FishMed-PhD Teaching week

March 3th, 2023

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

Photo by Andrea De Giovanni

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Ravenna Campus, UNIBO

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Summary

- Our ancestors and the coastline environment
- Marine resources from past to present
- Fishing: health benefits and contaminants
- Genetics and epigenetics of fishing communities

WATER IS LIFE

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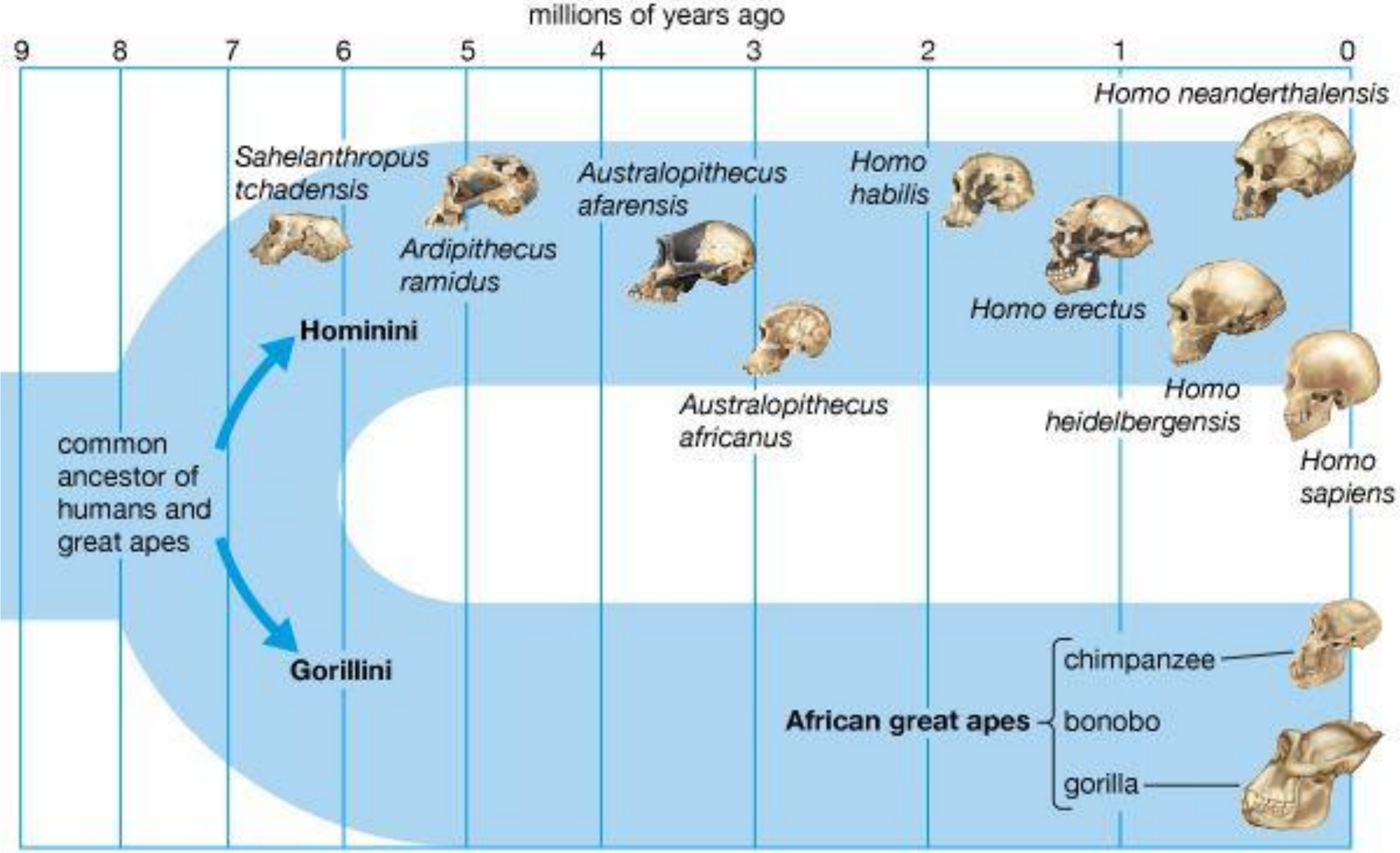
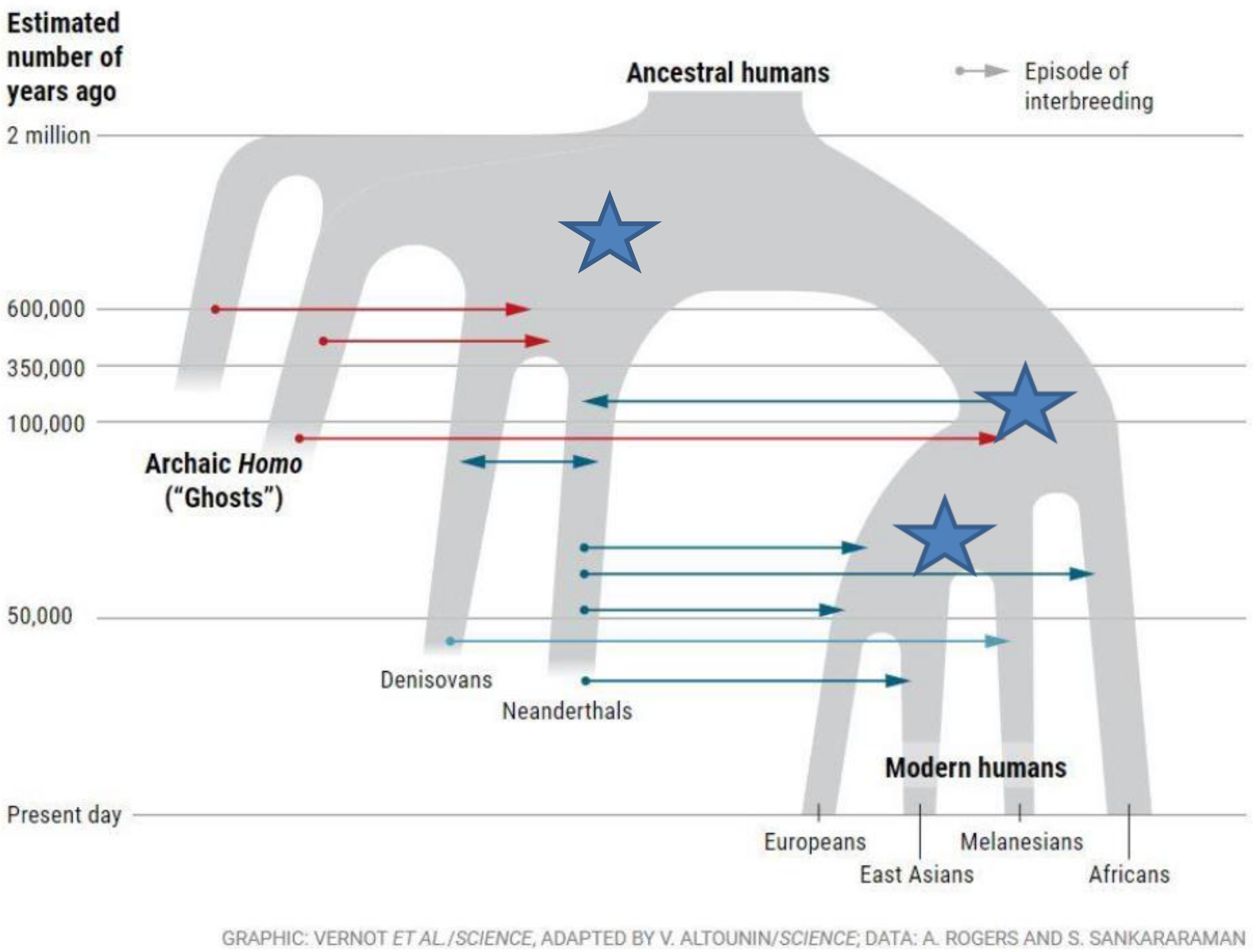


