

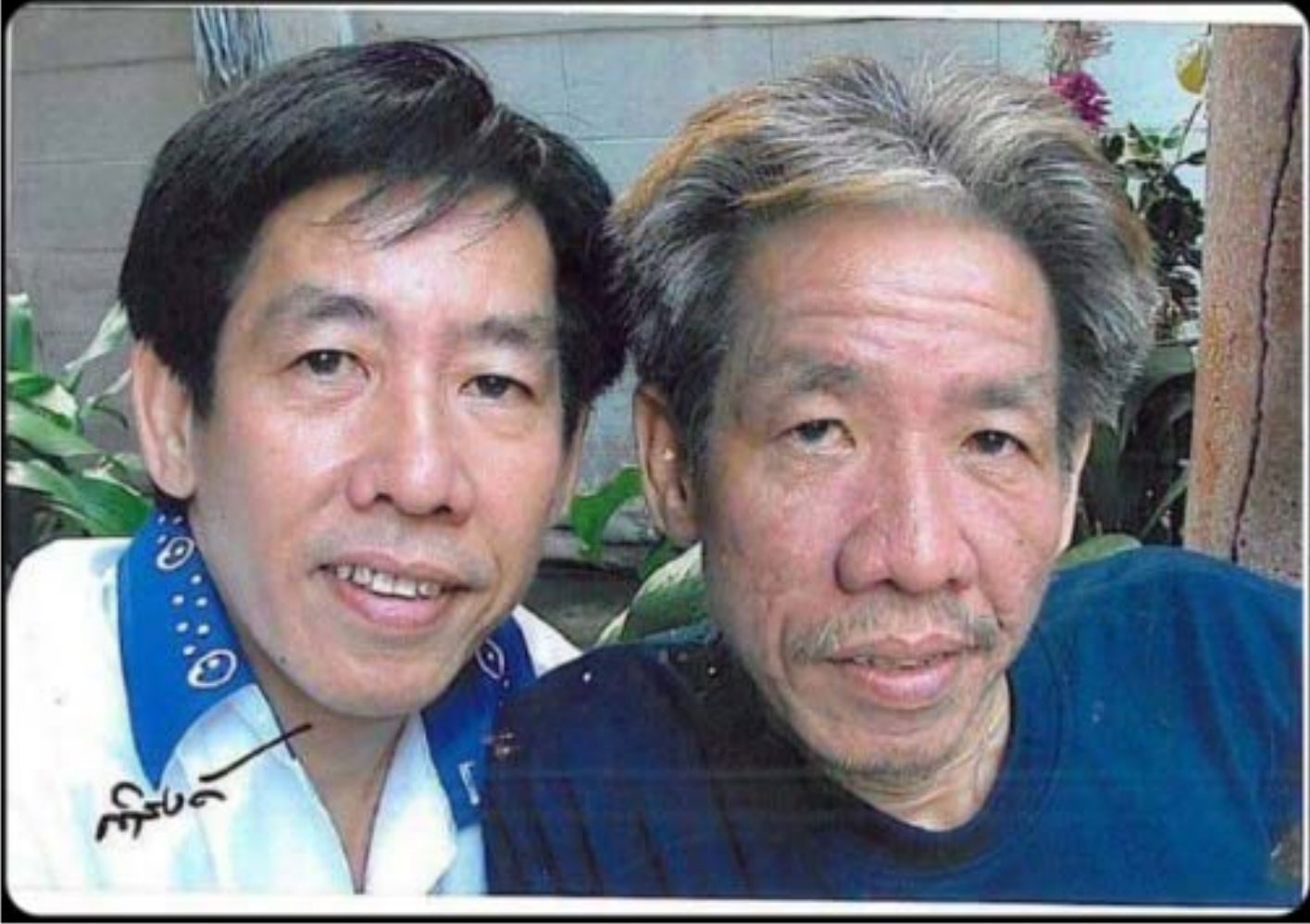
Genknowme

A couple of entrepreneurs'
journey



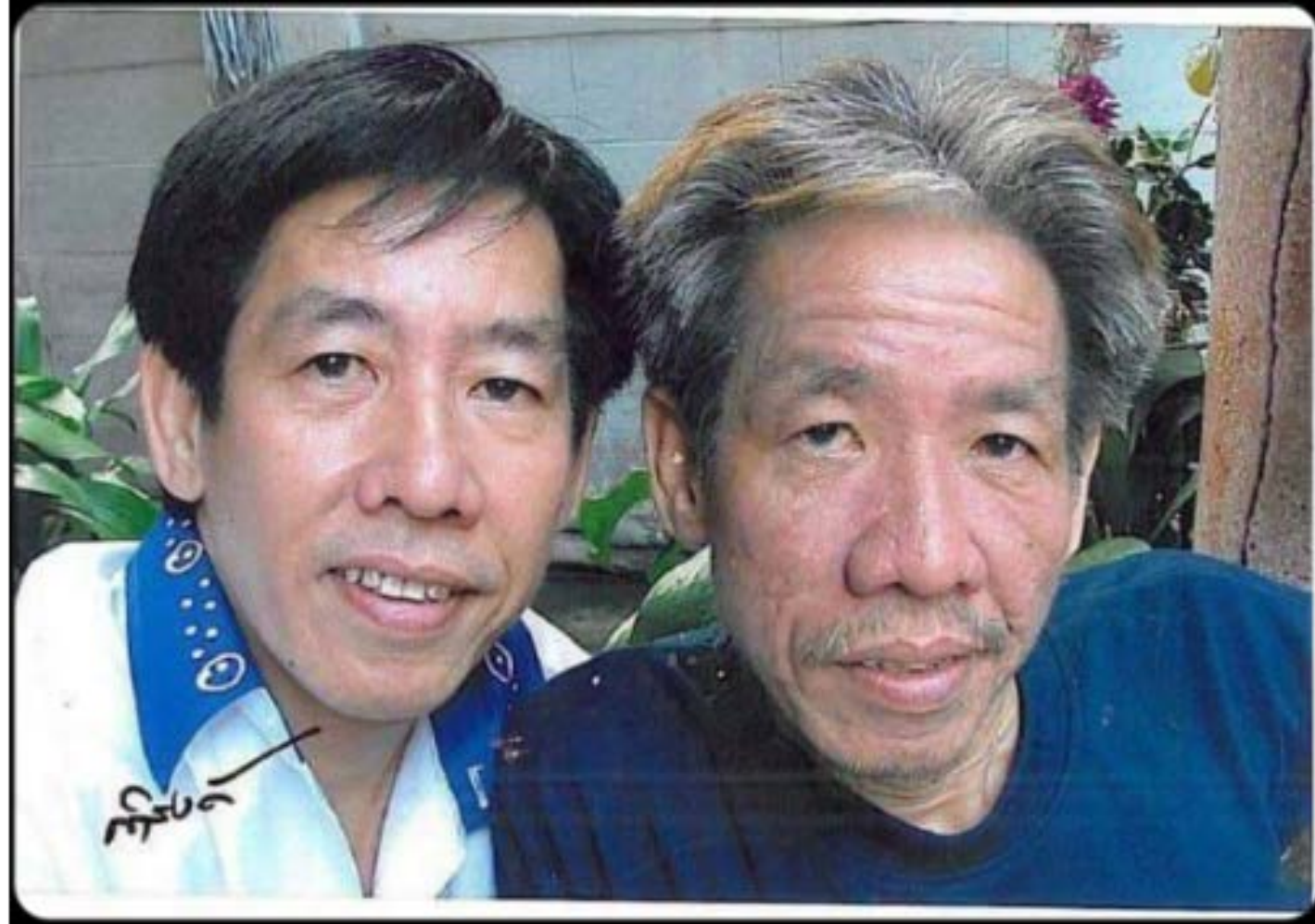
Sébastien Nusslé
Co-Founder, CEO
sebastien@genknowme.com
+41 79 460 20 69

Identical twins, different ...



Identical twins, different health status

Diet and air pollution



Diet



Smoker | Non Smoker



Sun exposure



BMI = 37, BMI = 23



Identical twins, different health status

Diet and air pollution



Diet



Smoker | Non Smoker



Sun exposure



BMI = 37, BMI = 23



EPIC GENETICS

Lets start in 2008...

PhD in Lausanne in evolutionary biology

Unil

UNIL | Université de Lausanne



Evolutionary Applications ISSN 1752-4571

ORIGINAL ARTICLE

**Fishery-induced selection on an Alpine whitefish:
quantifying genetic and environmental effects on
individual growth rate**

Sébastien Nusslé, Christophe N. Bornand and Claus Wedekind

Department of Ecology and Evolution, University of Lausanne, Lausanne, Switzerland

$$R = G + E + G \times E$$

- Response to selection (change through time)
- Genes
- Environment
- Gene-environment interactions

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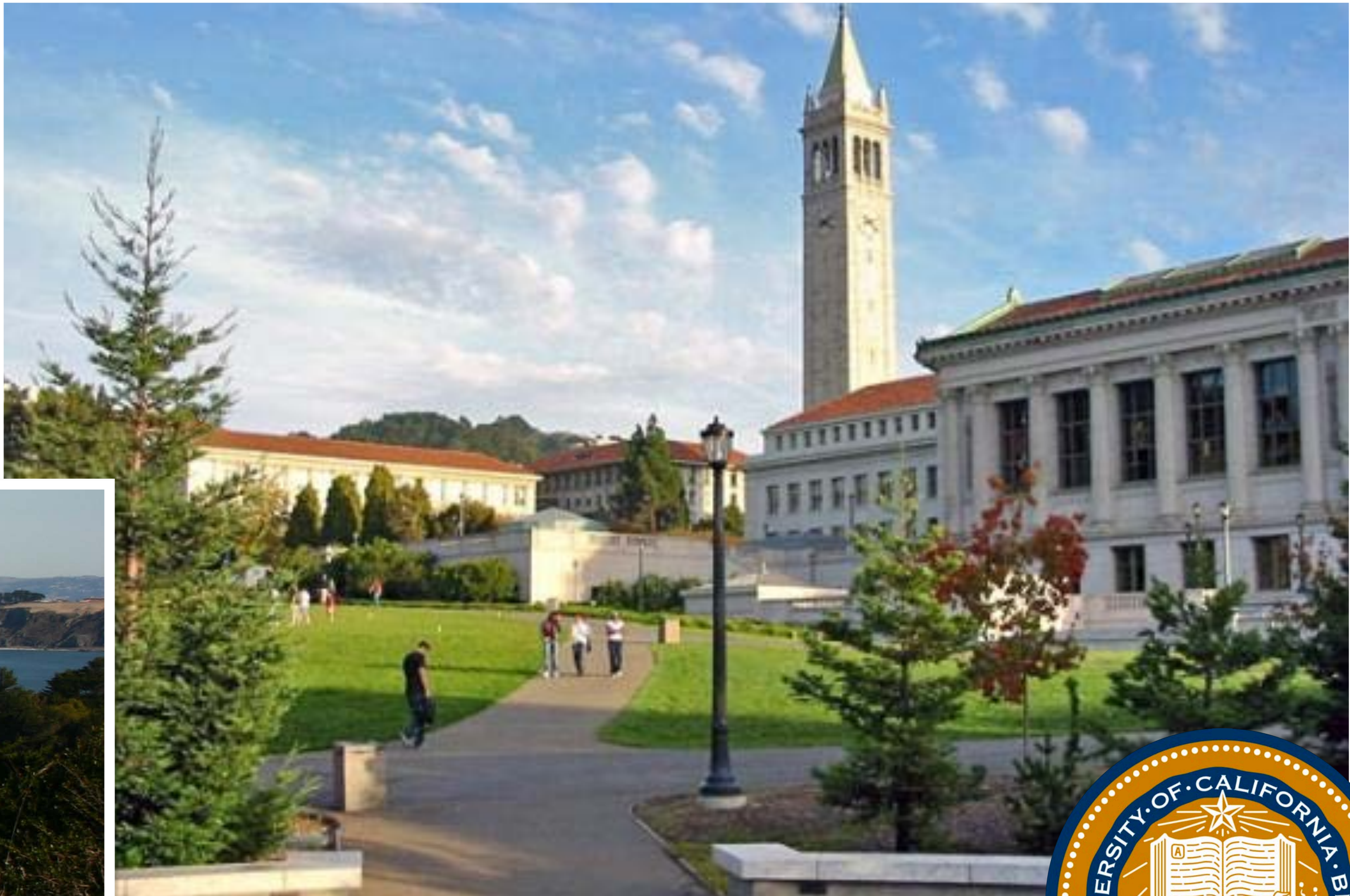
Department of Ecology and Evolution, University of Lausanne, Lausanne, Switzerland

$$R = G + E + \cancel{G \times E}$$

- Response to selection (change through time)
- Genes (22'000 genes)
- Environment (hundreds of parameters)
- Gene-environment interactions

Moving to California in 2013

Postdoc with an FNS grant



First steps in epigenetic measurements

Everything leaves a trace...



MD in prevention and public health
Specialist in chronic disease and epigenetics

RESEARCH PAPER

Epigenetics 10:12, 1166–1176; December 2015; © 2015 Taylor & Francis Group, LLC

Periconceptional folate consumption is associated with neonatal DNA methylation modifications in neural crest regulatory and cancer development genes

Semira Gonseth, MD^{1,*}, Ritu Roy, MA², E Andres Houseman, ScD³, Adam J de Smith, PhD¹, Mi Zhou, MD¹, Seung-Tae Lee, MD, PhD⁴, Sébastien Nusslé, PhD⁵, Amanda W Singer, PhD⁶, Margaret R Wrensch, PhD⁷, Catherine Metayer, MD, PhD⁶, and Joseph L Wiemels, PhD¹

¹Department of Epidemiology and Biostatistics; Laboratory for Molecular Epidemiology; University of California; San Francisco, CA, USA; ²Computational Biology Core; HDF Comprehensive Cancer Center; University of California; San Francisco, CA, USA; ³College of Public Health and Human Sciences; Oregon State University; Corvallis, OR, USA;

⁴Department of Laboratory Medicine; Yonsei University College of Medicine; Seoul, Republic of Korea; ⁵Department of Environmental Science; Policy & Management; University of California; Berkeley, CA, USA; ⁶School of Public Health; University of California; Berkeley, CA, USA;

⁷Department of Neurological Surgery; University of California; San Francisco, CA, USA

Keywords: cancer prevention, developmental origin of health and disease, DNA methylation, epigenetics, folate, neural tube defects
Abbreviations: β , regression coefficient; CCLS, California Childhood Leukemia Study; DFE, dietary folate equivalents; DMR, differentially methylated region; GEO, gene expression omnibus; IQR, inter-quartile range; LEF1, lymphoid enhancer-binding factor 1; MAZ, MYC-associated zinc finger protein; NTD, neural tube defect; TCF3, pre-B cell transcription factor 3



University of California
San Francisco

Identical twins, different health status

Diet and air pollution



Diet



Smoker | Non Smoker



Sun exposure



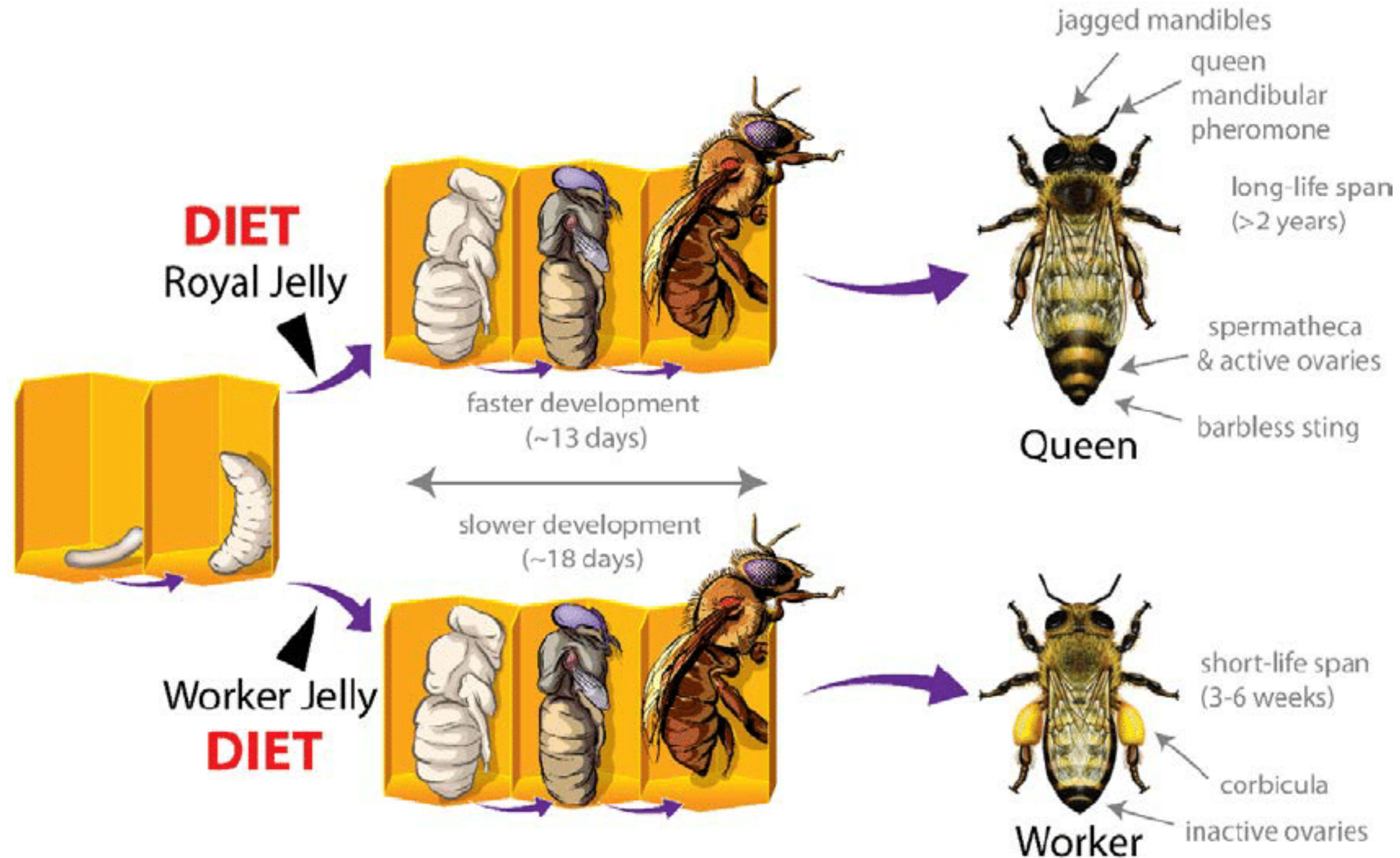
BMI = 37, BMI = 23



EPIC GENETICS

The epigenetics of queen-bee determination

Queens and workers have the same genes, but queens get royal jelly



Cridge, A.G. et al. (2015) What Do Studies of Insect Polyphenisms Tell Us about Nutritionally-Triggered Epigenomic Changes and Their Consequences? *Nutrients*, 7: 1787-1797.

