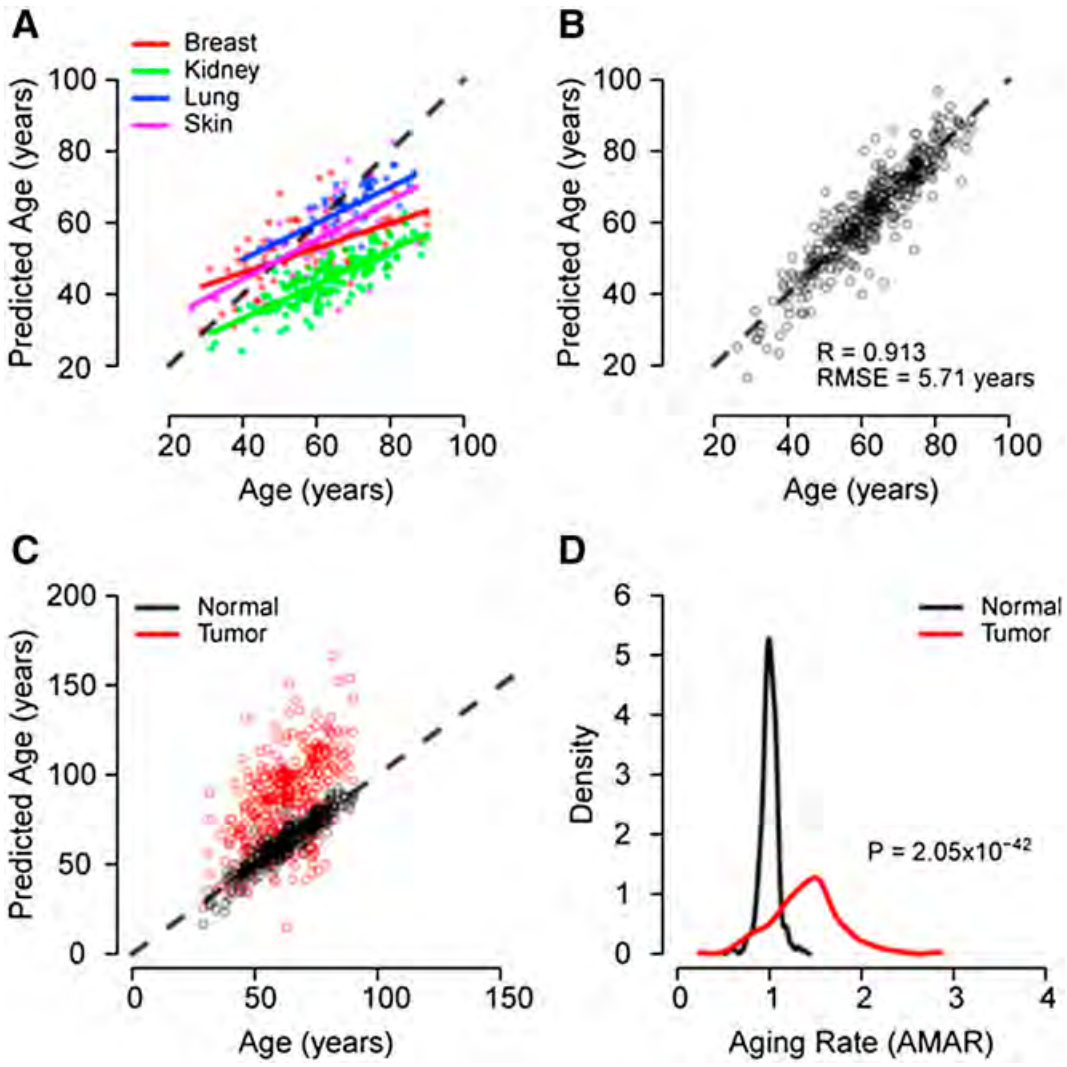

((A) Predictions of age made by the full aging model on the TCGA control samples. There is a high correlation between chronological and predicted age, but each tissue has a different linear intercept and slope.
(B) After adjusting the intercept and slope of each tissue, the error of the model is similar to that of the original whole-blood data.
(C) Age predictions made on matched normal and tumor samples from TCGA. Predictions are adjusted for the linear offset of the parent tissue (breast, kidney, lung, or skin).
(D) Tumor samples show a significant increase in AMAR.