Homo sapiens evolution and migration from Africa



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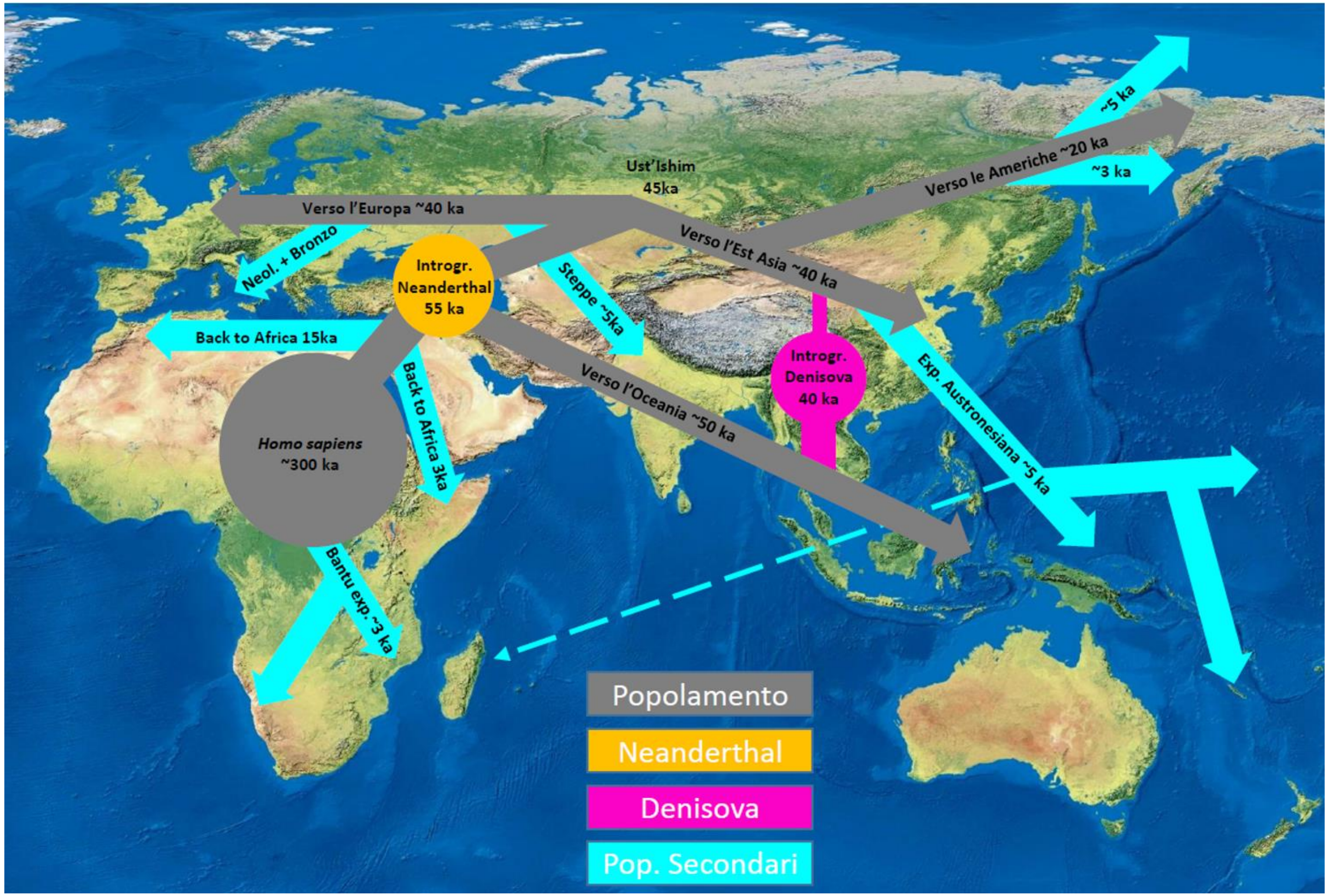
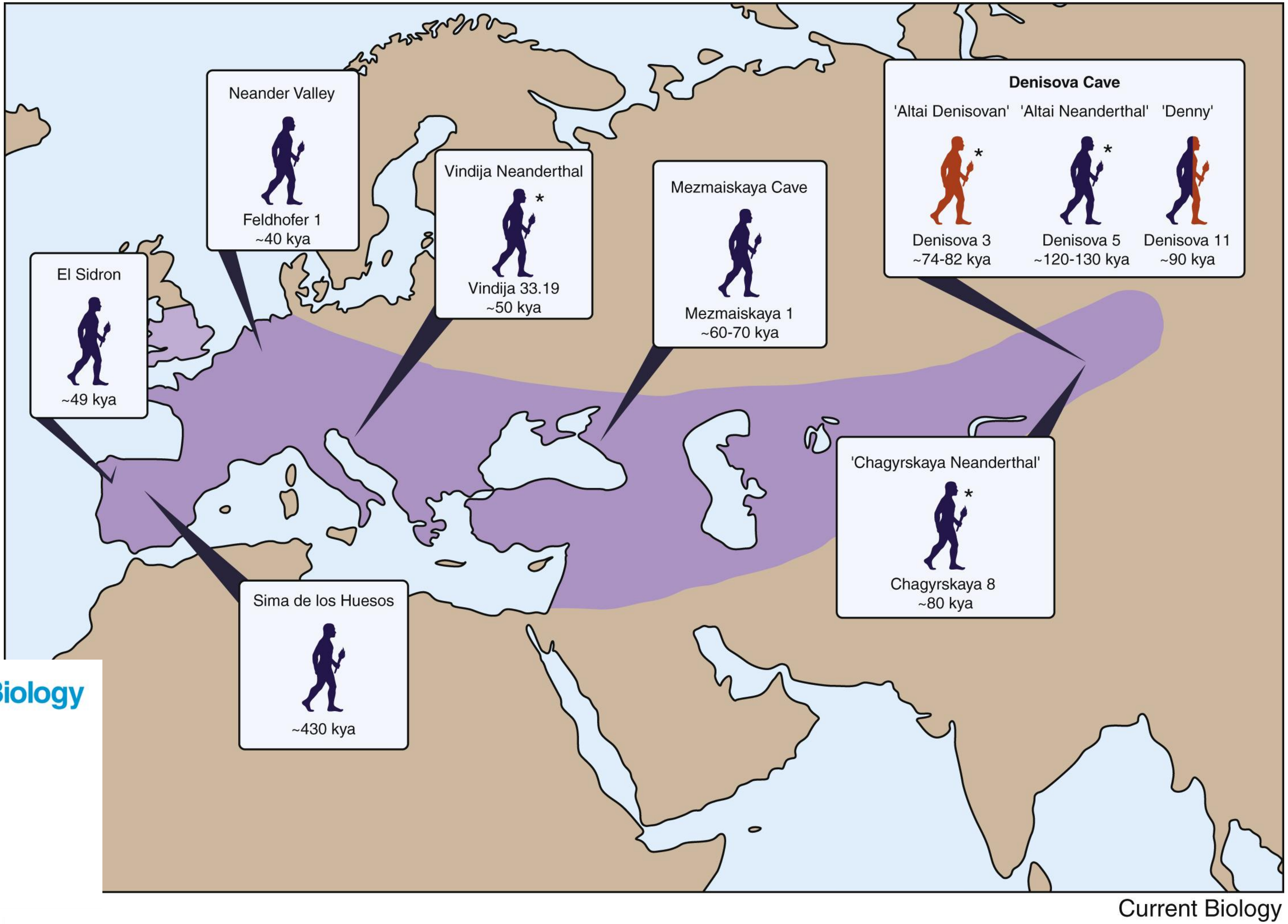
★ **Three key phases in our ancestry**