Chittka, A. & Chittka L. (2010) Epigenetics of royalty. *PLoS biology*, 8(11): e1000532

Epigenetic landscape

Conrad Waddington (1905 - 1975) - invented the term epigenetic in 1942

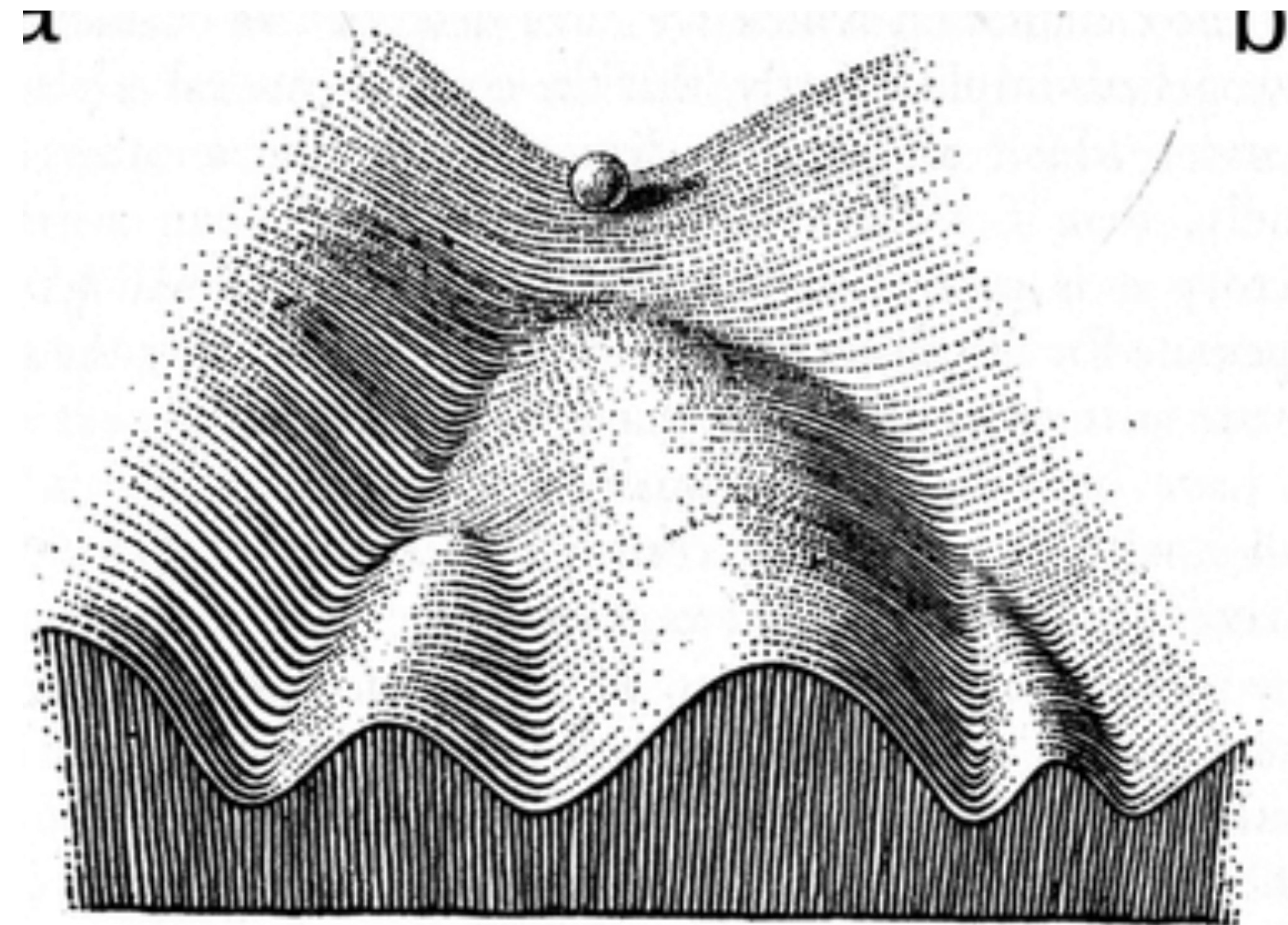
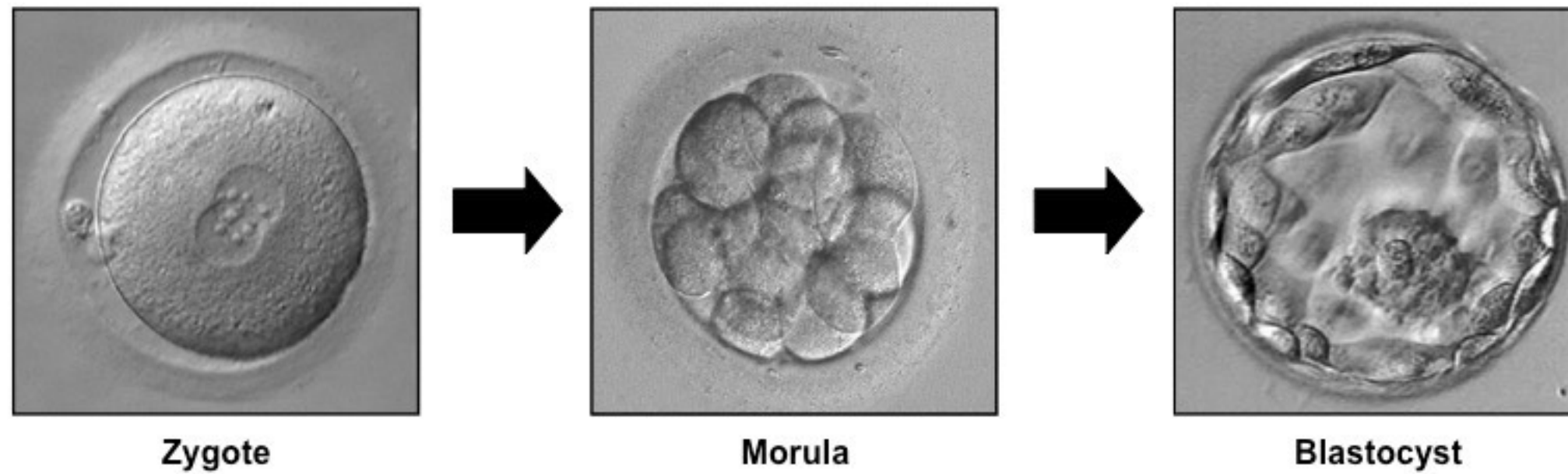
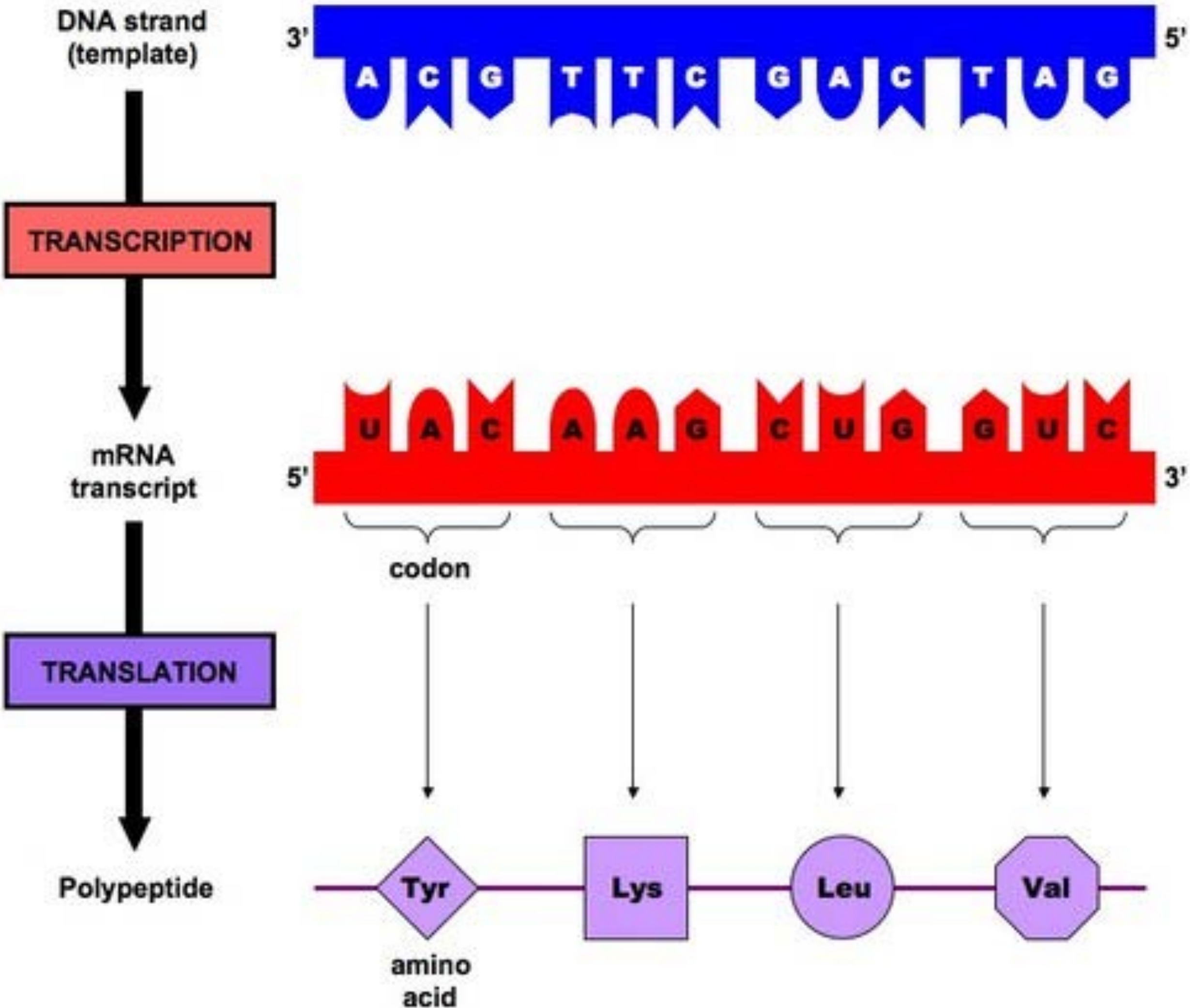
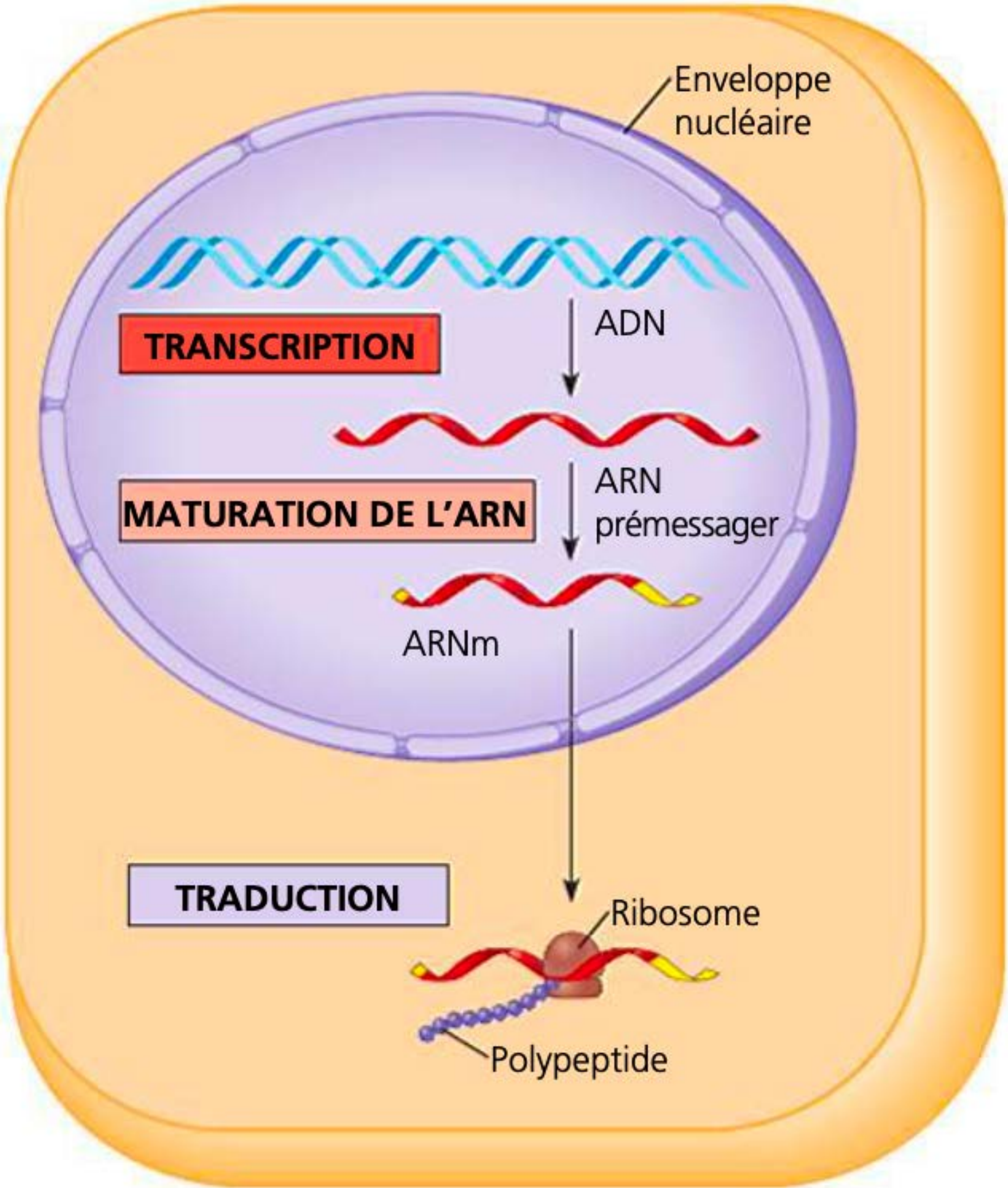


FIGURE 4

Part of an Epigenetic Landscape. The path followed by the ball, as it rolls down towards the spectator, corresponds to the developmental history of a particular part of the egg. There is first an alternative, towards the right or the left. Along the former path, a second alternative is offered; along the path to the left, the main channel continues leftwards, but there is an alternative path which, however, can only be reached over a threshold.

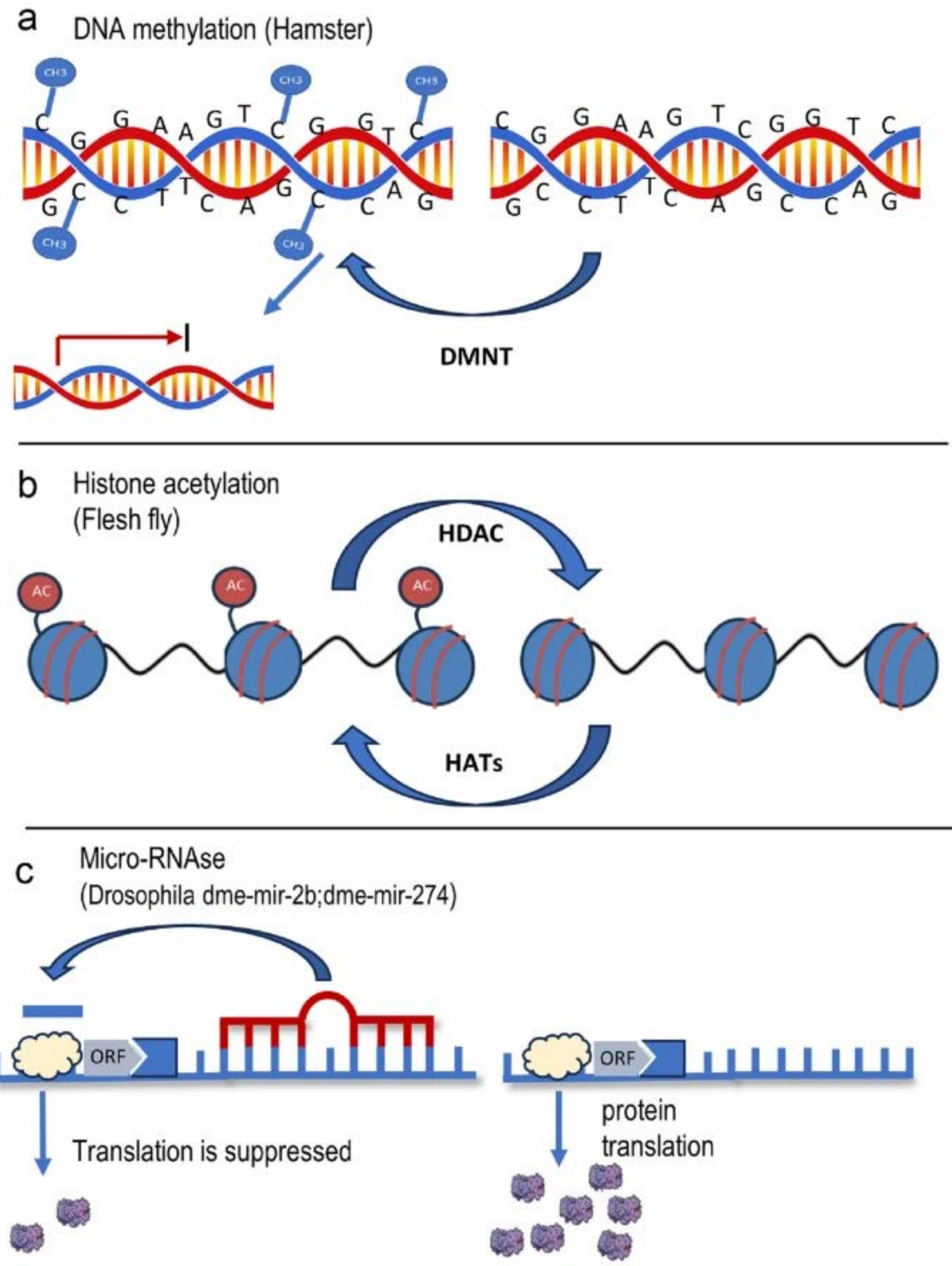
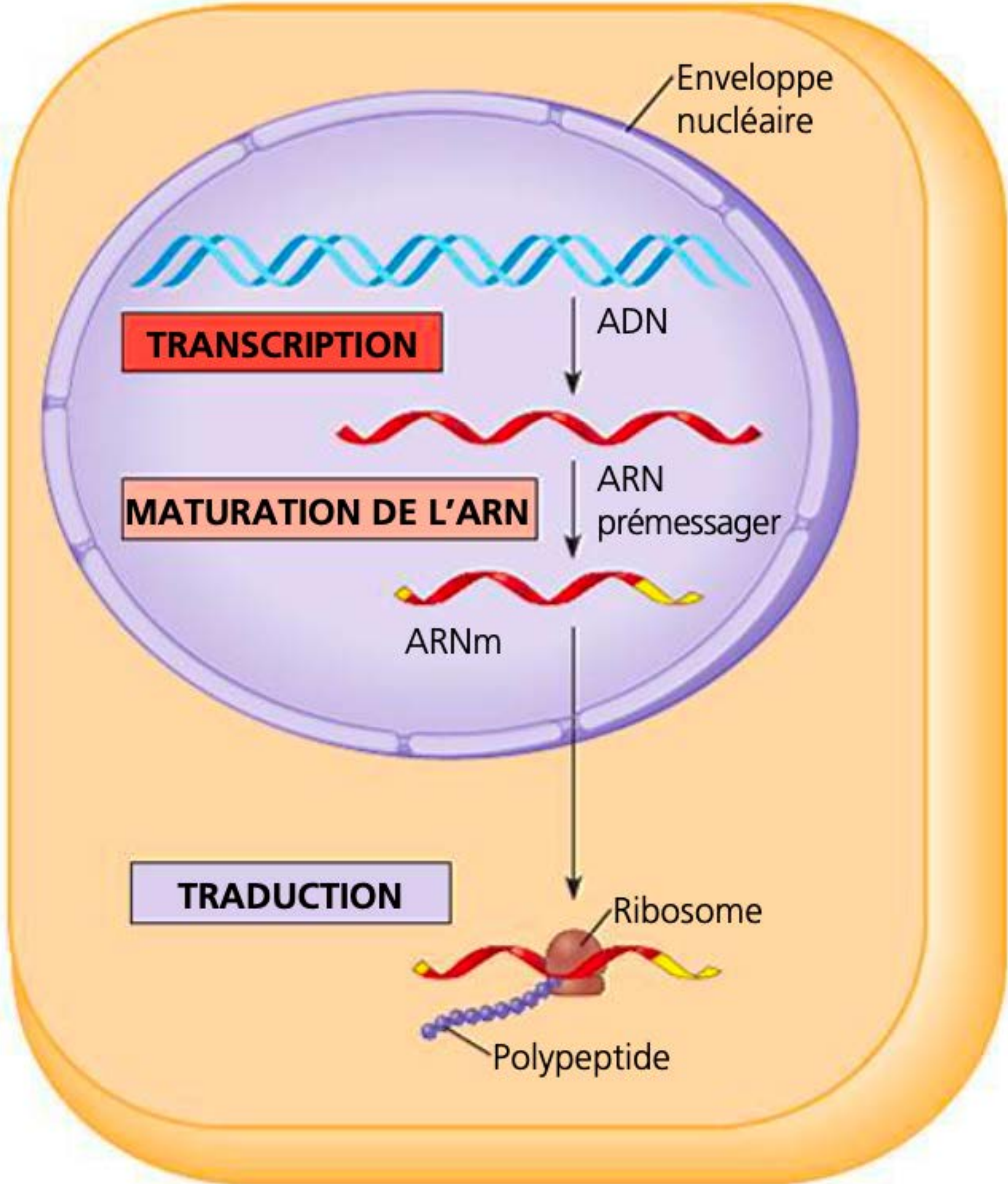
Reminder

