



FishMed-PhD Teaching week 2021

March 1st, 2021



Human population dynamics in traditional fishing communities: genetics, nutrition, health



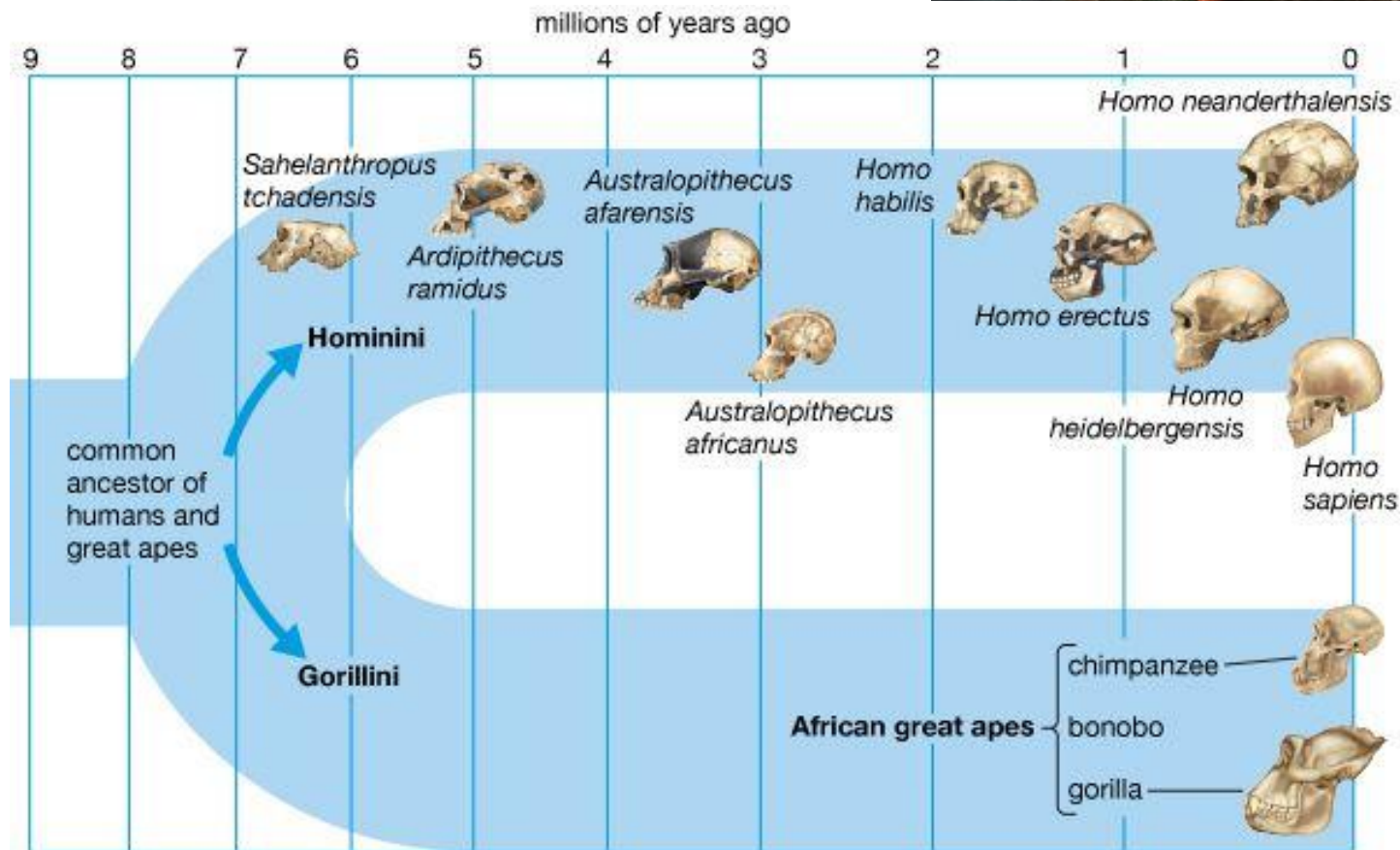
Photo by Andrea De Giovanni

Donata Luiselli
aDNALab, Department of Cultural Heritage
Ravenna Campus, UNIBO

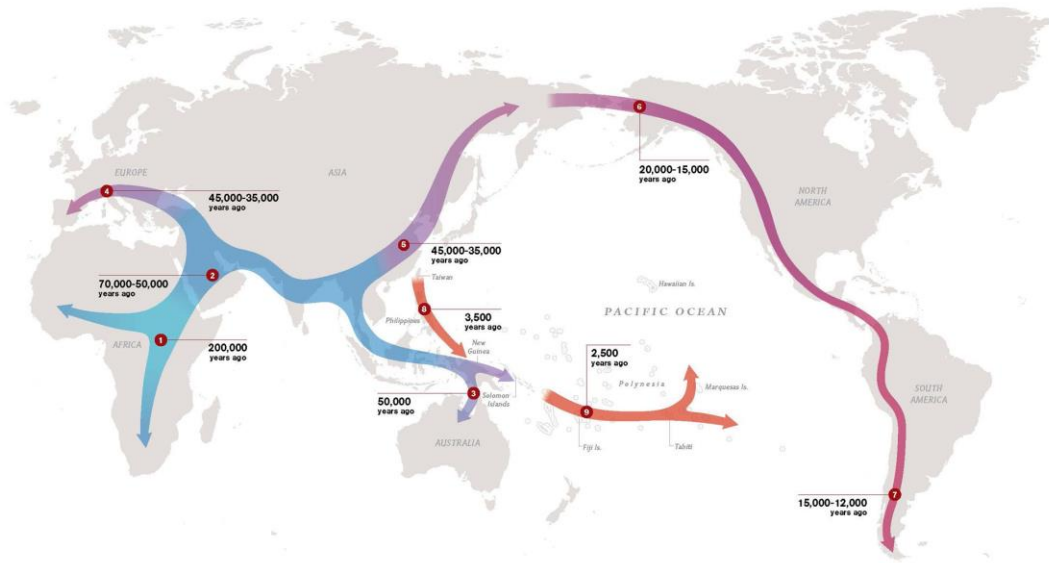
donata.luiselli@unibo.it



WATER IS LIFE



Why does the fish story from our evolutionary past matter today?



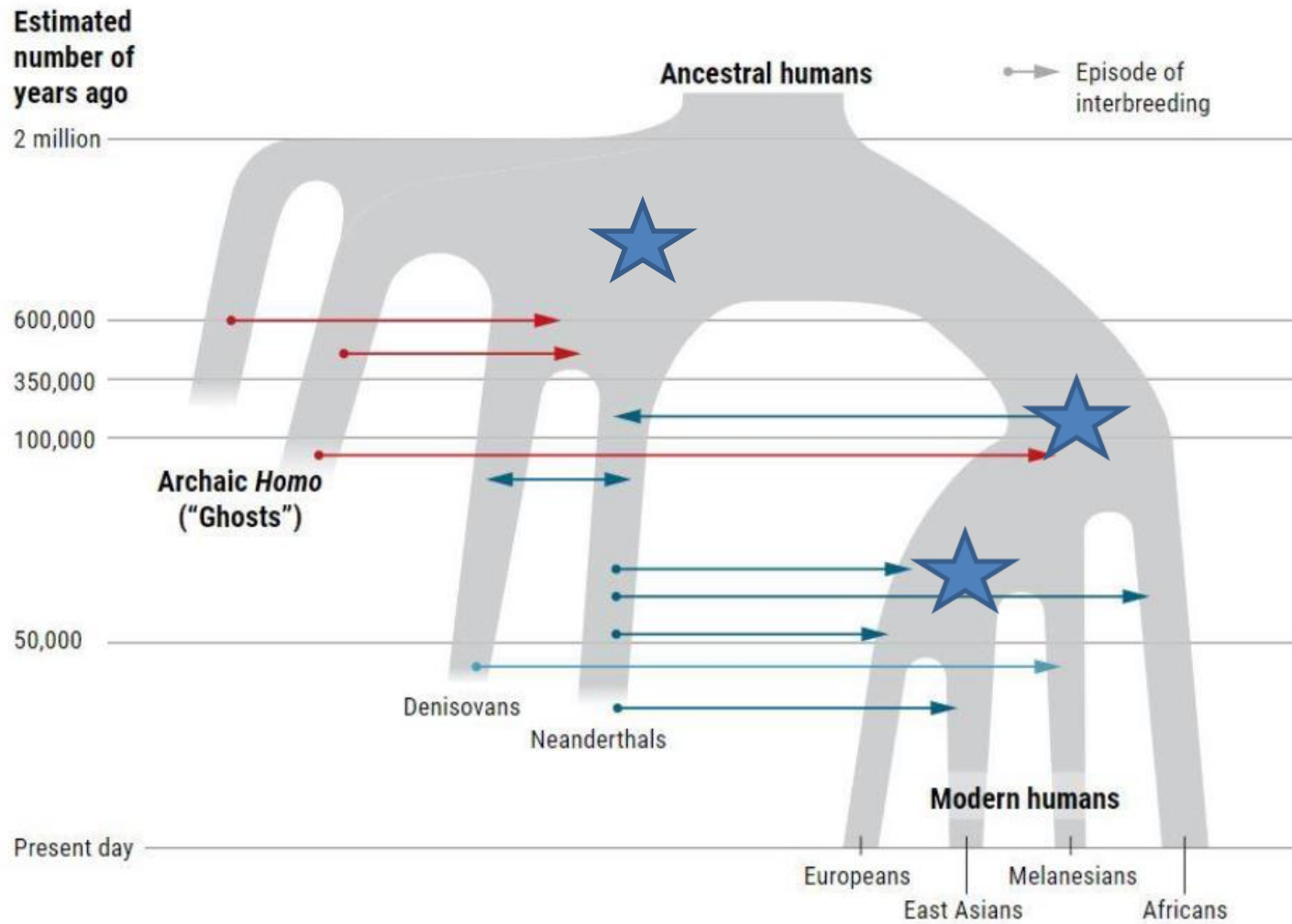
Coastal adaptations have become an important topic in discussions about the evolution and dispersal of *Homo sapiens*.

GLOBAL JOURNEY

Once modern humans began their migration out of Africa some 60,000 years ago, they kept going until they had spread to all corners of the Earth. How far and fast they went depended on climate, the pressures of population, and the invention of boats and other technologies. Less tangible qualities also sped their footsteps: imagination, adaptability, and an innate curiosity about what lay over the next hill.

MAP: INTERNATIONAL MAPS
SOURCE: JAMES SPENCER, NATURAL HISTORY MUSEUM, LONDON
SPENCER PELL, 2007

Homo sapiens evolution and migration from Africa



★ Three key phases in our ancestry

A complex interbreeding

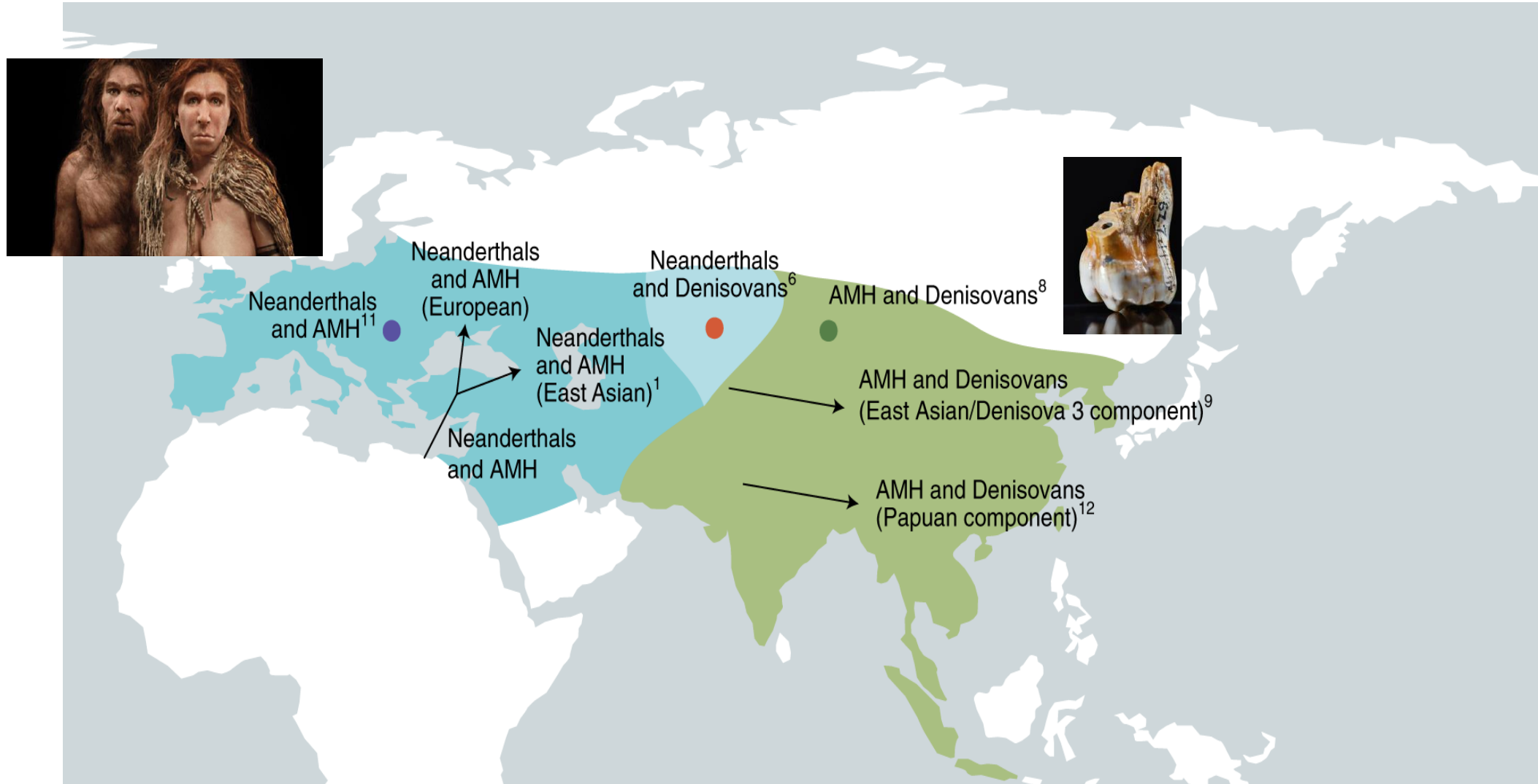
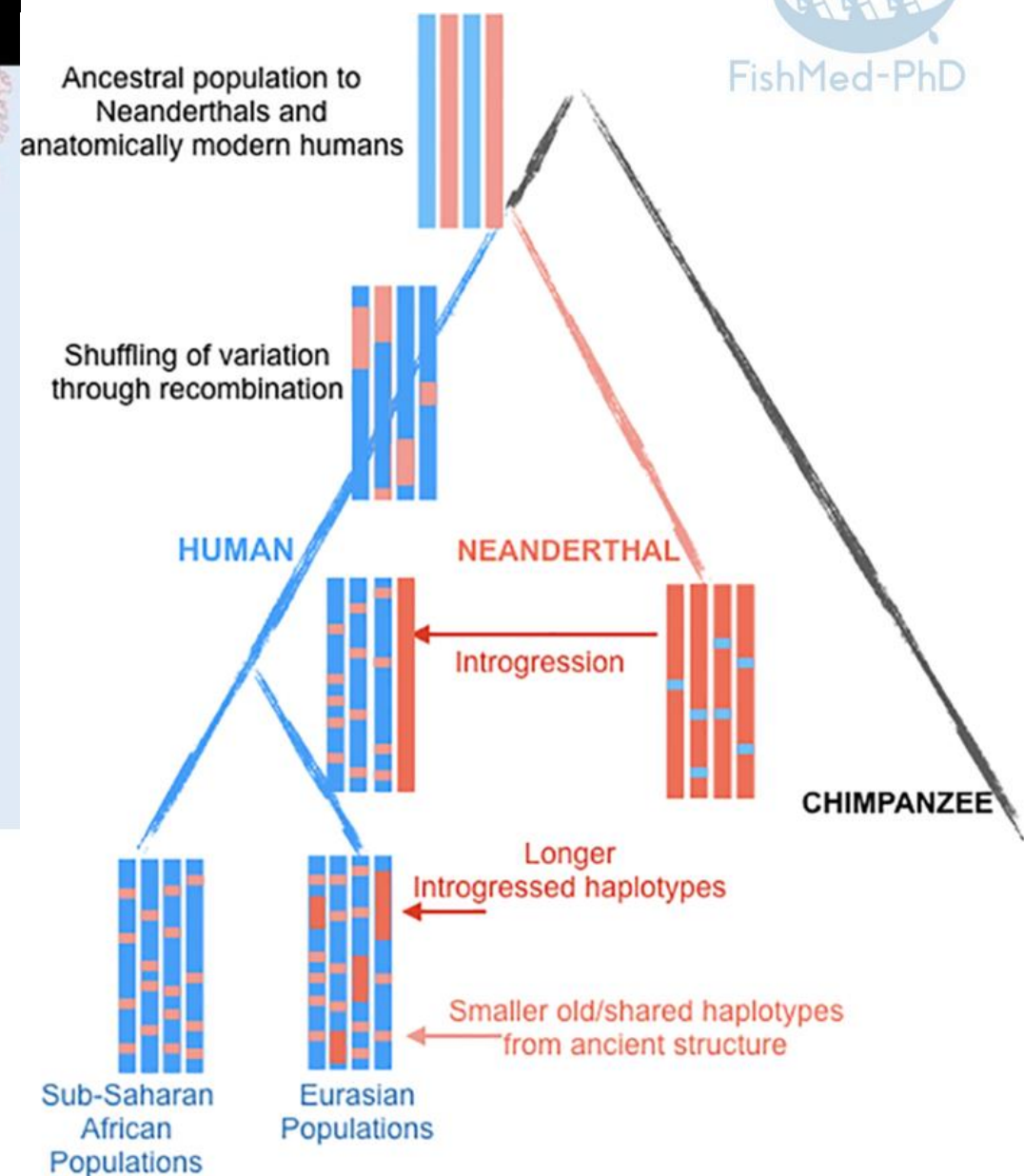
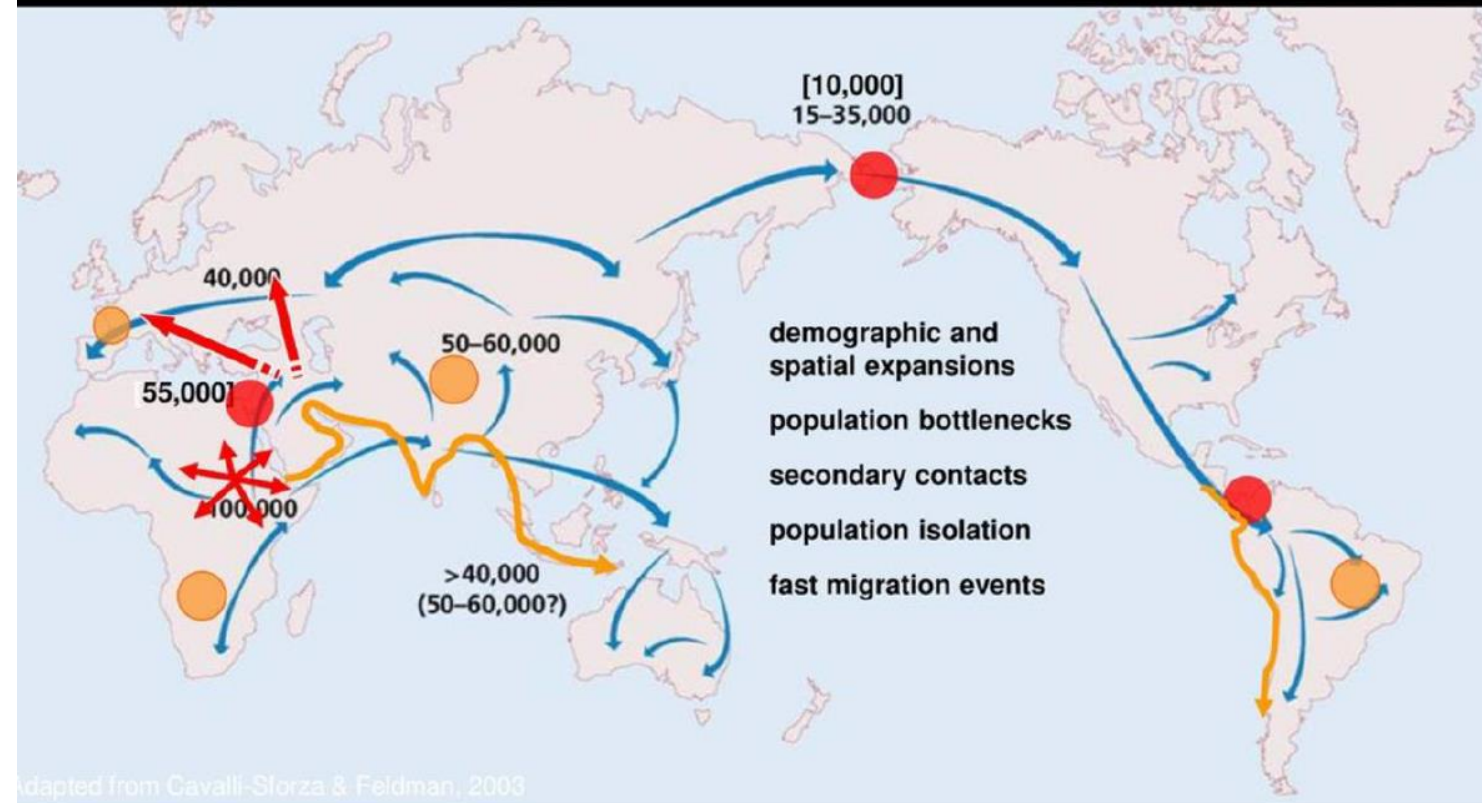


Fig. 1: Map of the encounters between different archaic hominins and ancient modern humans (AMH).

A complex demography

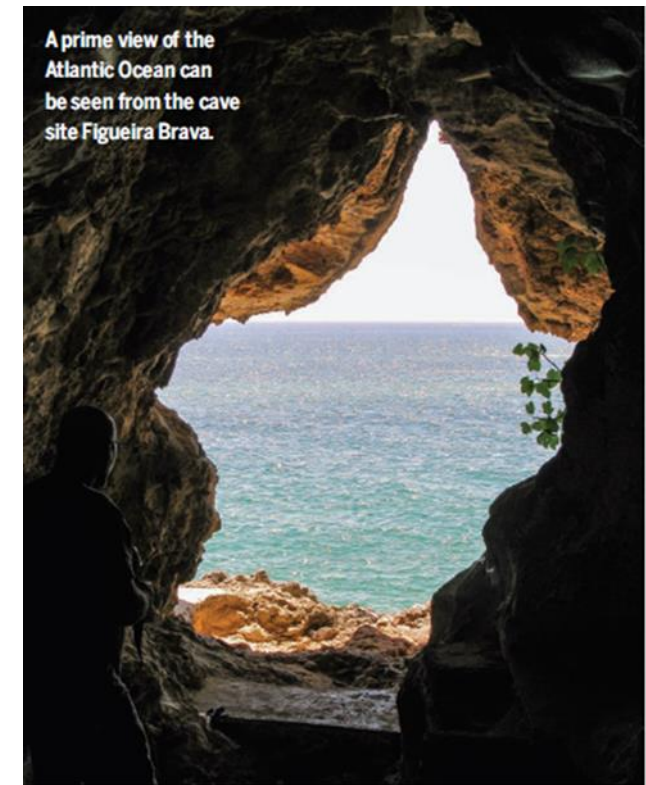


FishMed-PhD



Did Neanderthal adapt to the sea in the same way as early *Homo sapiens*?