Hannum, G et al. Molecular Cell 49(2): 359-67, 2012

DNA methylome and epigenetic clock
Horvath Clock

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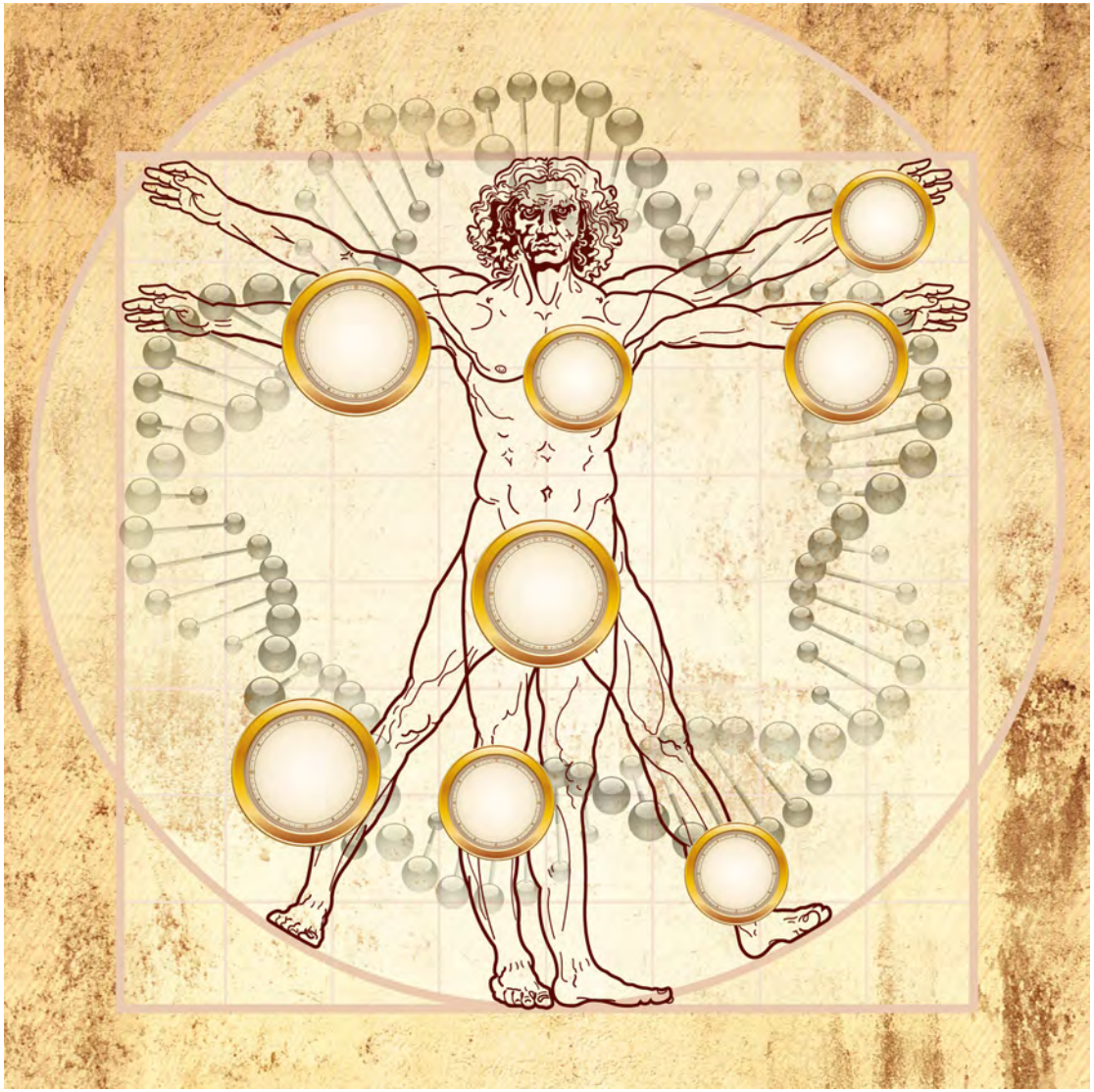

Horvath, S. Genome Biology 14(10):R115, 2013

DNAm age increases in all tissues as time passes; is accelerated in cancer

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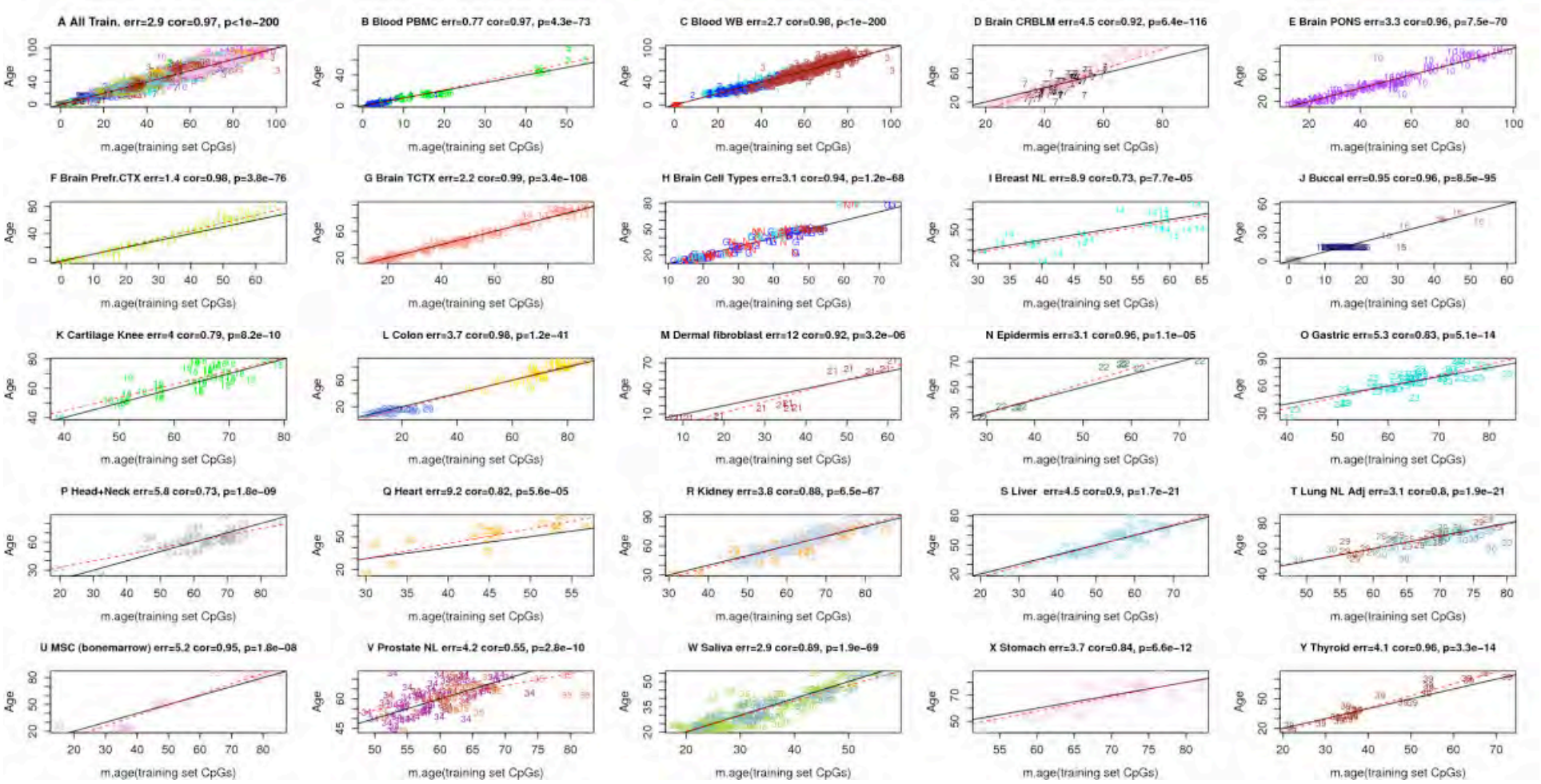