Basics of genetics



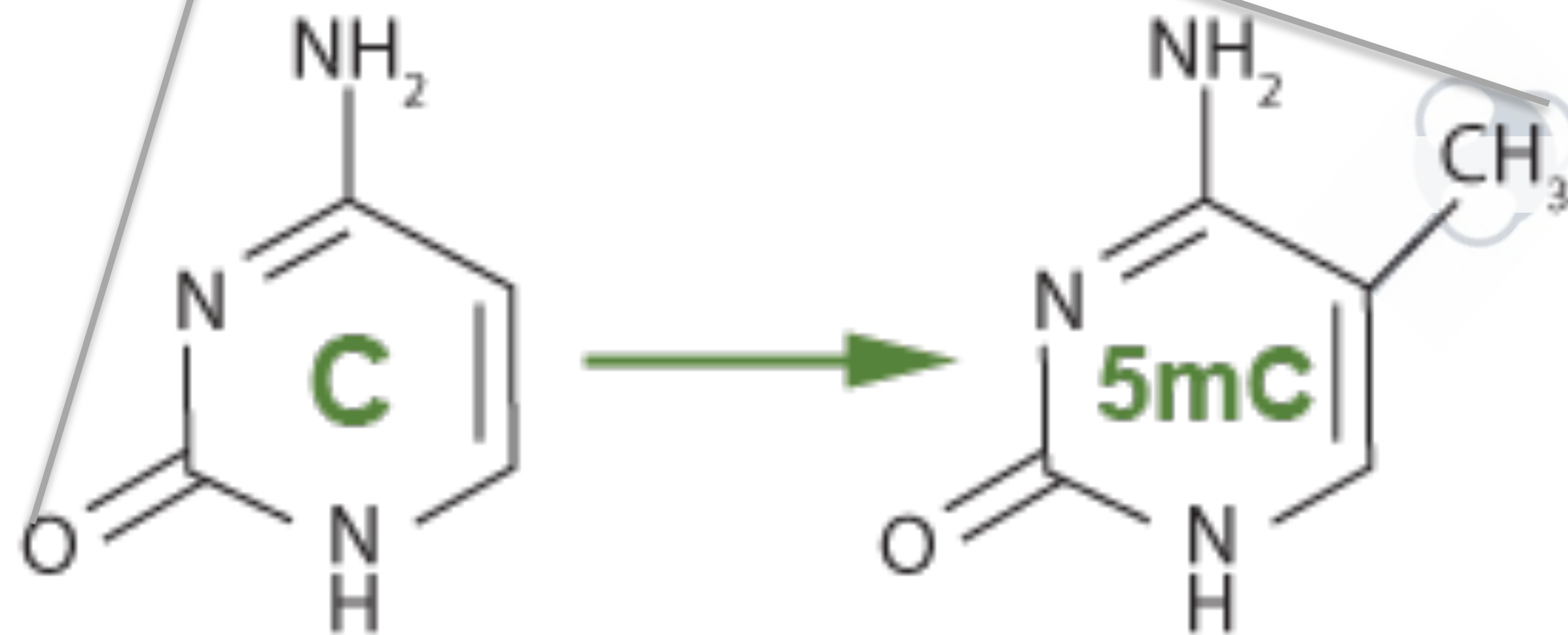
Reminder

Basics of genetics



Epigenetic processes : DNA methylation

Most proximal process

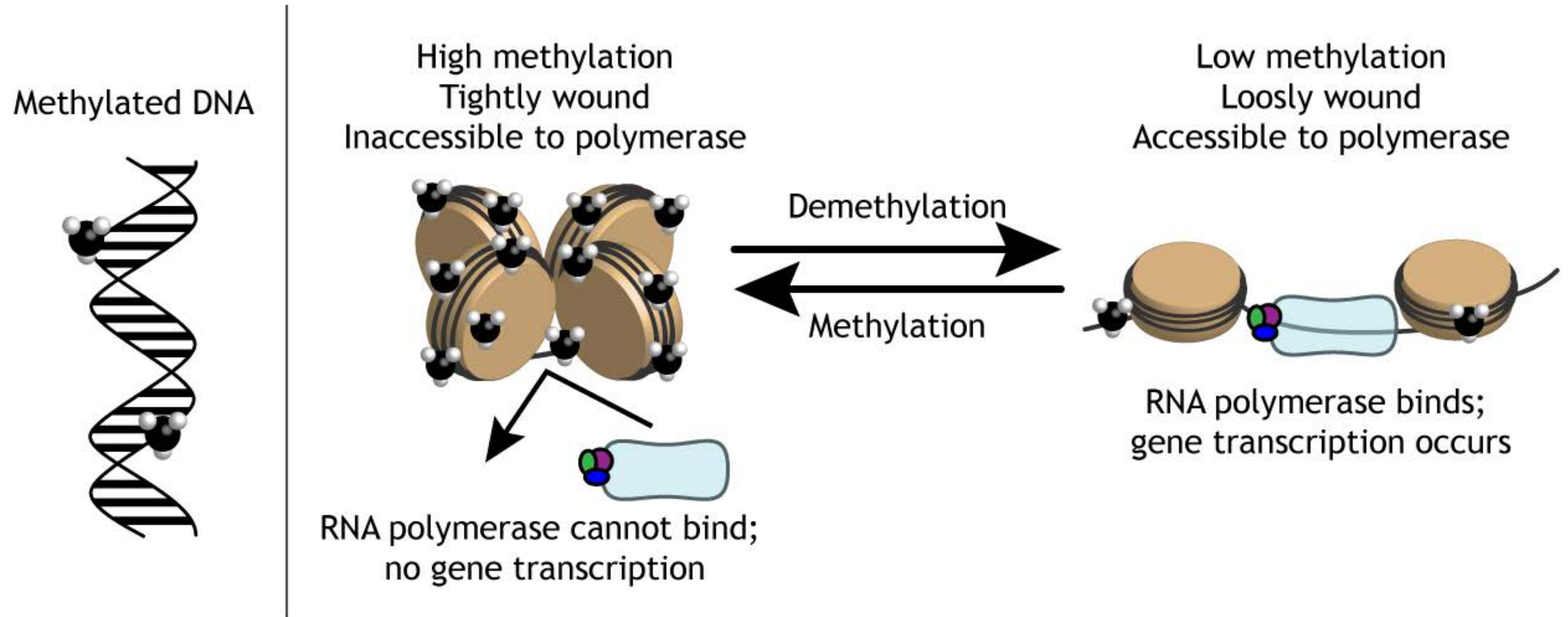


Unmethylated
cytosine

5-methylated
cytosine

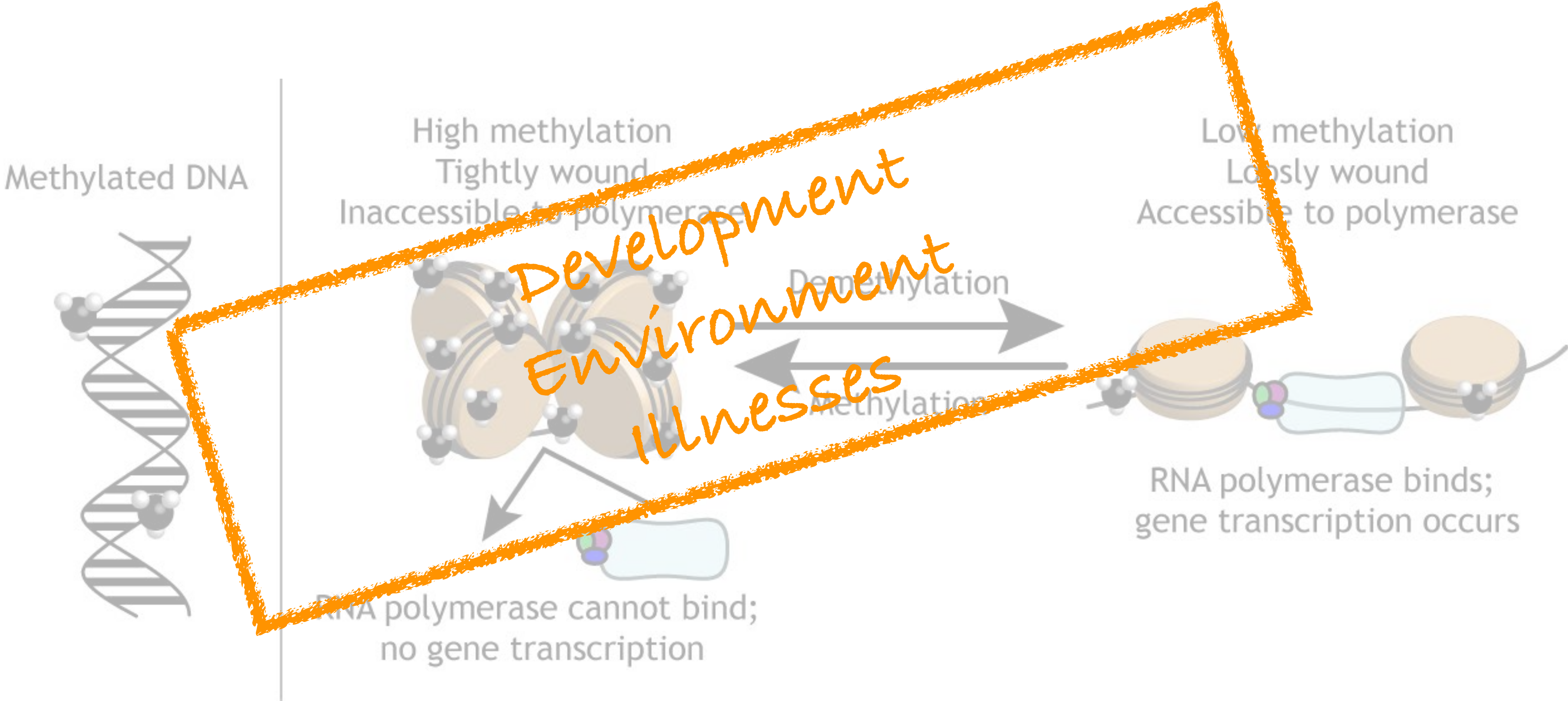
Epigenetic processes : DNA methylation

Most proximal process



Epigenetic processes : DNA methylation

Most proximal process



Foundations of Neurology. By Casey Henley. Libraries Michigan State University.

Early-life deficiencies have profound late-life epigenetic consequences

Dutch hunger winter study (Nov. 1944 - May 1945)

- Dutch famine organized by Nazis
- Cohort : 2400 children born between Nov. 1943 and Mar. 1947
- Metabolic disorders in adults
 - Obesity
 - Cardiovascular diseases
 - Preference for fatty food
 - Cancer, mental health and neurodegenerative disease

The Dutch Hunger Winter and the developmental origins of health and disease

Laura C. Schulz¹

Department of Obstetrics, Gynecology and Women's Health, University of Missouri, Columbia, MO 65211

In the early 1980s, David Barker and others noted a paradox: although overall rates of cardiovascular disease increase with rising national prosperity, the least prosperous residents of a wealthy nation suffer the highest rates. He and others proposed over a series of studies that an adverse fetal environment followed by plentiful food in adulthood may be a recipe for adult chronic disease, a claim referred to as the Barker Hypothesis. These studies generally correlated birth weight and other infant parameters to the incidence of adult disease. Detractors, including an editorial in *BMJ* in 1995, complained that "[e]arly nutrition is inferred indirectly from fetal and infant growth, and fetal growth especially is a doubtful surrogate measure" (1). Most of the epidemiological studies were also vulnerable to confounding factors, particularly social class, that influence

during mid- to late gestation had babies with significantly reduced birth weights. Babies whose mothers were exposed only during early gestation had normal birth weights; however, they grew up to have higher rates of obesity than those born before and after the war and higher rates than those exposed during mid- to late gestation (3). Thus, although reduced birth weight is the most easily measured proxy for intrauterine deprivation, it is not

Adverse fetal environment followed by plentiful food in adulthood may be a recipe for adult chronic disease.

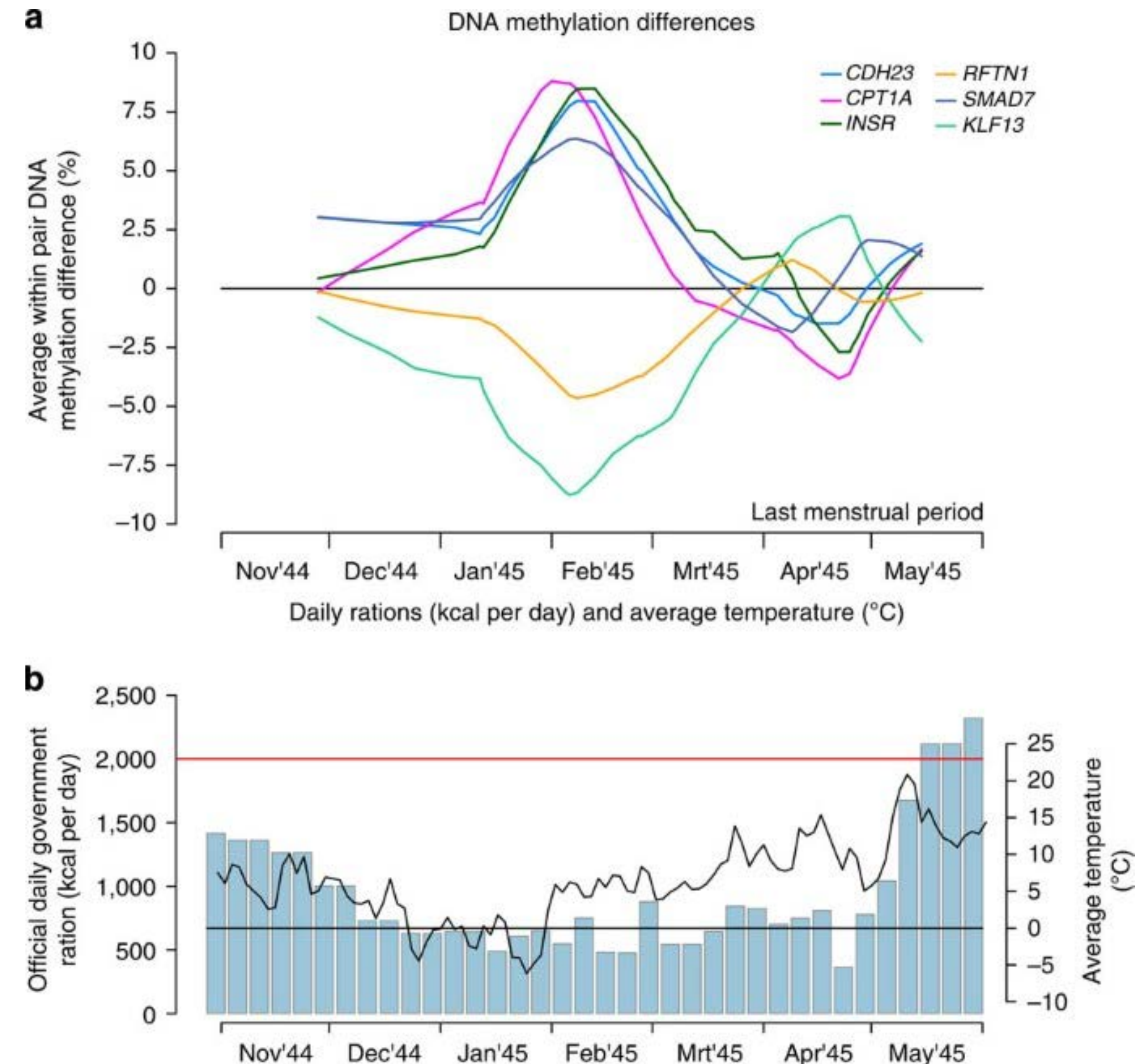
formation is almost impossible to glean from most epidemiological studies. Hence, the Dutch Hunger Winter study is important because of its ability to provide insight into how a starvation diet during limited periods of gestation influences subsequent health of the offspring.