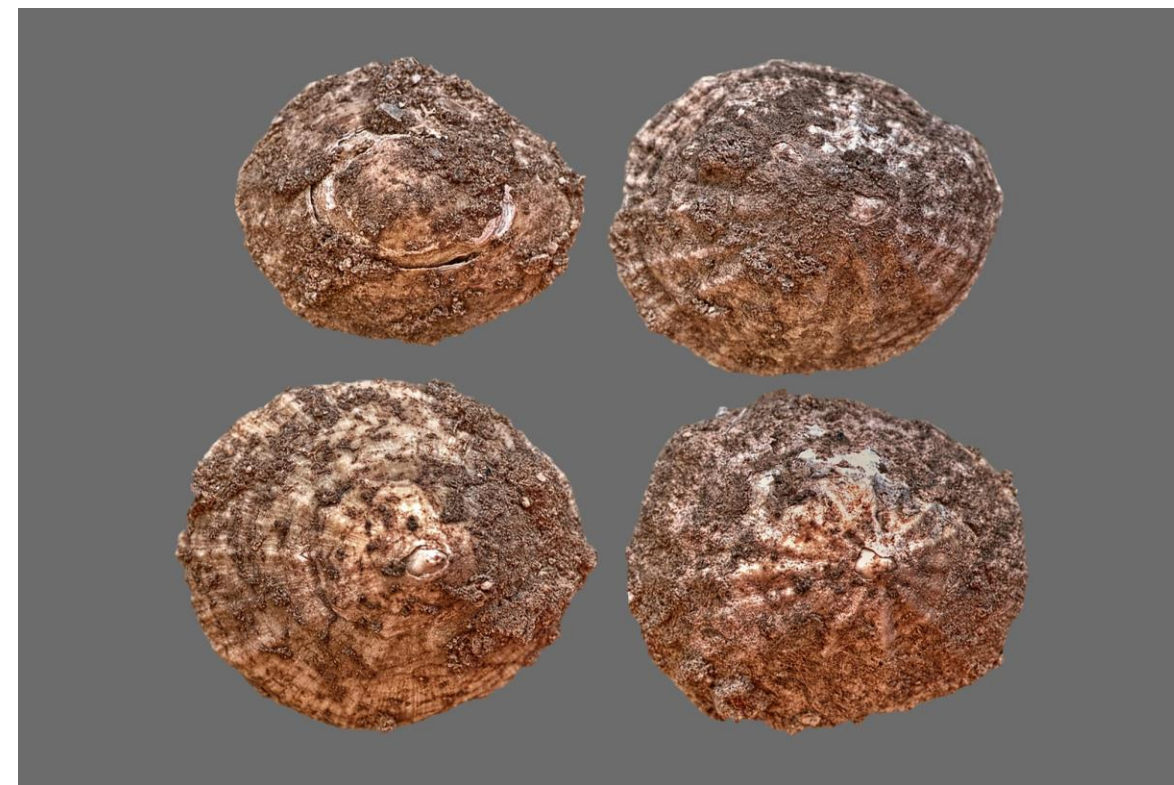
Archaeological research in southern Africa revealed early human coastal adaptations that occurred at least as far back as ~160,000 years ago in the Middle Stone Age (MSA)—the cultural period of the earliest *Homo sapiens*. **Paleolithic sites across Africa and elsewhere support the hypothesis that coastal adaptations have a long and lasting history.**



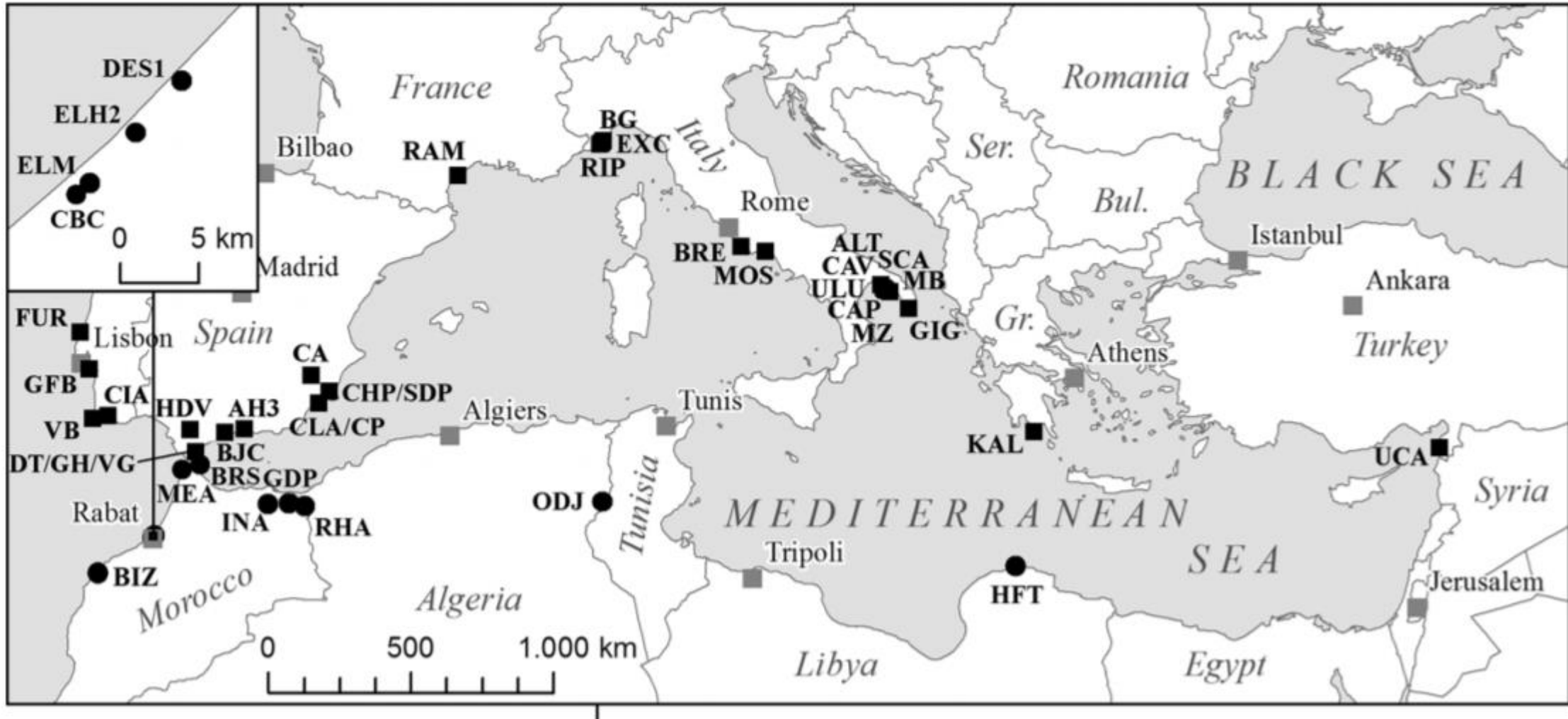


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Shells of *Patella vulgata*, or common limpet, a type of edible sea snail, recovered from a seaside cave in Portugal that was once inhabited by Neanderthals. Zilhao et al. Science, 2020

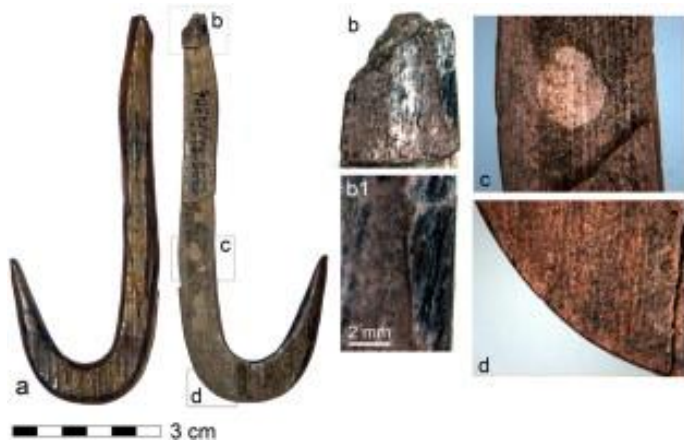


Map depicting the main sites with evidence of coastal adaptations by modern humans in north Africa (circles) and Neanderthals in Europe (rectangles).

There is good evidence for Neanderthal use of marine resources and coastal landscapes from 30 cave, rockshelter and open-air sites associated with MP archaeology.

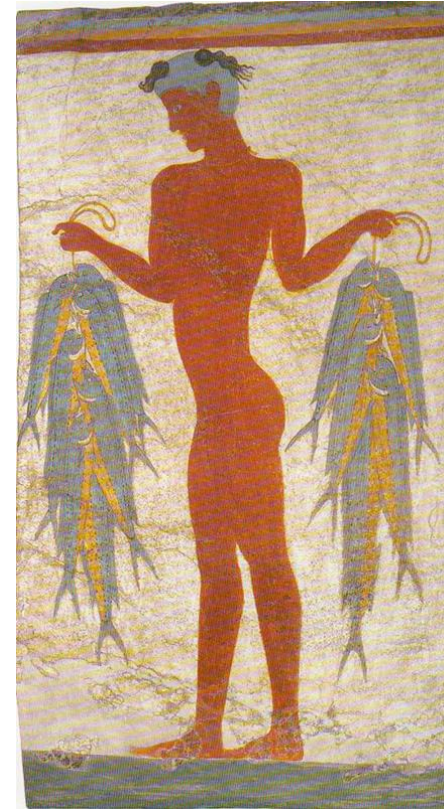
Fishing is a prehistoric practice dating back at least 40,000 years.

Since the 16th century, fishing vessels have been able to cross oceans in pursuit of fish, and since the 19th century it has been possible to use larger vessels and in some cases process the fish on board.



An ivory fishhook with a raw material age of about 19,000 years Final Palaeolithic, site Wustermark 22 (northeastern Germany)

► Mesolithic fishhook tradition has its roots in the Final Palaeolithic.



Little Fisherman. Wall painting, Akrotiri, Thera



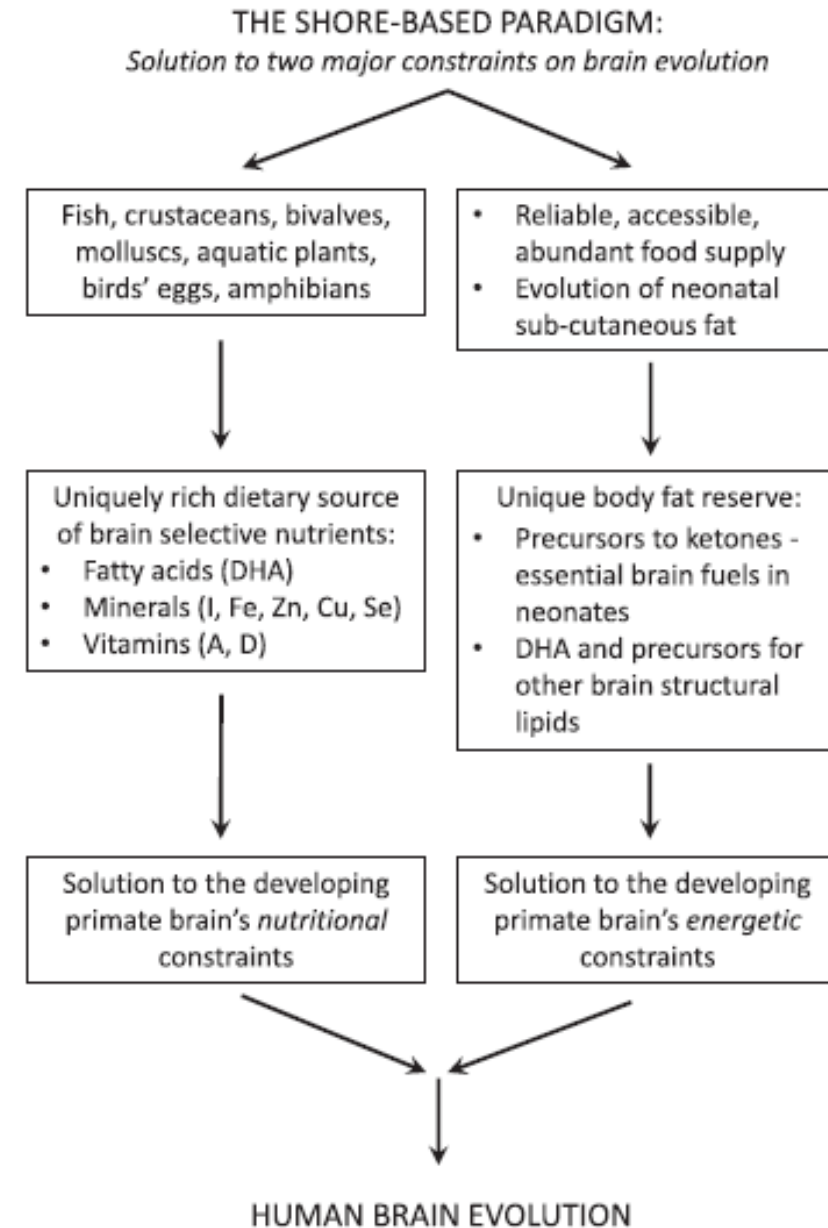
Aegean Talismanic seal with crab, ca. 1450 BC

What are the selective advantages conferred by adopting coastal adaptations?

Shore-based habitats provided abundant and sustained access to a wide selection of foods rich in brain selective nutrients



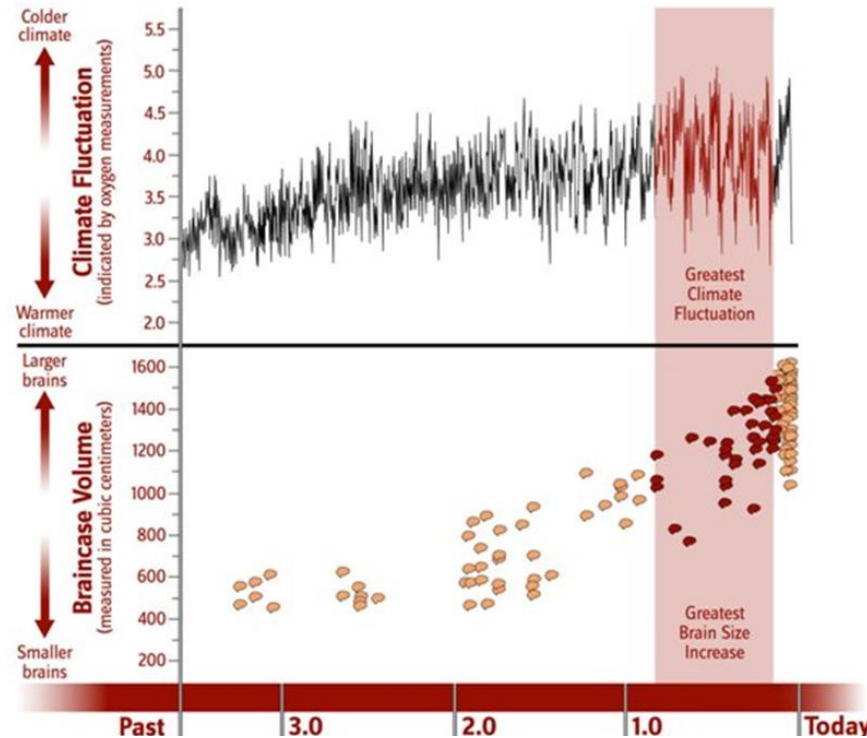
associated to the evolution of neonatal body fat reserves, which were just as important for optimal human brain development.



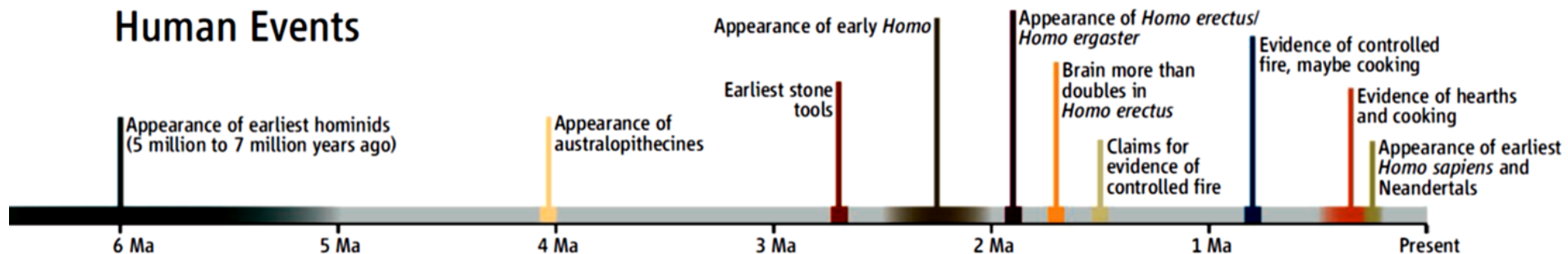
The 'brain hypothesis' for the causal impact of coastal adaptations for human evolution



Over the course of human evolution, brain size tripled



The human brain is nearly 60% fat by total weight, and that big, **powerful brain needs to be provided with certain types of fats (both saturated and unsaturated)** throughout life to provide a balance of structural integrity and fluidity to its cells.

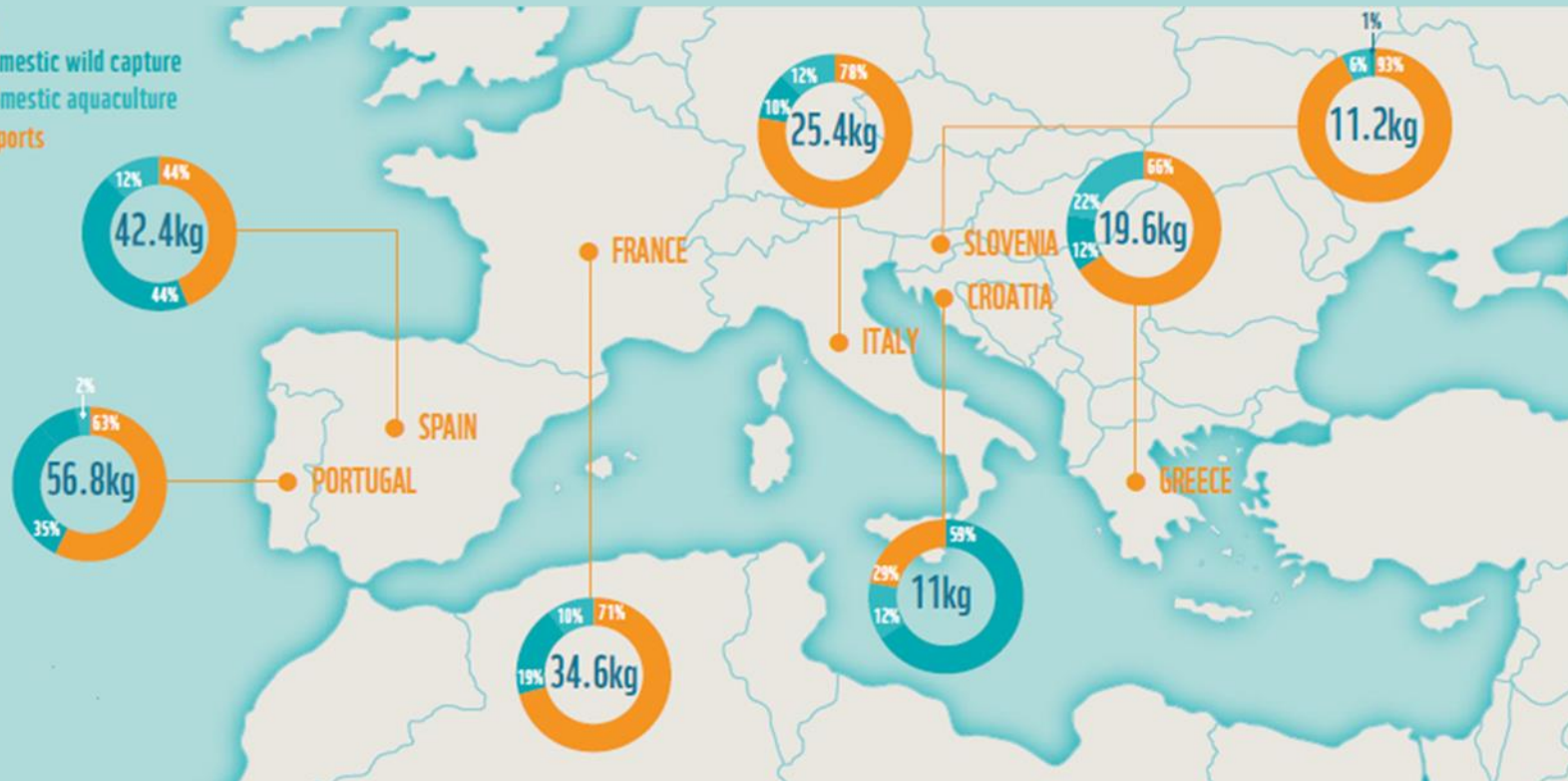


THE MEDITERRANEAN FISH IN A GLOBAL MARKET

EUROPEAN MEDITERRANEAN COUNTRIES: HOW MUCH FISH DO THEY CONSUME, AND HOW MUCH DO THEY IMPORT? KG/CAPITA/PER YEAR

KEY

- Domestic wild capture
- Domestic aquaculture
- Imports



Data: EUMOFA/EUROSTAT; FEAP; Statistical Office of the Republic of Slovenia, 2011; FAO 2013; Croatian Bureau for Statistics, 2015



- ω -3
- Vitamins (D, B2, etc.)
- Calcium
- Phosphorus
- Minerals (iron, zinc, iodine, magnesium, potassium)

- Organochlorine pesticides
- Organotin compounds
- Phthalates
- Brominated flame retardants
- Polyfluorinated compounds
- Polycyclic aromatic hydrocarbons (PAH)
- Dioxins
- Dioxin-like PCBs
- Non-dioxin-like PCBs
- Heavy metals (mercury, cadmium, lead)
- Radionuclides
- Arsenic

Evidence exist that environmental mercury could have been posing a risk to human health since ancient times.

1)

Serrano et al., 2013. Millennial scale impact on the marine biogeochemical cycle of mercury from early mining on the Iberian Peninsula

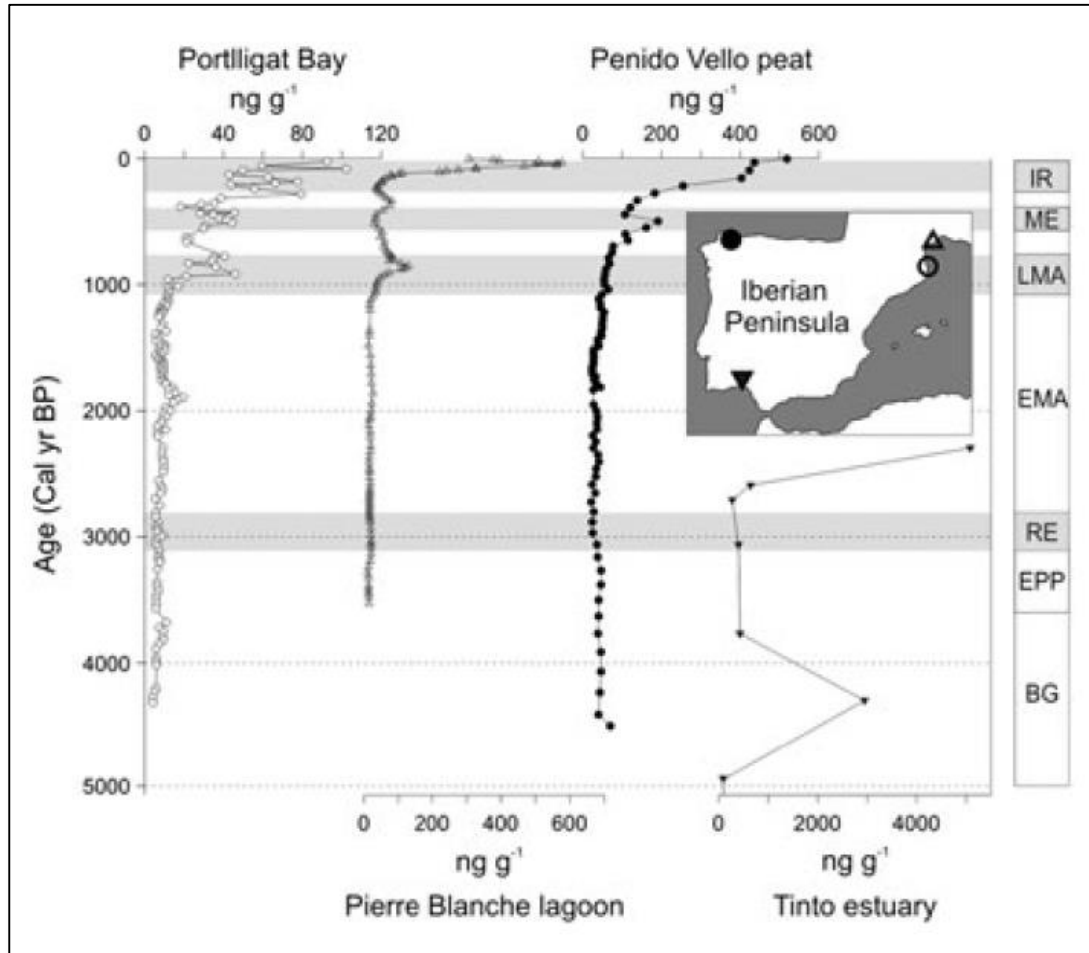
2)

López-Costas et al., 2020. Human bones tell the story of atmospheric mercury and lead exposure at the edge of Roman World

3)

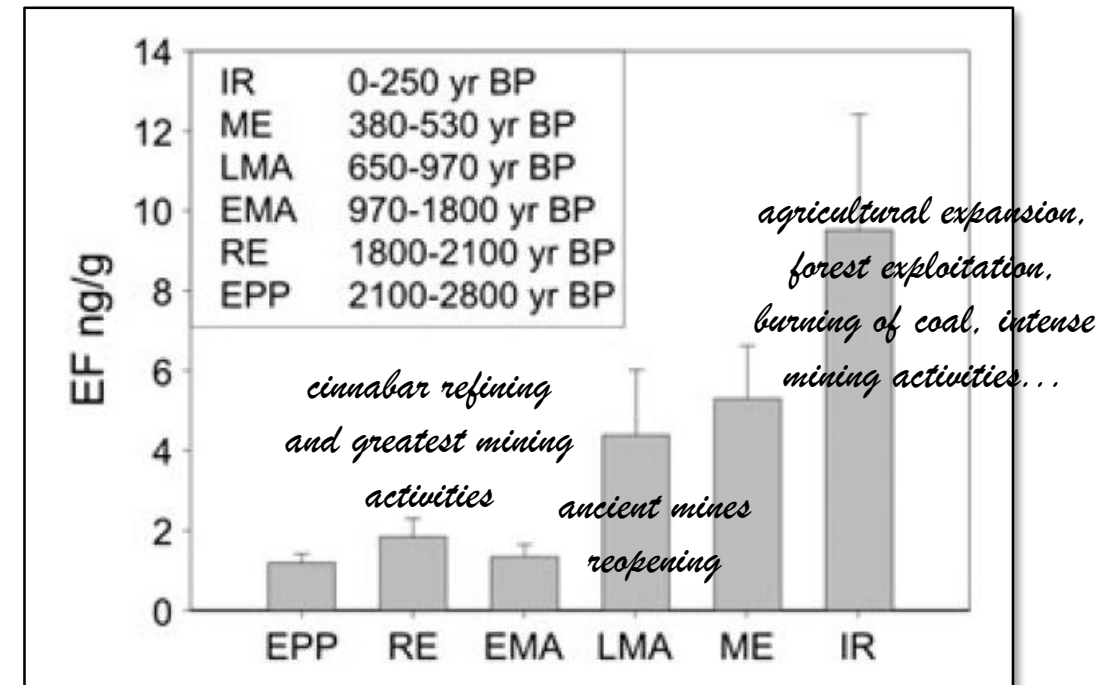
Blankholm et al., 2020. Dangerous food. Climate change induced elevated heavy metal levels in Younger Stone Age seafood in northern Norway

1) Serrano et al., 2013. Millennial scale impact on the marine biogeochemical cycle of mercury from early mining on the Iberian Peninsula

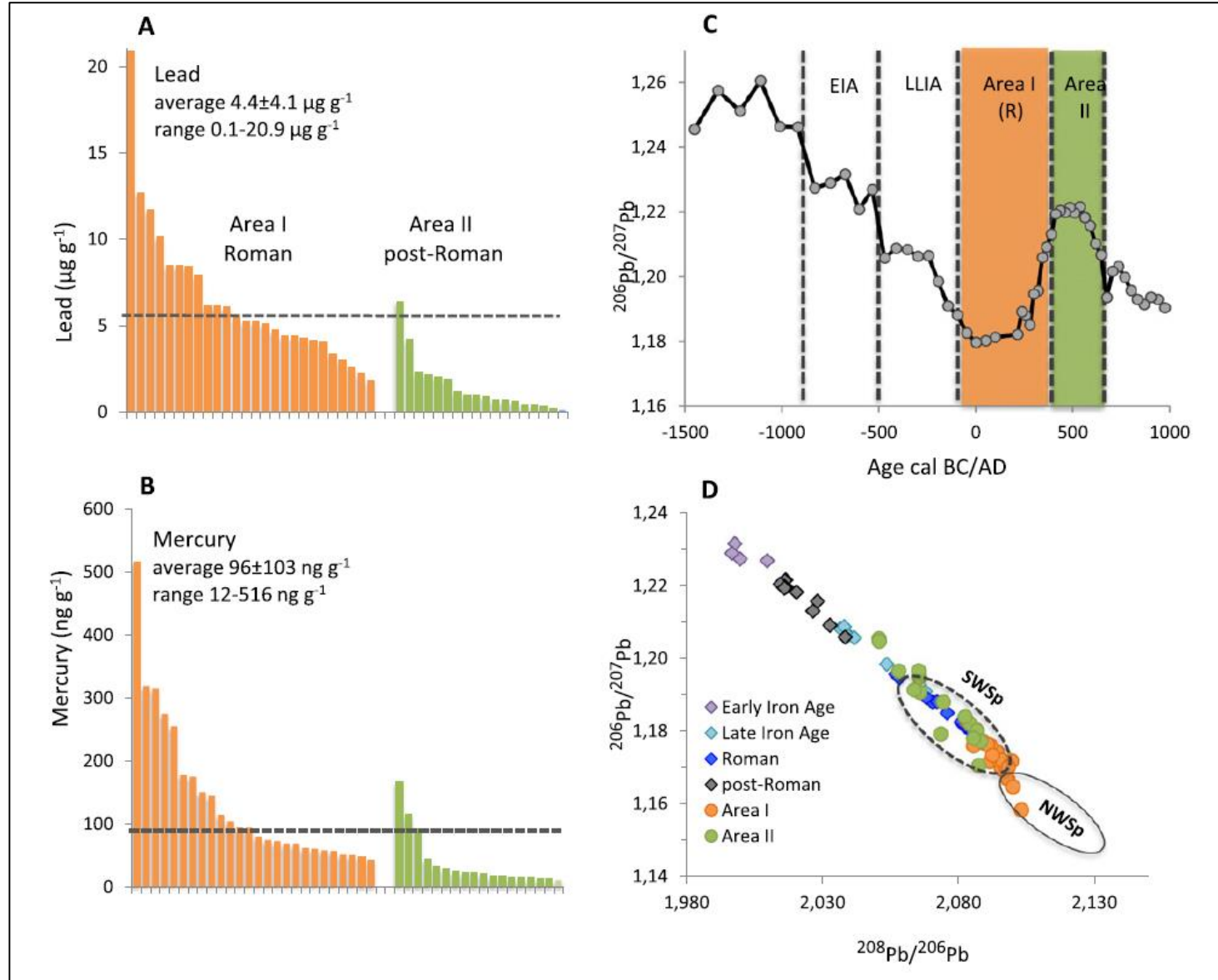


Chronology of Hg pollution in southern France and the Iberian Peninsula.