Horvath, S. Genome Biology 14(10):R115, 2013

DNAm Age and Chronological Age

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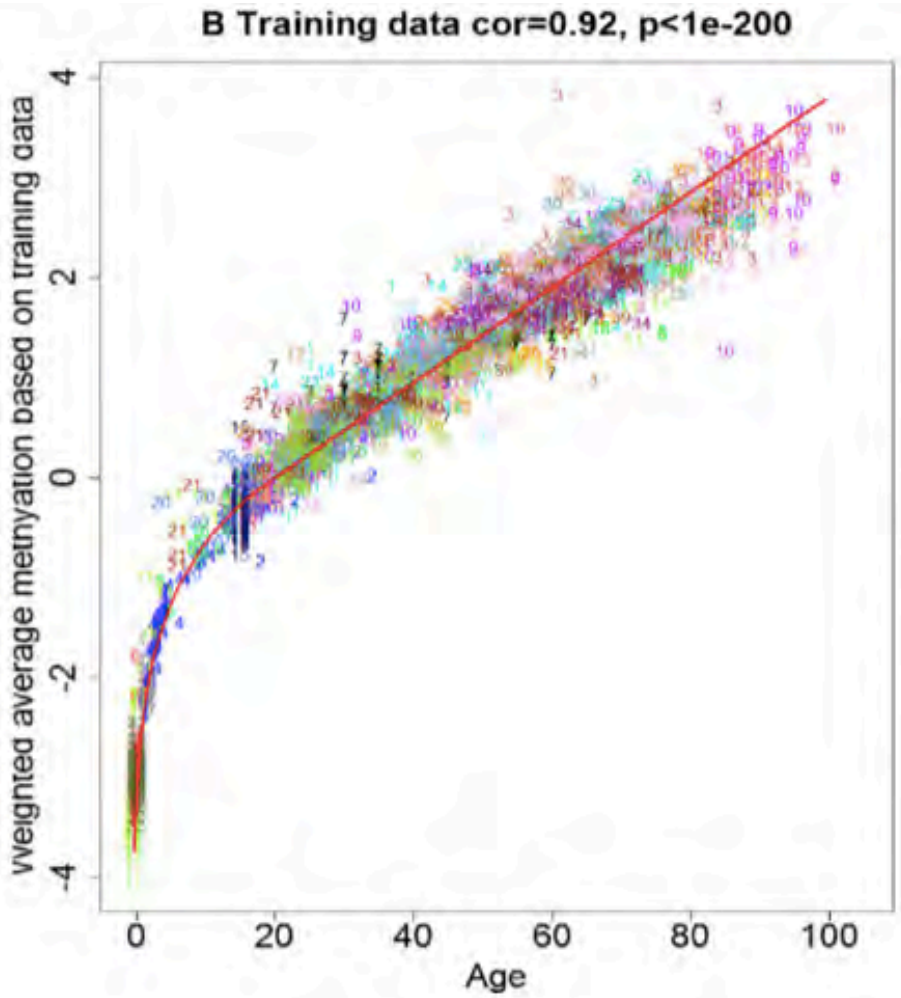