Interestingly, although the importance of exposure during early gestation was identified nearly 35 y ago, the reason that this period is important is still not fully understood. As discussed by Rooij et al. (2), CNS structures are formed in the first trimester of pregnancy, and changes underlying mental illness, altered appetite regulation centers, or even later declines in cognitive function likely occur during this period. Others have shown that alterations in placental growth, which outstrip that of the fetus in early gestation, are programmed by food restriction (6, 7). Because the placenta is responsible for

Early-life deficiencies have profound late-life epigenetic consequences

Dutch hunger winter study (Nov. 1944 - May 1945)

- Dutch famine organized by Nazis
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 - Preference for fatty food
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Fast-forward to 2017

Entrepreneurial spark...



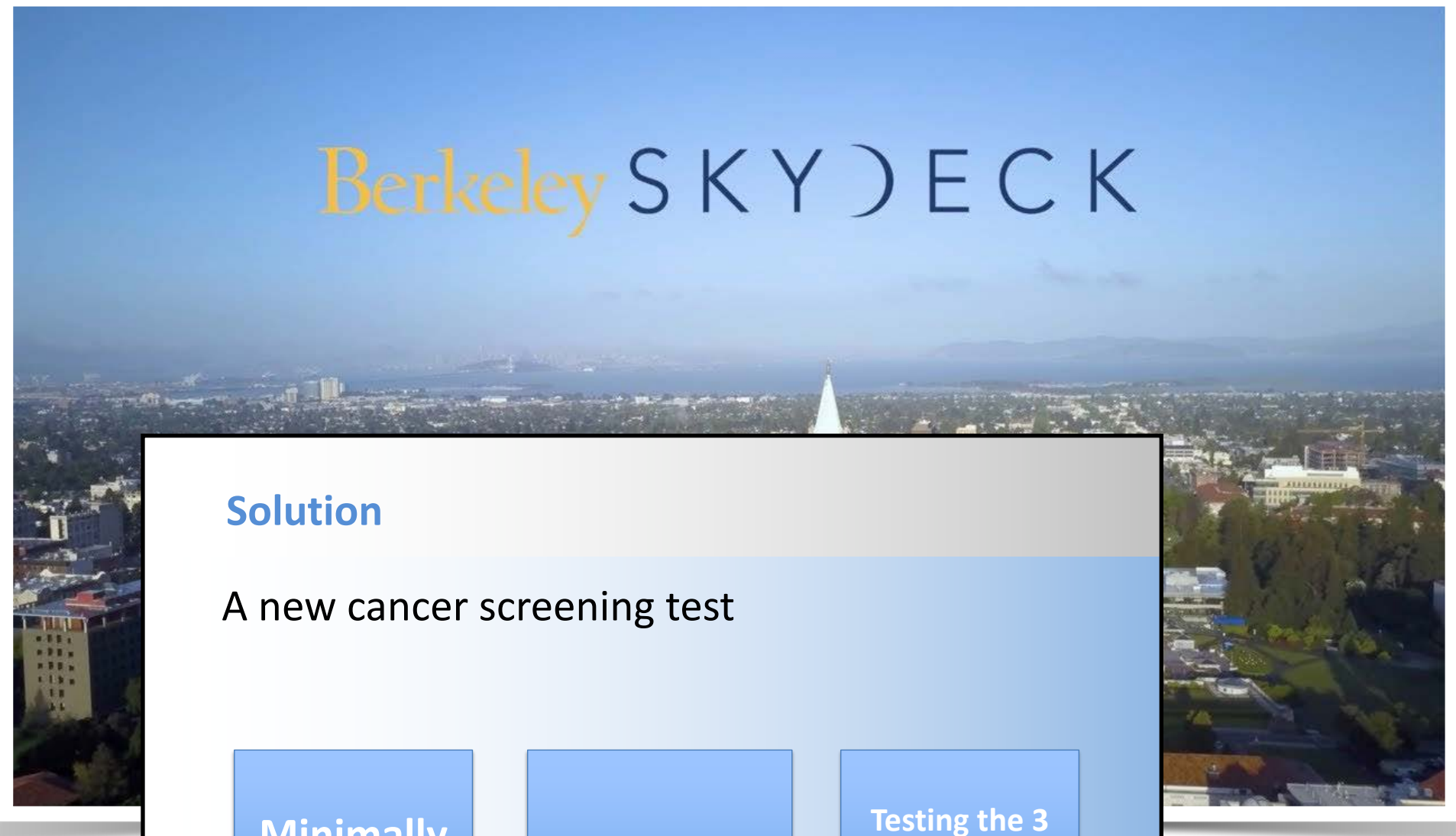
First-steps as entrepreneurs

First pitch deck

Genknowme
Bridging genetics and environment in cancer detection

Problem

- Cancer should be detected as soon as possible to enhance survival
- Cancer screenings are invasive and expensive
- No good screening tests exist for lung and prostate cancers yet



Solution

A new cancer screening test

Minimally invasive Requires a drop of blood	Inexpensive \$100-150	Testing the 3 most frequent cancers at once <ul style="list-style-type: none"> • Colon • Breast (women) • Prostate (men) • Lung
---	---------------------------------	---

Market size

120+ M People over 45 (USA, in 2010) Total available market in the US	131+ M Screening of top 4 cancers Screening for top 4 cancers available market	60 M GenKnowMe Screening tests Share of market
--	---	---

Product

Prick your finger (at home) → Send blood spot by postmail → Received your results online

Your test results:

Breast cancer: Low risk ✓

Colon cancer: High risk ✗

Lung cancer: Low risk ✓

Comment: We recommend that you contact your physician for scheduling a follow-up regarding your risk of colon cancer.

Competitive advantages

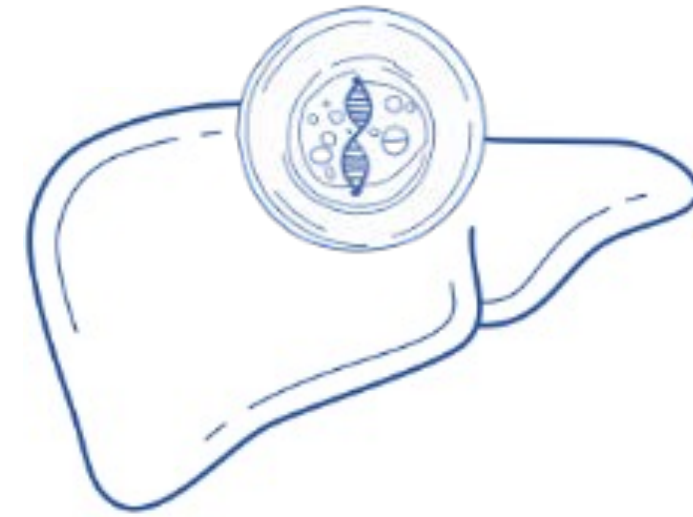
First to market No existing combined tests for the 3 most frequent cancers	Inexpensive 3 cancer tests for \$100-150	Minimally invasive Simple finger-prick at home
Industry connections We can launch a study quickly	Technical breakthrough Patent is pending	Speed to produce 3-day process

Refined idea : epigenetics for prevention

Our lifestyle has an impact that can be quantified with epigenetics



Alcohol consumption triggers cells to detoxify or mitigate damages



Specific maintenance or detox genes are activated



Gene activation adapts to lifestyle with detectable epigenetic marks

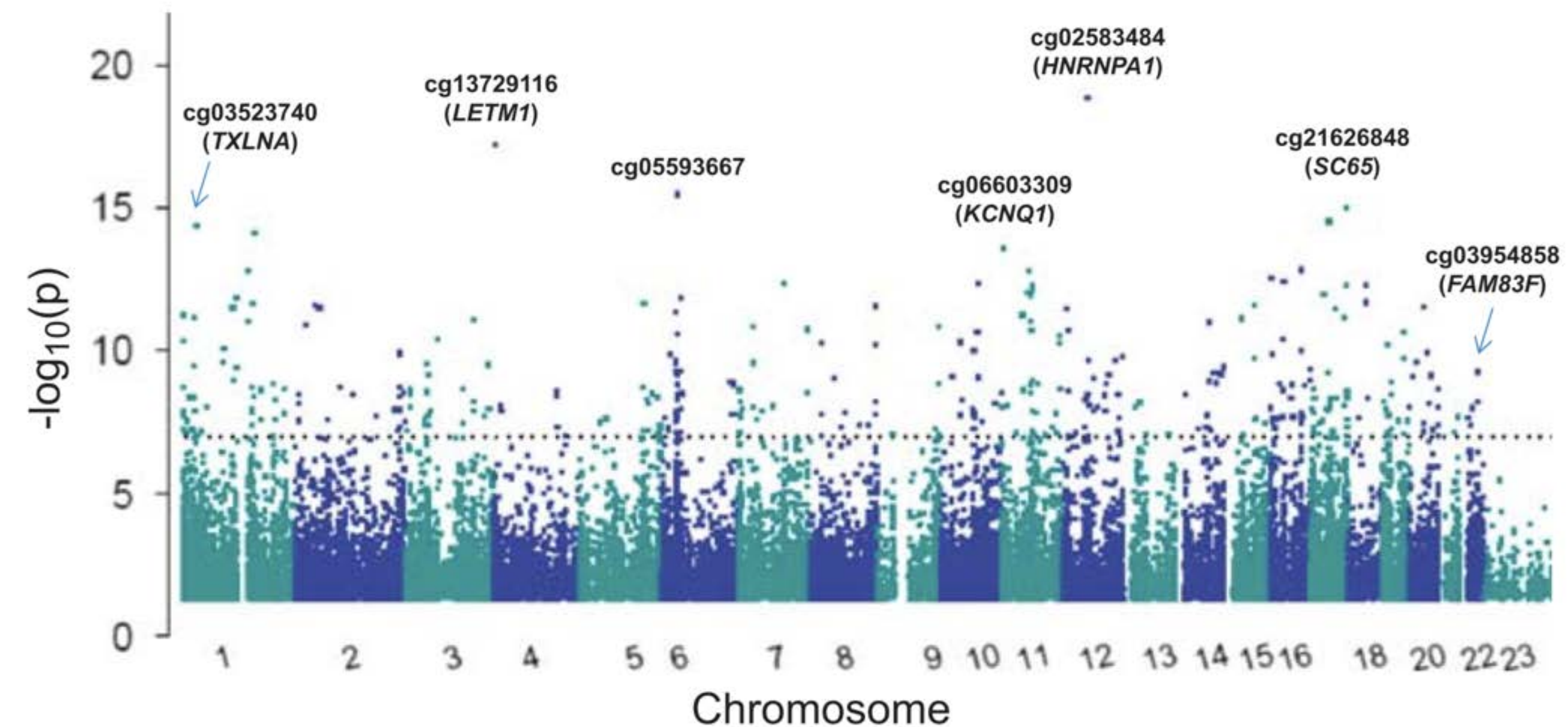


Epigenetic patterns are unique and allow personalized care

The epigenetics of alcohol intake

Epigenetic-Wide Association Studies

- Meta-analysis of EWAS studies on alcohol intake
- 13 populations and 13'000 participants
- 300 methylation loci linked to alcohol consumption
- High number of markers in GABA receptors genes (neurotransmitter receptors, calming effect)



Liu et al. (2018) A DNA methylation biomarker of alcohol consumption. *Molecular Psychiatry* 23: 422-433

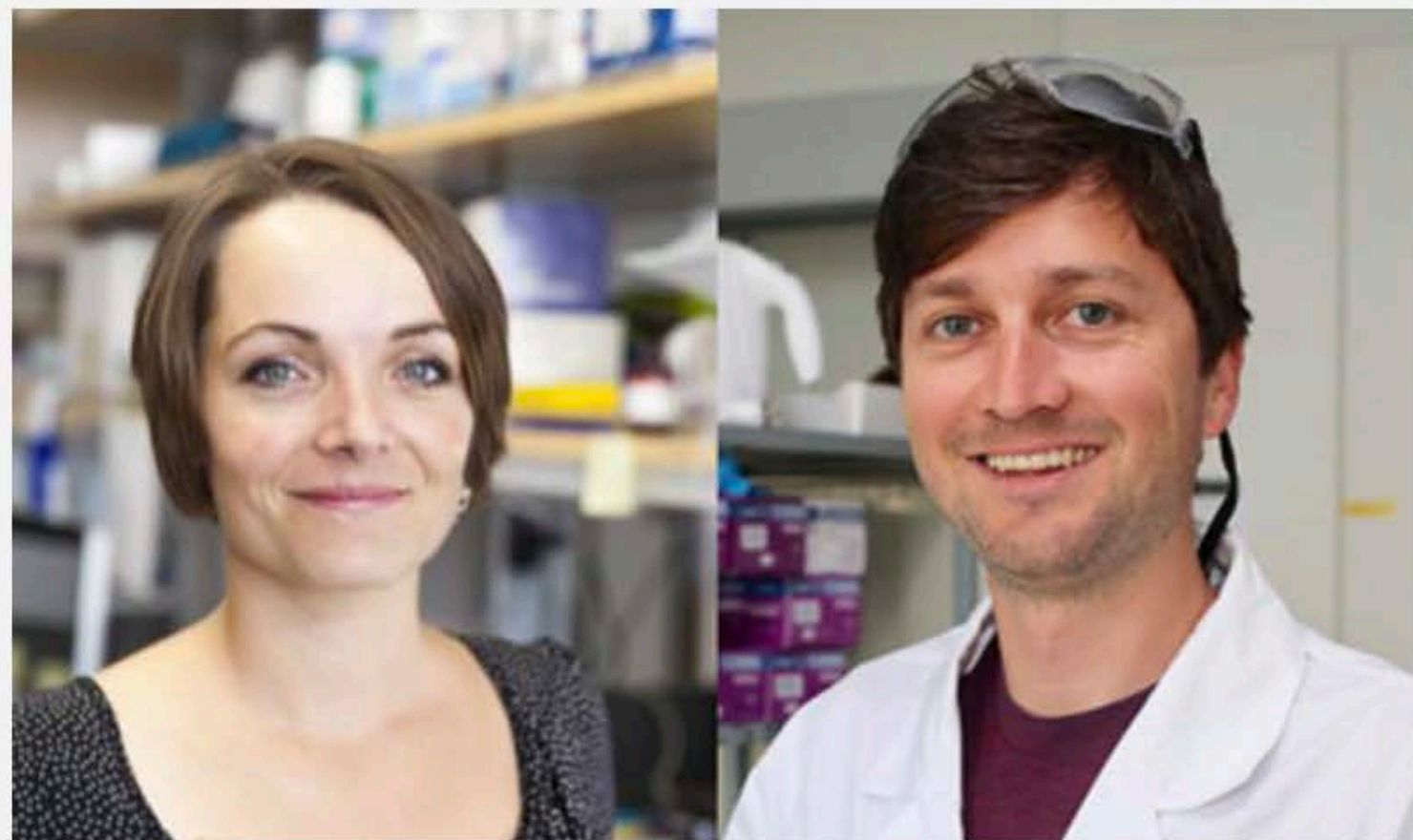
First grant - Innotreck (2019)

Collaboration with the CHUV, foundation of the company



[About PACTT](#) [Researcher](#) [Industry](#) [Documents](#) [InnoPACTT](#) [Contact](#)

TWO NEW INNOTREK GRANTS AWARDED TO SEMIRA GONSETH NUSSLÉ AND FLORENTIN COPPEY



In response to the 2018 spring call InnoTREK, Mrs. Semira Gonseth Nusslé and Mr. Florentin Coppey submitted two innovative projects. They were both chosen to benefit from the InnoTREK grant of CHF 100'000.-. These funds will be a great help to continue developing their project and subsequently create their own start-up.