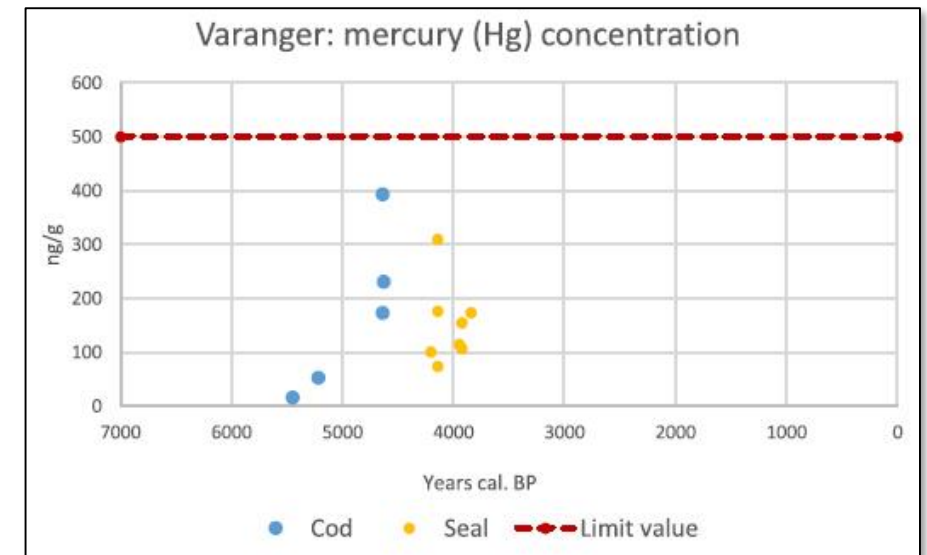
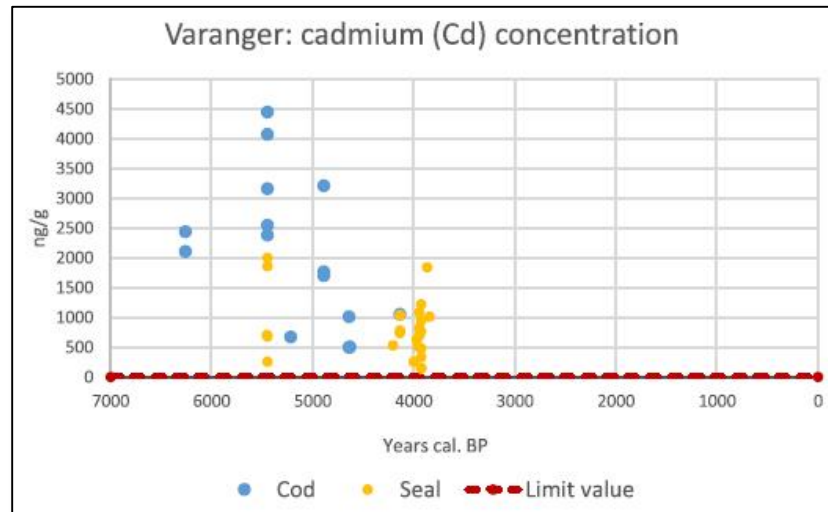
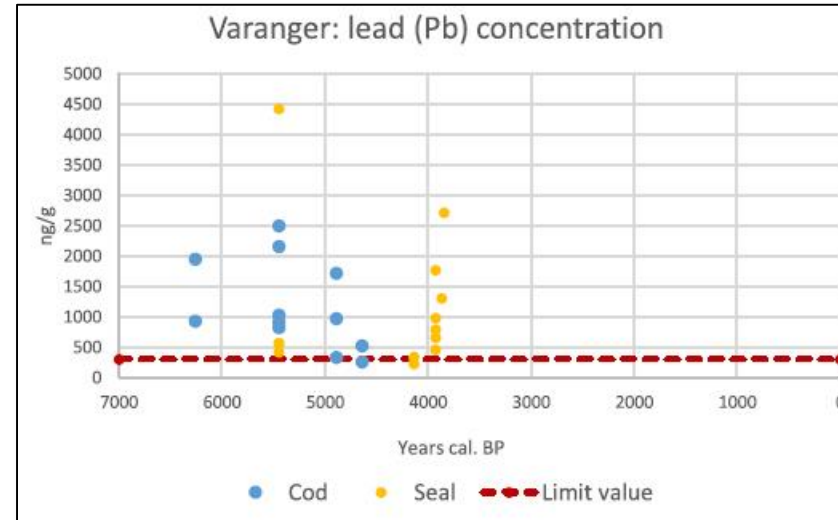
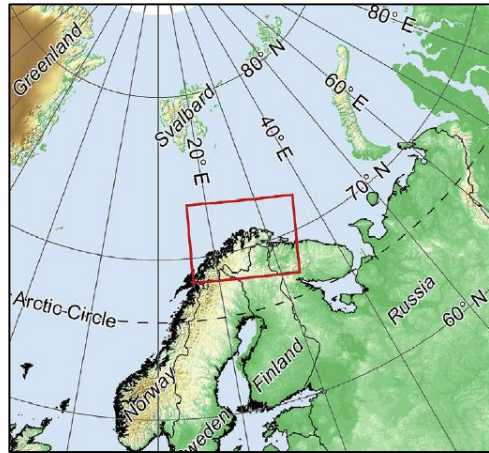
Average enrichment factors \pm SD with respect to background levels (samples older than 2800 cal yr BP) (EPP, early pollution period; RE, Roman Empire; EMA, Early Middle Ages; LMA, Late Middle Ages; ME, modern era; IR, Industrial Revolution)



2) López-Costas et al., 2020. Human bones tell the story of atmospheric mercury and lead exposure at the edge of Roman World



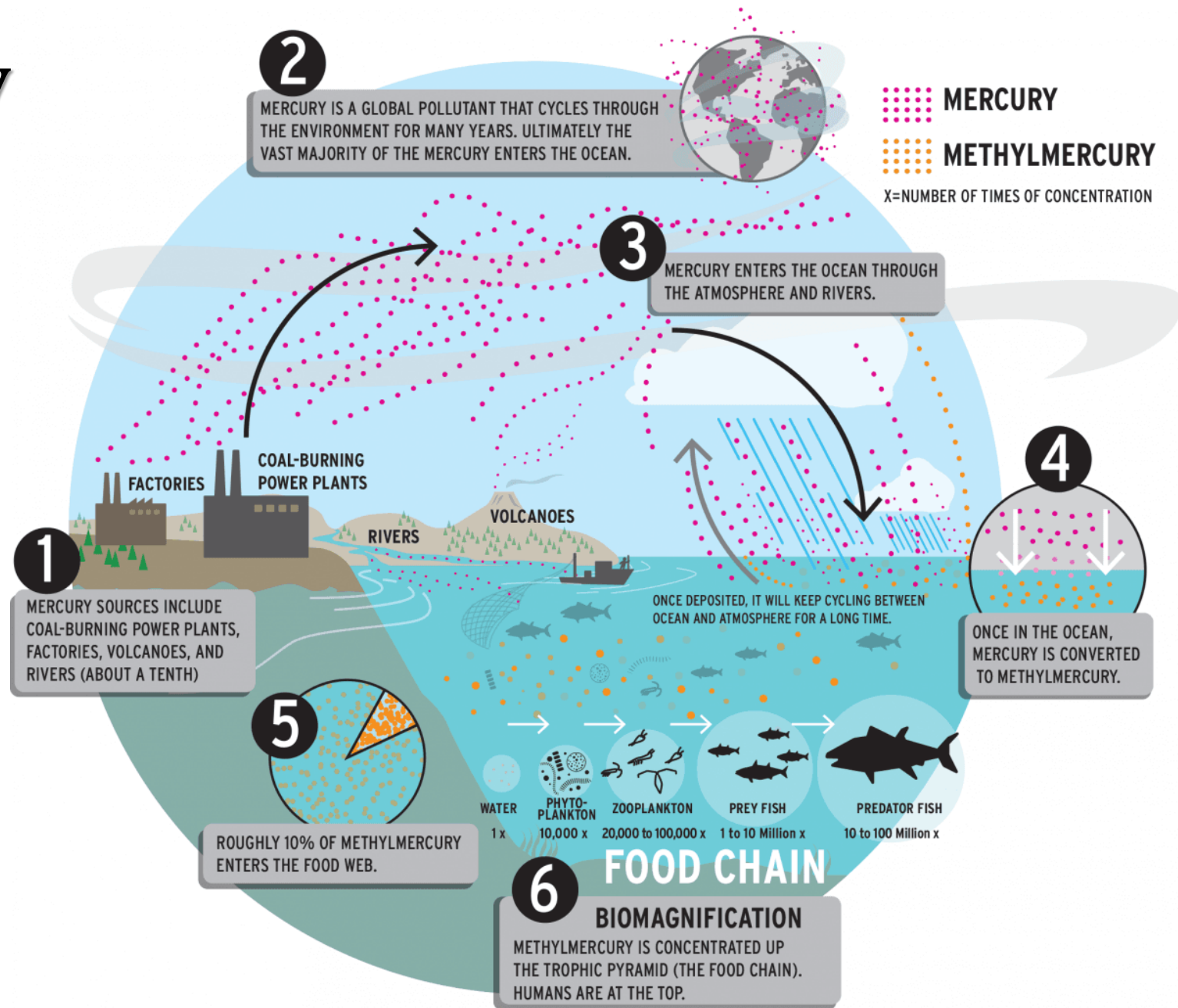
3) Blankholm et al., 2020. Dangerous food. Climate change induced elevated heavy metal levels in Younger Stone Age seafood in northern Norway



Mozzafarian and Rimm, 2006. Fish Intake, Contaminants, and Human Health Evaluating the Risks and the Benefits.

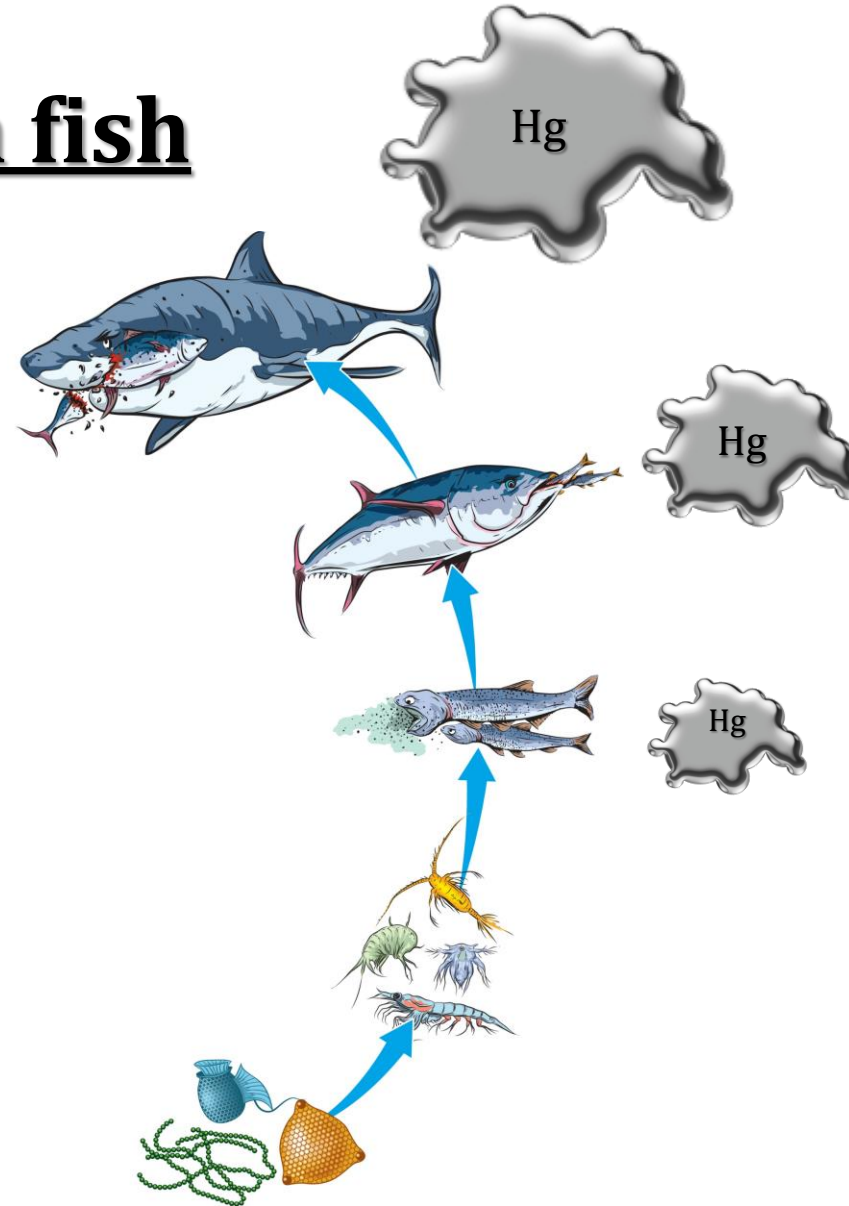


Global mercury (Hg) cycle

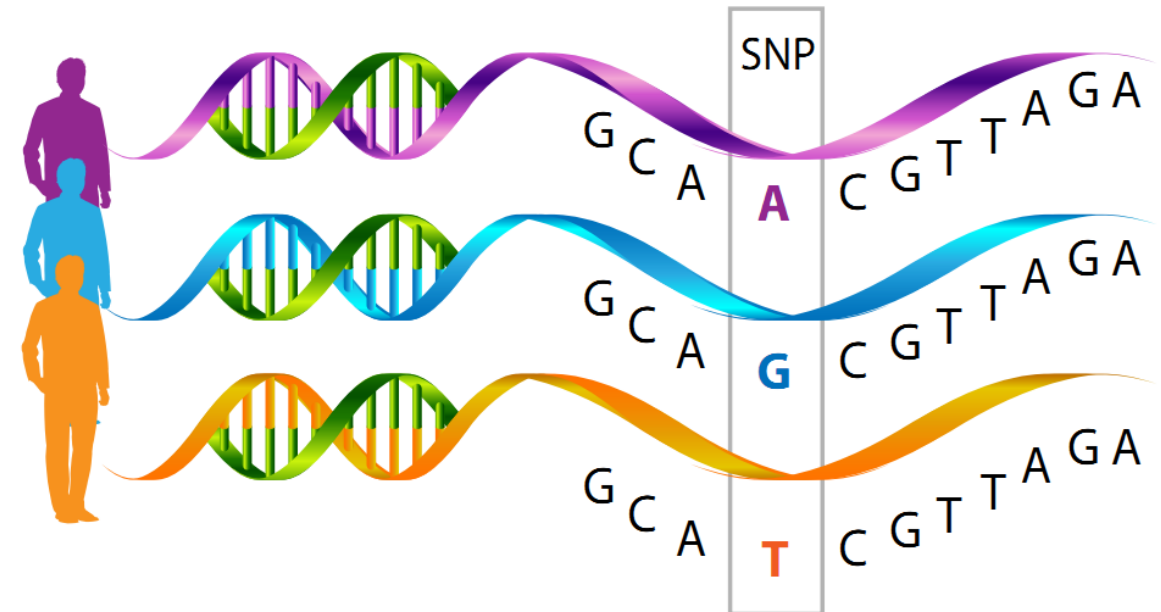
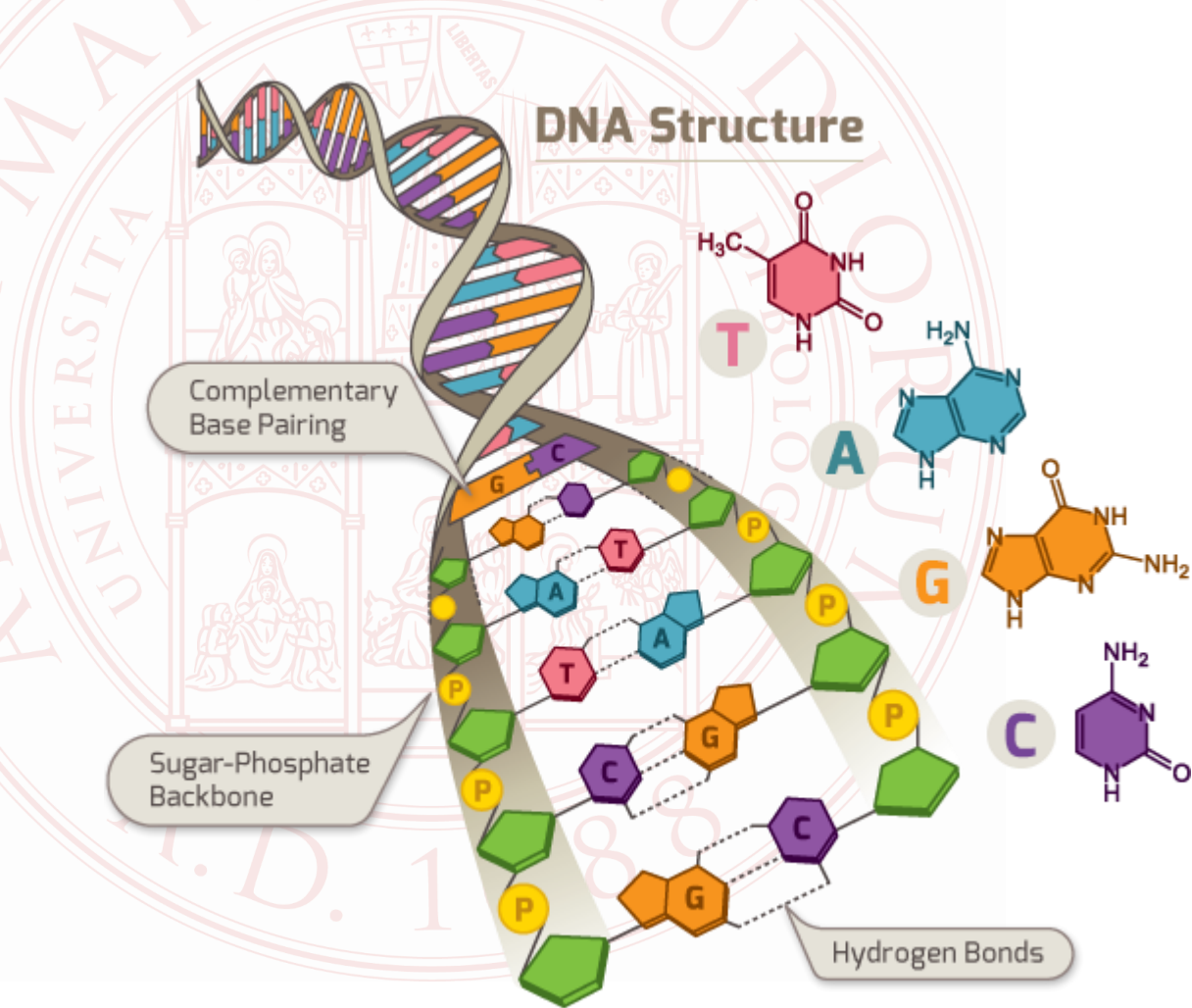


Mercury concentration in fish increases with:

- **Trophic level**
- **Size**
- **Age**
- **Demersal habitat**



- Basu et al., 2014. Ecogenetics of mercury: from genetic polymorphisms and epigenetics to risk assessment and decision-making
- Andreoli and Sprovieri, 2017. Genetic Aspects of Susceptibility to Mercury Toxicity: An Overview
- Joneidi et al., 2019. The impact of genetic variation on metabolism of heavy metals: Genetic predisposition?



Goodrich et al., 2011. Glutathione enzyme and selenoprotein polymorphisms associate with mercury biomarker levels in Michigan dental professionals

This work assumes that polymorphisms in key genes underlie inter-individual differences in mercury body burden as assessed by mercury measurement in urine and hair, biomarkers of elemental mercury and methylmercury, respectively.



Elemental Hg
(main source: dental amalgams)



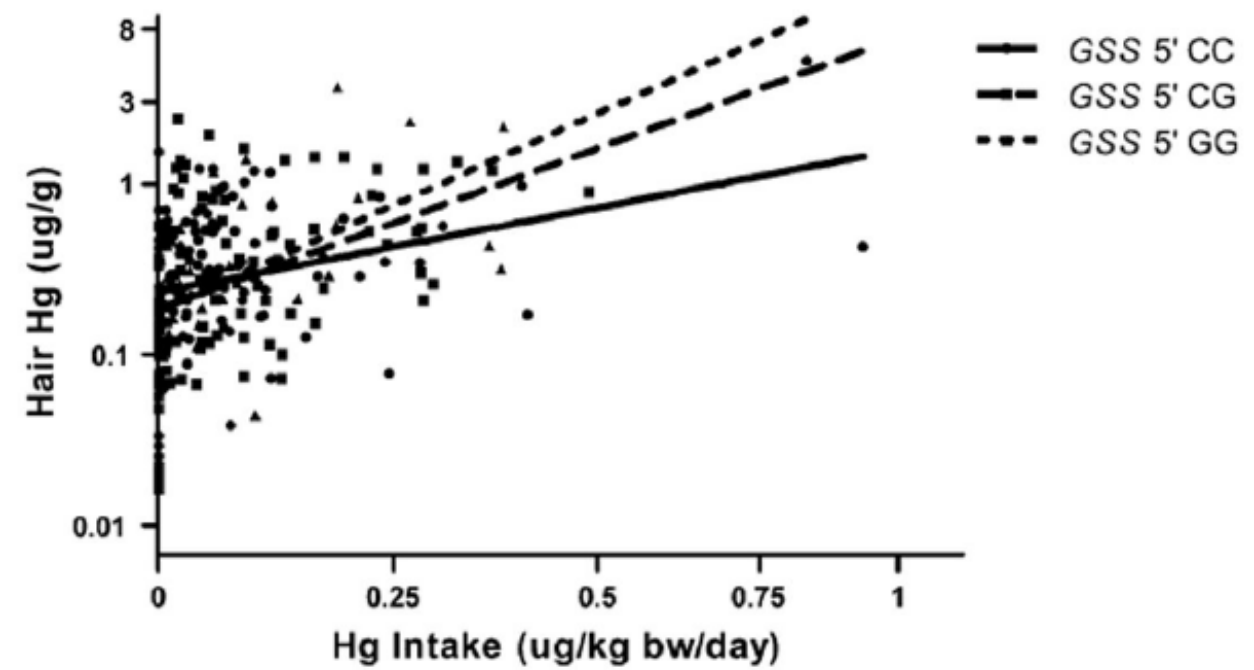
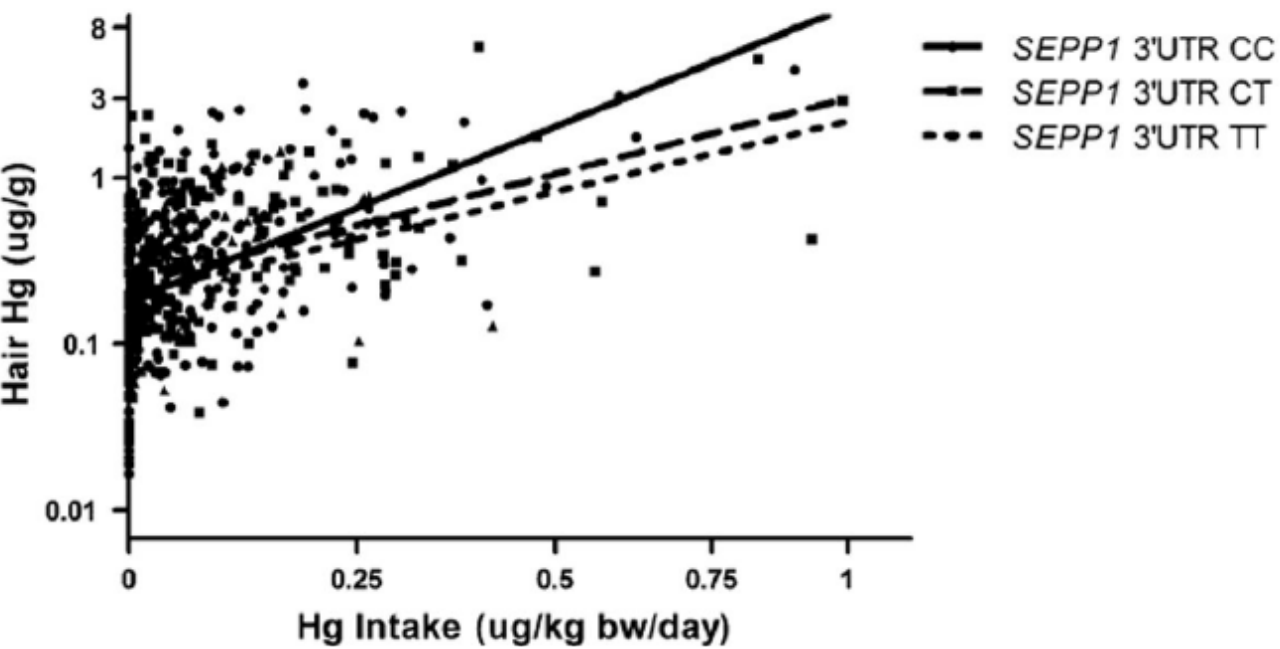
MeHg
(main source: seafood)

1) Fish consumption as estimated by a self-administered survey was the best predictor of measured hair mercury level

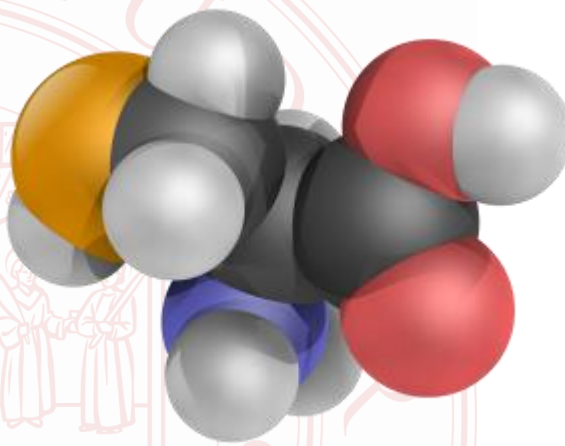
2) Regression model:

TaqMan SNP Genotyping Assay

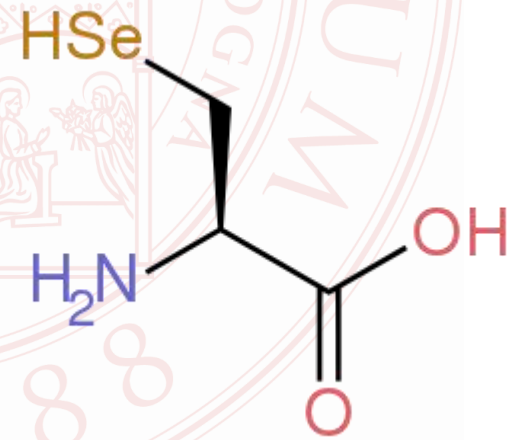
- Major homozygote
- Heterozygote
- Minor homozygote



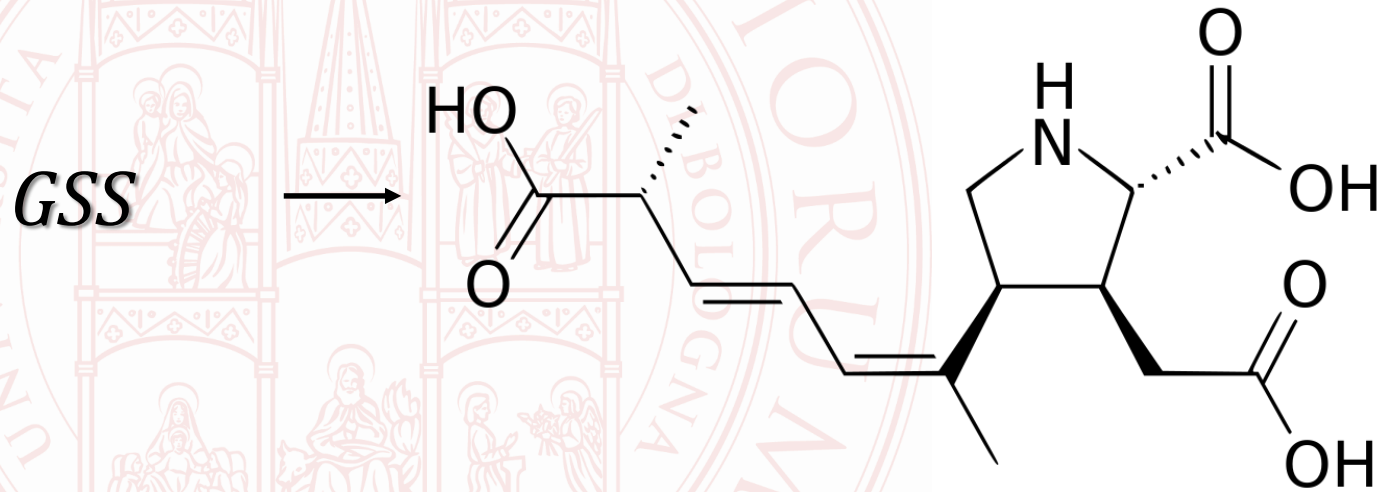
SEPP1



Selenoprotein P plasma 1



SEPP1 3'UTR T allele is linked to greater *SEPP1* expression and mercury binding capacity.