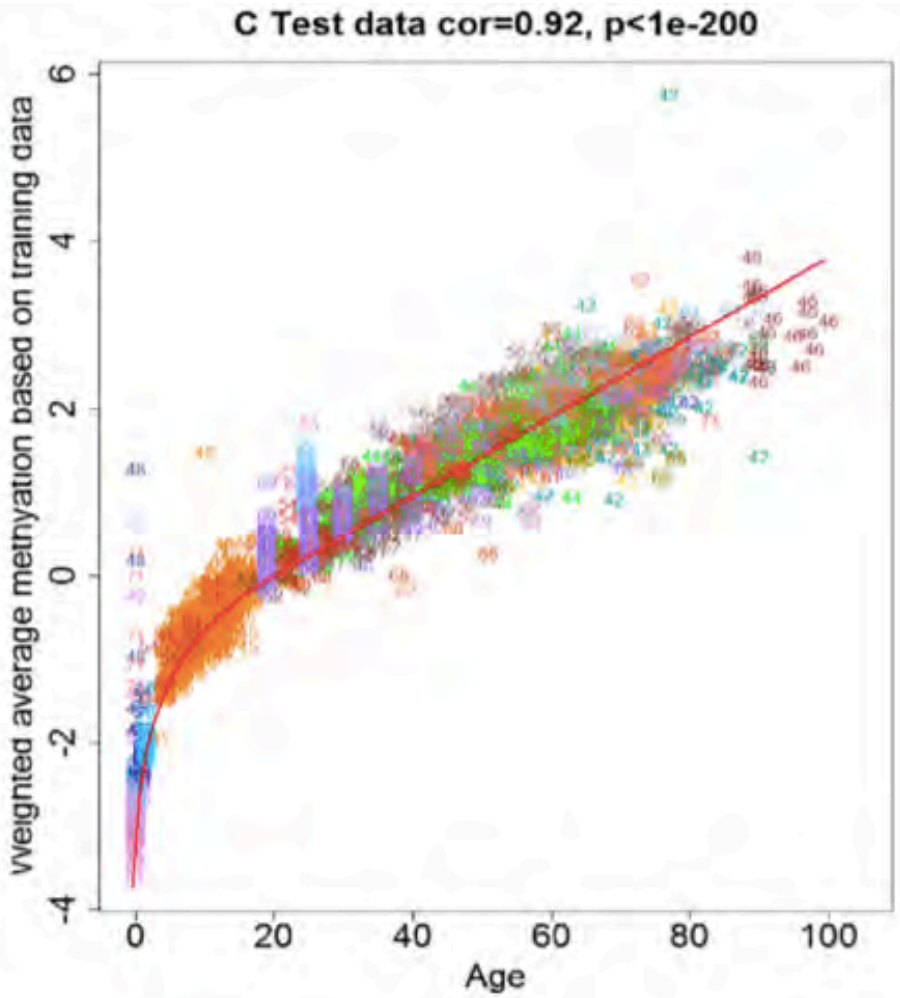

Horvath, S. Genome Biology 14(10):R115, 2013

Longer Lifespan of the CA Loma Linda SDAs

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Table 1. Life Expectancy of CA SDAs Compared to Others

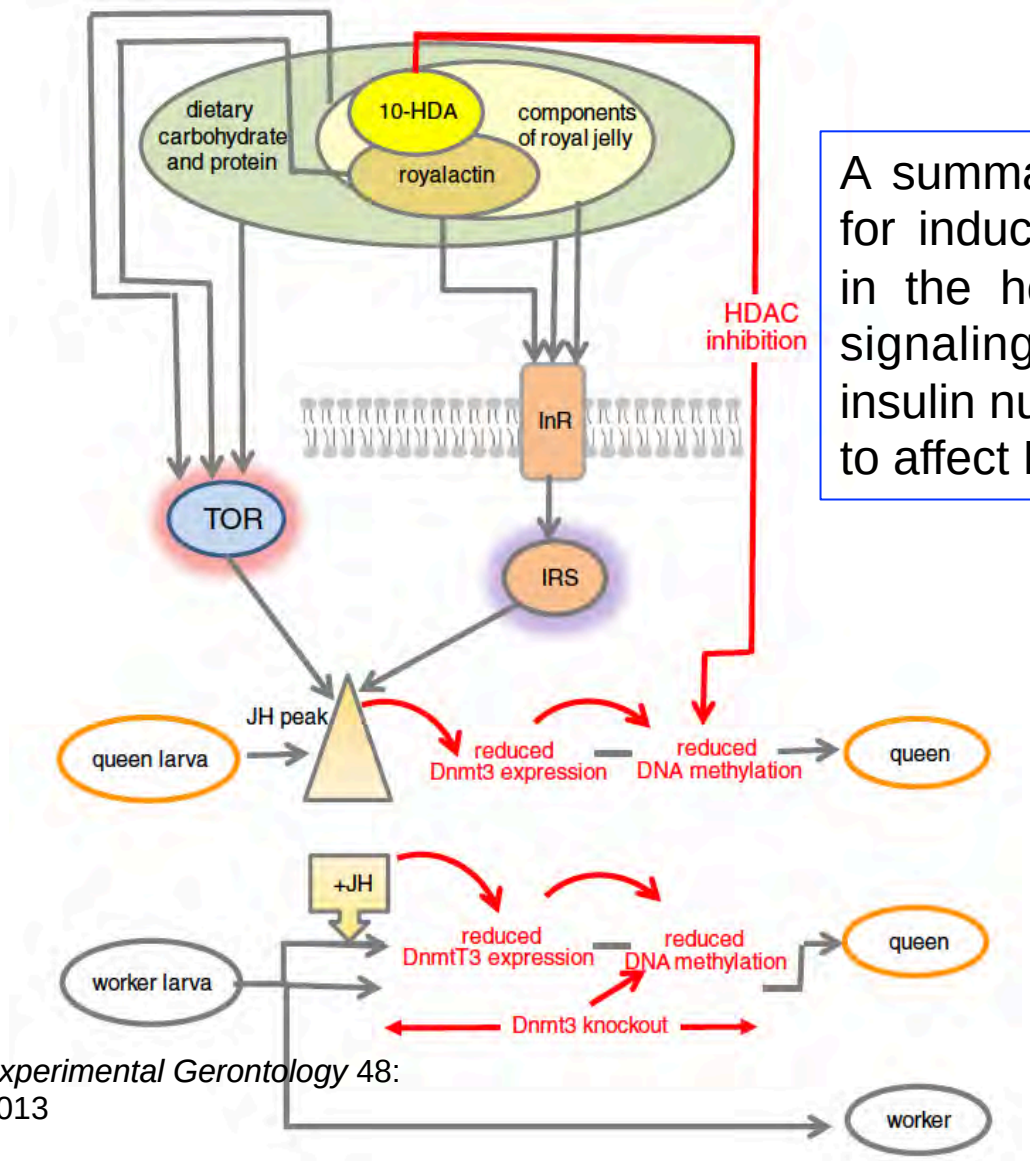
Country/Population	Men		Women	
	At Birth	At 65 YO	At Birth	At 65 YO
Australia (1990)	73.9	15.2	80.0	19.0
Canada (1985-1987)	73.0	14.9	79.7	19.1
Denmark (1989-1990)	72.0	14.1	77.7	17.9
Finland (1989)	70.9	13.8	78.9	17.7
Iceland (1989-1990)	75.7	16.1	80.3	19.3
Japan (1990)	75.9	16.2	81.8	19.9
New Zealand (1987-89)	71.6	14.1	77.6	17.8
Norway (1990)	73.4	14.6	79.8	18.6
UK (1985-1987)	71.9	13.4	77.6	17.3
United States (1990)	73.0	14.9	79.7	19.1
CA SDAs (1980-1988)	78.5	19.1	82.3	21.6
Vegetarians	80.2*	20.3	84.8*	22.6