Flashback in 2005

Side quest...



unine
UNIVERSITÉ DE
NEUCHÂTEL

Diplôme postgrade en statistique
Master degree in statistics
Années académiques:
Academic years: 2006-2007

Message du Directeur des études
A Message From the Director of Studies

4

La statistique: un pari vers l'avenir

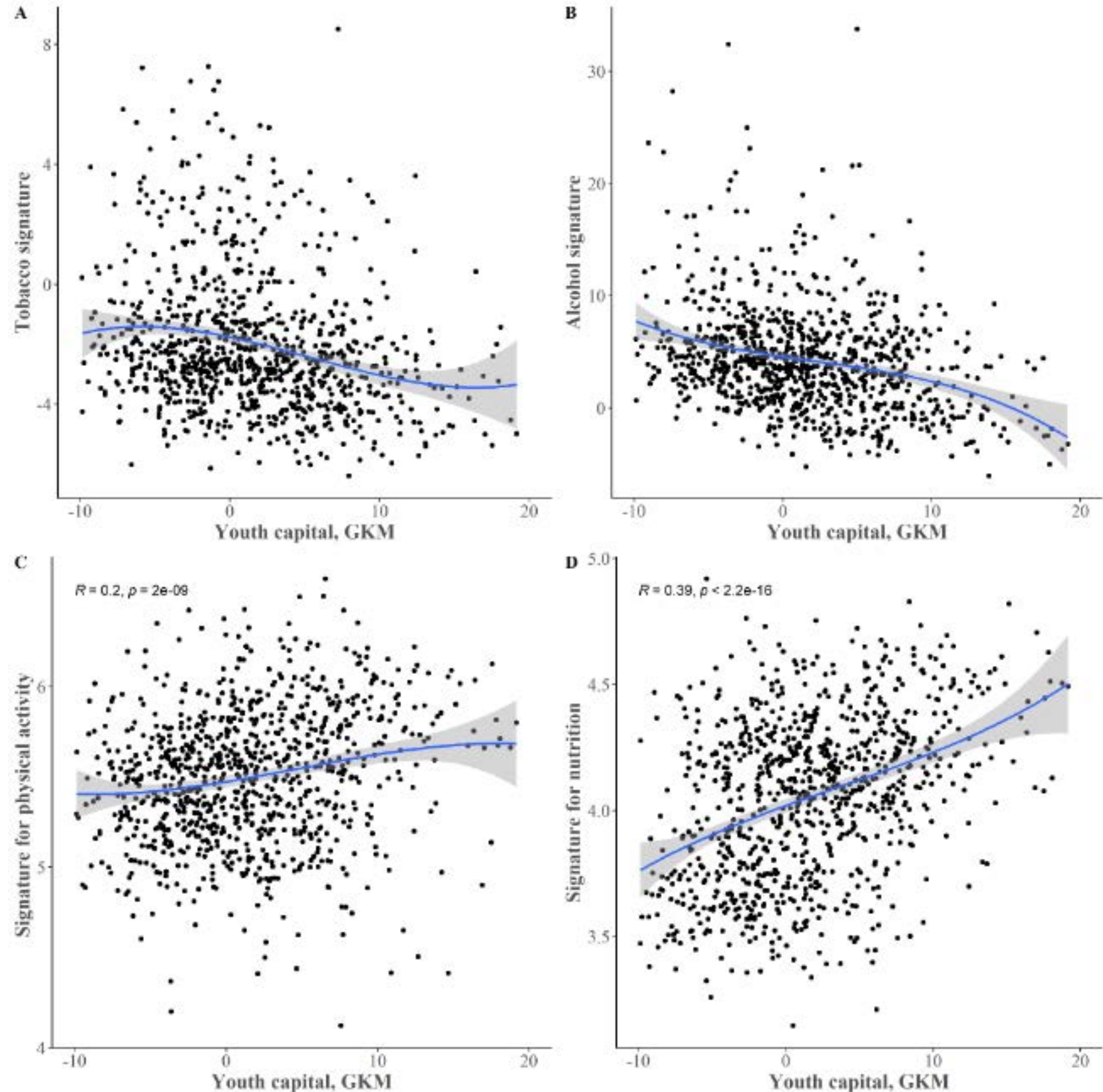
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Statistics: A Challenge For the Future

6

Les activités du statisticien
What Does the Work of a Statistician Entail?

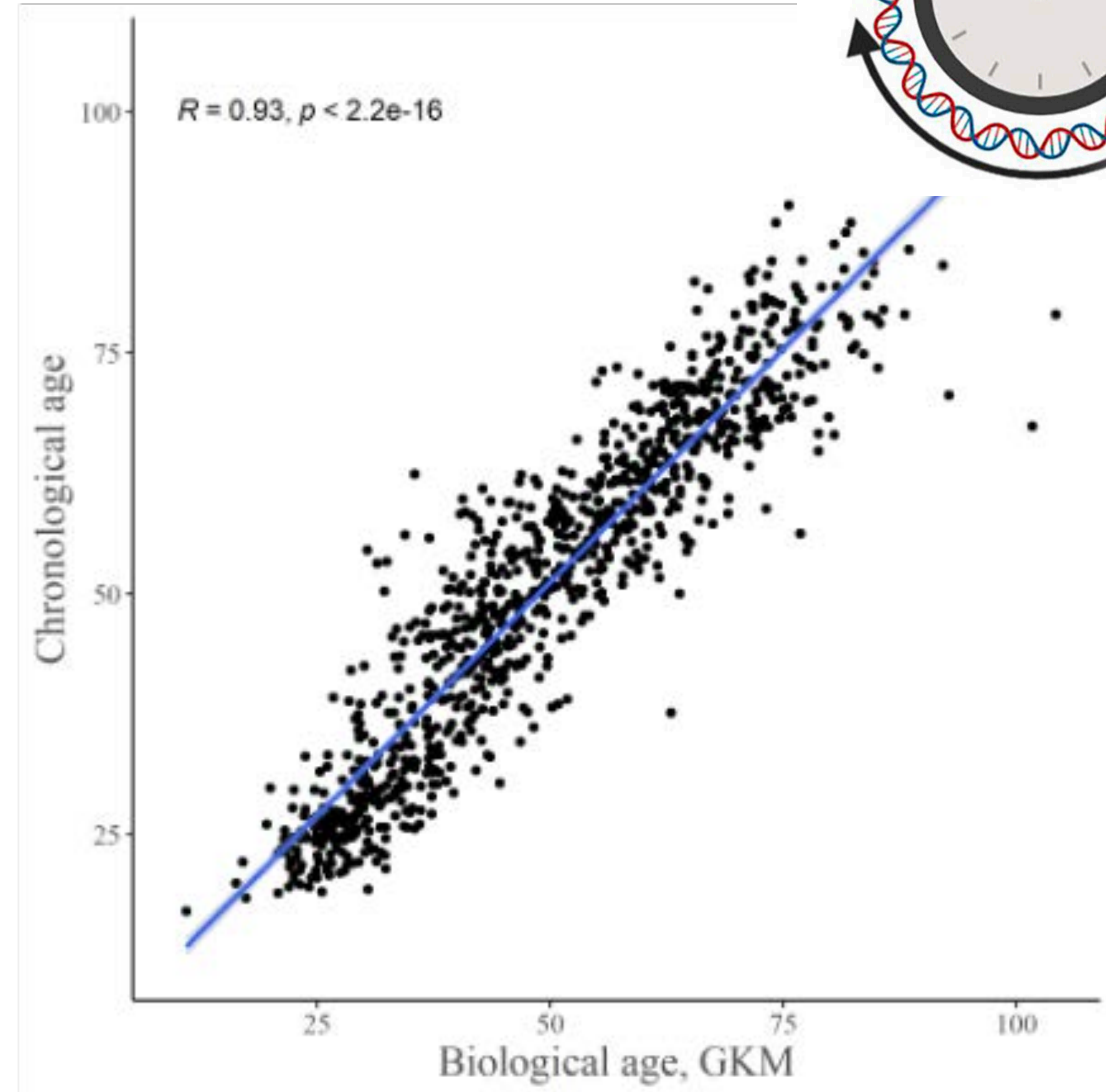
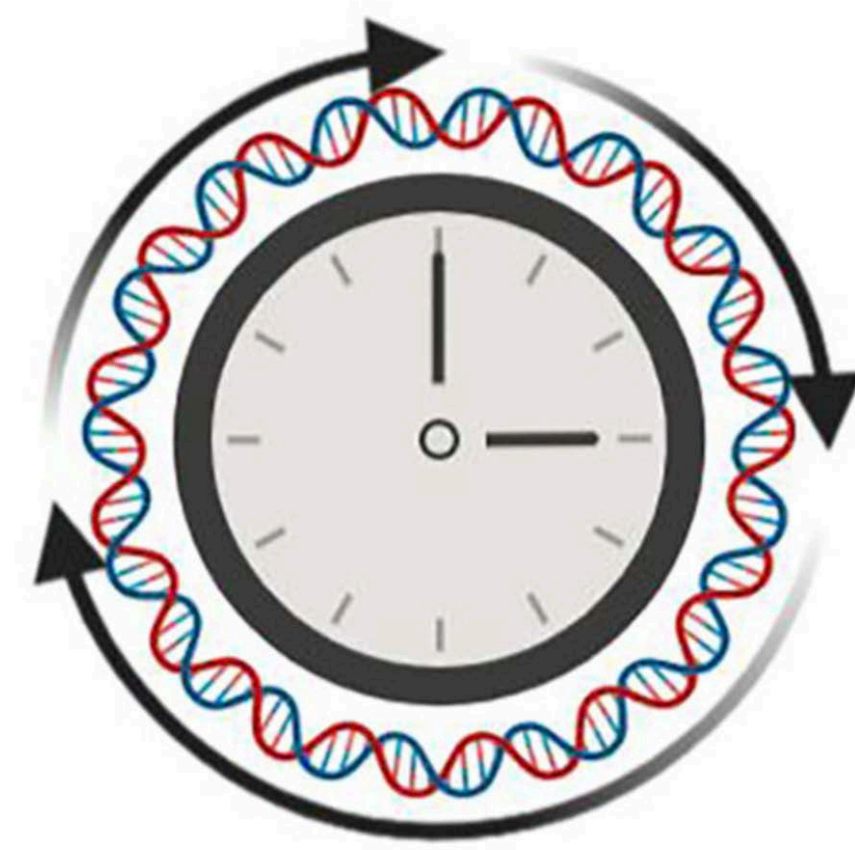
7



Invention of the “Swiss clock”

Collaboration with the SKIPOGH population cohort

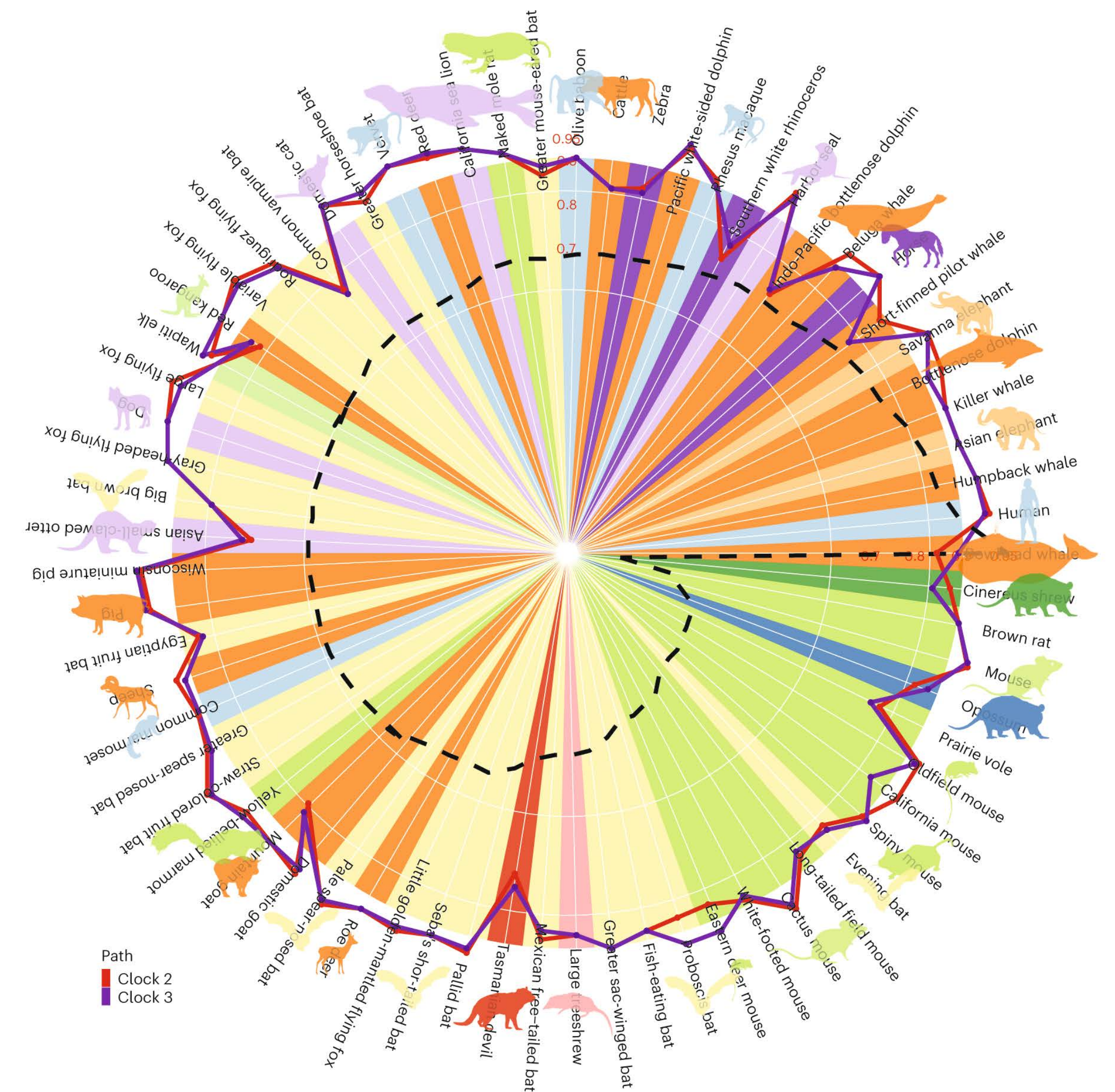
- CpG site identification
 - Longevity, lifestyle
 - EWAS Atlas
- Lifestyle-specific signatures
 - Tobacco, alcohol, diet, physical activity
- Random models (~10 million)
 - Age as response
 - Residual regression
 - **Bayesian Framework**



Epigenetic clocks of aging and disease

Most proximal process

- Global DNA methylation levels decrease with age
- Specific markers of the time that passes → epigenetic clocks of ageing
- Association with:
 - mortality
 - time-to-death
 - cancers incidence
 - cardiometabolic and neuro-degenerative diseases
- Pan-mammalian clock



Heyn, Holger, et al. "Distinct DNA methylomes of newborns and centenarians." *Proceedings of the National Academy of Sciences* 109.26 (2012): 10522-10527.

Horvath, S., Raj, K. DNA methylation-based biomarkers and the epigenetic clock theory of ageing. *Nat Rev Genet* **19**, 371–384 (2018)

Fransquet, P. D., et al. (2019). The epigenetic clock as a predictor of disease and mortality risk: a systematic review and meta-analysis. *Clinical epigenetics*, 11(1), 1-17.

Lu, A.T., Fei, Z., Haghani, A. et al. Universal DNA methylation age across mammalian tissues. *Nat Aging* **3**, 1144–1166 (2023). <https://doi.org/10.1038/s43587-023-00462-6>

Breaking The Barriers Of Ageing: M'Sia's First Biological Age Testing Collaboration



DNA methylation age of human tissues and cell types (Horvath 2013)

Epigenetic Aging - DNA methylation as an age marker

Home > [Genome Biology](#) > Article

DNA methylation age of human tissues and cell types

Research | [Open access](#) | Published: 10 December 2013
Volume 14, article number 3156, (2013) [Cite this article](#)



- **Epigenetic Maintenance System (EMS)** - Protective role against instability
- **Cross-Species Comparison** - DNAm age in humans, chimpanzees, evolution insights
- **Cancer Methylation Patterns** - Accelerated DNAm age, genome stability
- **Rejuvenation & Stem Cells** - DNAm age reset in iPSC, regenerative potential
- **Biomarker Potential** - DNAm age in disease, anti-aging interventions
- **Predictive Power** - Multi-tissue applicability, tissue-specific variations
- **Future Research** - DNAm age as an aging marker vs. aging effector

The epigenetic clock as a predictor of disease and mortality risk

Fransquet *et al.* 2019 Clinical Epigenetics

Table 2 Studies investigating the association between the epigenetic clock and the incidence of age-related diseases