A summary of the peopling of continents by H. sapiens



The gray traces show the first population to have left a genetic mark in modern human populations. The orange and fuchsia circles summarize the interactions with archaic groups while the blue arrows refer to the main secondary population movements

Neanderthals inhabited this vast geographical region from **300-430 thousand years ago (kya) up to 40 kya**, overlapping in time and space with modern humans



CellPress Current Biology

Review

The contribution of Neanderthal introgression to modern human traits

Patrick F. Reilly[1], Audrey Tjahjadi[1], Samantha L. Miller[1], Joshua M. Akey[2,*], and Serena Tucci[1,3,*]
[1]Department of Anthropology, Yale University, New Haven, CT, USA
[2]Lewis Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ, USA
[3]Department of Ecology and Evolutionary Biology, Yale University, New Haven, CT, USA
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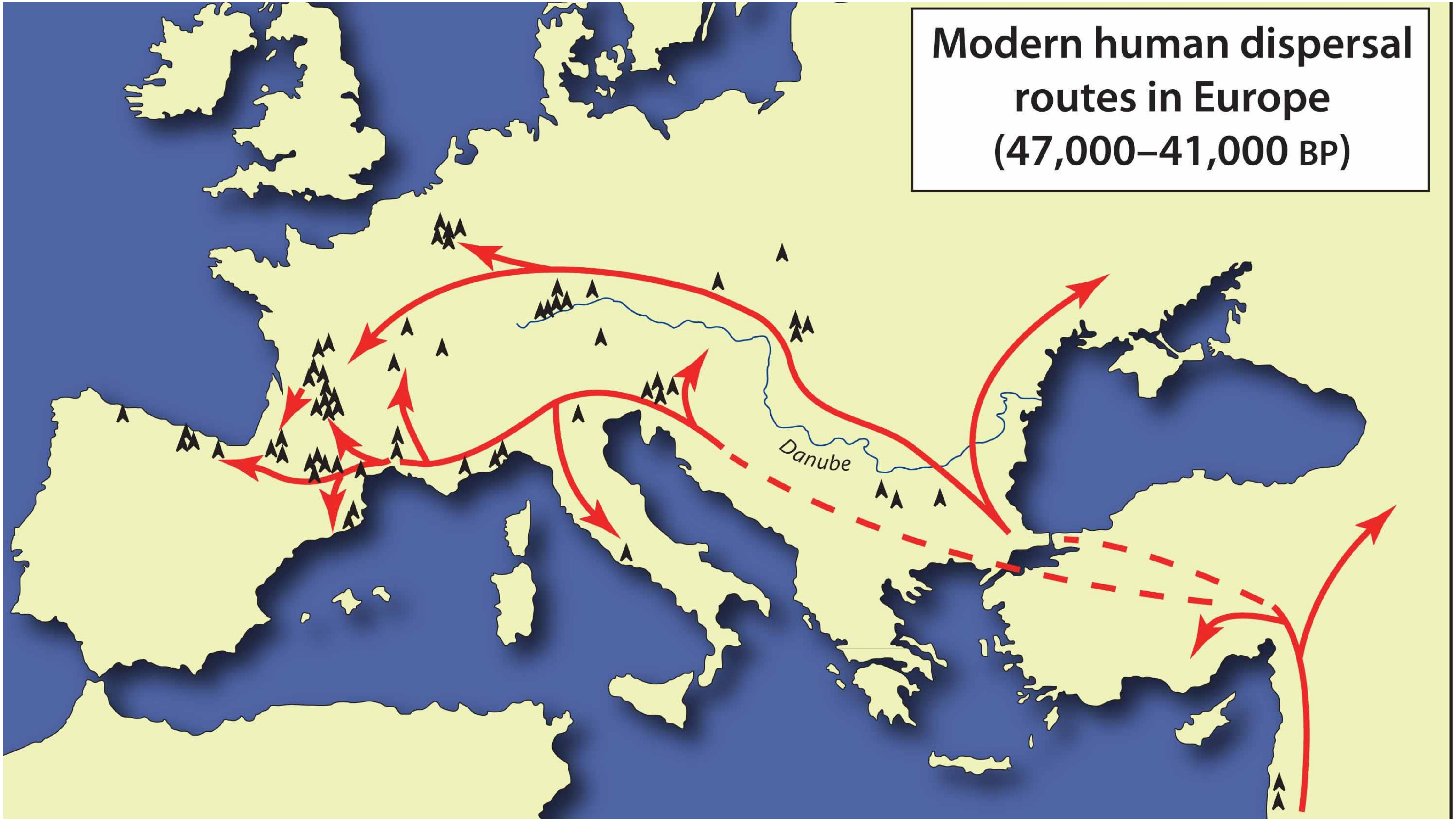
https://doi.org/10.1016/j.cub.2022.08.027