**Glutathione synthetase is
a potent antioxidant**

Minor allele (G)

Decreased expression of GSS

**Reduced MeHg
elimination**

de Oliveira et al., 2014. Genetic Polymorphisms in Glutathione (GSH-) Related Genes Affect the Plasmatic Hg/Whole Blood Hg Partitioning and the Distribution between Inorganic and Methylmercury Levels in Plasma Collected from a Fish-Eating Population

The aim of the study was to evaluate the effects of polymorphisms in glutathione (GSH-) related genes on the distribution of mercury species (MeHg and IHg) in the plasma compartment.



- 80% of the protein intake from fish
- No industrial activities
- No gold-mining
- No dental amalgam fillings

Questionnaires on sociodemographic, lifestyle,
and health information

+
7-day recall food consumption frequency
questionnaire

Blood sample collection

Genomic analysis

+

Mercury level measurements

Multiplex PCR

GSTM1

GCLC

glutathione S-transferase

glutamate-cysteine ligase

***GSTM1* – Null homozygotes showed higher plasmatic methylmercury levels**

***GCLC* – TT and CT showed higher plasmatic methylmercury levels**

Wahlberg et al., 2018. Maternal polymorphisms in glutathione-related genes are associated with maternal mercury concentrations and early child neurodevelopment in a population with a fish-rich diet

The authors hypothesized that maternal genetic variation linked to GSH pathways could influence MeHg concentrations in pregnant mothers and children and thereby also affect early life development.

- ➔ **Maternal genotypes**
- ➔ **Maternal hair and blood Hg**
- ➔ **Cord blood Hg**
- ➔ **Children's Mental Developmental Index (MDI)
and Psychomotor Developmental Index (PDI)**

TaqMan SNP
Genotyping Assay

GCLC



Glutamate-Cysteine Ligase Catalytic Subunit

GSTP1



Glutathione S-transferase

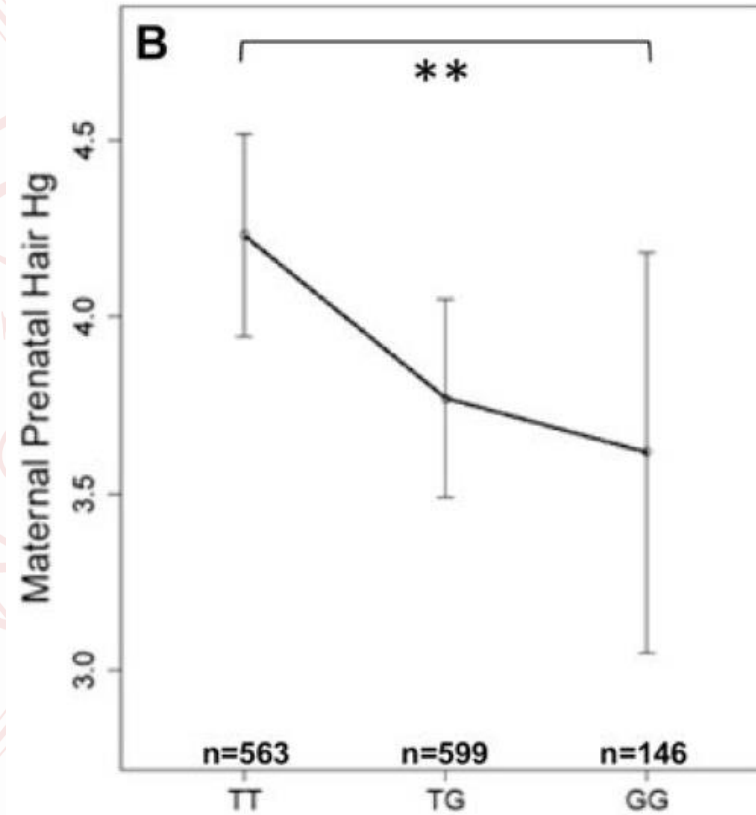
Pyrosequencing

GCLM

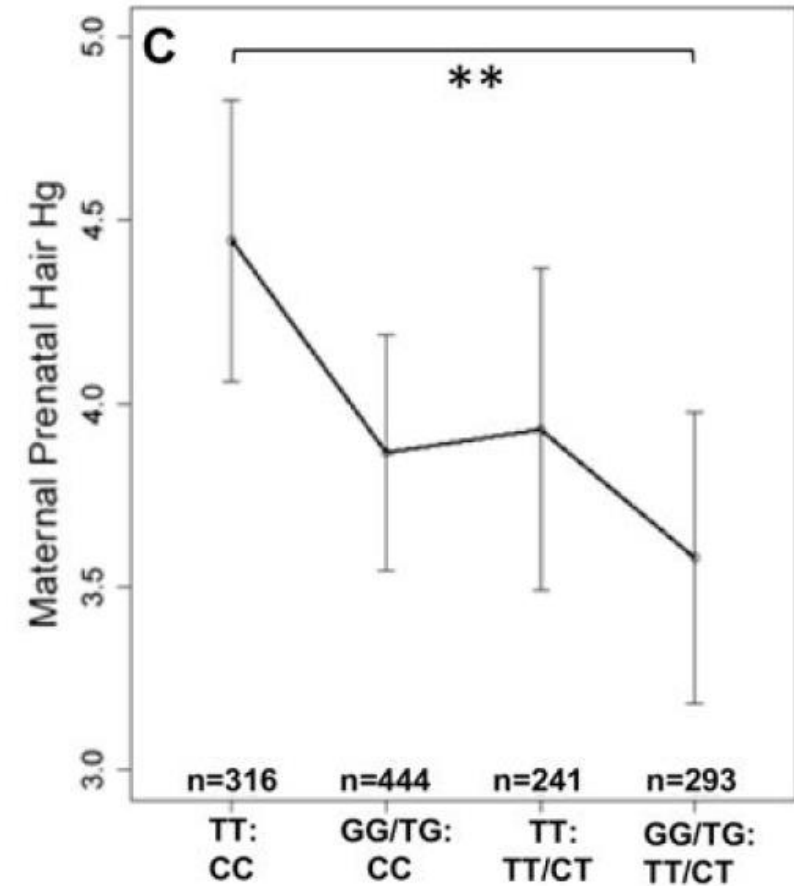


Glutamate-Cysteine Ligase Modifier Subunit

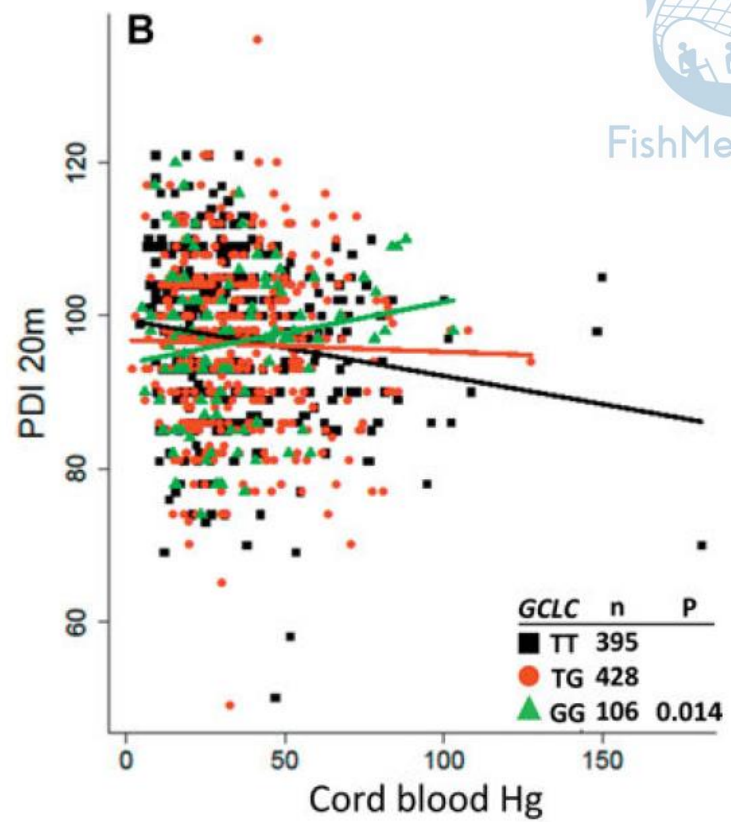
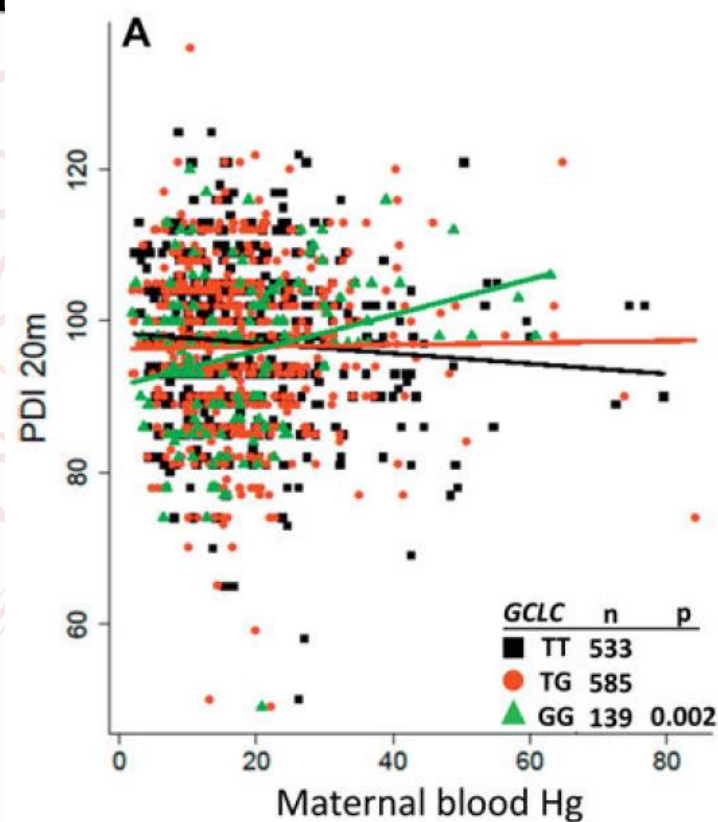
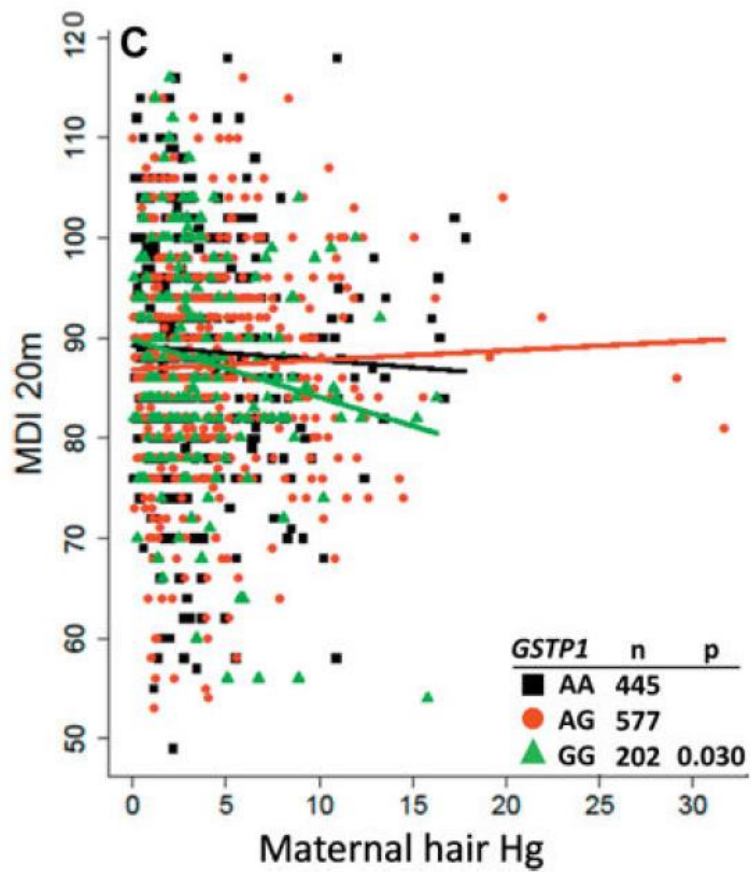
***GCLC* – TT homozygotes showed higher hair Hg levels**



***GCLC GCLM* – TT CC homozygotes showed higher hair Hg levels**



Increasing Hg in maternal and cord blood was associated with lower PDI among GCLC rs761142 TT carriers



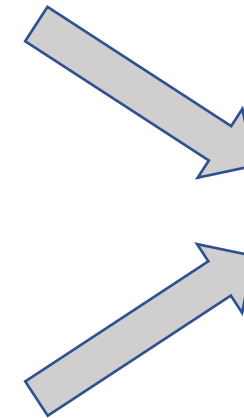
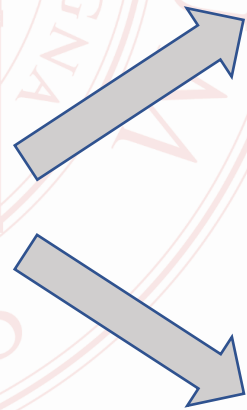
Increasing mercury in hair was associated with lower MDI among GSTP1 rs1695 GG carriers

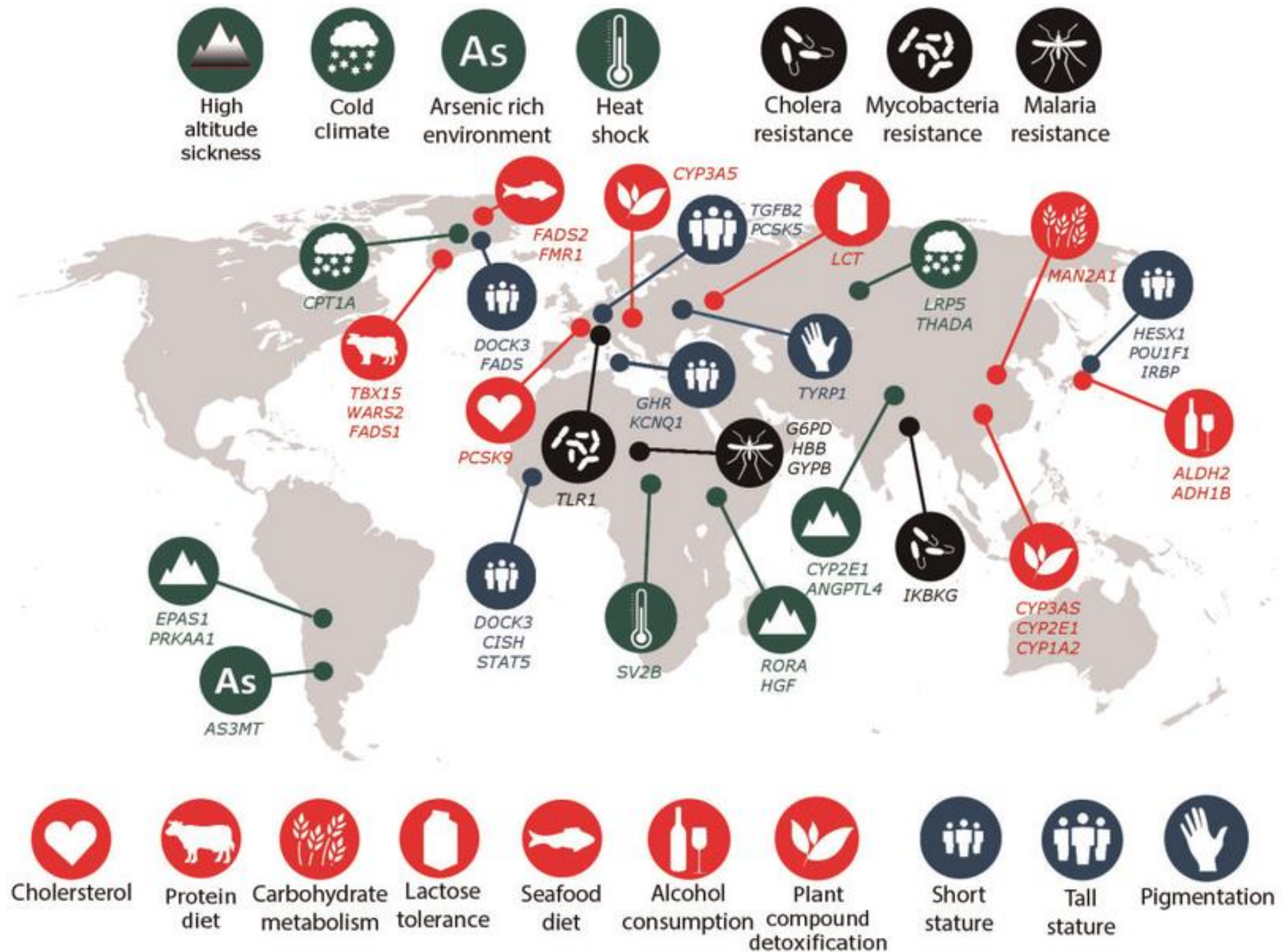
**SEAFOOD NUTRIENTS AND
CHEMICALS MOLECULAR
IMPACT**

**Selective pressure on
genetic and epigenetic
variants**

PHENOTYPIC CHANGES

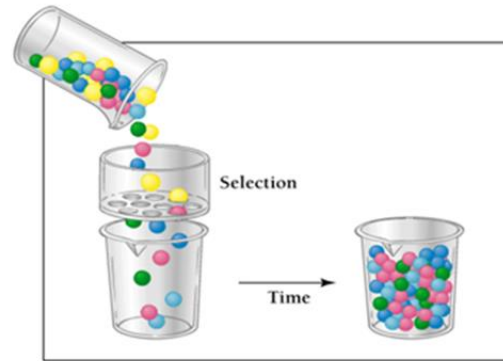
Epigenetic changes





Shaping diversity:

Selection



Differential reproduction of genotypes in succeeding generations

Positive selection

Advantageous mutations increase in frequency

Negative selection

Disadvantageous mutations decrease in frequency

Balancing selection

Multiple alleles are positively selected

Finding selection...

Assumptions

**Comparison of the
variability of genomic
regions**

Genomic regions under selective pressure tend to show less genetic variability than others (e.g. nucleotide diversity, heterozygosity...)

**Comparison of the
allele frequencies**

An allele that has been positively selected is present at a higher frequency than expected for simple chance (e.g. Tajima's D)

**Analysis of the genetic
divergence between
populations**

Genomic regions under selection tend to be more divergent between populations (e.g. Fst, PBS...)

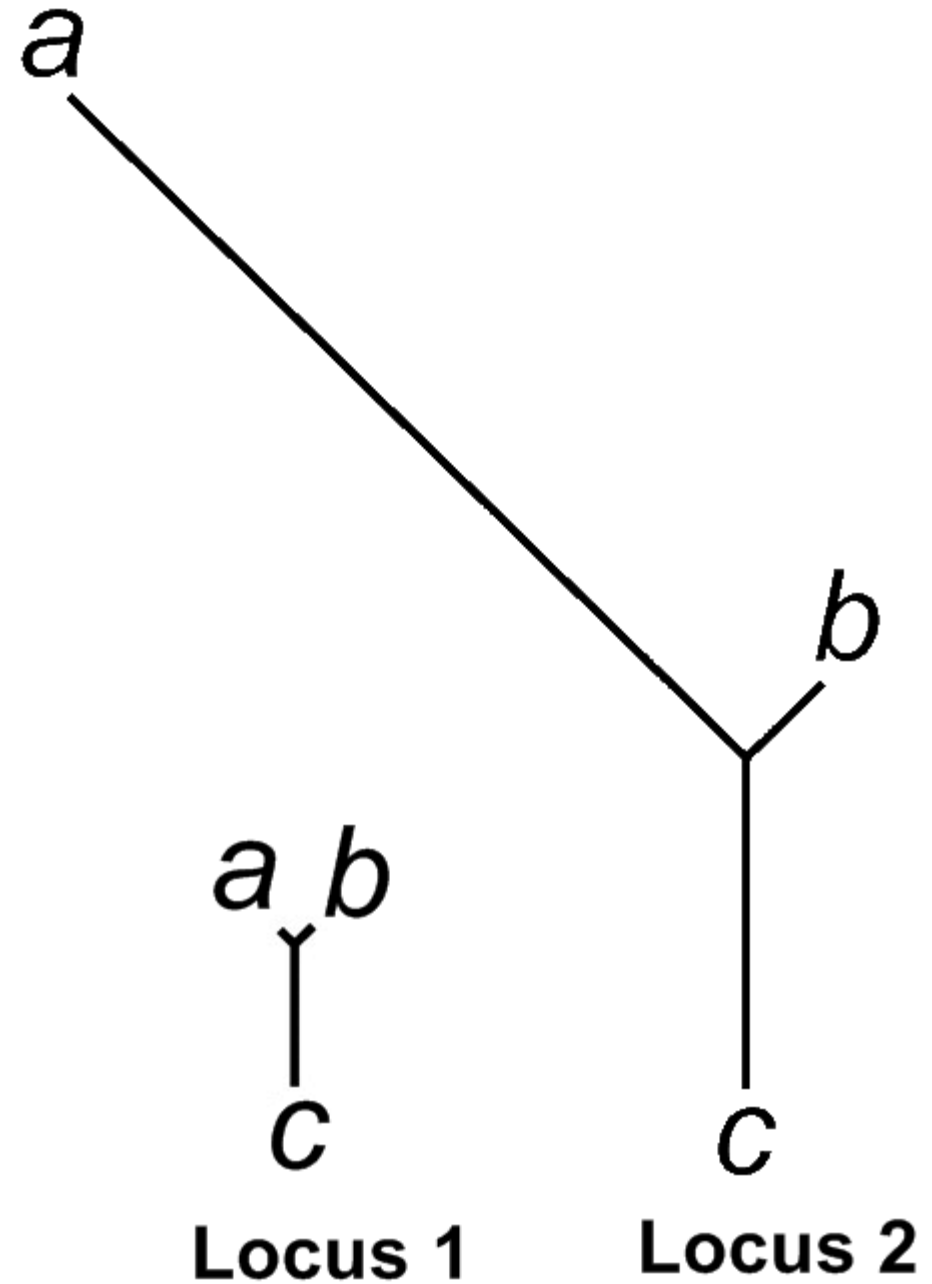
**Analysis of the linkage
disequilibrium
extension**