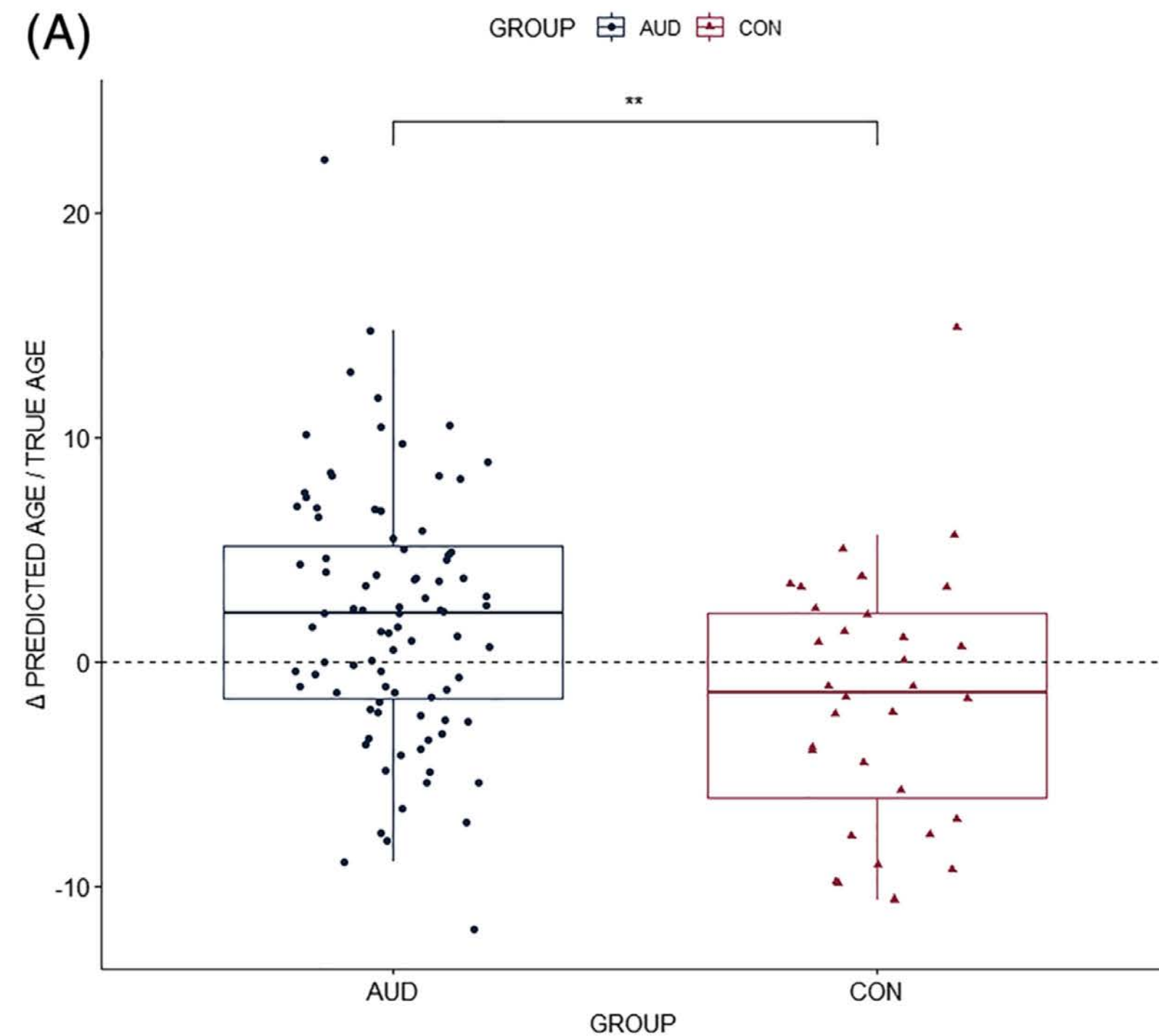
Paper	Study (country)	Characteristics: n, mean (SD) age, sex	Outcome	Sample; platform	Clock*	DNAme associations [correlation with chronological age]	Adj.
[69]	Cohort study WHI (USA)	2029, age 65.3 (7.1) 100% ♀ (post-menopause). 20 years FU	Lung cancer incidence; n=43	Blood; 450K	IEAAH	↑ risk of lung cancer (HR 1.50; $p=0.003$), especially septuagenarians (HR:2.51, $p=0.0008$) and current smokers (HR 6.17, $p=0.0004$) [NS]	Age, ethnicity, smoking, and pack years
[70]	Cohort study NAS (USA)	442, 71.7 (6.7), 0% ♀, 370 seen pre 2003, 306 in cohort 2003 to 2013. 3–5 years FU	Cancer incidence, n=132	Buffy coat (3 years FU); 450K	IEAAHa	↑ cancer incidence (HR 1.06, $p=0.004$ per year) in 2003–2013 cohort only [NS]	Age, BMI, education, smoking, alcohol
[63]	Case-control EPIC (10 countries)	902 Total, 52.3 (8.9), 100% ♀ 451 cases 451 CT	Breast cancer	Blood; 450 K	IEAAH	↑ breast cancer (4%, $p=0.016$). In stratified analysis, only significant for postmenopausal ♀ [0.76]	BMI, hormonal factors, various others
[64]	Case-control EPIC (10 countries)	845 Total, 52 (7.4), 77.8% ♀ 235 BC 166 CRC	Breast/colorectal cancer	Blood; 450 K	AAH AAHa IEAAH IEAAHa	In males, ↑ AAH in CRC (1.6 years older, $p=0.04$) NS all in females [NS]	Cell %
[13]	Seven case-control studies nested in MCCS Case-control (Australia)	6432 total, 27–76, 59% ♀ 3216 cancer cases** 3216 CT Median 8.3 years FU	Cancer	Blood; 450 K	All	↑ cancer risk (7 of 35 associations, $p < 0.05$, mainly kidney ↑ 35–63% and B cell lymphomas ↑ 15–27%). [EAH: $r=0.73$, EAHa:0.78]	Age and sex, matched, various others
[23]	10 cohorts (Δ ethnicities) WHI, BHS, PEG (USA), cohorts from Bolivia, Asia, and Africa	Total 4296 (individual cohorts 41–1462), 2–92 (NS), between 0% and 100% ♀	Incident coronary heart disease (CHD), n = not stated	Blood (3x saliva) 450 K (2 x 27 K)	IEAAH EEAA	NS [EAH assumed: $r=0.65$ to 0.93 depending on cohort, 3 of 10 > 0.80]	Age, sex, cell %, education
[62]	Cohort study IS: BASICMAR CT: REGICOR (Spain)	IS: 82, 63.9 (10.3), 45.1% ♀ CT: 41, 62.8 (14.2), 48.8% ♀	Ischemic stroke	Whole blood; 450 K	AAH AAHa	↑ stroke patients (AAHa: 2.5 years, $p=0.008$; AAH NS), especially younger patients [All samples, EAH: $r=0.87$, EAHa:0.80]	Sex
[67]	Two cohorts of ischemic stroke (IS) patients (Spain)	Discovery: 551, 65–81 (NS), 41.9% ♀; Replication: 85, 66–80 (NS), 29.4% ♀	IS outcome at 3 months (from 0 = no symptoms to 6 = death)	Whole blood; 450 K	AAHa	↑ worse 3-month stroke outcome (OR:1.04, $p=0.008$ and OR 1.16, $p < 0.001$ in 2 cohorts). [$r=0.81$]	Age, sex, smoking, treatment, various others
[74]	Cohort study PIVUS (Sweden)	832, 70 (NS), 50% ♀ 10years FU	Incident CVD, n = 153	Whole blood; 450 K	AAH AAHa	↑ incident CVD (3.3% per year, $p=0.02$) with AAH. AAHa NS [NS]	Sex, smoking, BMI, various others
[16]	Case-control PEG (USA)	Caucasians: 289 PD, 37–91 (NS), 43% ♀; 219 CT, 35–92 (NS), 47% ♀. Hispanics: 46 PD, 37–83 (NS), 30% ♀	Parkinson's disease (PD)	Blood; 450 k	AAH IEAAH EEAA	Associated with PD after logistic regression (AAH: $p=0.037$; EEAA $p=0.031$. Effect sizes not stated. [Caucasians: $r=0.82$, Hispanics: $r=0.81$]	Age, sex, cell %, smoking, ethnicity, coffee, pesticides

Significant associations:

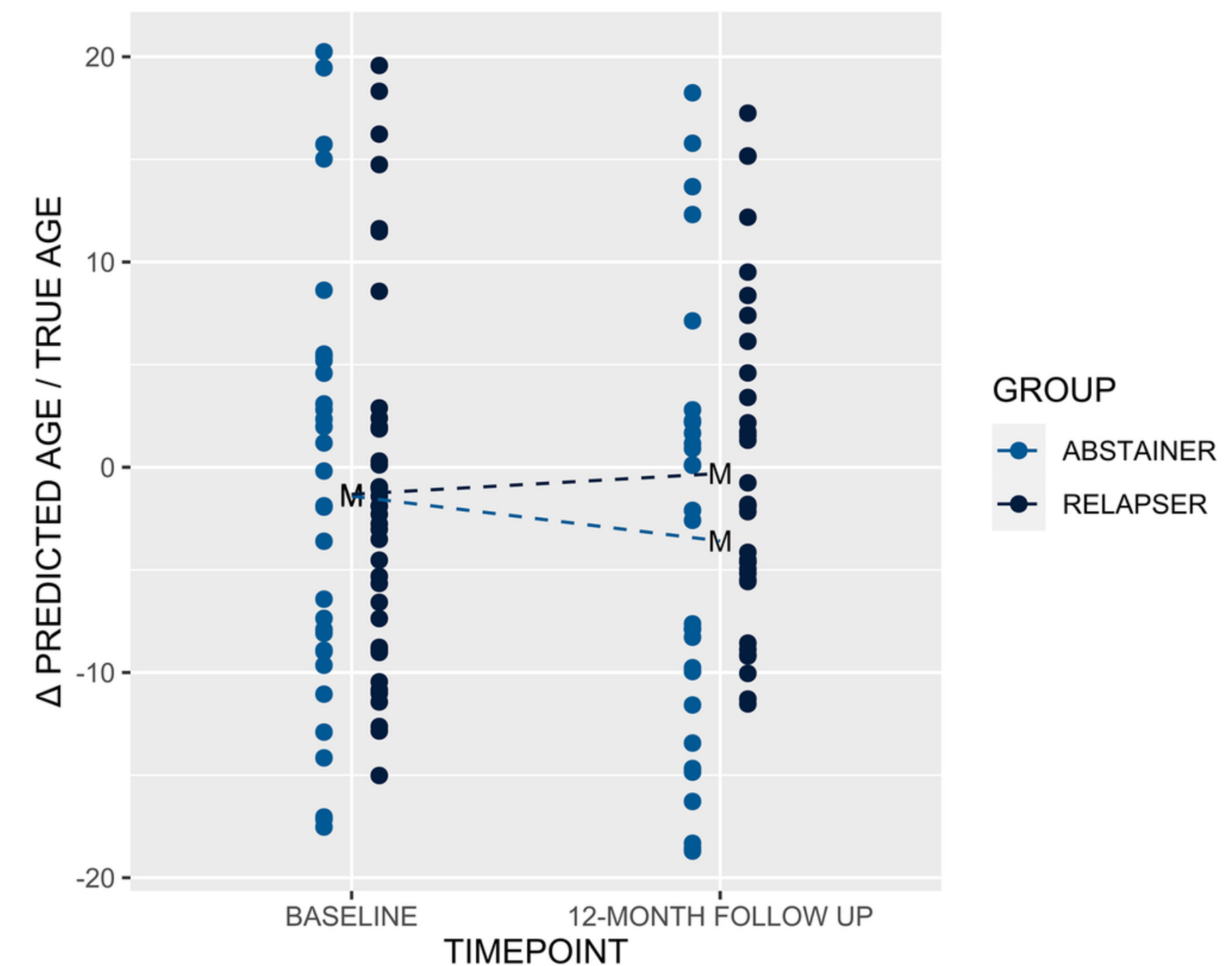
- Lung cancer
- Cancer incidence
- Breast cancer
- Colorectal cancer (males, females NS)
- Stroke
- Worse clinical outcome after stroke (3 mo)
- Incidence of CVD
- Parkinson disease

Reversibility of epigenetic age: alcohol use

Fransquet *et al.* 2019 Clinical Epigenetics



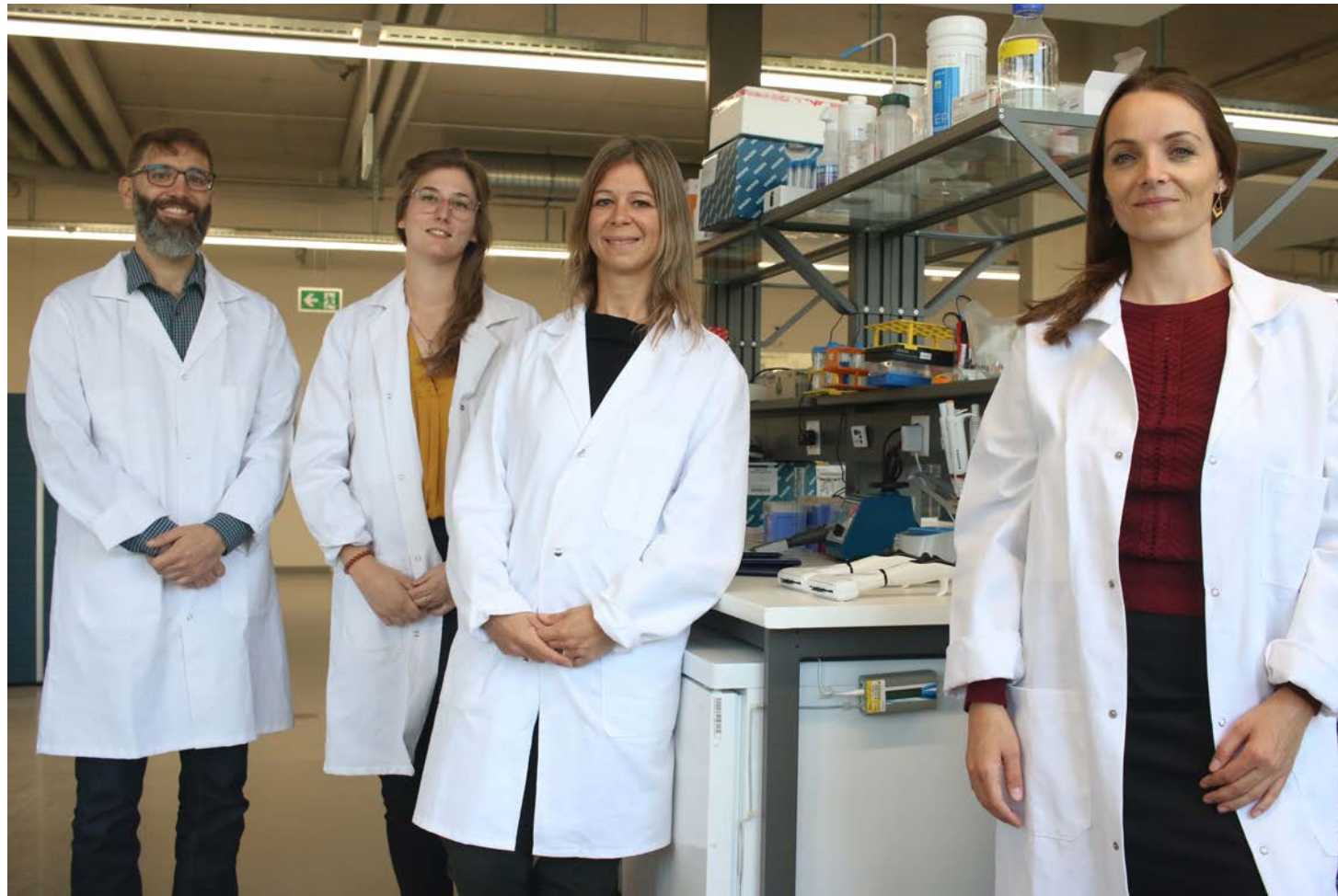
- Ageing was accelerated by **3.64 years** in epigenetic age of patients with alcohol use disorder compared with the control group



- Abstaining patients displayed a decrease in epigenetic clock by **3.1 years** after 12 months
- Increase by **2.7 years** in those who relapsed

2019 - Foundation of Genknowme

Real entrepreneurship starts...



Le panel d'évaluation de BRIDGE Proof of Concept a été impressionné par la qualité de votre présentation et trouve votre feuille de route détaillée et bien rédigée. Cependant, il n'est pas convaincu par l'idée du produit et le groupe cible. Le panel considère que l'impact de votre projet pourrait être marginal et s'interroge sur l'utilité d'un test à utiliser sans l'interprétation d'un médecin. Il aurait souhaité voir une réflexion sur les raisons qui poussent le client vers un tel produit. En outre, le panel s'interroge sur la manière d'atteindre les clients cibles et se demande si votre produit répond à un réel besoin. Pour ces raisons, bien que le panel ait jugé votre dossier et votre présentation excellents, il ne peut recommander le financement de votre projet en raison de l'absence d'une stratégie convaincante de ciblage de la clientèle.



Epigenetic clock and signatures development

Innovation requires constant developments

Filed patents :

Method Determining The Difference Between The Biological Age And The Chronological Age Of A Subject, filing number: EP 22 162 216.0 (15.03.2022)

Method determining a value of allostatic load: EP 23 179 588.1 (15.06.2023)

Scientific publications and contributions:

- A novel, lifestyle-based epigenetic clock, Chamberlain, (...), & Nusslé. Presented on June, 29, 2022, IMB Conference Mainz
- Chamberlain JD, Nusslé S, ... & Nusslé SG (2022). Blood DNA methylation signatures of lifestyle exposures: Tobacco and alcohol consumption, Clinical Epigenetics
- Chamberlain JD, Nusslé S, ... & Nusslé SG (2023). Investigating the association of measures of epigenetic age with COVID-19 severity, Swiss Medical Weekly
- Chamberlain JD, Nusslé S, ... & Nusslé SG (submitted). MethAL: An epigenetic signature of allostatic load

Two *Innosuisse research and developments grants* with the University center for primary care and public health, Lausanne, and the Lausanne University Hospital.

Chamberlain et al. *Clinical Epigenetics* (2022) 14:155
<https://doi.org/10.1186/s13148-022-01376-7>

Clinical Epigenetics

RESEARCH

Open Access

Blood DNA methylation signatures of lifestyle exposures: tobacco and alcohol consumption



Jonviea D. Chamberlain^{1*}, Sébastien Nusslé², Laurence Chapatte², Cassandre Kinnaer², Dusan Petrovic¹, Sylvain Pradervand^{3,4}, Murielle Bochud¹, Sarah E. Harris⁵, Janie Corley⁵, Simon R. Cox⁵ and Semira Gonseth Nusslé^{1,2}

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Centre universitaire
de médecine générale
et santé publique · Lausanne

genknowme
Personalized prevention solutions



Innosuisse unisanté

Novel epigenetic signatures: A lifestyle-based epigenetic clock and lifestyle exposures

Presentation for the IMB conference in Mainz, DE:
"Epigenetics of Ageing: Responses to Adversity across Scales"
June 29, 2022

JD Chamberlain, PhD (Chargée de recherche)
Unisanté, Lausanne, Switzerland

smw swiss medical weekly

Original article | Published 24 April 2023 | doi:<https://doi.org/10.57187/smw.2023.40076>
Cite this as: Swiss Med Wkly. 2023;153:40076

Investigating the association of measures of epigenetic age with COVID-19 severity: evidence from secondary analyses of open access data

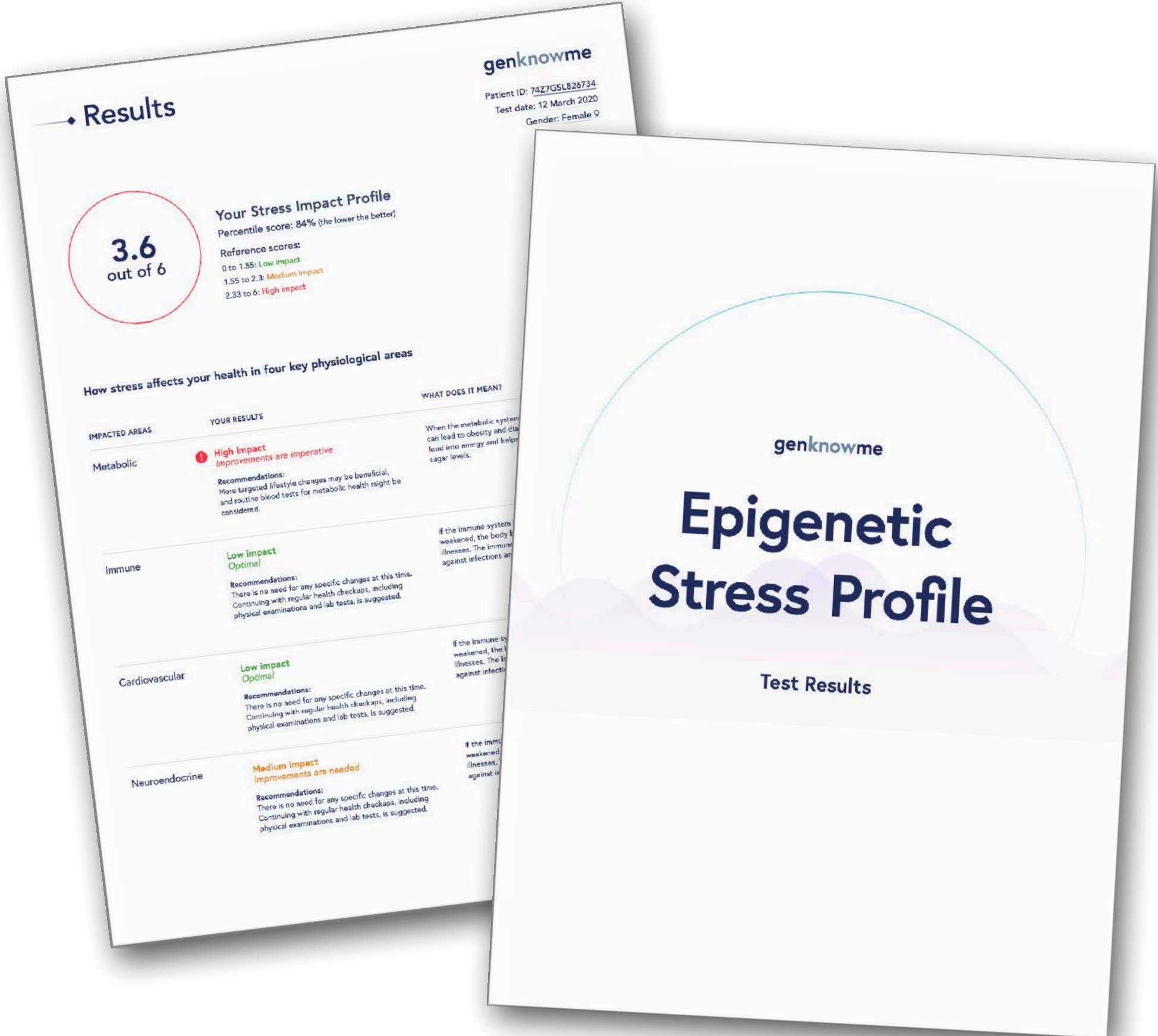
Jonviea D. Chamberlain^a, Sébastien Nusslé^b, Murielle Bochud^{a,c}, Semira Gonseth-Nusslé^{a,b}