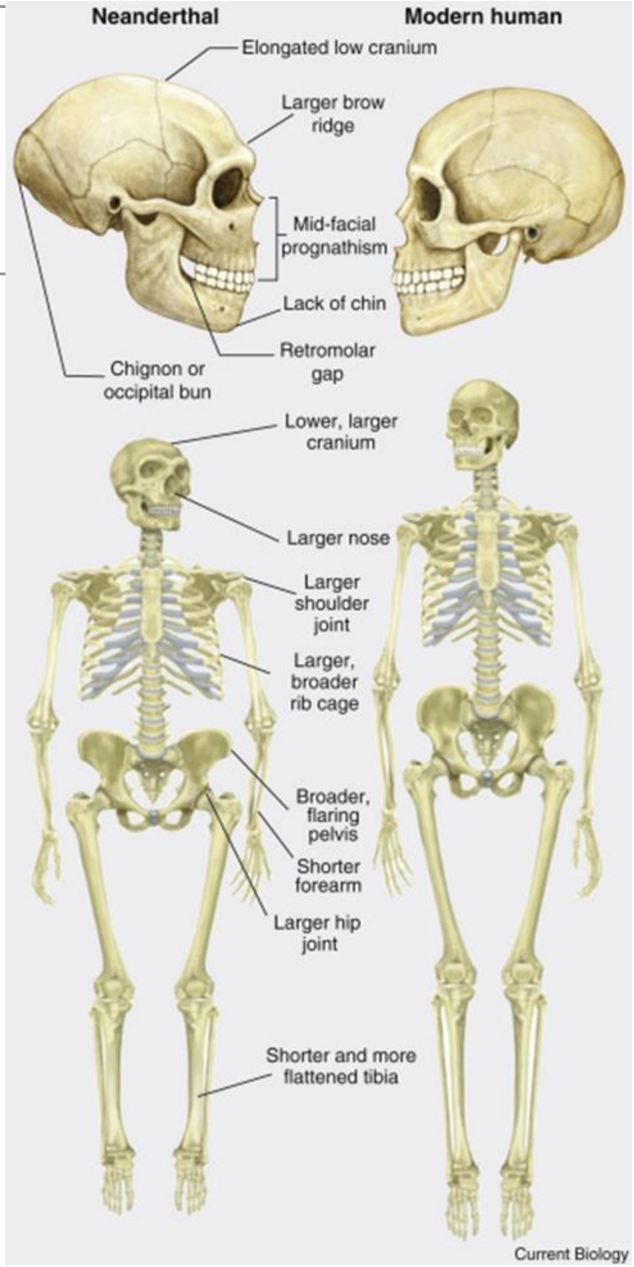
R970 Current Biology *32*, R970–R983, September 26, 2022 © 2022 Elsevier Inc.

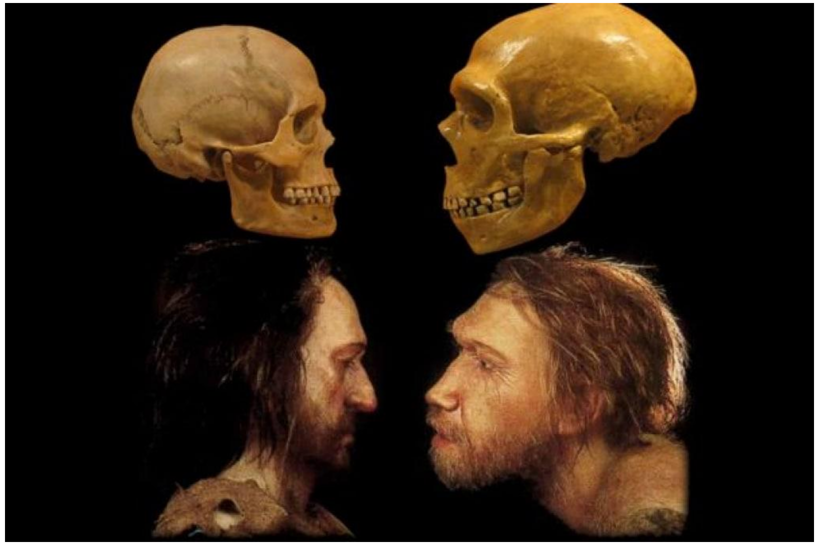

Modern human dispersal routes in Europe (47,000–41,000 BP)
Danube

PIONEER OF RESEARCH ON ANCIENT DNA WINS MEDICINE NOBEL

Svante Pääbo has used genomic analysis to unmask the lives of ancient human species such as Neanderthals.

Svante Pääbo's work helped to spawn the competitive field of palaeogenomics.