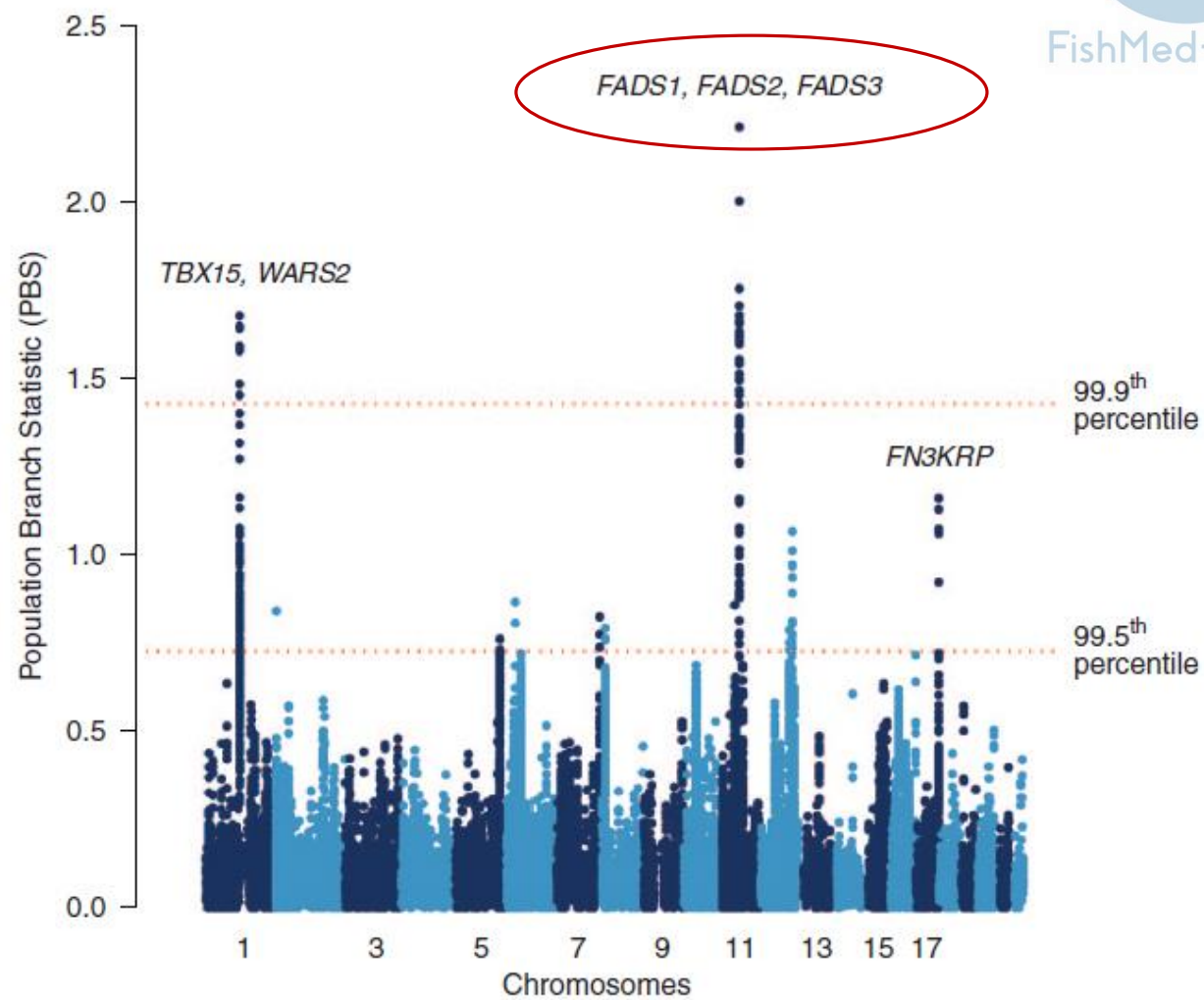
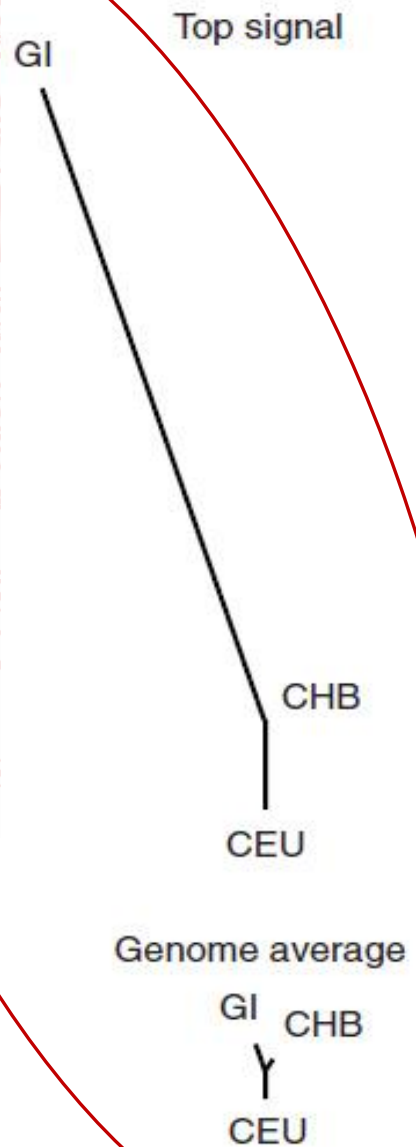
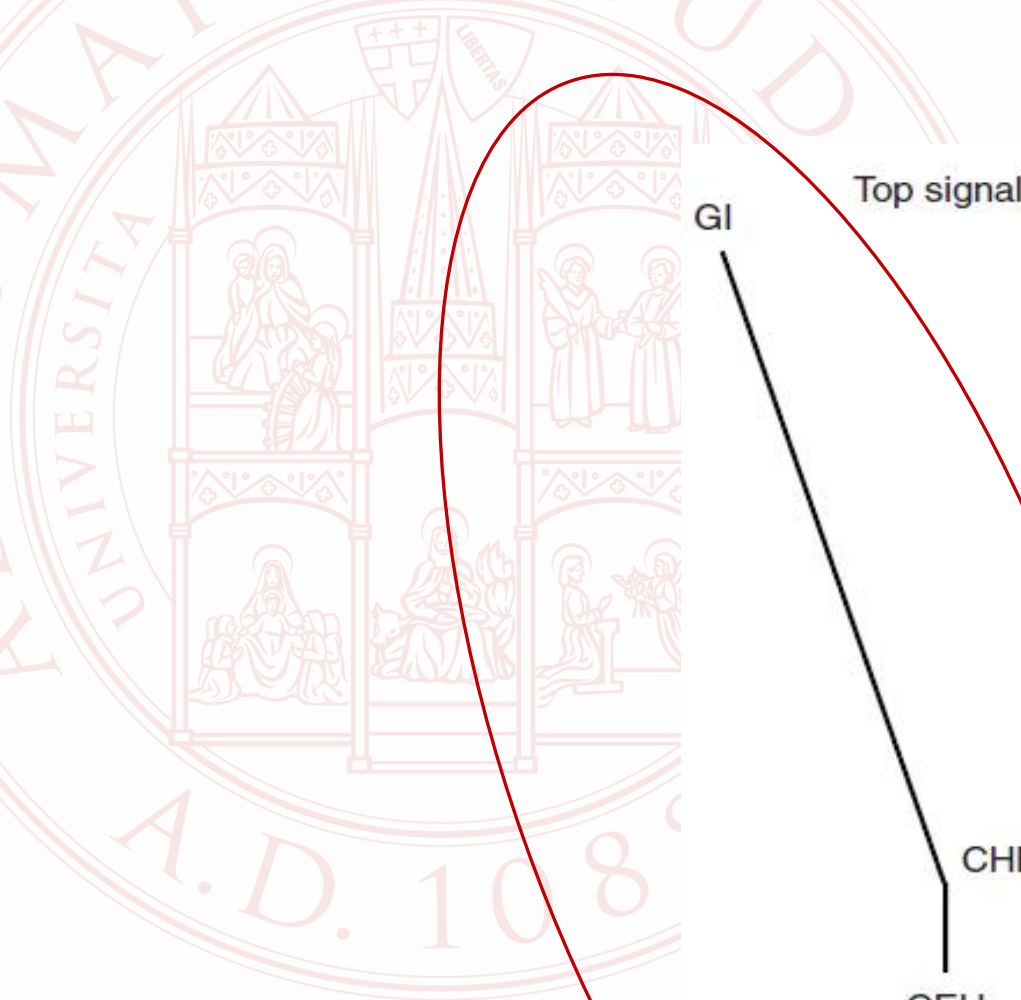
Linkage disequilibrium blocks that are long and frequent among the population have probably been subjected to positive selection, which led to a rapid increase in their frequency, before recombination could split them (e.g. EHH, DIND...)

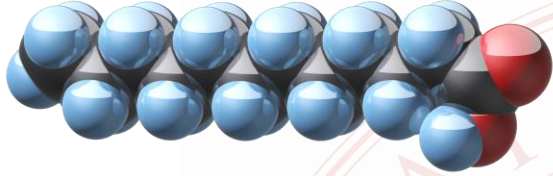
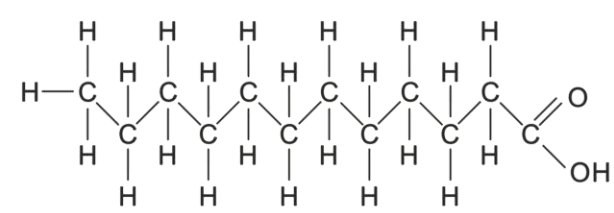
Fumagalli et al., 2015. Greenlandic Inuit show genetic signatures of diet and climate adaptation

A scan of Inuit genomes for signatures of adaptation revealed signals at several loci, with the strongest signal located in a cluster of fatty acid desaturases that determine PUFA levels.

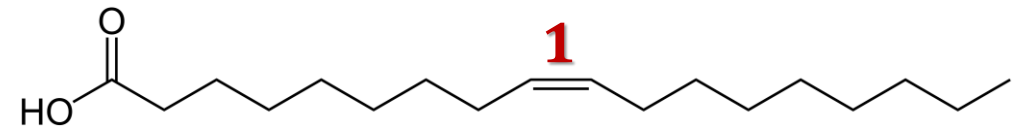
Population branch statistic (PBS)



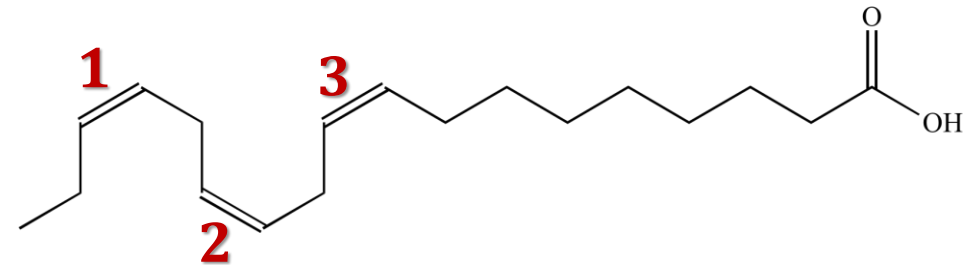




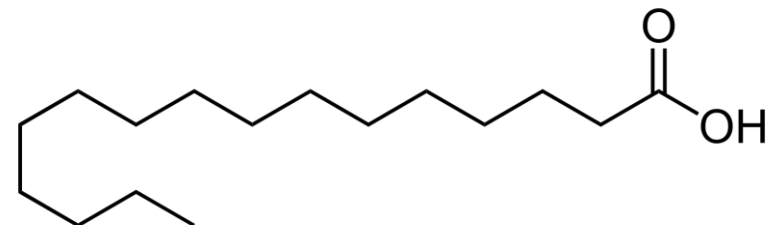
Monounsaturated fatty acids (MUFA)



Polyunsaturated fatty acids (PUFA)

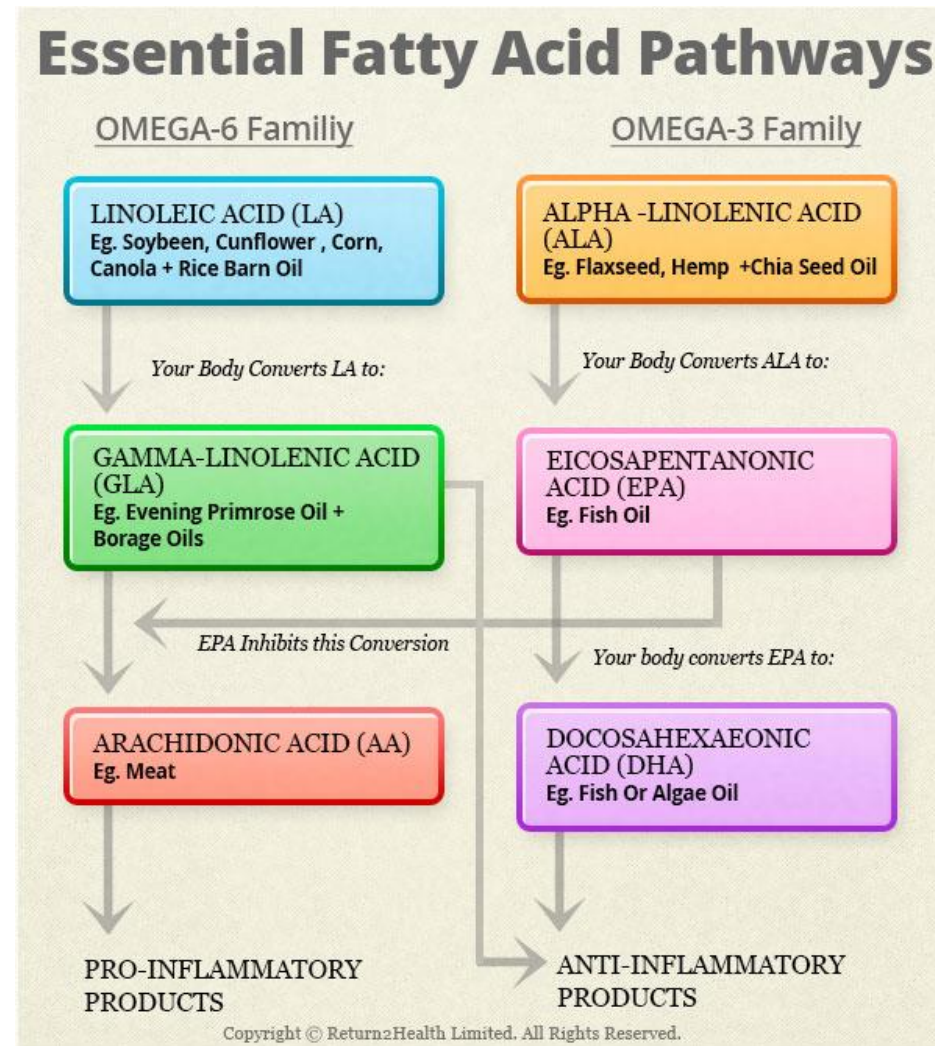


Saturated fatty acids (SFA)



EVOLUTIONARY ASPECTS OF THE DIETARY OMEGA6/OMEGA 3 FATTY ACID RATIO

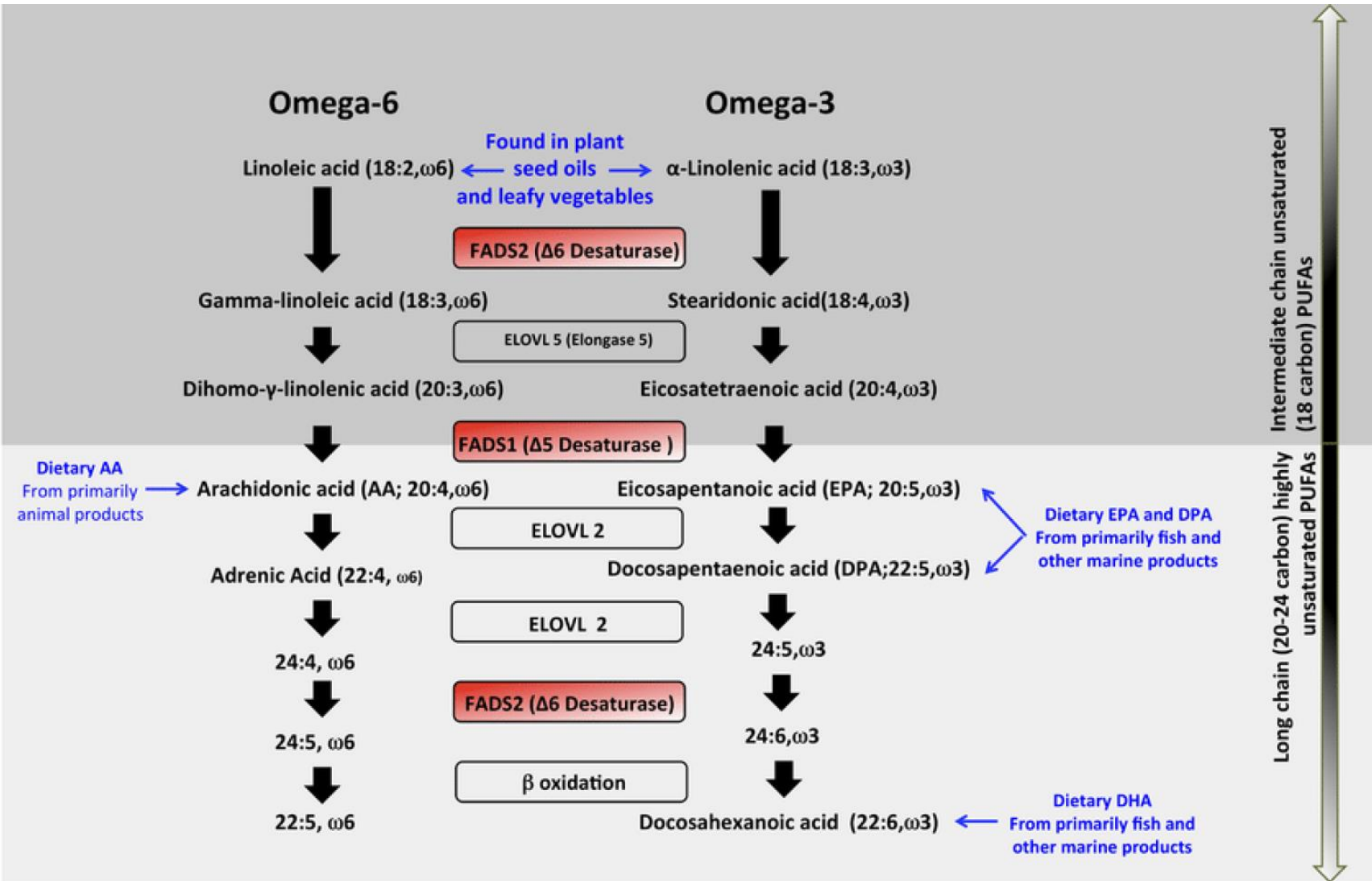
- a balance existed during the long evolutionary history of genus *Homo*;
- ***essential to humans in the sense that they cannot be synthesized de novo but need to be supplied through dietary intake***;
- lack of the converting enzyme, omega-3 desaturase (omega-6 to omega-3 fatty acids);
- a **balance** is a physiological state (important physiological effects)



The metabolic conversion of dietary omega-3 and omega-6 18 carbon (18C) to long chain (>20 carbon) polyunsaturated fatty acids (LC-PUFAs) is vital for human life.

The rate-limiting steps of this process are catalyzed by fatty acid desaturase FADS 1 and 2

FADS GENES - LCPUFA METABOLISM

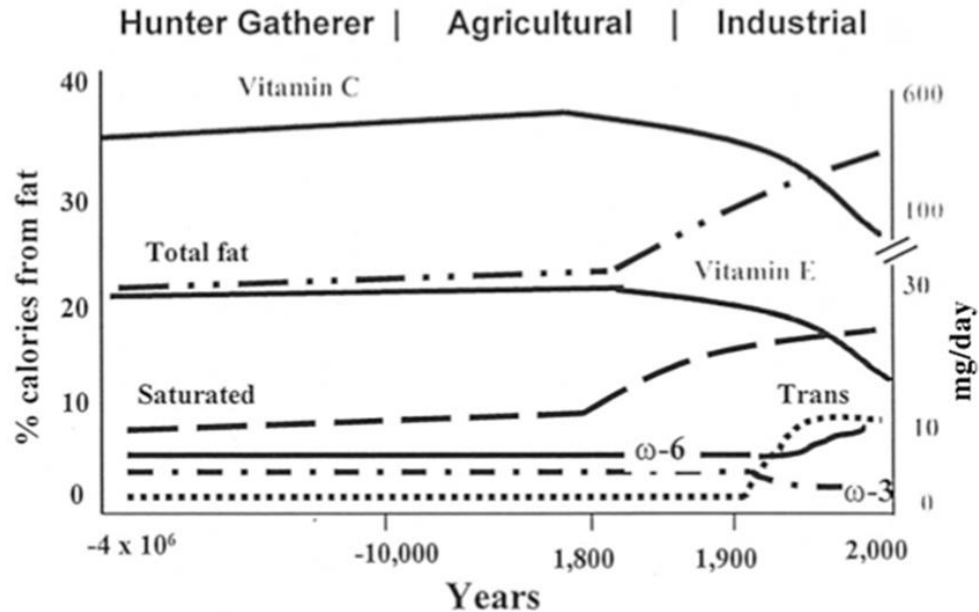


Omega-6 and omega-3 long chain polyunsaturated fatty acids (LCPUFAs) and their metabolites:

- ☐ play **signaling** and **structural** roles in the cell
- ☐ are involved in the **development and cognitive function** of the human brain
- ☐ are related to **immune, cardiovascular and inflammatory responses**
- ☐ their **biosynthesis** is crucial in meat-poor diets
- ☐ have **different precursors** introduced by **different food sources**

During the Paleolithic period, the diets of humans included equal amounts of omega-6 and omega-3 fatty acids from plants (LA+ ALA) and from the fat of animals in the wild and fish (AA + EPA + DHA).

Rapid dietary changes over short periods of time have occurred over the past 100–150 years → totally new phenomenon in human evolution.



Population	ω -6/ ω -3
Paleolithic	0.79
Greece prior to 1960	1.00–2.00
Current Japan	4.00
Current India, rural	5–6.1
Current UK and northern Europe	15.00
Current US	16.74
Current India, urban	38–50

Urbanization and industrialization processes change the ratio

Omega-6/Omega-3 ratios in different populations



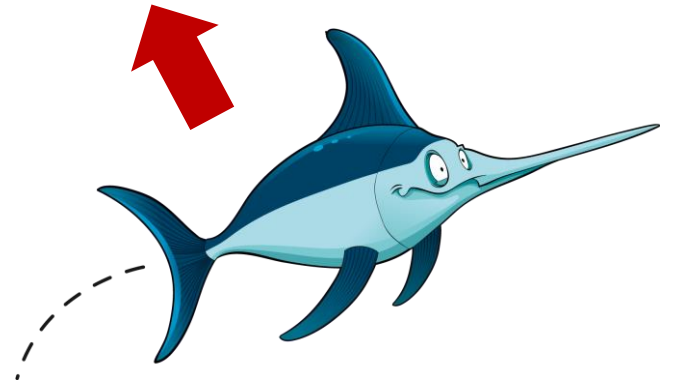
FishMed-PhD

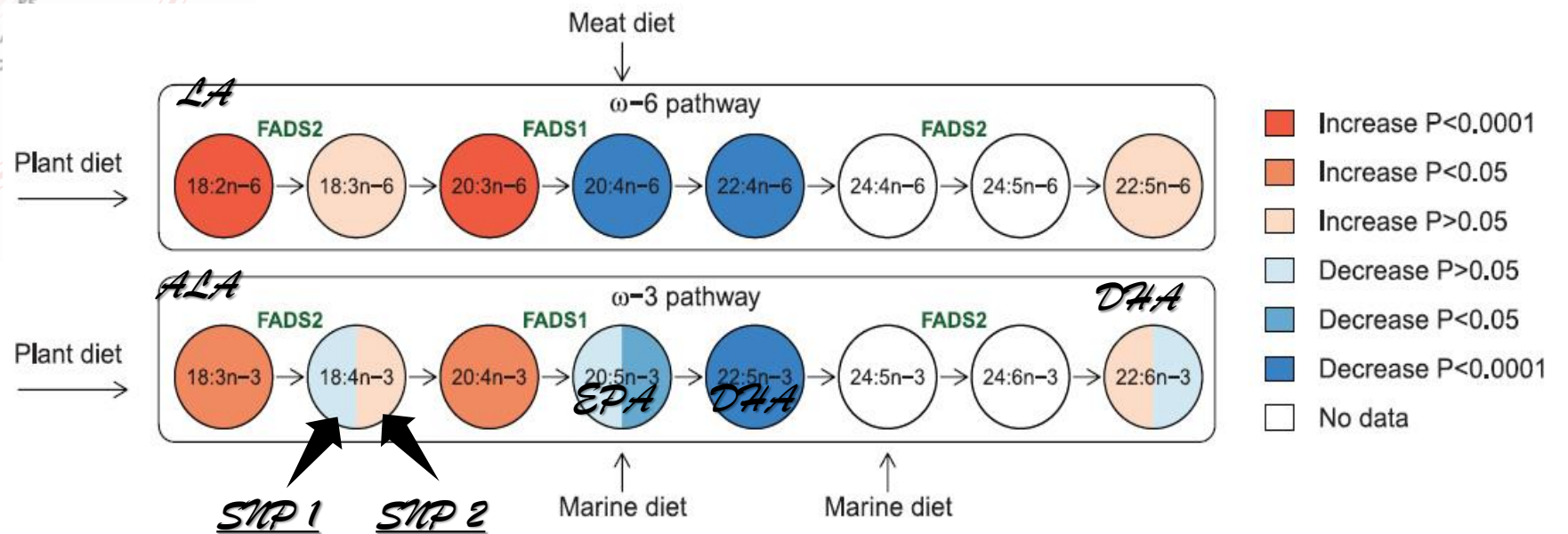
FADS1
FADS2

delta-5 and delta-6
desaturases

eicosapentaenoic acid (EPA)
docosapentaenoic acid (DHA)

linoleic acid (LA)
 α -linolenic acid (ALA)





Site Frequency
Spectrum-based
method

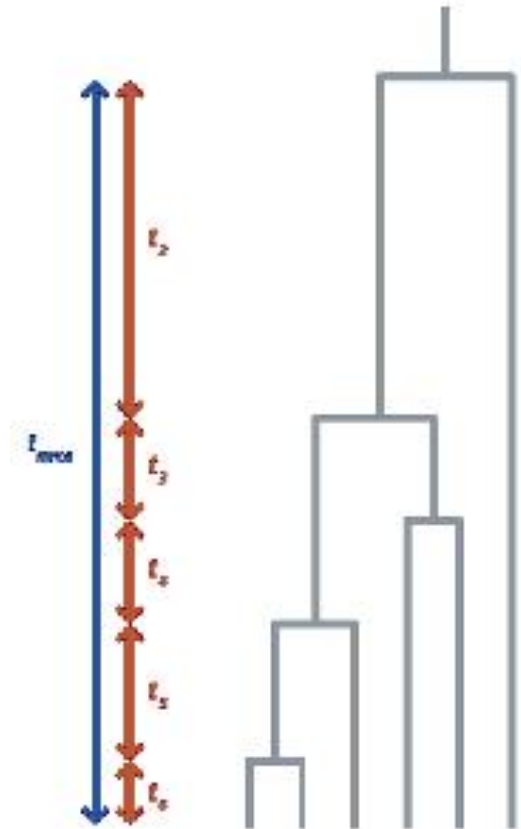
Joint demographic history of Han Chinese and
Greenlandic Inuit (split-time, gene flow, population
size)

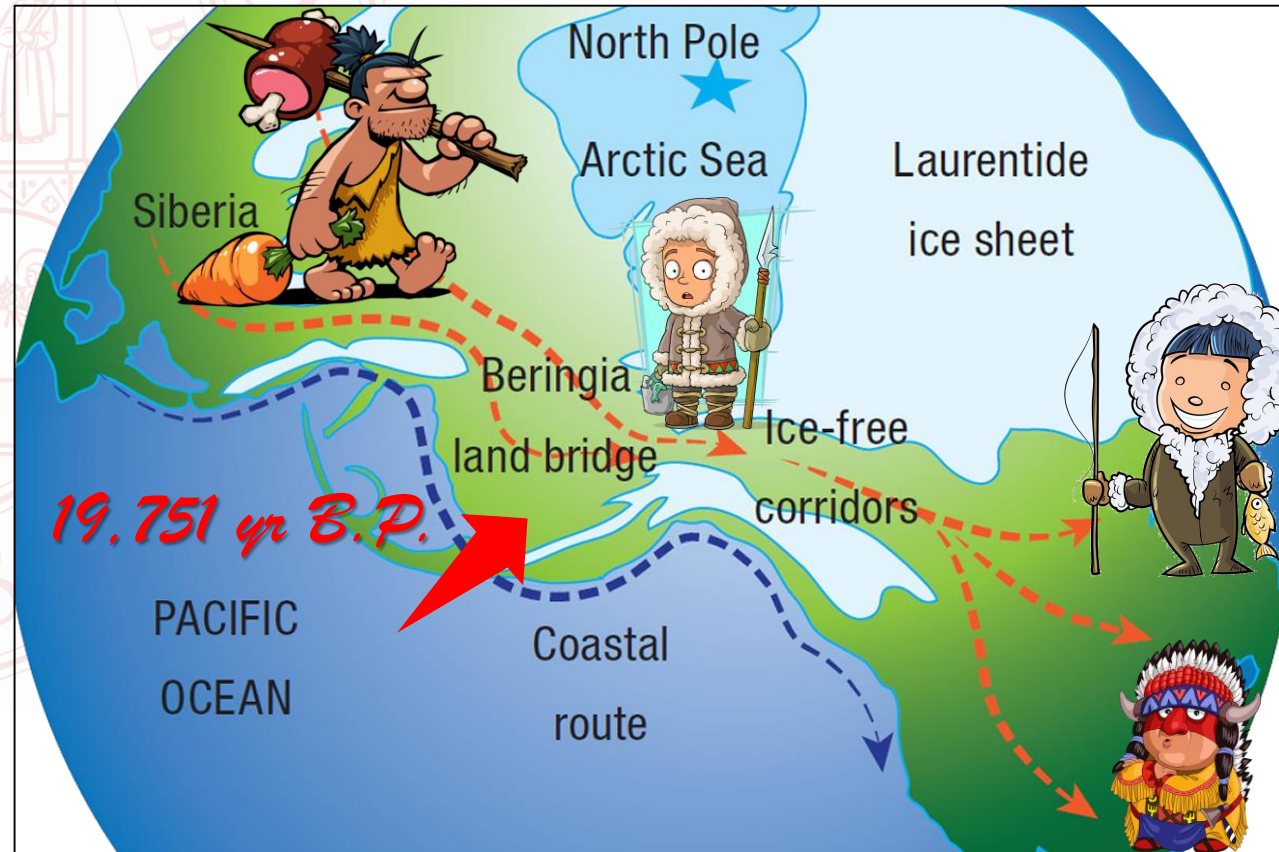
COALESCENT ANALYSIS

Simulated data based on neutrally
evolving population model

Observed genetic diversity

Has selection been acting? And when it started?