10 extra years?!

Fraser et al. JAMA Internal Medicine, 2001


MEAT

Diet signaling through TOR and IGF1/insulin nutrient sensing pathways to affect DNA methylation



A summary of experimental evidence for induction of the queen phenotype in the honeybee as a result of diet signaling through TOR and IGF1/ insulin nutrient sensing pathways to affect DNA methylation.

JH — juvenile hormone; **TOR** — target of rapamycin; **HDAC** — histone deacetylase; **10-HDA** — 10-hydroxydecanoic acid.

Ford, D. *Experimental Gerontology* 48: 614–19, 2013

Characteristics of Selected Lifestyle of AHS2 Participants

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Selected Lifestyle Characteristics of Participants	
Smoking Status	%
Never smoked	80.06
Past smoker	18.79
Current smoker	1.15
Alcohol Use	
Never	59.43
Past use	33.82
Current use	6.75
Dietary Status	
Vegan 1	8.05
Lacto-ovo-veget. 2	28.14
Pesco-vegetarian 3	9.87
Semi-vegetarian4	5.64
Non-vegetarian 5	48.31
Meat Consumption	
Never6	39.11
<1 time/week	10.02
1-4 times/week	31.00
5+ times/week	19.87
Coffee Consumption	
Never	69.03
≤ 1 cup/day	22.48
2+ cups/day	8.49

Selected Lifestyle Characteristics of Participants	
Soy Milk Consumption	
Never	45.64
<1 time/week	5.52
1-4 times/week	22.95
5+ times/week	25.89
	Mean (Svgs/wk)
Cruciferous vegetables (zeroes = 4.5%)	4.27
Fish (zeroes = 50.7%)	0.84
Citrus fruits (zeroes = 11.2%)	4.20
Berries (zeroes = 13.8%)	1.75
All fruits	20.44
Legumes	4.69
Tomatoes/tomato prods	6.16