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^b Genknowme, Lausanne, Switzerland

Blood test quantifying the impacts of lifestyle and environment on health

Two products currently on the market



We provide the only estimate of chronic stress impact, and how body systems are differentially impacted

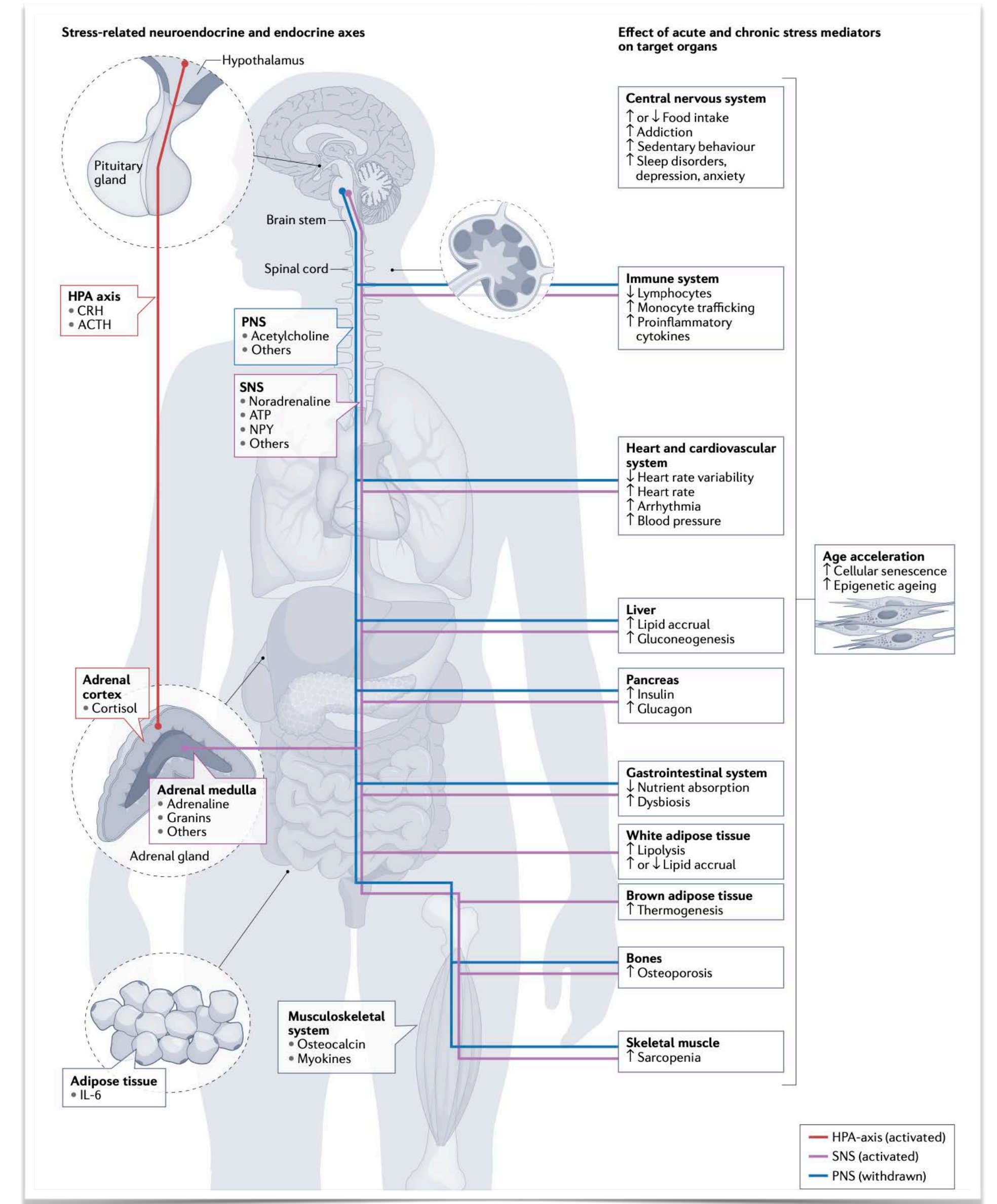
We measure premature aging and disentangle the effects of lifestyle and environment on biological age



Score of Allostatic load: a measure of stress overload

Development of a chronic stress epigenetic signature

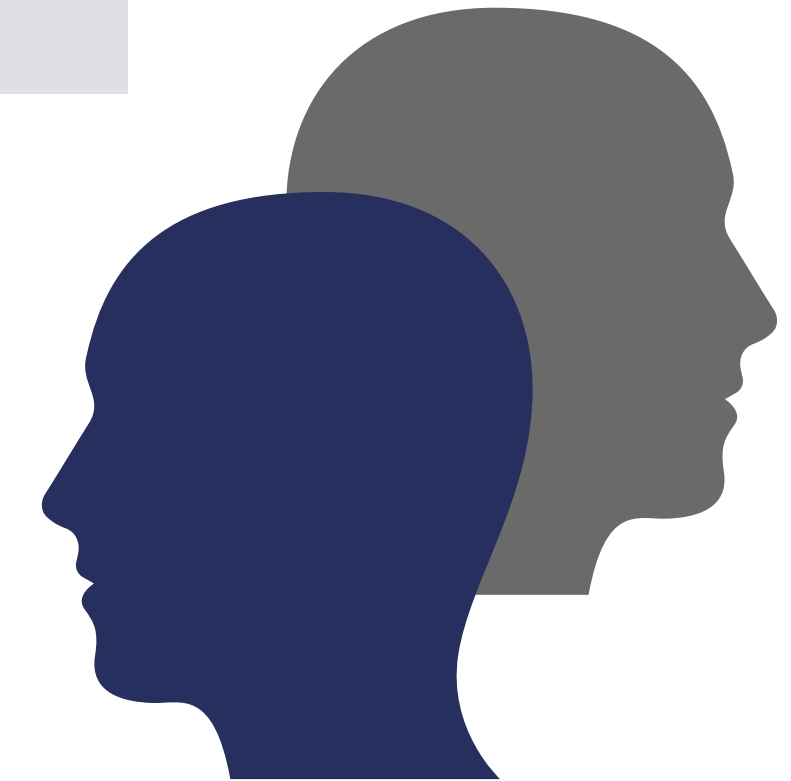
- **Neuroendocrine system**
 - Hypothalamic-pituitary-adrenal axis
 - Central nervous system
 - Sleep
- **Immune system**
 - Long-term immunosuppressive effects
- **Alterations in multiple body functions**
 - Cardiovascular system
 - Metabolic balance
 - ...



Score of Allostatic load: a measure of stress overload

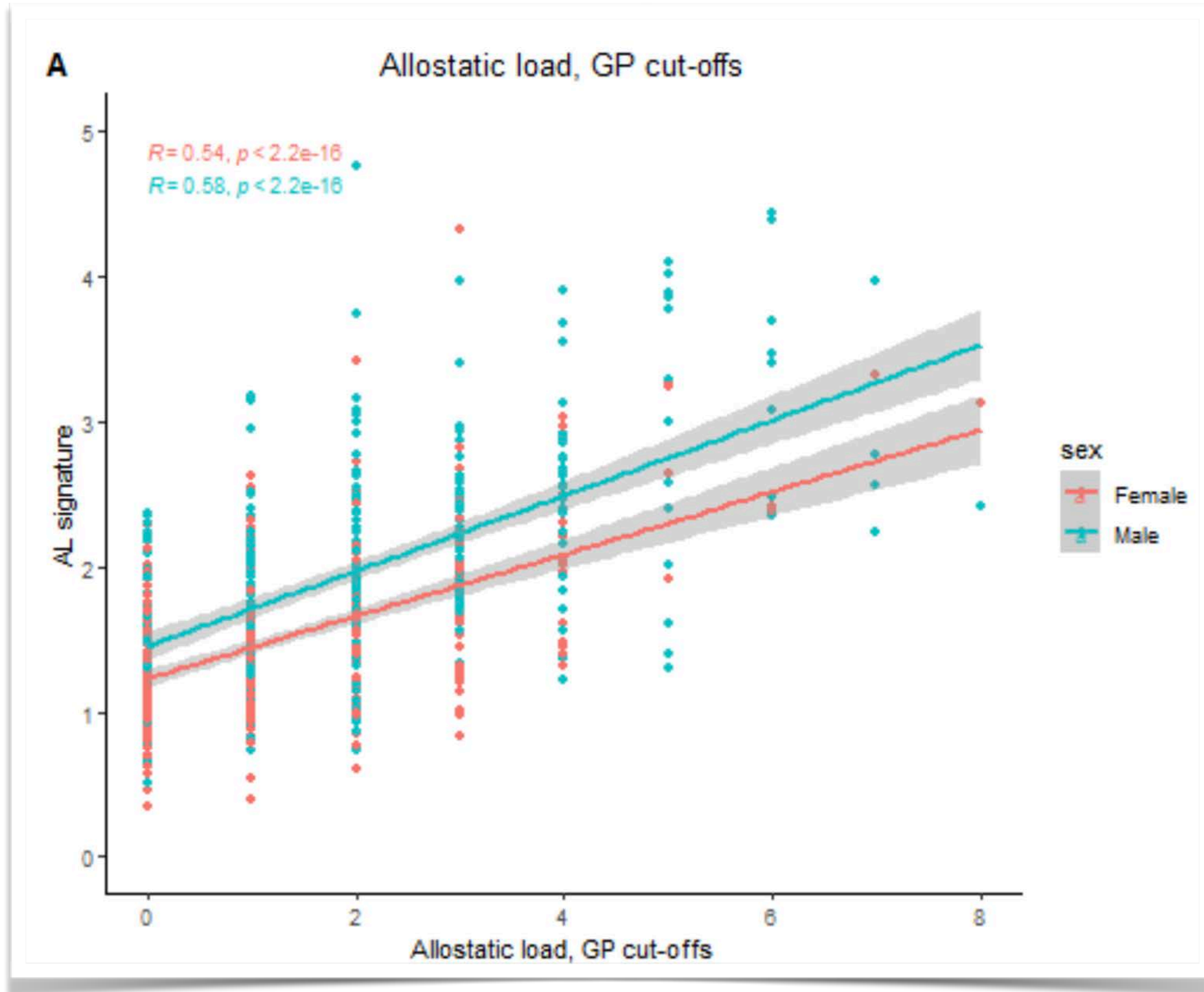
Development of a chronic stress epigenetic signature

System	Biomarkers
Immune	IL-6, IL-10, IL-1b, IFNg, CRP, TNF- α , fibrinogen
Cardiovascular	Systolic Blood Pressure, Diastolic Blood Pressure, Heart Rate
Metabolic	Total Cholesterol, Triglycerides, Insulin, Albumin, Glyceamia, Alanine Transaminase, GammaGT, Uric acid
Neuroendocrine	DHEA, Cortisol, Androsterone, stress (questionnaire)
Anthropometric	BMI, Waist-to-hip ratio, Body surface

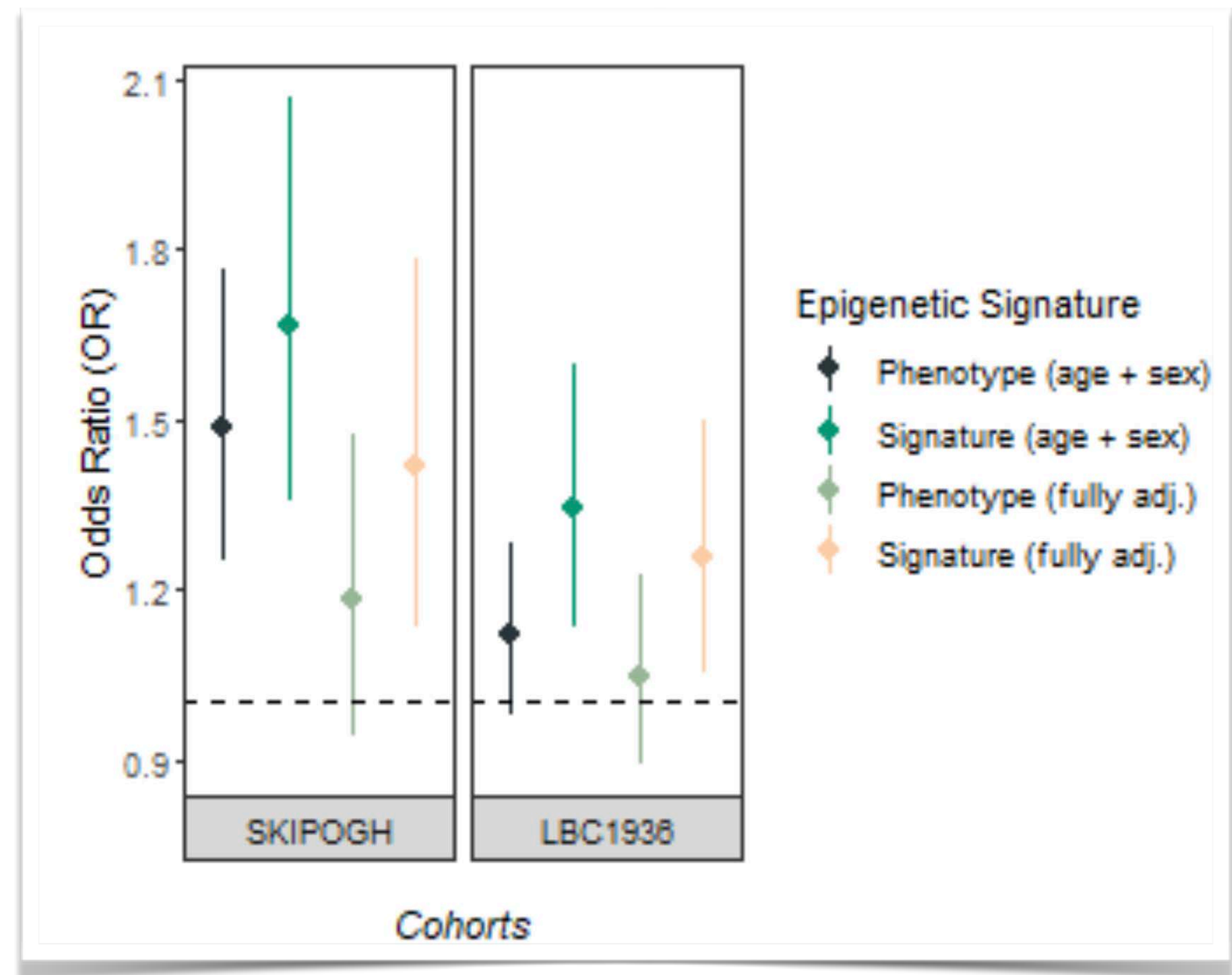


Score of Allostatic load: a measure of stress overload

Epigenetic signature derived from allostatic load measurements



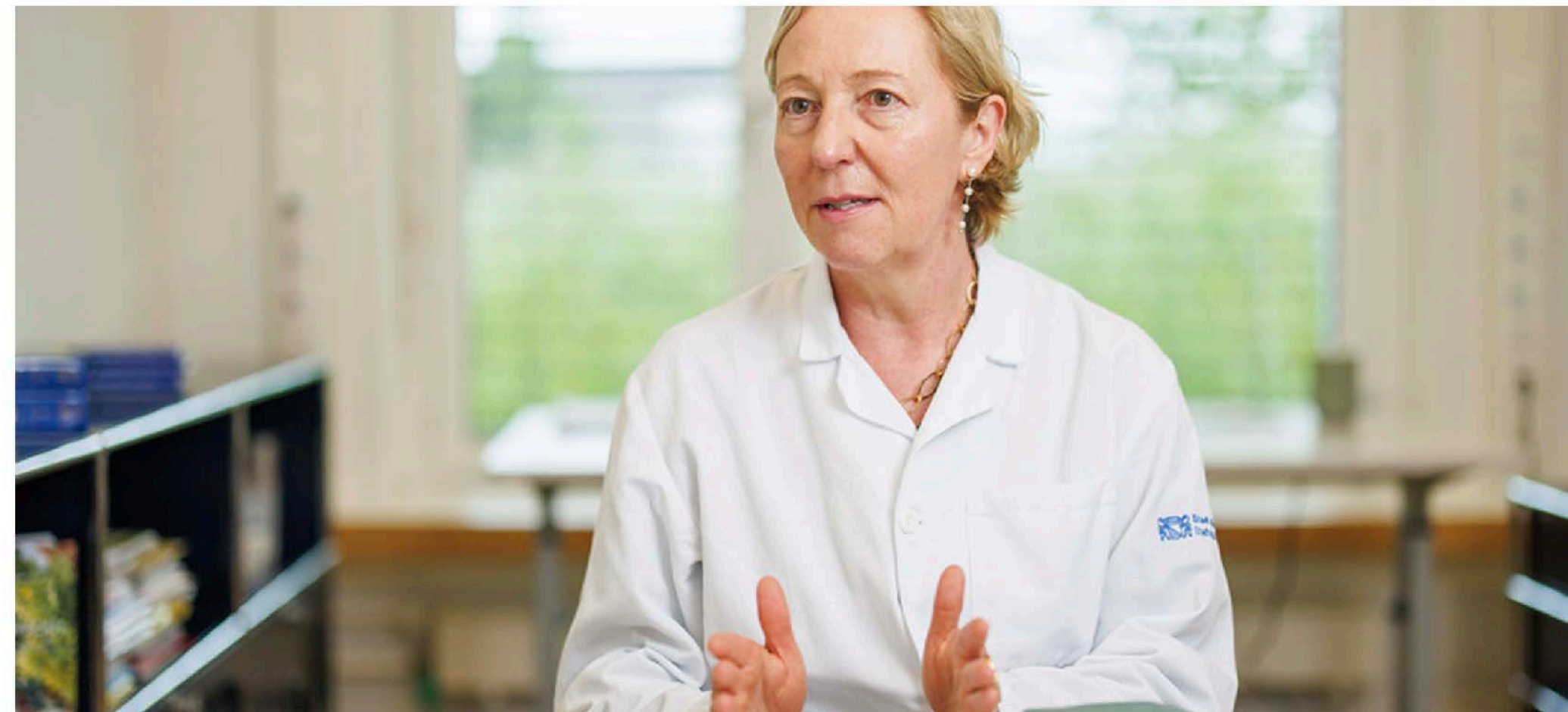
Plot of the correlation between phenotypic allostatic load and the epigenetic signature in the SKIPOGH cohort



Plot of odds ratios and 95% confidence intervals for probability of history of cardiovascular disease corresponding to different measures of allostatic load

Our vision is to transform health care with epigenetics, one step at a time

Personalized medicine needs biomarkers to understand how environment and lifestyle affect future health.