LD Block 1

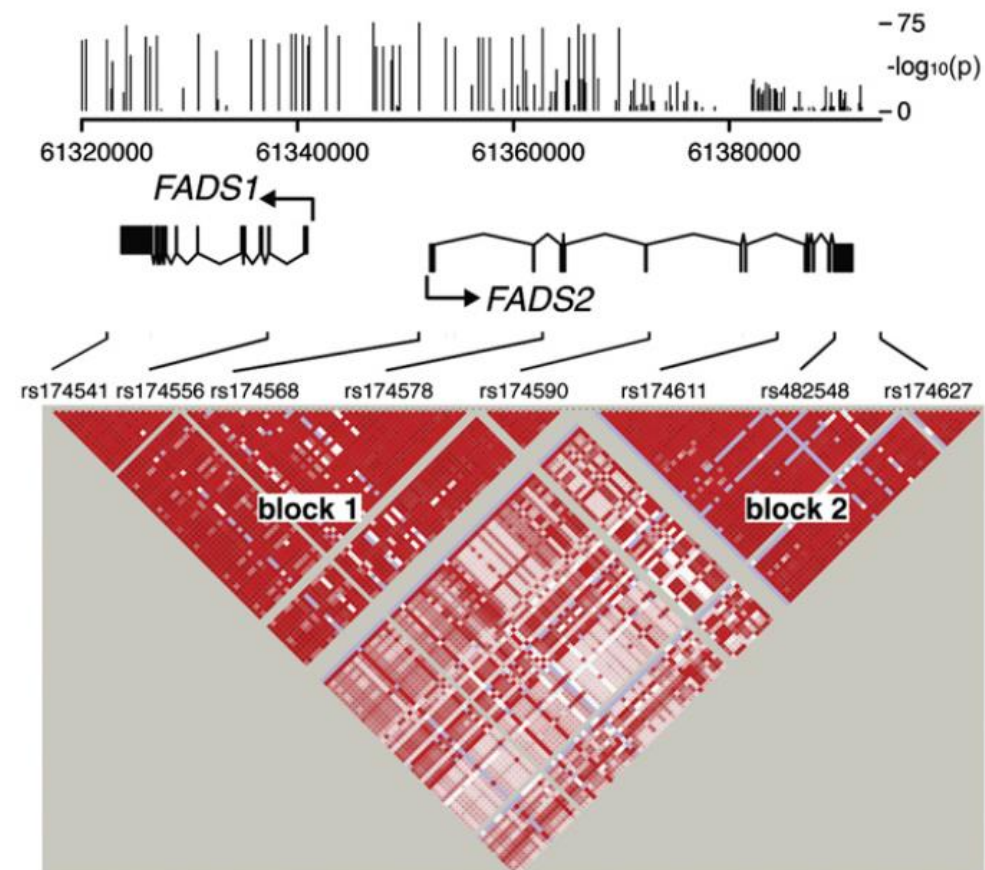
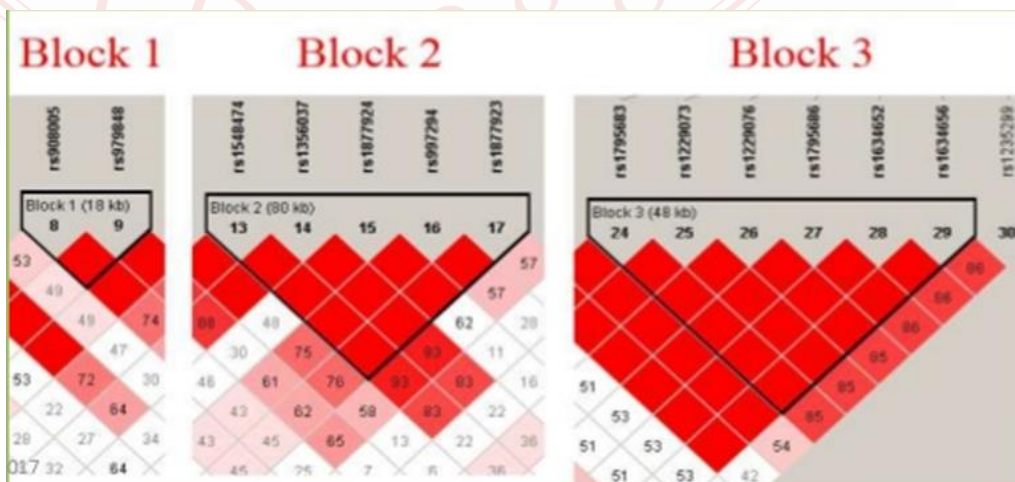
LD Block 2

FADS1

FADS2

FADS3

LD and HAPLOTYPE BLOCK



Haplotype D increases expression of FADS1 and is hypothesized to be an adaptation to a diet relatively low in PUFA, whereas haplotype A is hypothesized to be advantageous in a PUFA-rich environment.

LD block 1 is also where the strongest genome-wide association study signals for lipid levels are detected in European ancestry populations.

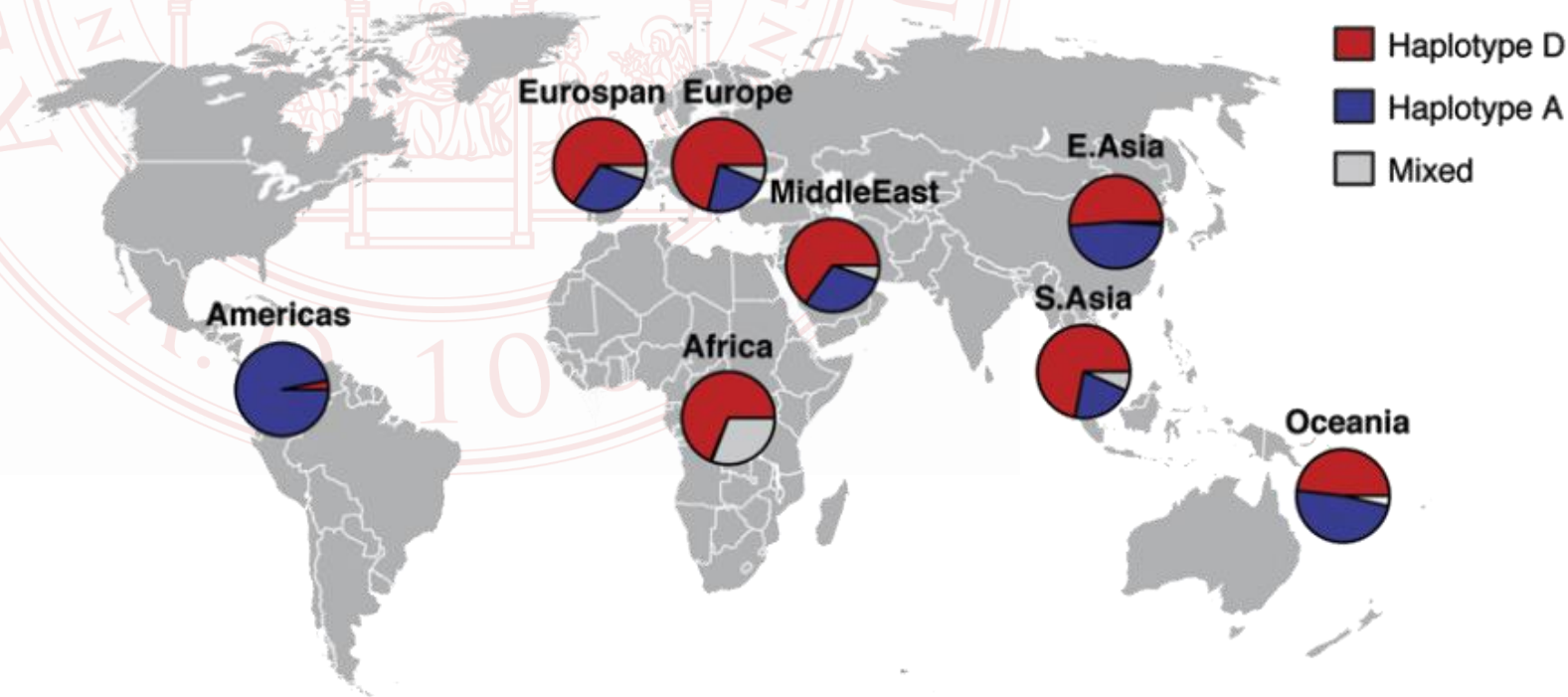
Haplotype D appears to have been under selection in Africa—indeed, this selection may have preceded the out-of-Africa bottleneck and it is virtually fixed in present-day African populations.

LD BLOCK 1: FADS1 + 1° half of FADS2

HAPLOTYPE A

HAPLOTYPE D

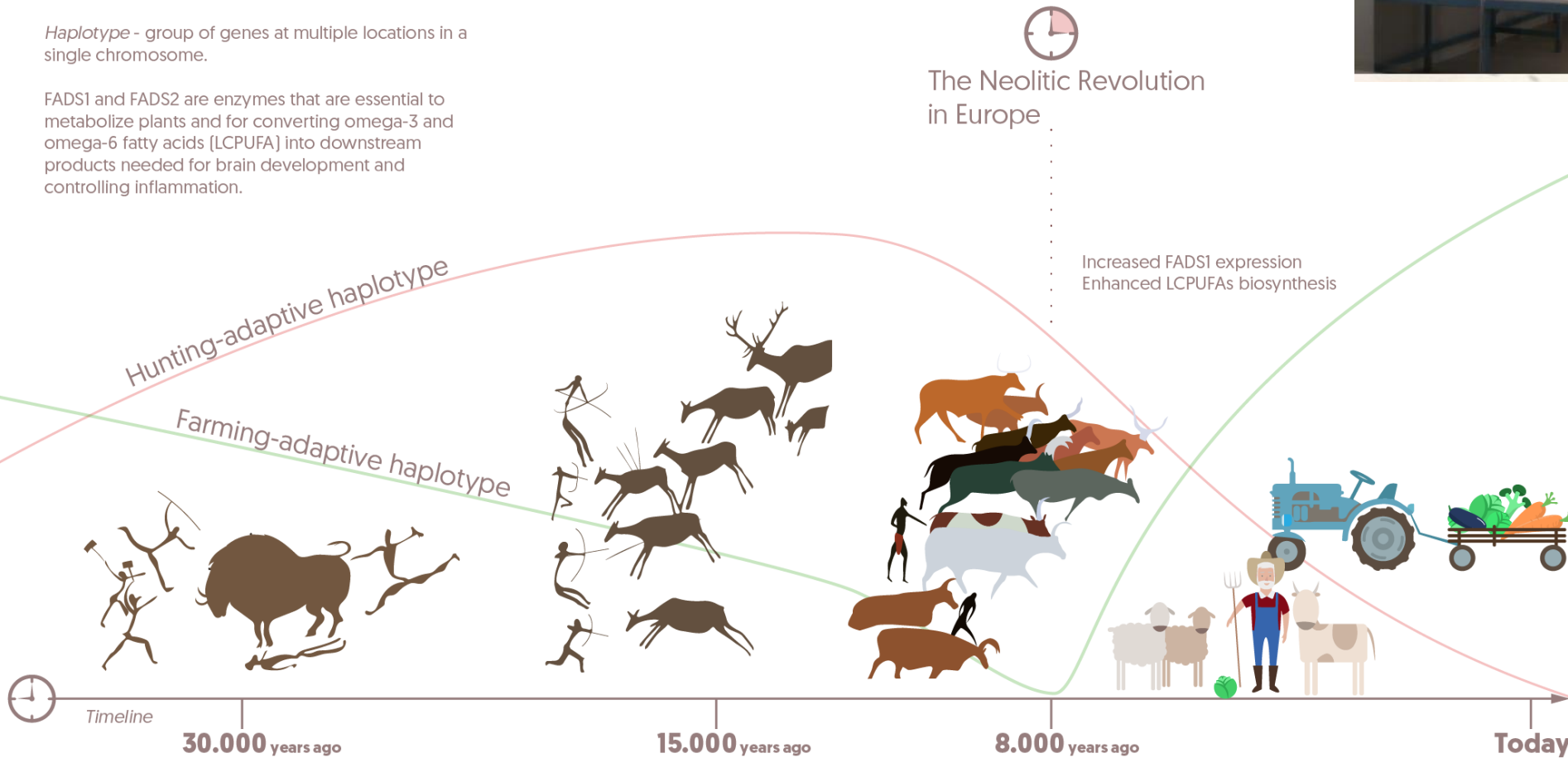
(increased FADS1 activity and is hypothesized to be an adaptation to a diet relatively low in PUFA, whereas haplotype A is hypothesized to be advantageous in a PUFA-rich environment).



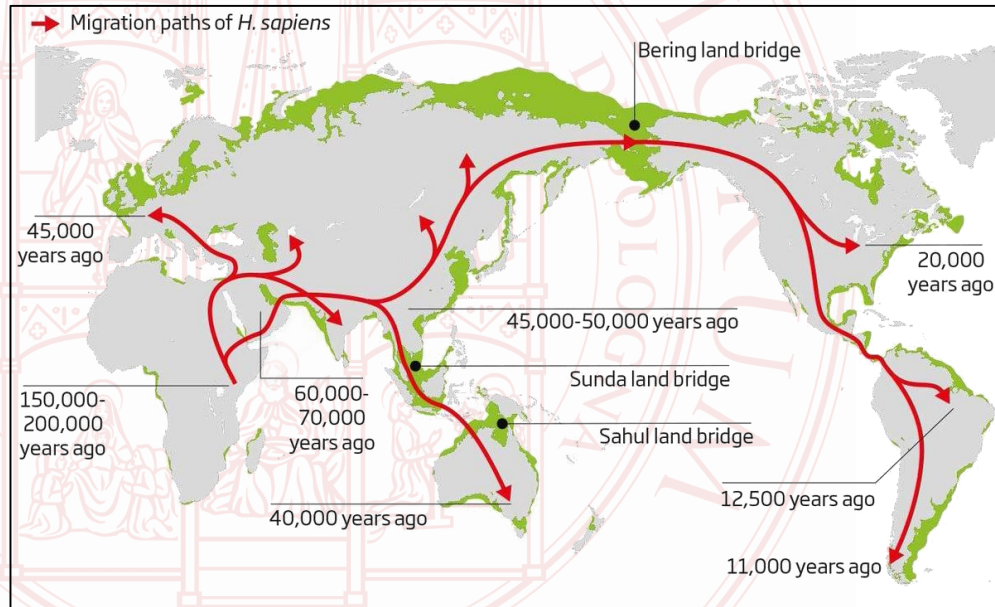
The importance of paleogenomics

Haplotype - group of genes at multiple locations in a single chromosome.

FADS1 and FADS2 are enzymes that are essential to metabolize plants and for converting omega-3 and omega-6 fatty acids [LCPUFA] into downstream products needed for brain development and controlling inflammation.

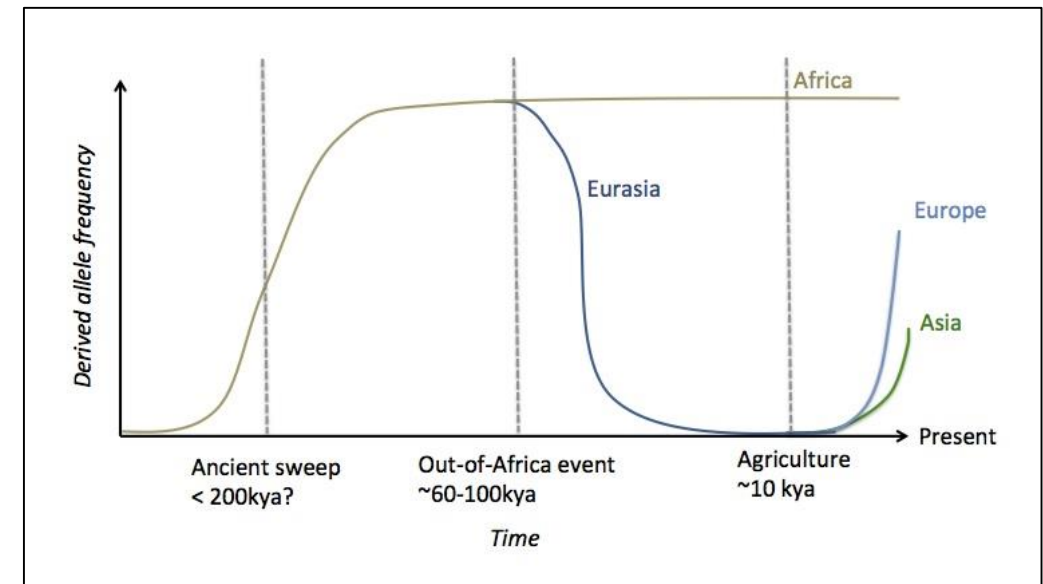


aDNA Lab_Ravenna



- 1) Haplotype D appeared before Neanderthal-Denisovan_Modern human split
- 2) First Non-Africans all had derived haplotype
- 3) Ancestral haplotype introgressed into early Non-Africans from some archaic population (maybe Neanderthals)

- 4) In Africa, a selective sweep led to the fixation of the derived haplotype
- 5) In Europe the ancestral haplotype was positively selected because of a diet rich in meat and fish
- 6) With the spread of agriculture, derived haplotype was reintroduced in Europe, where it underwent positive selection from 4.000 years ago.



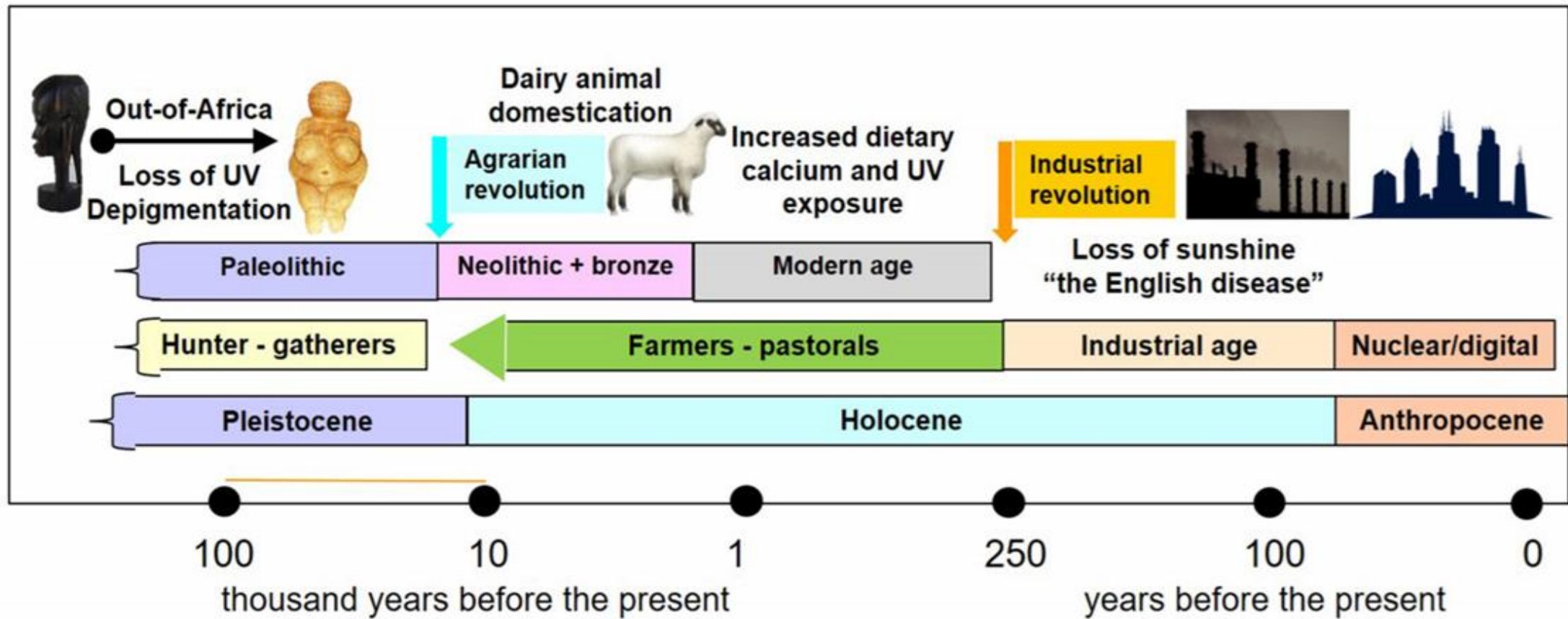
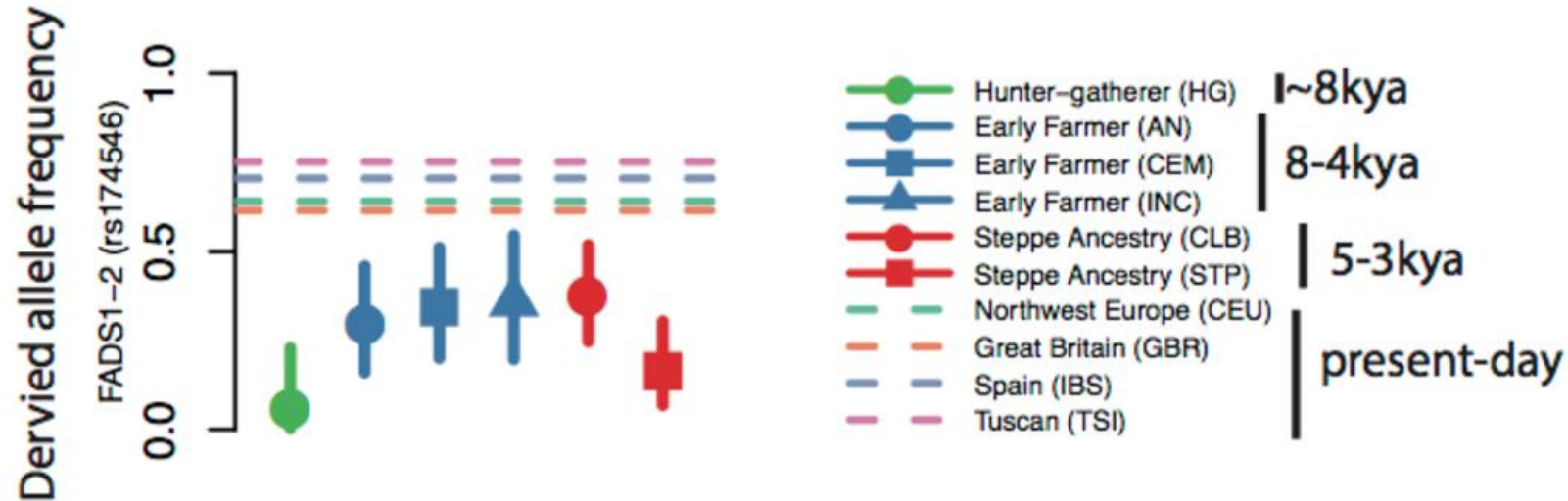


FIGURE 1 | Timeline of geological epochs, archeological periods in human prehistory and history, and the effects of sunshine and dietary calcium. The migration of man out of Africa to northern and southern latitudes 60–130 k.y.a was associated with depigmentation. Transition from the geological Pleistocene epoch to the Holocene epoch coincided with the “agrarian revolution” 10–12,000 years ago and from the archeological Paleolithic period (hunter gatherer tool makers) to the Neolithic farmers. The agrarian revolution happened at different times in different parts of the world, and wherever it happened, it was associated with an increase in dietary calcium and crowding of people in cities. The industrial revolution, which began in Europe in the second half of the 18 century, was associated with rickets – “the English disease” due to industrial air pollution. The transition to the nuclear age, also called the digital age, define also the transition to the Anthropocene epoch, which is associated with further diminution of UVR exposure in humans.

Selection has targeted **different alleles in the FADS genes in Europe than it has in South Asia or Greenland.**

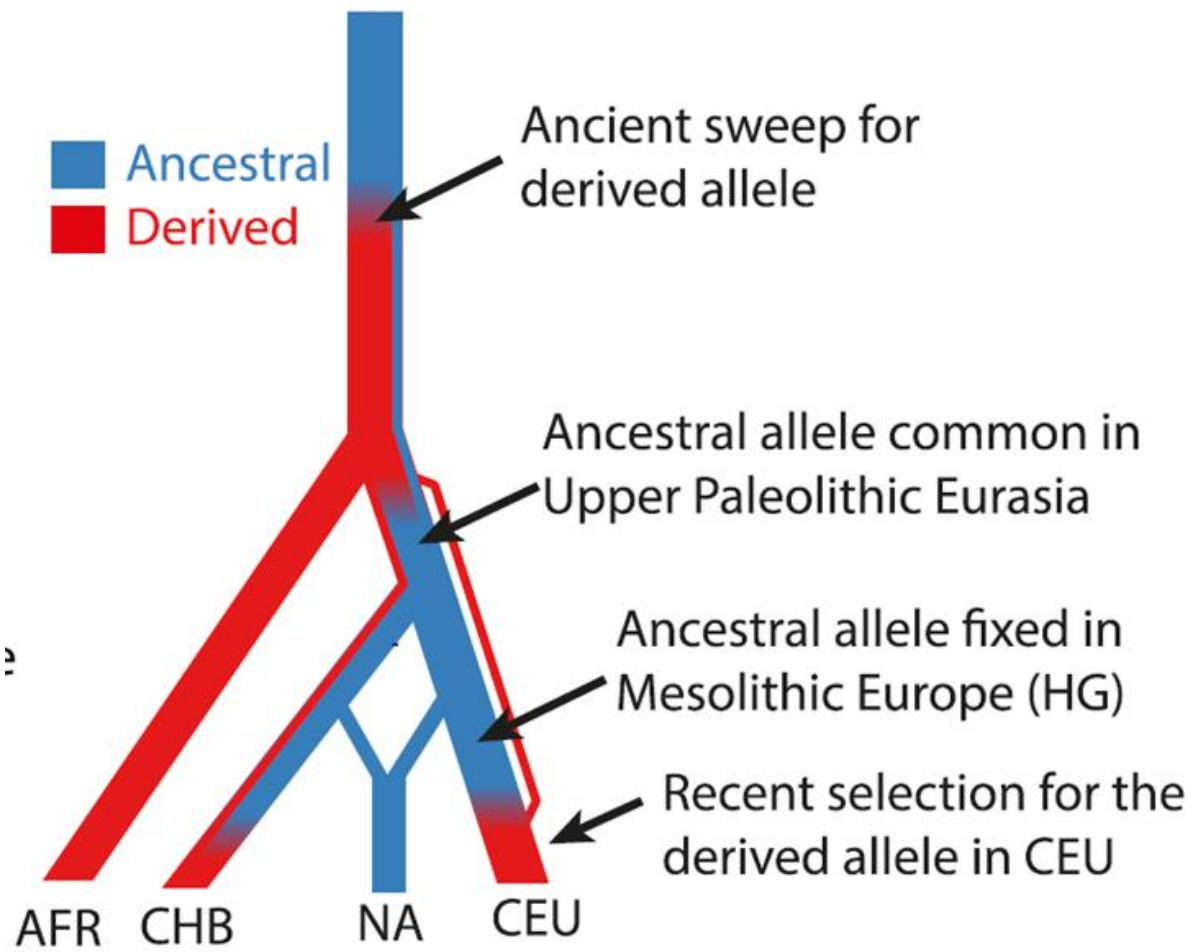


The derived haplotype was reintroduced to Europe in the **Neolithic** by the migration of **Early Farming populations from Anatolia**, experienced **strong positive selection during the Bronze Age** and is now at a **frequency of around 60%**.