LLU AHS2: Diet-modulated Epigenomic Reprogramming in SDAs

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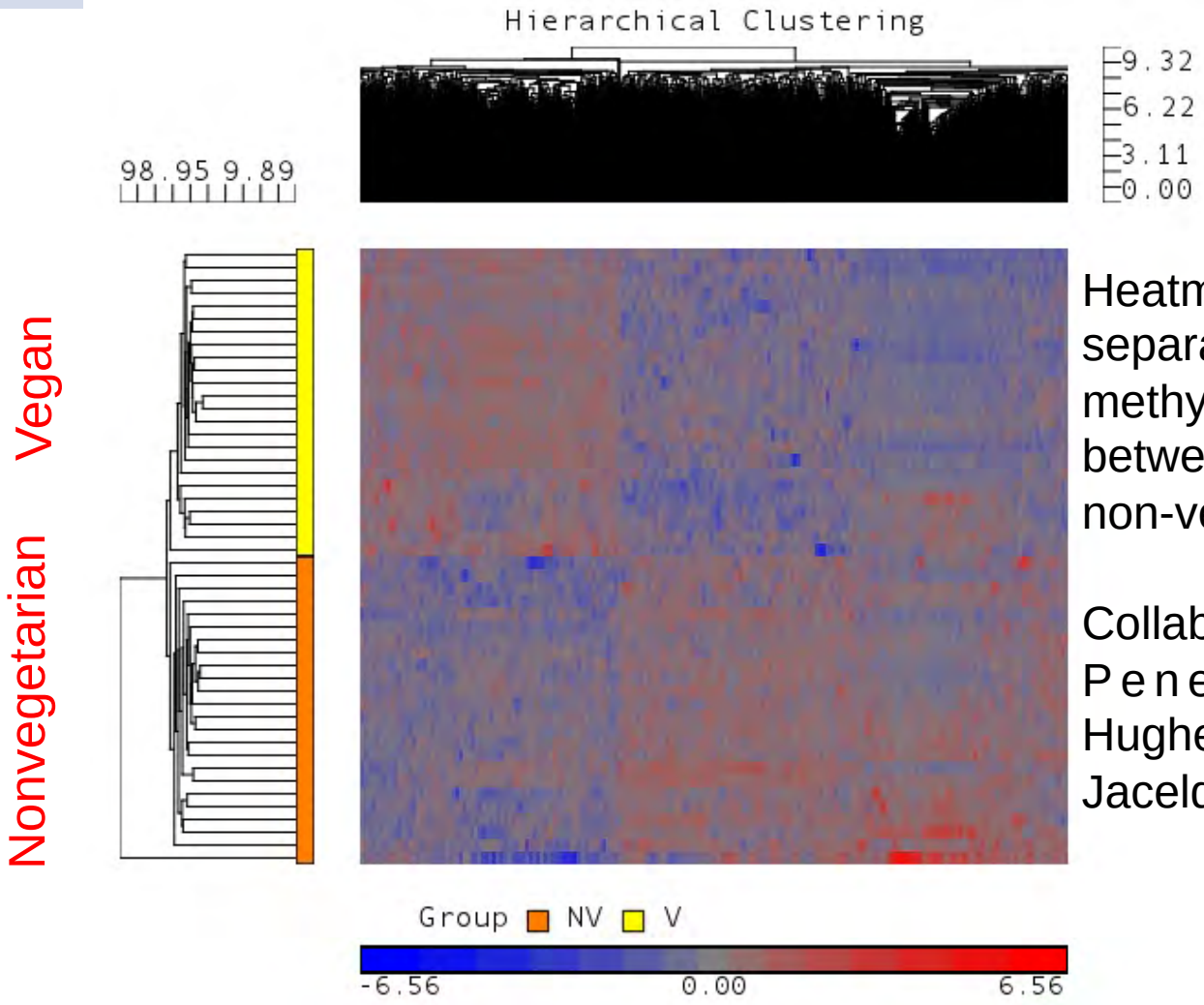
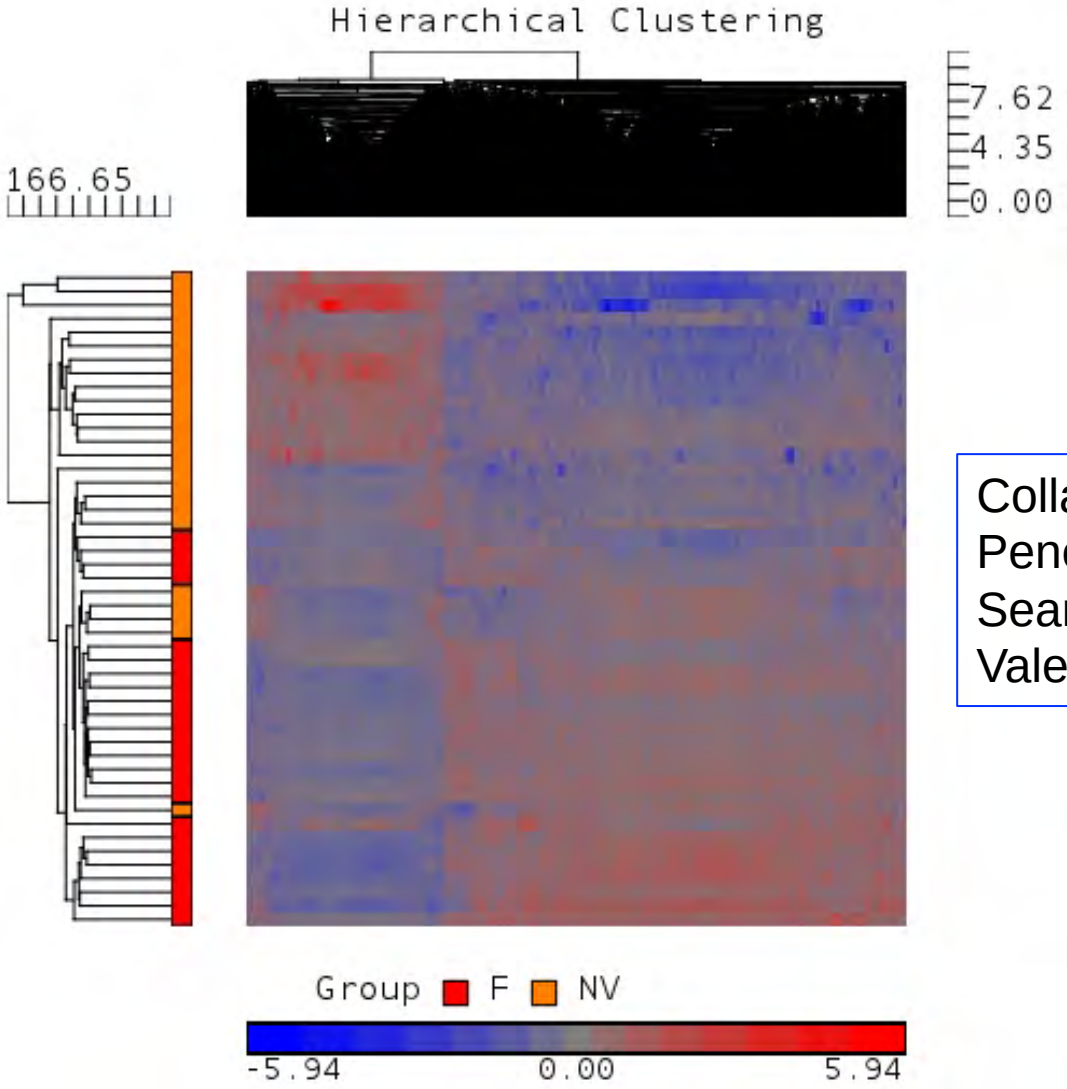


Heatmap showing distinct separation of DNA methylation pattern between vegans (V) and non-vegetarians (NV)

Collaborators: Gary Fraser, Penelope Duerksen-Hughes, Sean Chen, Karen Jaceldo, Valeri Filippov

Methylation status at individual sites is shown in X-axis, and subjects are listed top-to-bottom (Y-axis).