Science

«Nous sommes une espèce vieillissante»

Partagez

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Commentez (0)

PROF. DR. MED. HEIKE A. BISCHOFF-FERRARI



Prof. Dr. med. Heike A. Bischoff-Ferrari, DrPH
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Professor of Geriatrics and Age Research
Head of Internal Medicine - Oncology USZ
Member of the Cantonal Ethics Committee Zurich

With a biomarker detecting biological changes earlier, before they trigger diseases, prevention would leap forward.

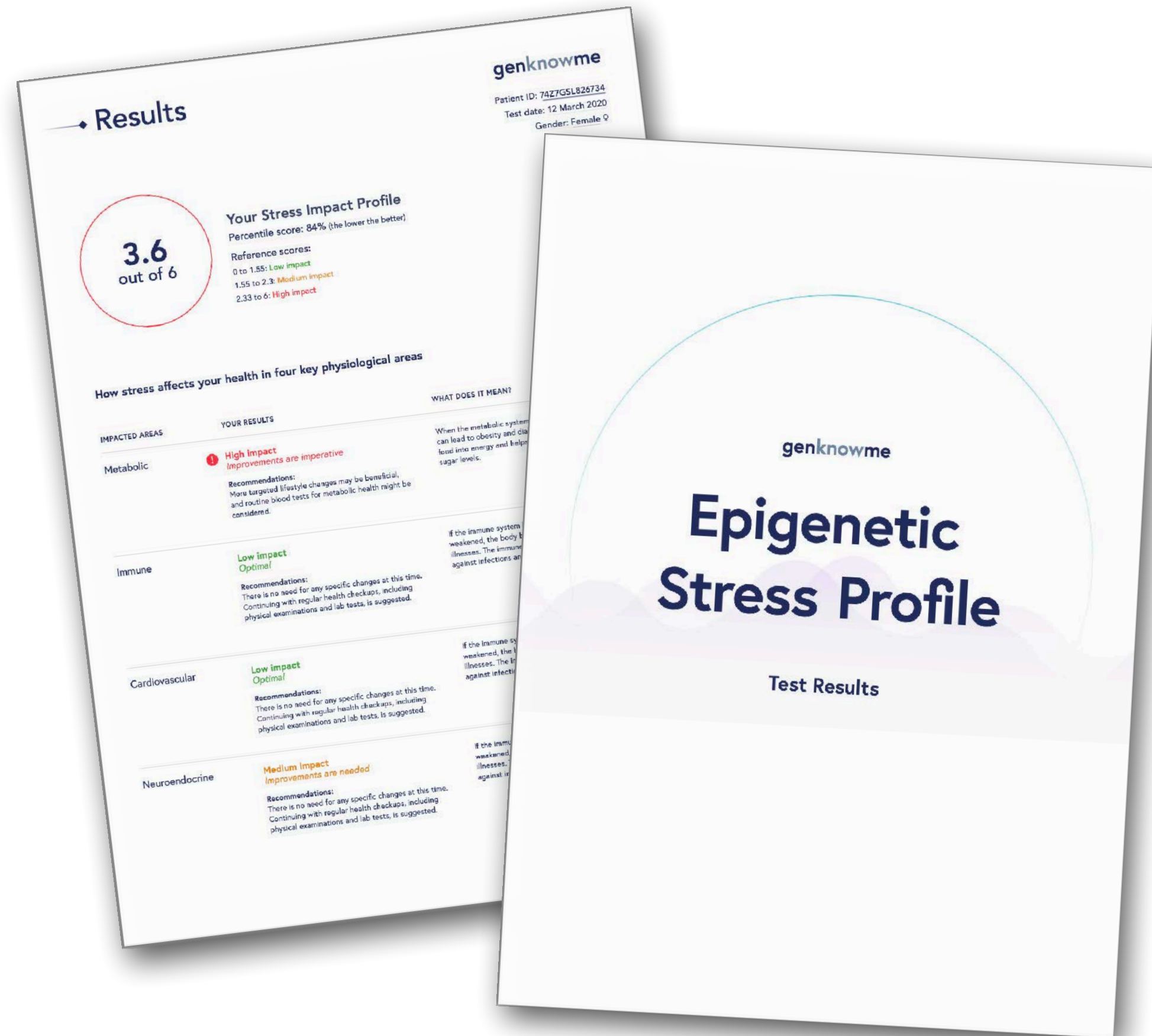
Among the promising biomarkers are epigenetic clocks based on DNA methylation.

Prof. Dr. Med HA Bischoff-Ferrari

By enabling early detection of disease risks and personalized prevention, Genknowme aims to contribute to longer, healthier lives, reducing the burden of chronic diseases.

First step : blood test quantifying the impacts of lifestyle and environment

Two products currently on the market



We measure premature aging and disentangle the effects of lifestyle and environment on biological age



We provide the only estimate of chronic stress impact, and how body systems are differentially impacted

Second step : chronic disease prognostic and diagnostic tests (medical)

Pioneering chronic disease early detection with medical epigenetic testing

We are developing a prognostic risk test for cardiovascular disease prediction years before an incident

- Collaboration with Unisanté and Lausanne University Hospital (CHUV, among the best hospitals in the world)
- Validation on several thousand patients in 2025
- Data shows that our unique epigenetic signature is a better predictor of cardiovascular disease than current methods using traditional biomarkers such as blood pressure, lipid concentration, etc.



Epigenetics as a primary prevention tool



Prof. David Nanchen, MD
Cardiovascular disease prevention
Swiss Clinical Guidelines
Unisanté

PRÉVENTION CARDIOVASCULAIRE

6 mars 2024

Modifications épigénétiques et maladies cardiovasculaires : nouvel Eldorado

Olivier Emery , David Nanchen , Jonviea Chamberlain 

DOI: 10.53738/REVMED.2024.20.864.496

- Ongoing clinical study led by Prof. David Nanchen (CHUV & Unisanté) to validate the link between our epigenetic signatures and cardiovascular risk.
- Proposed integration of our tests into the Health Screening Bus for large-scale cardiovascular risk screening.
- Swiss National Science Foundation (SNSF) grant application underway to study the relationship between severe hypercholesterolemia and DNA methylation.
- New project in preparation to explore the association between fertility and epigenetic markers.

Epigenetics as a secondary prevention tool



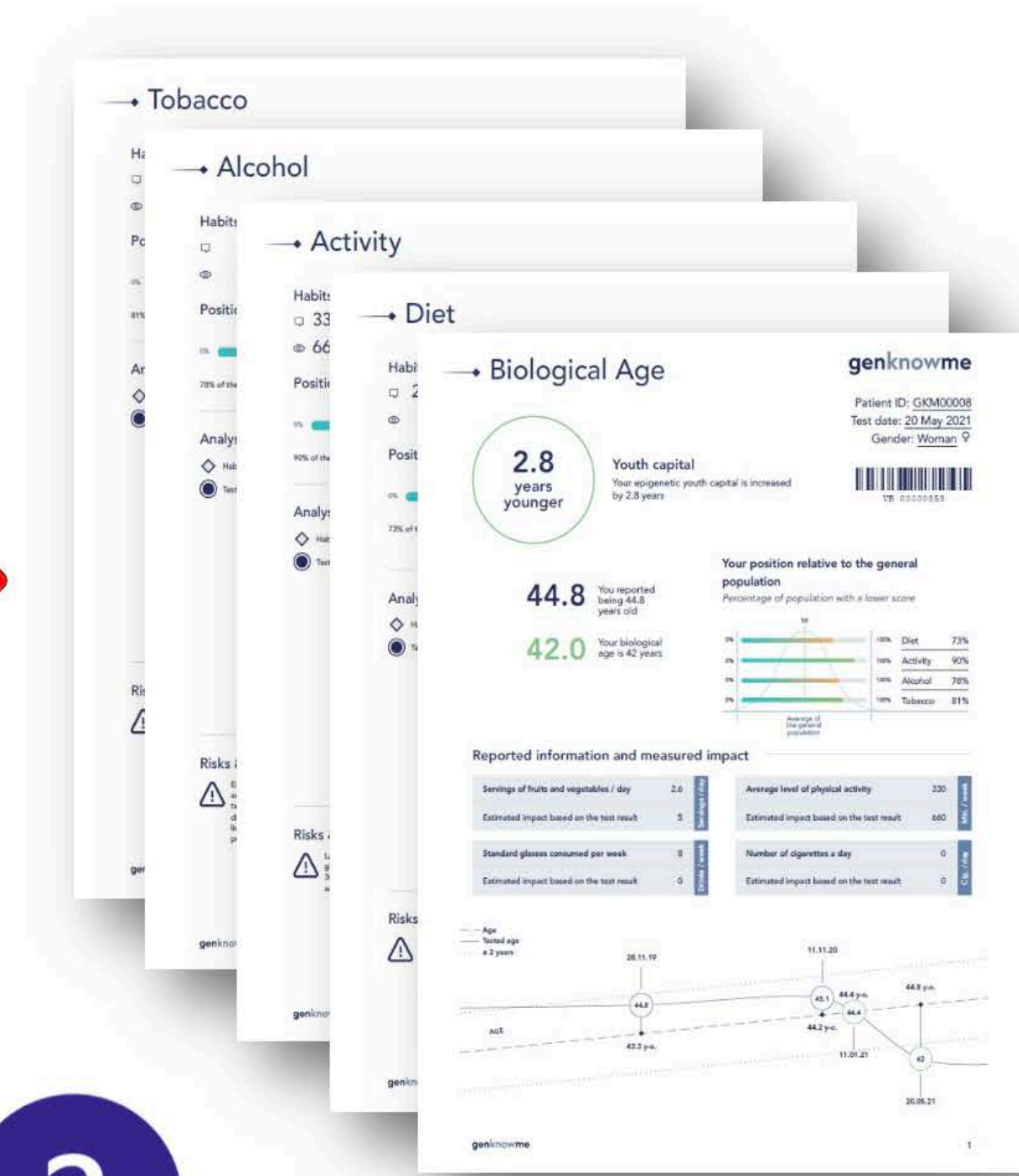
Prof. Baris Gencer, MD
Secondary Prevention
Patient-Centered Cardiovascular Research
Motivational Preventive Strategy
CHUV

- Pilot study on secondary prevention after myocardial infarction using our epigenetic tests
- Compared to wearables, patients unanimously preferred epigenetic feedback for lifestyle motivation
- Strong motivational impact confirmed in initial cohort (5 test patients)
- Grant application submitted to expand the study to 400 post-MI patients

Precisely customized Supplements

based on epigenetic profile

genknowme
Personalized prevention solutions



Made in Switzerland 

1

Epigenetic testing

2

Report with epigenetic profile.
Simple and easy to understand

3

Fully customized supplement with
a unique formula based on the
patient's profile.

Personalized Prevention Plan

First step dietary and lifestyle recommendations based on test results



GenknowStress results: Dietary and dietary supplementation recommendations

Metabolic system

Fibersⁱ

Fiber is beneficial for both healthy individuals and those with diabetes. It helps control blood sugar levels and may lower the risk of type 2 diabetes. Soluble fibers, such as beta-glucan, slow down carbohydrate absorption, aiding in blood sugar control. Insoluble fibers enhance insulin sensitivity and help remove carcinogens from the body. The Adequate Intake for fiber is 38 g for men and 25 g for women, with adult daily recommendations ranging from 25 to 38 g.

Fish oilⁱⁱ

Fish oil, rich in omega-3 fatty acids EPA and DHA, is found in salmon and anchovies and is available as both a dietary source and a prescription medication. It is extensively studied for its benefits in reducing cardiovascular risks and managing conditions like hypertension. Fish oil has been shown to lower triglyceride levels and modestly decrease blood pressure, particularly in those with hypertension. For maintaining general health, a minimum of 1,000 mg of combined EPA and DHA is recommended, which can be sourced from diet or supplements.

L-carnitineⁱⁱⁱ

L-carnitine, synthesized from amino acids lysine and methionine, is essential for the transport of fatty acids into mitochondria for energy production. As a supplement, its variant, acetyl-L-carnitine, crosses the blood-brain barrier efficiently. Supplementation has shown benefits in nonalcoholic fatty liver disease, improving metabolic syndrome, blood pressure, glucose levels, and lipid profiles, and reducing inflammation. The standard dose for L-carnitine is between 1,000 and 3,000 mg daily.

1

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Immune system

Zinc^{iv}

Zinc is an essential mineral important for numerous aspects of cellular function, including immune function and protein synthesis. It is particularly known for its role in enhancing immune response and wound healing. Zinc can be obtained from dietary sources with high levels found in meat, shellfish, legumes, and seeds. It is often recommended for boosting immune health, especially in reducing the severity and duration of colds. Typical supplementation doses range from 15–30 mg per day, which is absorbed when taken with a meal.

Vitamin D^v

Vitamin D is crucial for bone health, immune function, and overall cellular health. It is synthesized in the skin through sun exposure. It is also naturally present in fatty fish and eggs and is often fortified in dairy products. The recommended daily allowance (RDA) for vitamin D is 400–800 IU, but doses of 1,000–2,000 IU are often used to ensure adequate levels in most adults. It is best absorbed when taken with a source of fat.

Fish oil (see above)^{vi}

Fish oil is valued for its rich content of omega-3 fatty acids, namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are beneficial for cardiovascular conditions and general health. Fish oil can be sourced from diet or supplements and is effective in various forms including dietary supplements and prescription medication.

Echinacea^{vii}

Echinacea, native to North America, has been used historically in traditional herbal medicine. A meta-analysis of double-blind randomized trials found that echinacea could reduce the incidence of upper respiratory infections. Echinacea is administered in doses of 800 mg twice daily and has been used for up to six months in adults.

Curcumin^{viii}

Curcumin, derived from the turmeric plant (*Curcuma longa*), is recognized for its anti-inflammatory properties and its ability to enhance the body's antioxidant production. While it is effective in reducing inflammation markers in general, its effects may be less pronounced in individuals with chronic inflammatory diseases. Common dosages for curcumin range from 300 mg to 4,000 mg daily, and absorption is significantly improved when combined with piperine (black pepper extract) or lipids (e.g., BCM-95®, Meriva®).

2

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Cardiovascular system

Cocoa^{ix}

The cardioprotective properties of cocoa are largely due to its high polyphenol content, especially flavanols like epicatechin and proanthocyanidins. These compounds enhance nitric oxide levels in the bloodstream, which aids in vasodilation and can reduce blood pressure. Cocoa flavanols also help mitigate oxidative stress and inhibit LDL oxidation, contributing to lower cardiovascular disease risk and notably reducing stroke incidence.

Garlic^x

Garlic supplementation is known to reduce oxidative stress markers such as malondialdehyde, as well as inflammatory markers like C-reactive protein and TNF-α. It is also effective in reducing cholesterol levels, particularly in individuals with cardiovascular conditions, enhancing overall cardiovascular health. Typical daily doses range from 600–1,200 mg, often divided across meals. Aged garlic is favored in supplements for its lack of strong odor.

Nitrate-rich vegetables^{xi}

Nitrates in vegetables convert into nitrites and circulate within the body, transforming into the vasodilator nitric oxide (NO) when needed. Common nitrate-rich vegetables include arugula, beetroot, spinach, and kale, among others. These vegetables are often consumed directly or through dietary supplements like beetroot juice to leverage their vascular benefits.

3

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Sérotonine	Score			
Dépression	0	1	2	3
Difficulté à s'endormir	0	1	2	3
Maux de tête	0	1	2	3
Envie de sucres	0	1	2	3
Vite irrité	0	1	2	3
Intestin agité	0	1	2	3
Peu flexible	0	1	2	3
Inébranlable (ne pas s'écarter de ses idées et de ses convictions)	0	1	2	3
Goût pour la solitude	0	1	2	3
Triste	0	1	2	3
Total				

*0 = jamais 1 = parfois 2 = souvent 3 = toujours

Score:






EPISEEK™

EPISEEK™ to detect and monitor cancers.

A liquid biopsy is a simple and non-invasive alternative to surgical biopsies that provides physicians information about a tumor through a simple blood draw. Traces of the tumor's DNA can be found in the blood (cell-free DNA) and can provide insights into the type of cancer, staging (disease progression) and which treatments are more likely to work. EPISEEK™ interrogates cancer specific aberrant DNA methylation cell-free DNA from the liquid biopsy for a proprietary set of biomarkers that always indicate the presence of cancer, as this molecular signature is not found on normal cells. Our technology is cost-effective, precise, may detect cancer earlier than imaging and is more accessible than a tissue biopsy.

Patent issued 2023.

Should we know everything possible about our health ?

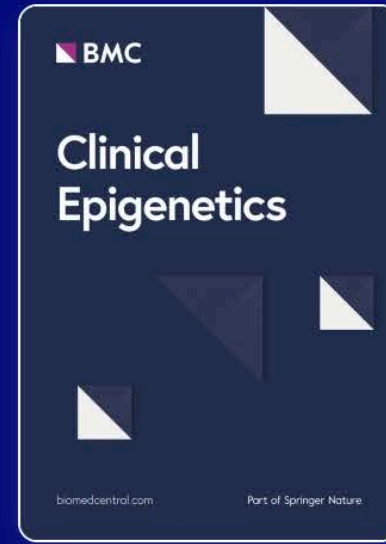
When will I die ?

How will I die ?

Blood DNA methylation signatures of lifestyle exposures: tobacco and alcohol consumption

Research | Open access | Published: 28 November 2022

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Clinical Epigenetics

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