The trajectory of the derived haplotype in East Asian populations is less clear. It is common today in East Asia (40%), and the locus does exhibit a signal of selection in East Asian populations. But, with **limited ancient DNA evidence**, it is **unclear whether this represents recent selection or ancient shared ancestry with African lineages**.

Conclusions FADS genes:

Model of the evolution of LD block 1



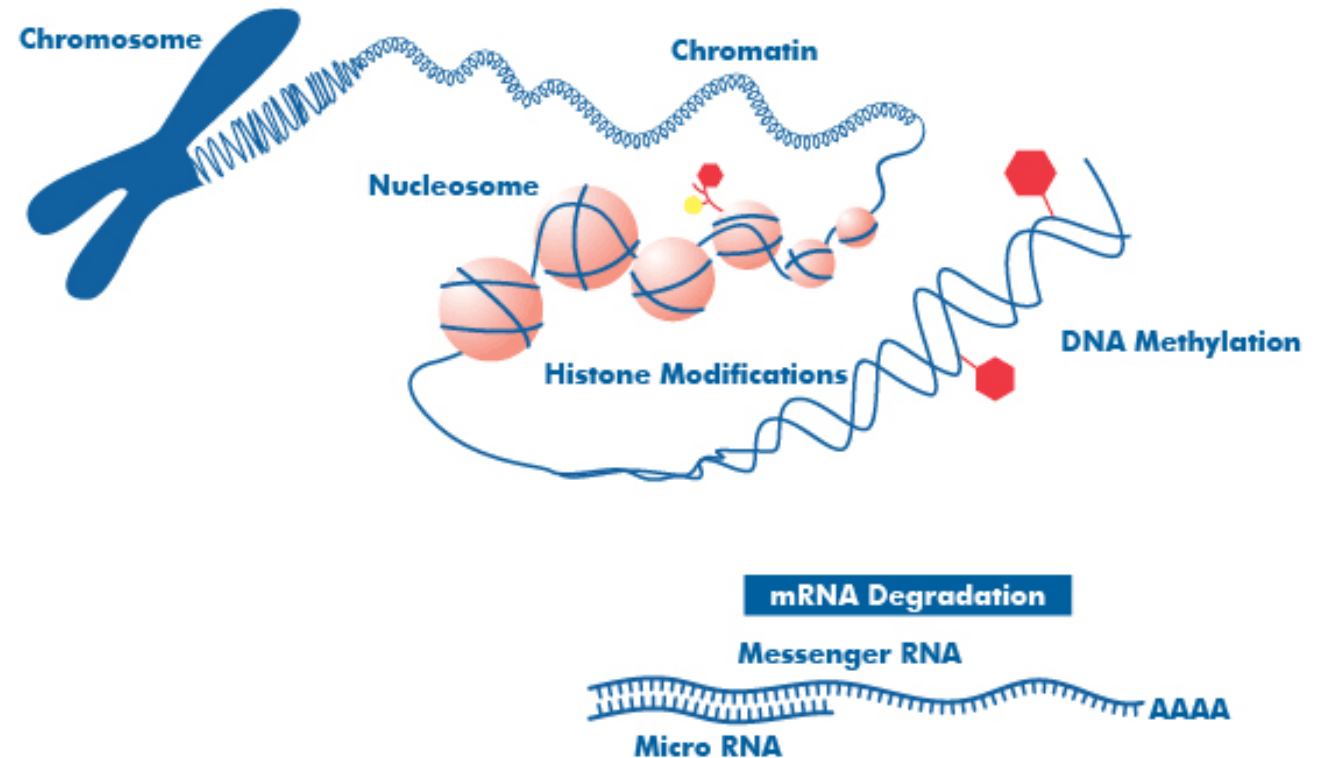
The alleles showing the **strongest changes in allele frequency since the Bronze Age** show associations *with expression* changes and multiple lipid-related phenotypes.

Multiple SNPs in the region affect expression levels and PUFA synthesis.

Feil and Fraga, 2012. Epigenetics and the environment: emerging patterns and implications

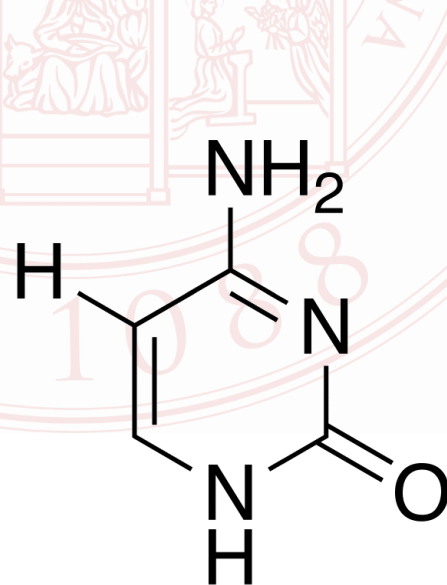
Epigenome = the full set of any stable changes in the chromatin structure that are heritable from one cell generation to the next, and can result in alteration of gene expression without altering DNA sequences.

- DNA methylation
- Histone methylation
- Histone acetylation
- Histone phosphorylation
- ncRNAs

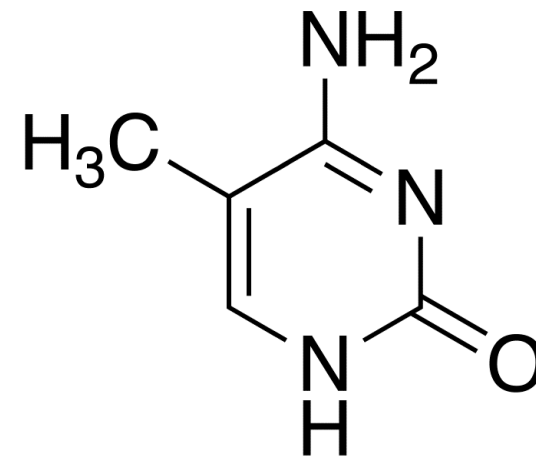
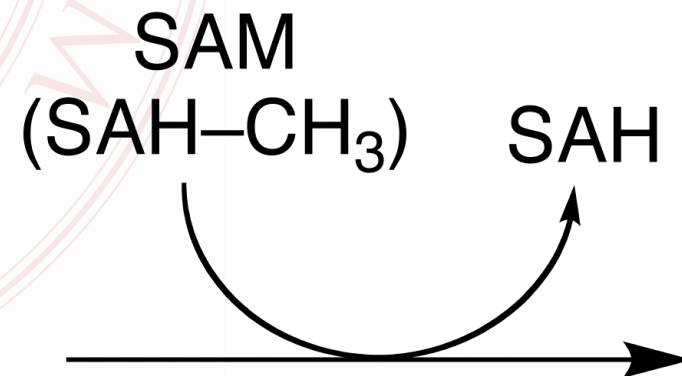




CpG dinucleotides

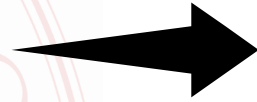


Cytosine

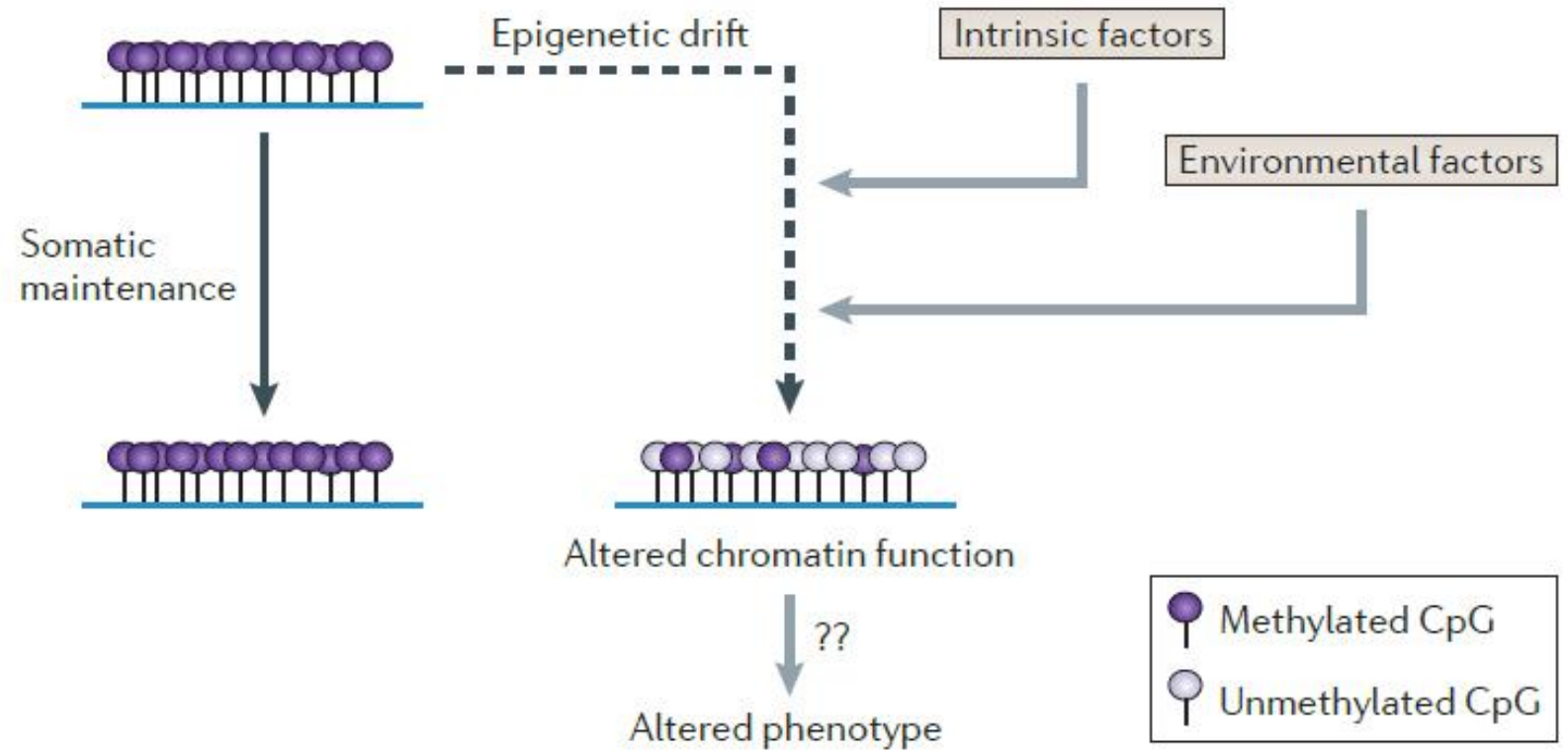


Methylated
Cytosine

Epigenetic changes

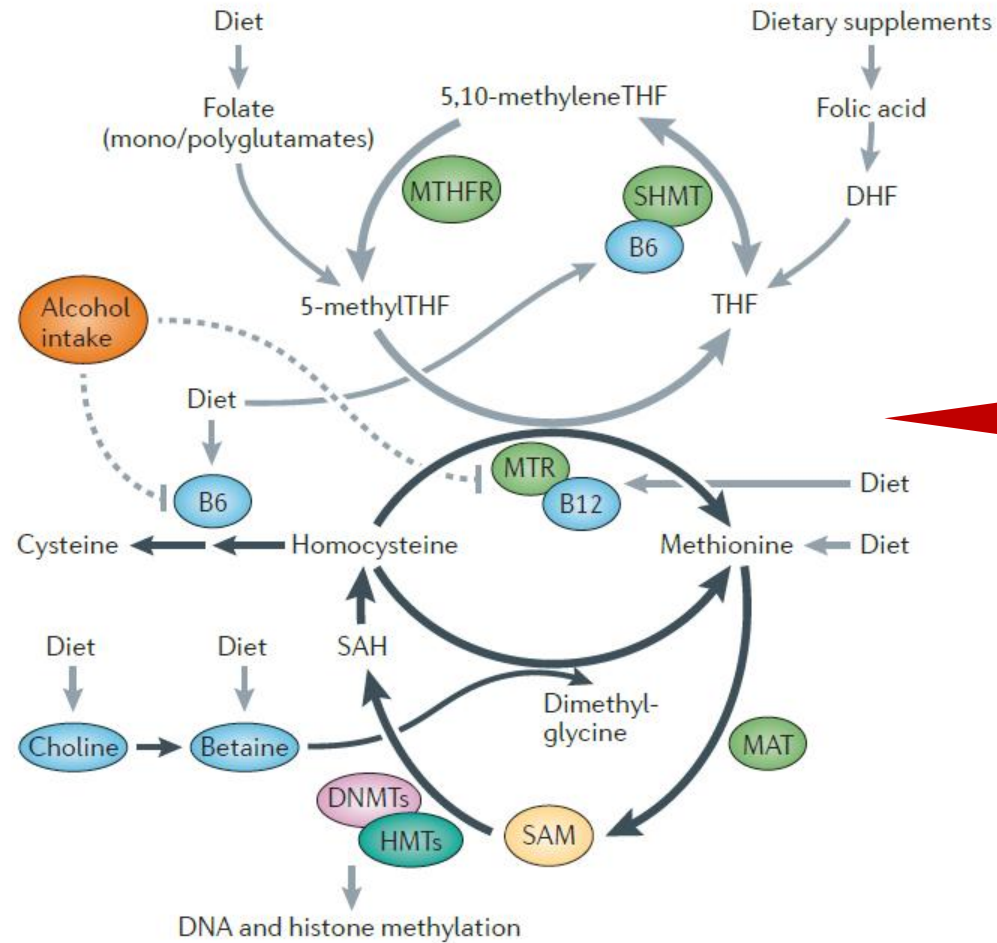


Gene expression changes



Synthesis of methylation enzymes

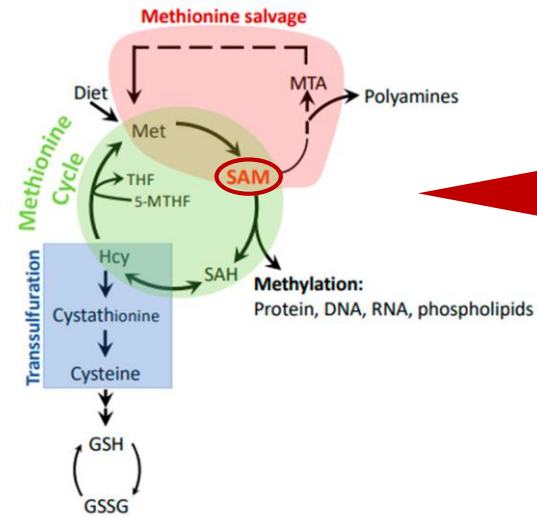
DIET
ENVIRONMENTAL
POLLUTANTS



METHYLATION
CHANGES

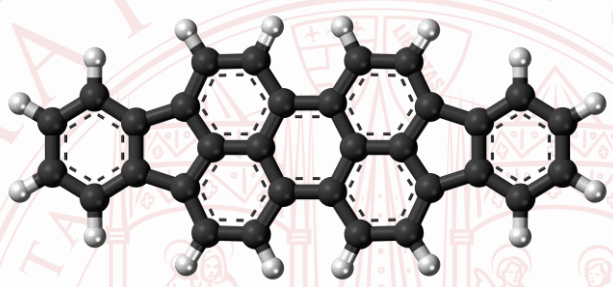


Reduced
expression or
activity of DNMT



Changes in SAM
availability

METHYLATION
CHANGES



PAHs



OXIDATIVE STRESS



**DNMT suppression
+
SAM consumption**



**METHYLATION
CHANGES**

Heyn et al., 2013. DNA methylation contributes to natural human variation

Giuliani et al., 2016. Epigenetic Variability across Human Populations: A Focus on DNA Methylation Profiles of the KRTCAP3, MAD1L1 and BRSK2 Genes

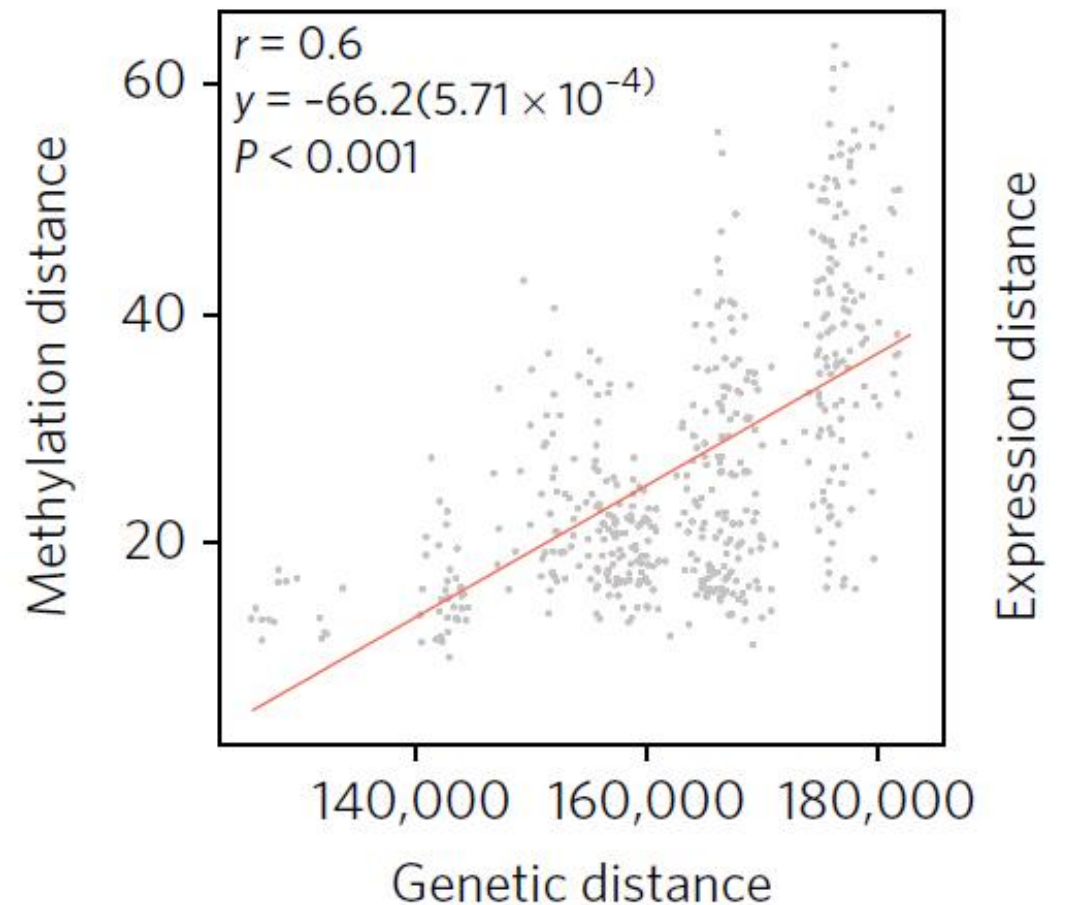
Carja et al., 2017. Worldwide patterns of human epigenetic variation

Methylation variability across human populations

Environment

- Diet
- UVA exposure
- Pathogens load
- ...

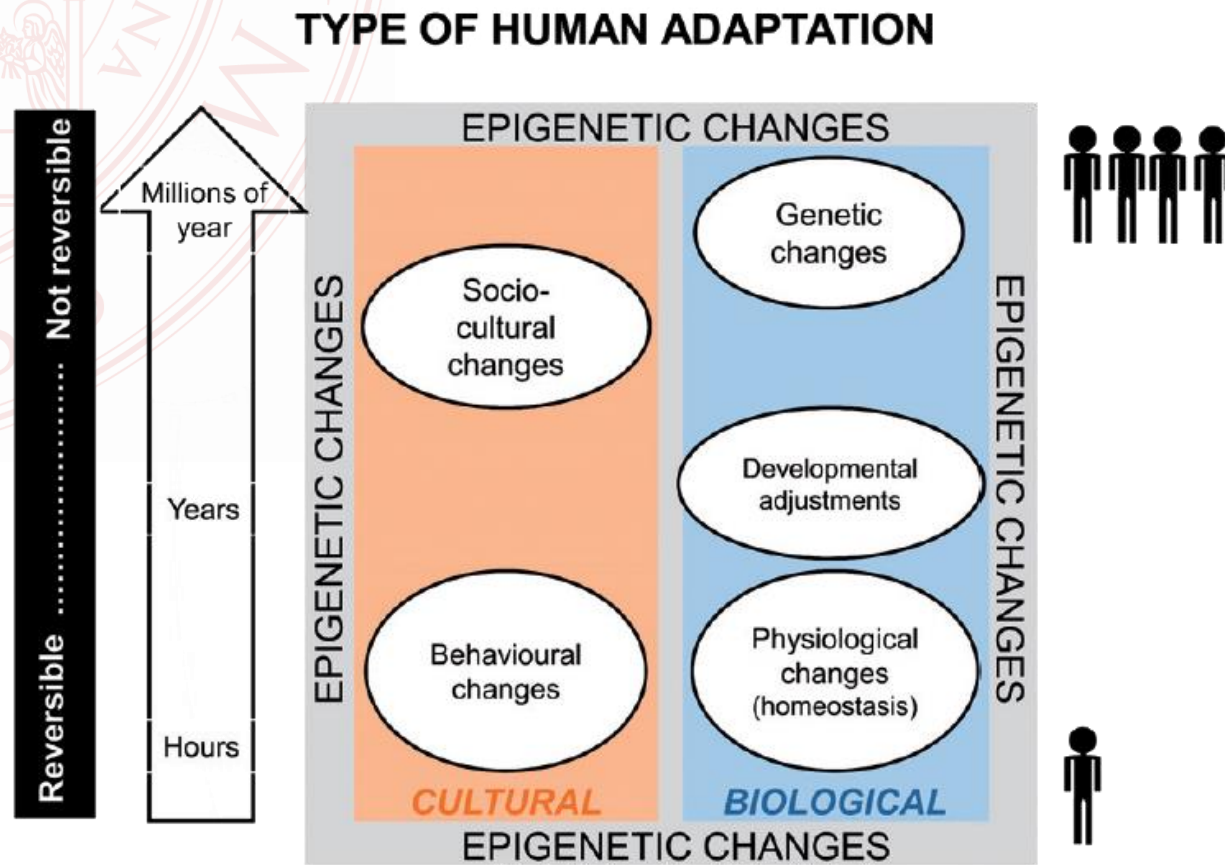
Genetic background



Could methylation changes contribute to human adaptation?

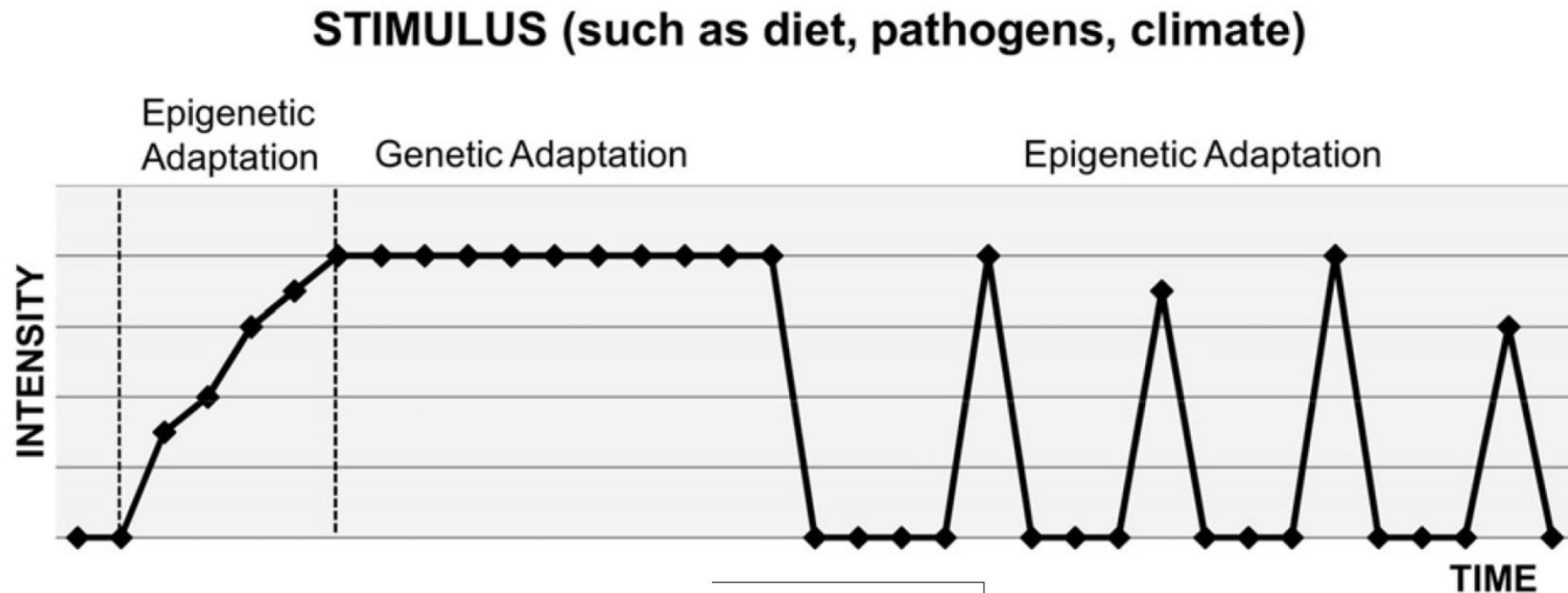
Giuliani et al., 2014. The epigenetic side of human adaptation: hypotheses, evidences and theories

Epigenetics mechanisms could represent “medium-term” strategies to cope with a demanding environmental condition, such as high altitude hypoxia.



EPIGENETIC SIDE OF HUMAN ADAPTATION

“When natural selection acts on pure epigenetic variation in addition to genetic variation, populations adapt faster, and adaptive phenotypes can arise before any genetic changes.” (Klironomos et al., 2013- Bioessay)



Review Paper

The epigenetic side of human adaptation: hypotheses, evidences and theories

Cristina Giuliani, Maria Giulia Bacalini, Marco Sazzini, Chiara Pirazzini, Claudio Franceschi, Paolo Garagnani & Donata Luiselli ... show less

Pages 1-9 | Received 10 Jul 2014, Accepted 02 Sep 2014, Published online: 21 Nov 2014

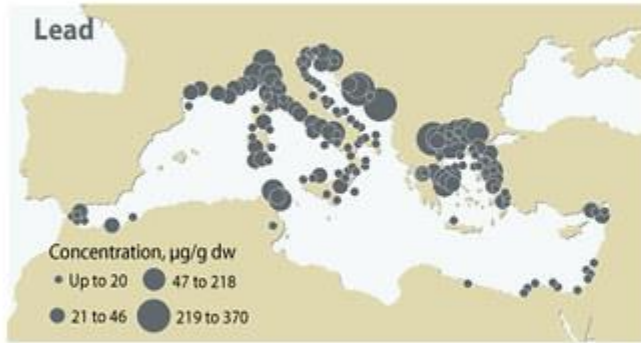
Mediterranean fishing communities as an informative case study

What is the potential impact of seafood consumption on the human genome?