LLU AHS2: Diet-modulated epigenomic reprogramming



Collaborators: Gary Fraser, Penelope Duerksen-Hughes, Sean Chen, Karen Jaceldo, Valeri Filippov

Heat map showing distinct separation of DNA methylation pattern between pescetarians and non-vegetarians

Lifestyle/Diet-modulated Epigenomic Reprogramming

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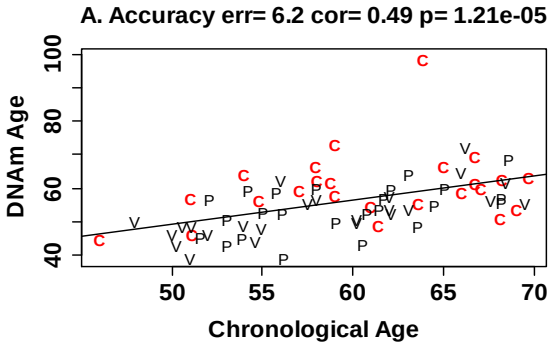

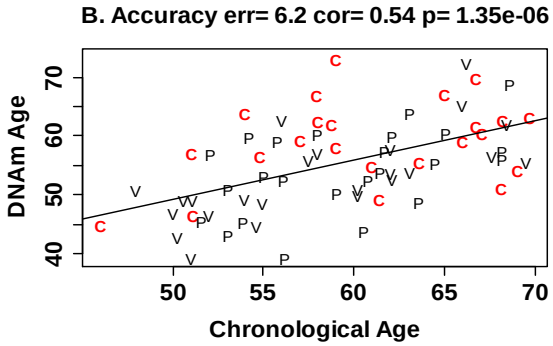

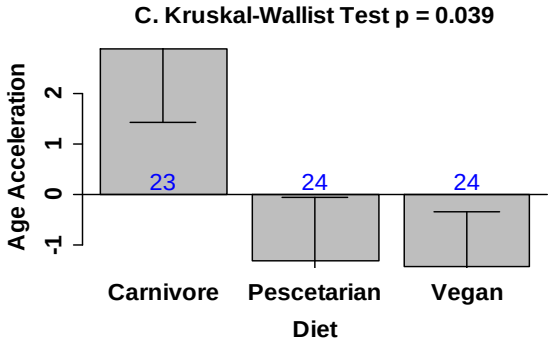

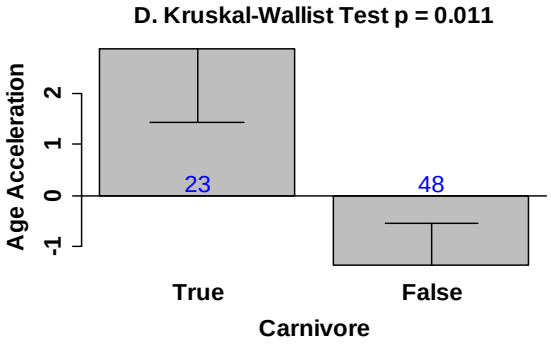

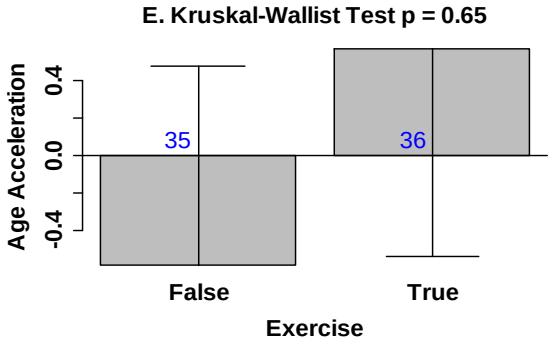

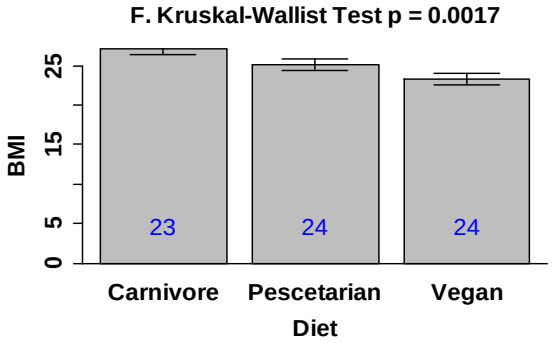

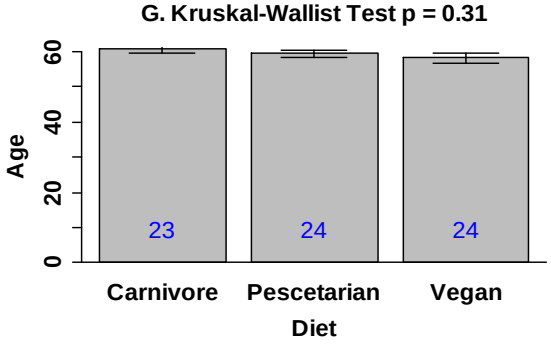

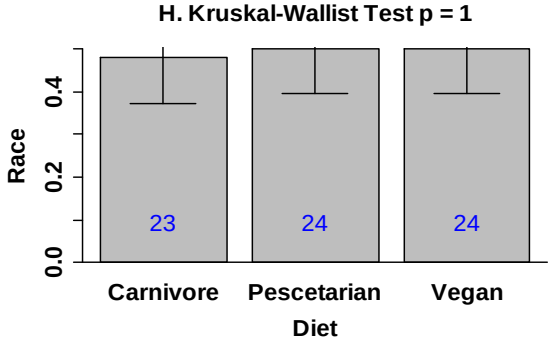

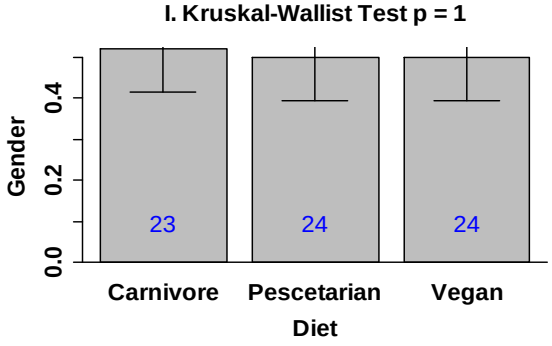

LLU AHS2: Diet-modulated Epigenetic Clocks and Longevity in SDAs

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Table 1. Δ_{age} Based on Hannum and Horvath DNAm age predictions

	Vegan M ± SD (N= 24)	Pescetarian M ± SD (N= 24)	Carnivore (NV) M ± SD (N= 24)
Chronological age (years)	58.1 ± 6.6	59.3 ± 5.3	60.9 ± 6.5
Hannum DNAm age (years)	61.0 ± 8.0	60.9 ± 6.9	66.7 ± 8.7
Hannum Δ_{age} (years)	2.9 ± 4.3	1.6 ± 5.4	5.7 ± 7.0
Horvath DNAm age (years)	53.3 ± 7.5	54.1 ± 7.1	61.0 ± 10.7
Horvath Δ_{age} (years)	-4.9 ± 5.4*	-5.2 ± 6.5*	0.1 ± 10.8

Δ_{age}: difference between DNAm predicted age and chronological age.

Study Design: A larger sample size is needed to validate the findings!

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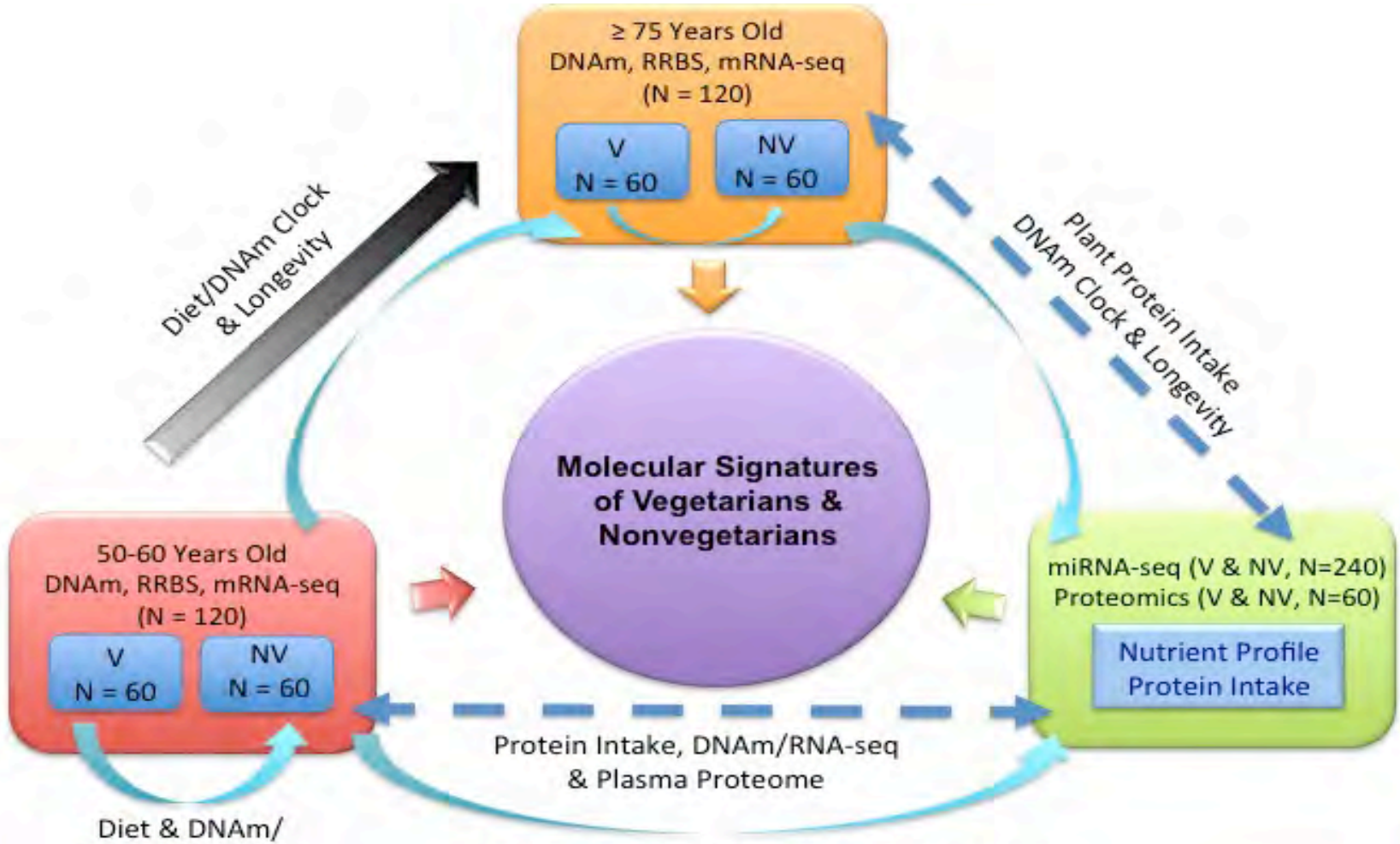

Fig. 5. Three-Dimension Study Design

V: Vegetarians/Vegans; NV: Non-Vegetarians