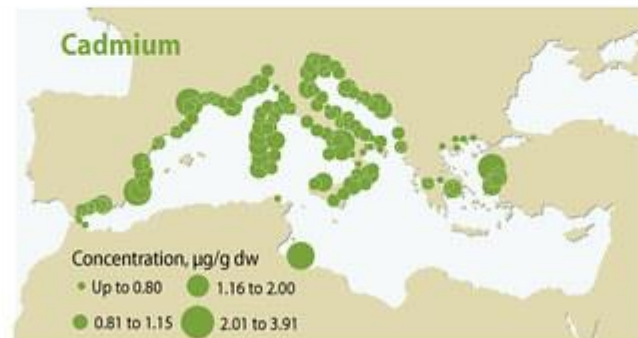
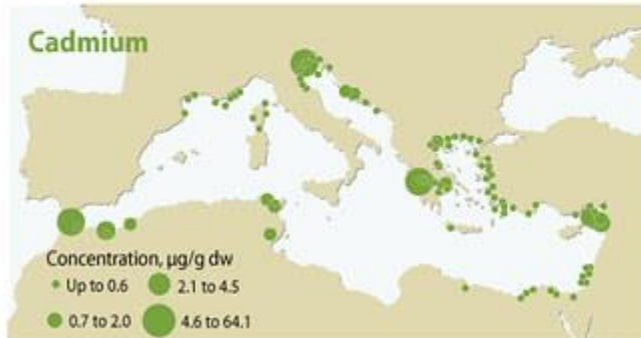
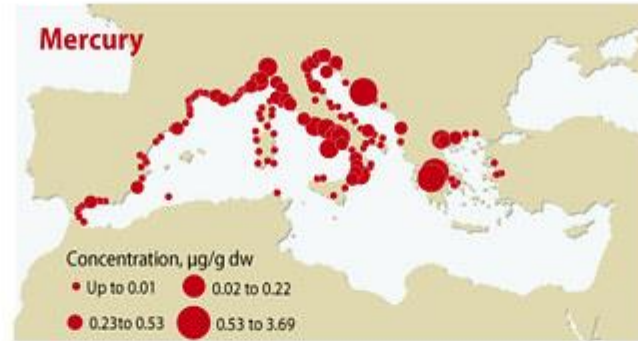
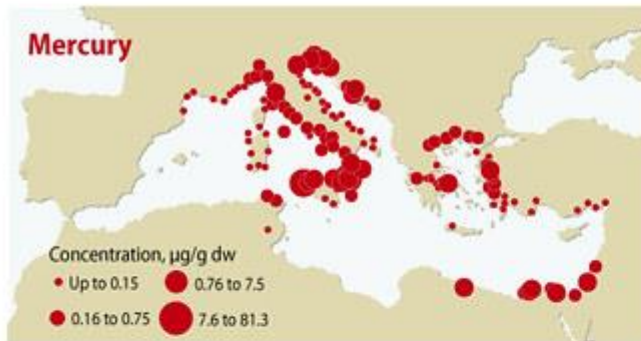
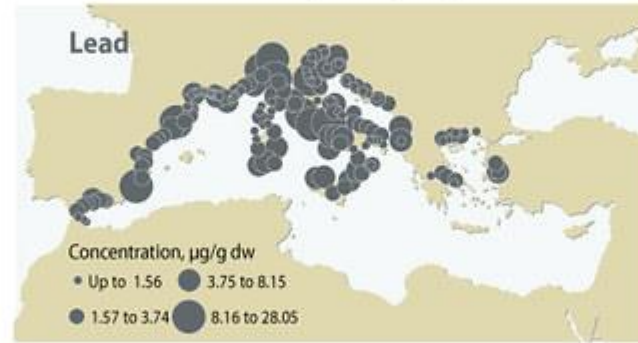


Mean concentrations of trace metals

In sediments

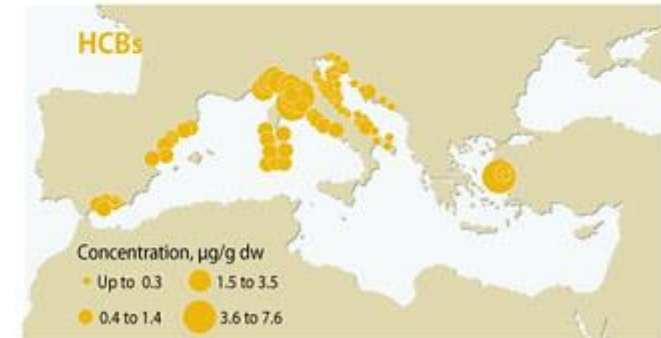
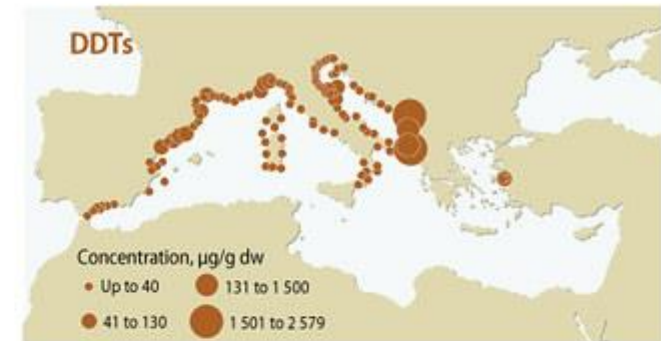
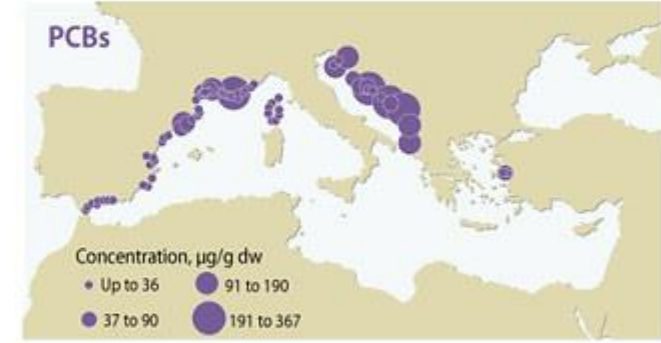


In Blue Mussels (*Mytilus galloprovincialis*)



Mean concentrations of Persistent Organic Pollutants (POPs)

In Blue Mussels (*Mytilus galloprovincialis*)



Source: UNEP/MAP, Hazardous Substances in the Mediterranean: A Spatial and Temporal Assessment, 2011

Ferrante et al., 2018. PAHs in seafood from the Mediterranean Sea: An exposure risk assessment

Annibaldi et al., 2019. Determination of Hg in Farmed and Wild Atlantic Bluefin Tuna (*Thunnus thynnus* L.) Muscle

Cinnirella et al., 2020. Mercury concentrations in biota in the Mediterranean Sea, a compilation of 40 years of surveys



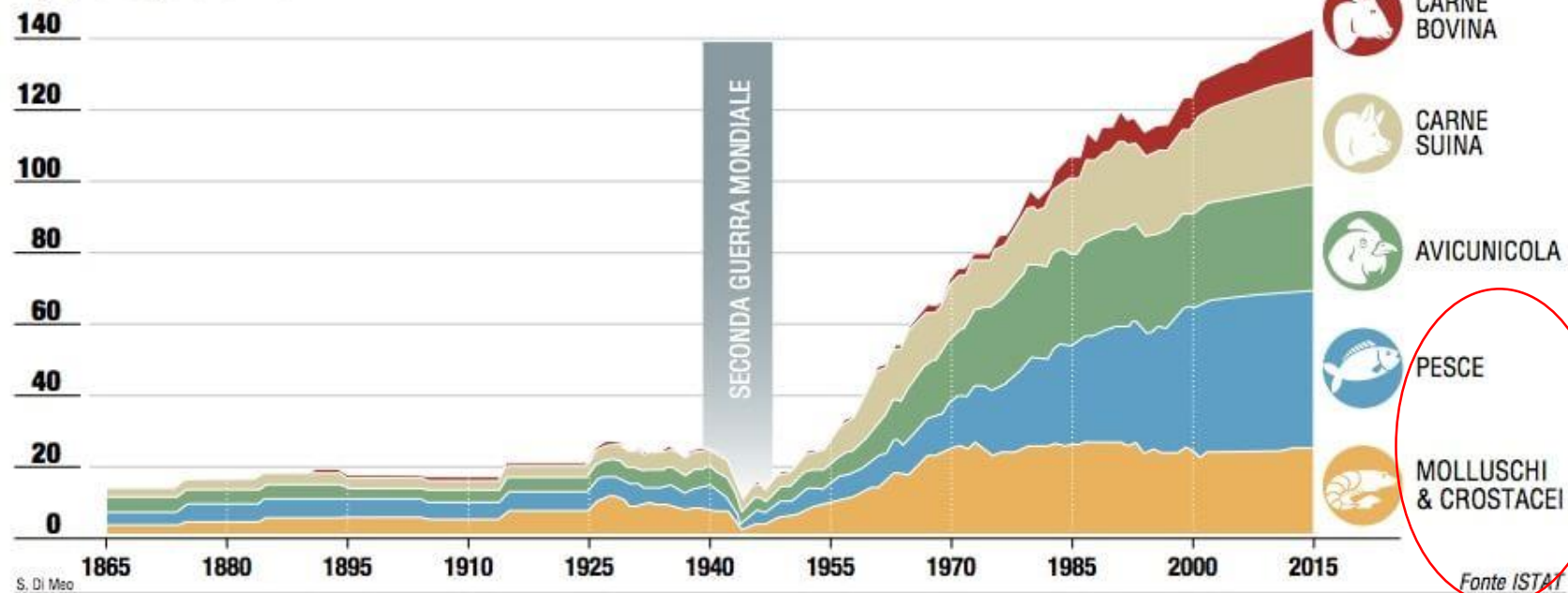
GLOBAL AVERAGE
FISH CONSUMPTION
PER CAPITA



EUROPEAN MEDITERRANEAN
AVERAGE FISH CONSUMPTION
PER CAPITA

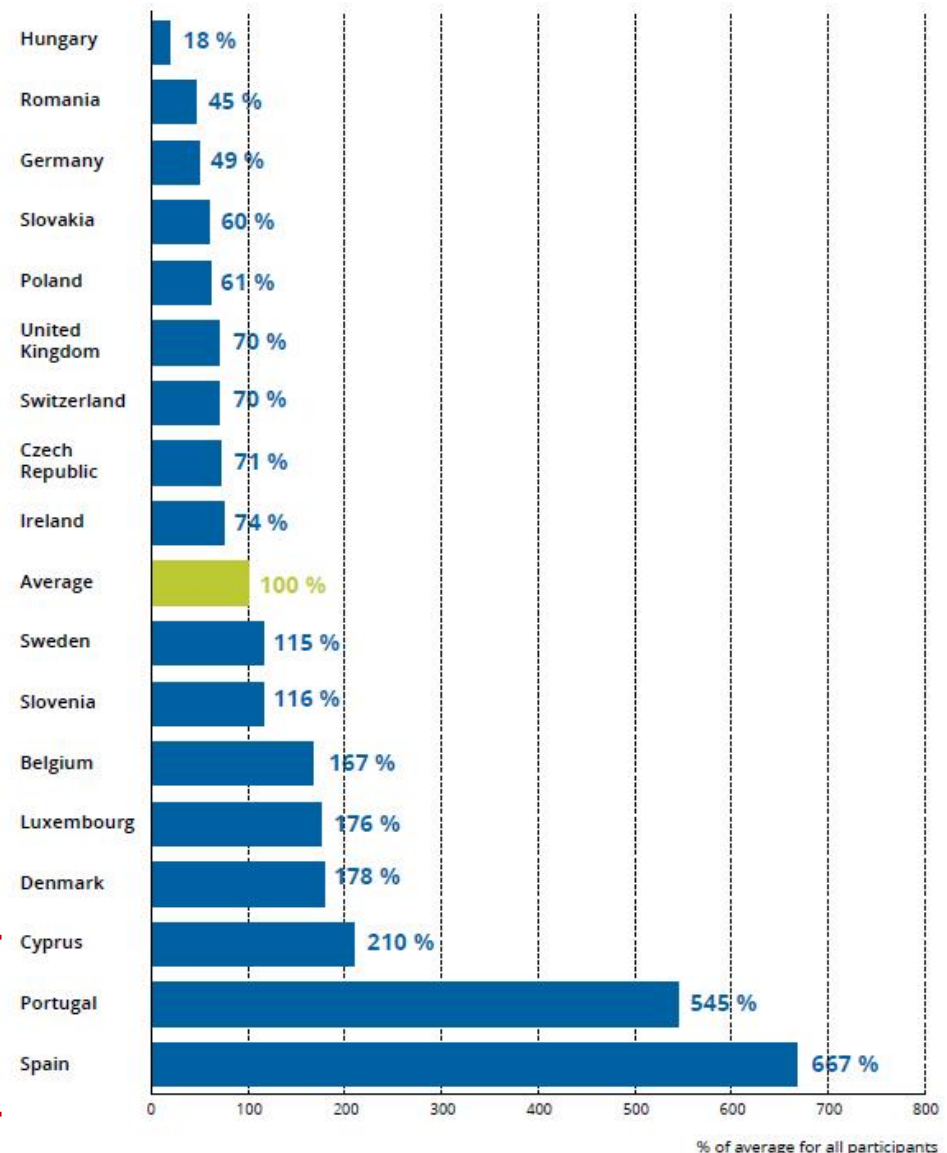
I CONSUMI DI CARNE E PESCE IN ITALIA

Kg pro-capite annui



Mercury levels in hair of mothers as a percentage of the Europe-wide average

Mediterranean countries



Junqué et al., 2018. Drivers of the accumulation of mercury and organochlorine pollutants in Mediterranean lean fish and dietary significance

Diez et al., 2008. Hair mercury levels in an urban population from southern Italy: Fish consumption as a determinant of exposure

Llop et al., 2014. Exposure to mercury among Spanish preschool children: trend from birth to age four

Elhamri et al., 2007. Hair mercury levels in relation to fish consumption in a community of the Moroccan Mediterranean coast

Giangrosso et al., 2016. Hair Mercury Levels Detection in Fishermen from Sicily (Italy) by ICP-MS Method after Microwave-Assisted Digestion

ECOGENETIC APPROACH

1) Communities selection



Control group



2a) Sampling for genetic and epigenetic data collection



2b) Interviews



3) Analyses



ECOGENETIC APPROACH

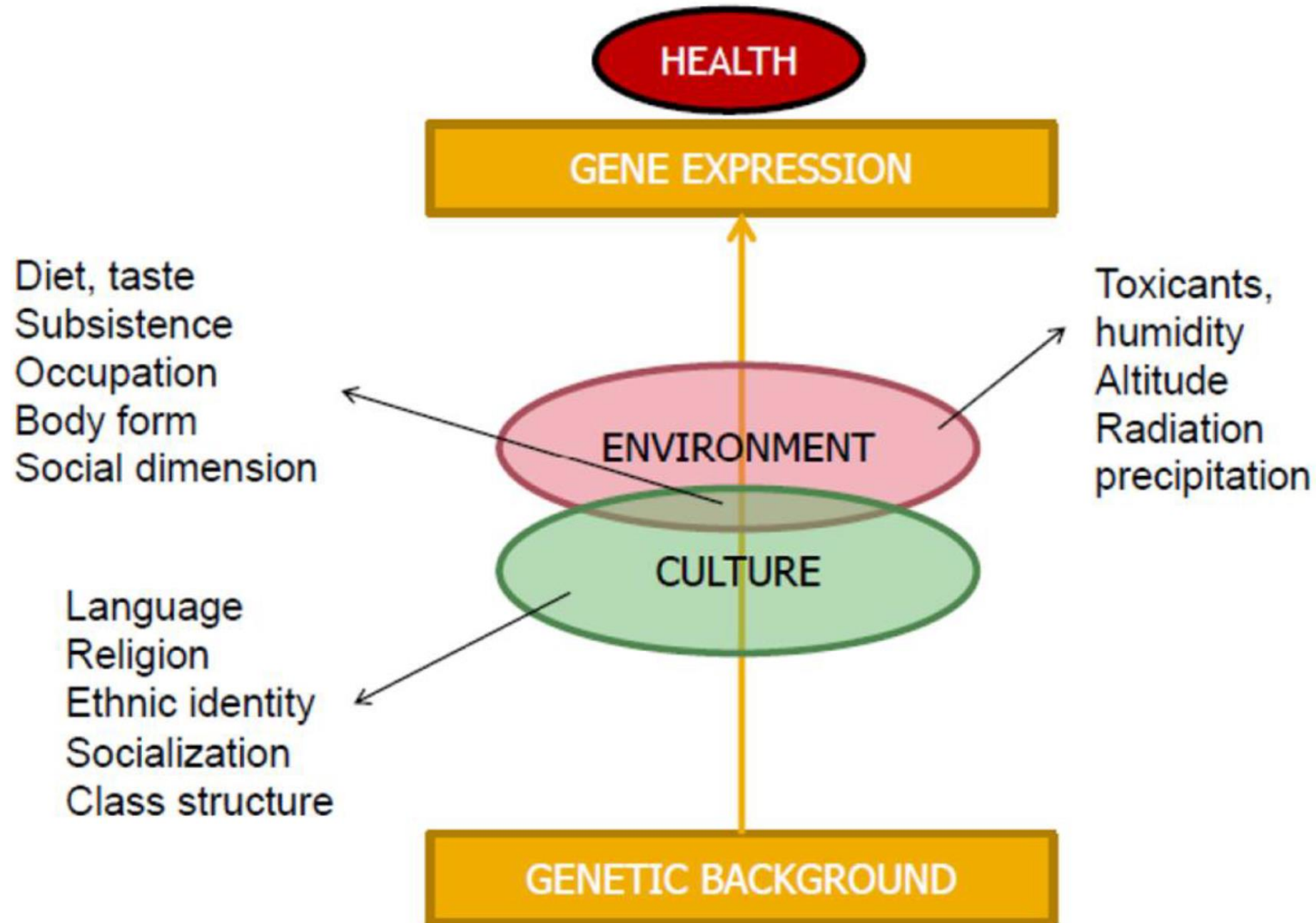


1) Are there any biological differences between fishing and non-fishing communities, that could have been caused by the different seafood intake?

- Genes under selection
- Epigenetic changes
- ...


2) Are there any differences in the biological predisposition of Mediterranean communities to the health effects of seafood intake?

- SNPs associated with differences in the tolerance to pollutants exposure
- SNPs associated with differences in FADS metabolism
- ...





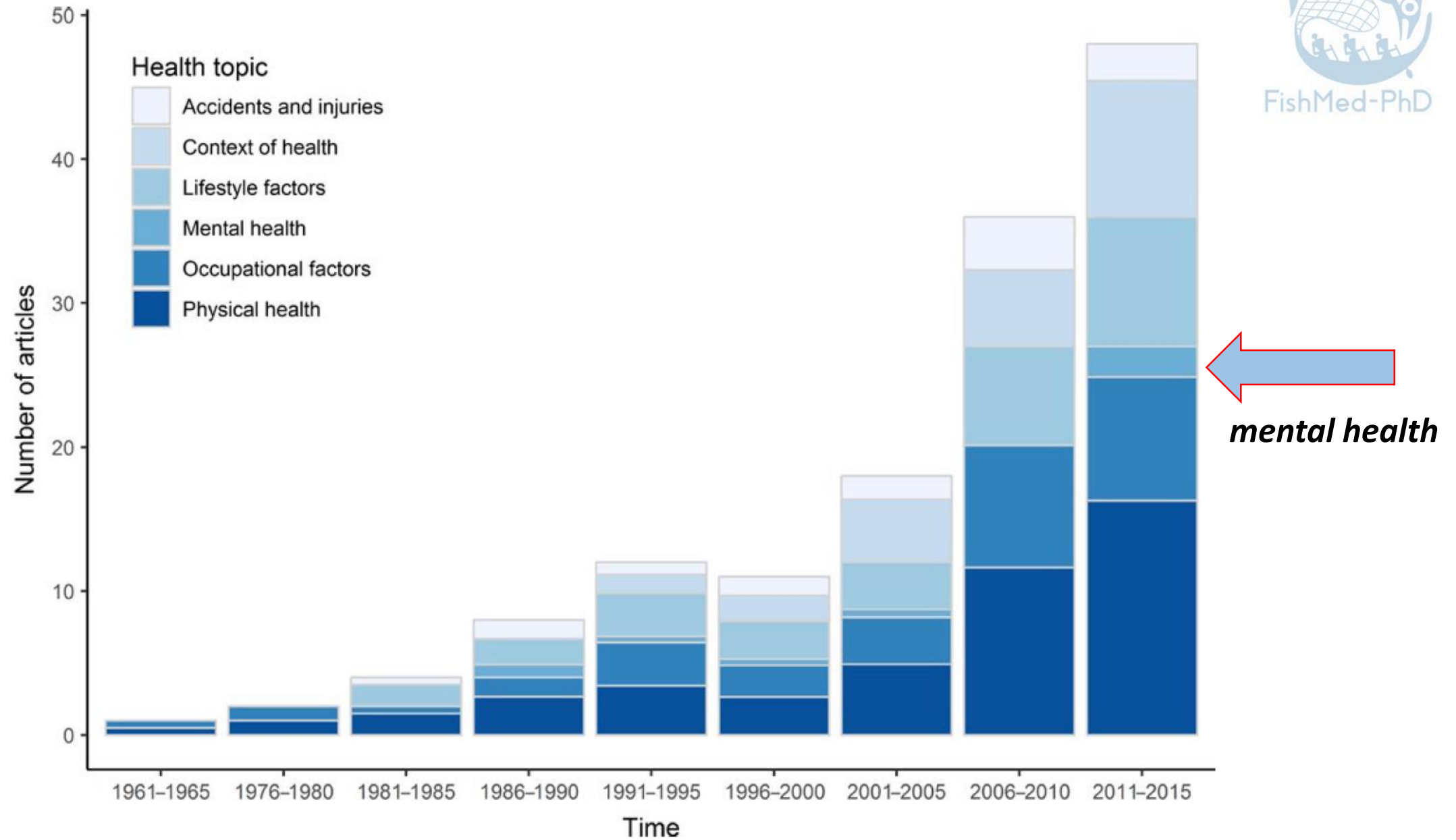
Health in fishing communities: A global perspective

Anna J. Woodhead  | Kirsten E. Abernethy | Lucy Szaboova | Rachel A. Turner 

In resource-dependent communities such as fishing communities, human health underpins the ability of individuals and families to maintain viable livelihoods. Fishing is a **dangerous occupation, in which fishers are exposed to health risks both on and offshore.**

Many of these **risks and associated health concerns also extend to fishing families and wider communities.**

Despite the importance of health, there is a **lack of understanding of the breadth of health issues affecting people associated with fishing.**



From the past to disease risk

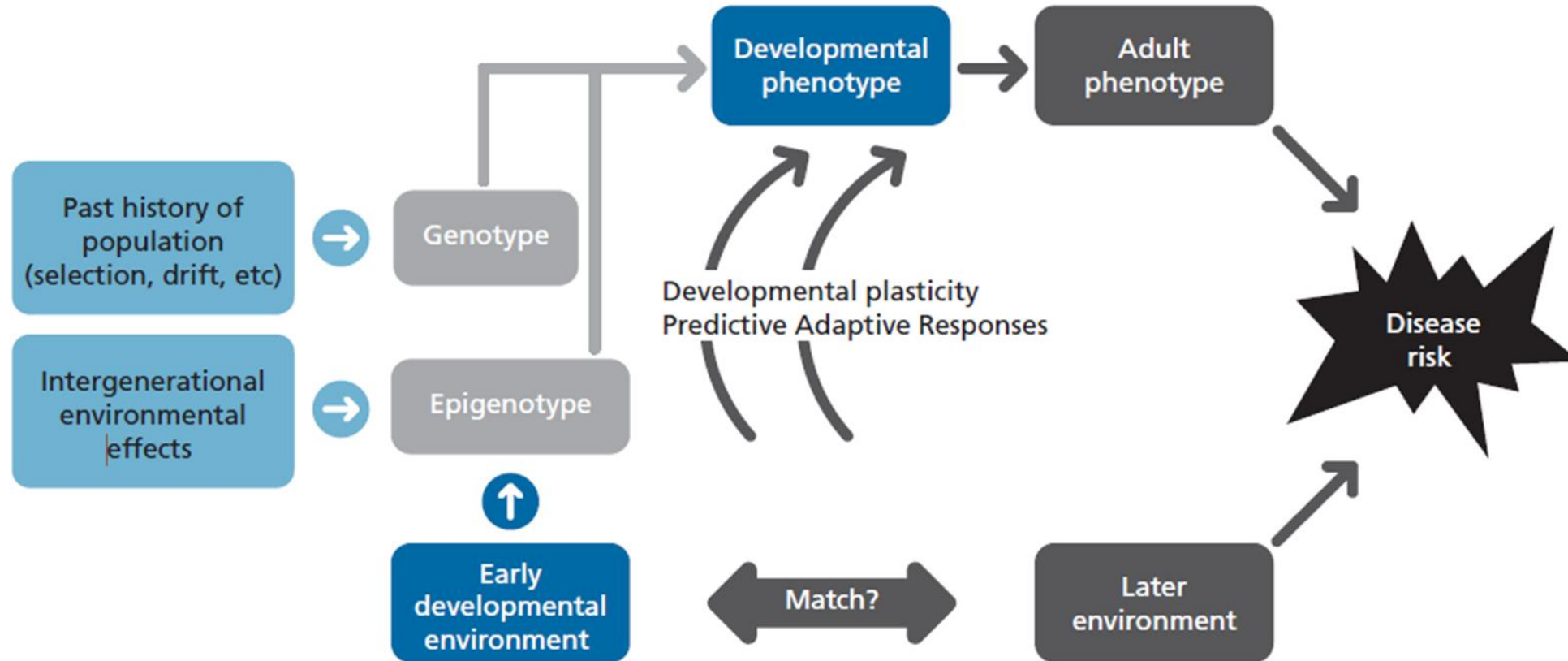


Figure 4.4 Disease risk in adulthood is influenced by a complex interplay between an organism's early developmental environment, later environment, intergenerational effects, and its evolutionary history. These factors shape the genetic and epigenetic repertoires to contribute to a particular developmental phenotype. Cues during development prompt predictive adaptive responses by the fetus to shift its developmental trajectory to match the perceived environment. If the inducing environment predicts the later environment well—that is, there is a match—then the individual has the appropriate physiological settings to be well prepared for the post-natal environment and the risk of disease is low. Conversely, if there is a mismatch between the predicted environment and the later environment, then the risk of disease is enhanced.

Diet during early development can have long-lasting effects



Maternal stress, malnutrition, low birth weight, and other factors affecting development in the womb can create long-term changes in basic biological functioning.

EARLY EVENT -> LATE ONSET
DISEASE

Suboptimal maternal nutrition



Placental abnormalities



Other maternal factors:
Stress
Infection
Drugs



Changes in fetal gene expression



Altered fetal growth metabolism



Reduced birth weight



Conflicting postnatal environment
Aging

Metabolic syndrome

The developmental programming hypothesis

These responses become maladaptive if the environment changes after birth.

The outcome of these maladaptations is increased susceptibility to disease in later life. One example is when birth weight is reduced as a result of inadequate fetal nutrition; if, in contrast, the postnatal environment allows overnutrition, abnormalities such as metabolic syndrome might result.

For adults, a methyl deficient diet still leads to a decrease in DNA methylation, but the changes are **REVERSIBLE** with resumption of a normal diet.



Over half a century ago, the American geographer Carl Sauer formally proposed the **importance of coasts in becoming human** (Sauer 1962).



If the past is a guide to the future, this topic is
designate to go on!





FishMed-PhD Teaching week 2021

March 1st, 2021



Thank you for your attention

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