ANCIENT HUMAN GENOMES

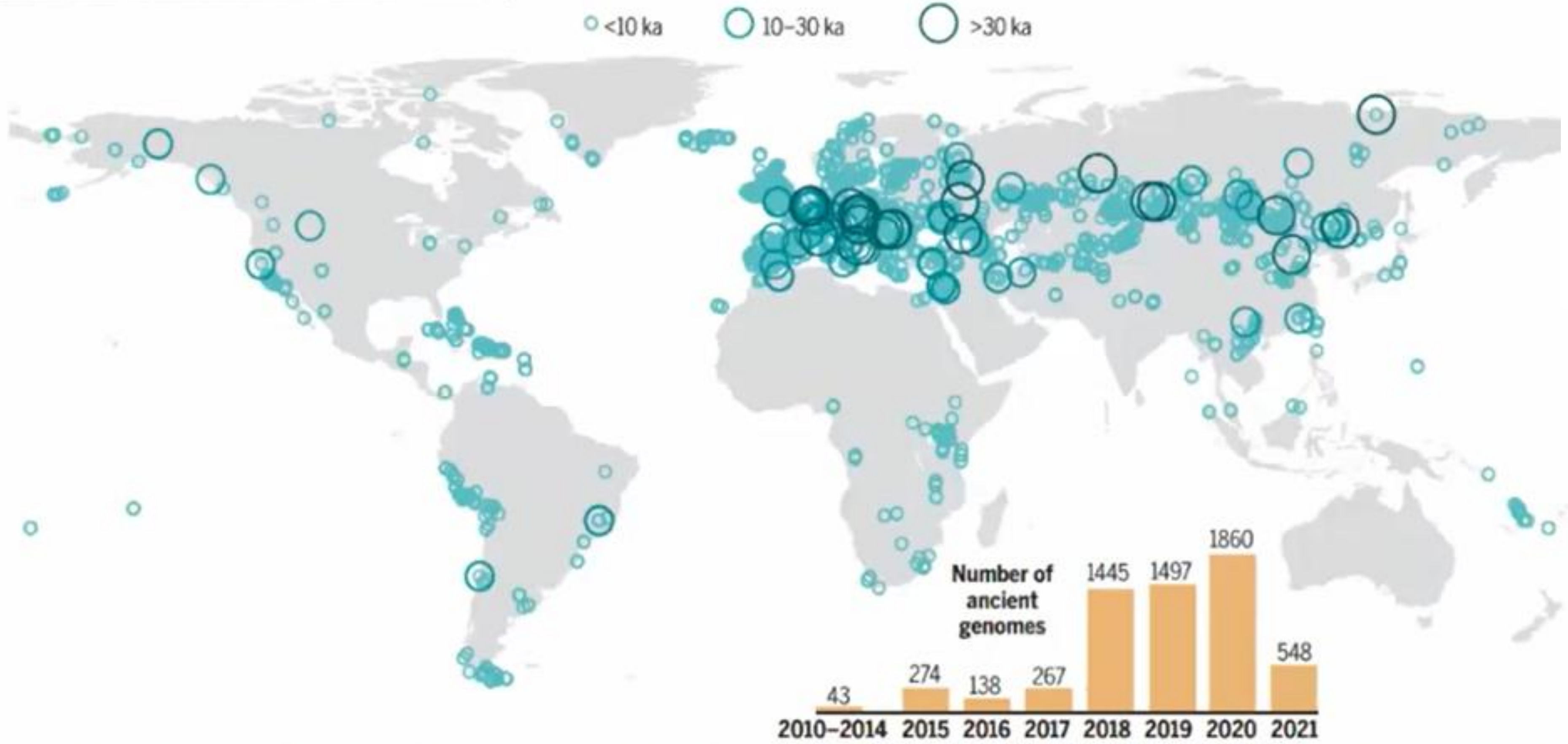
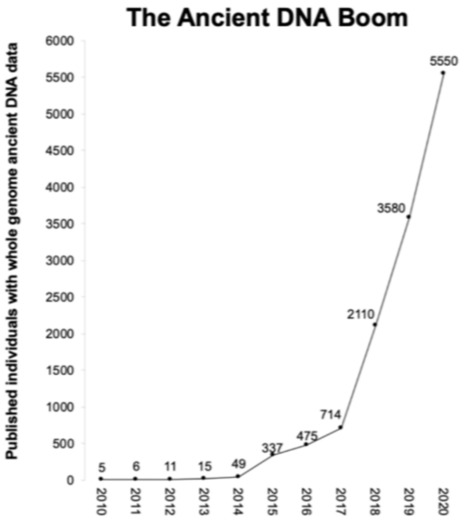
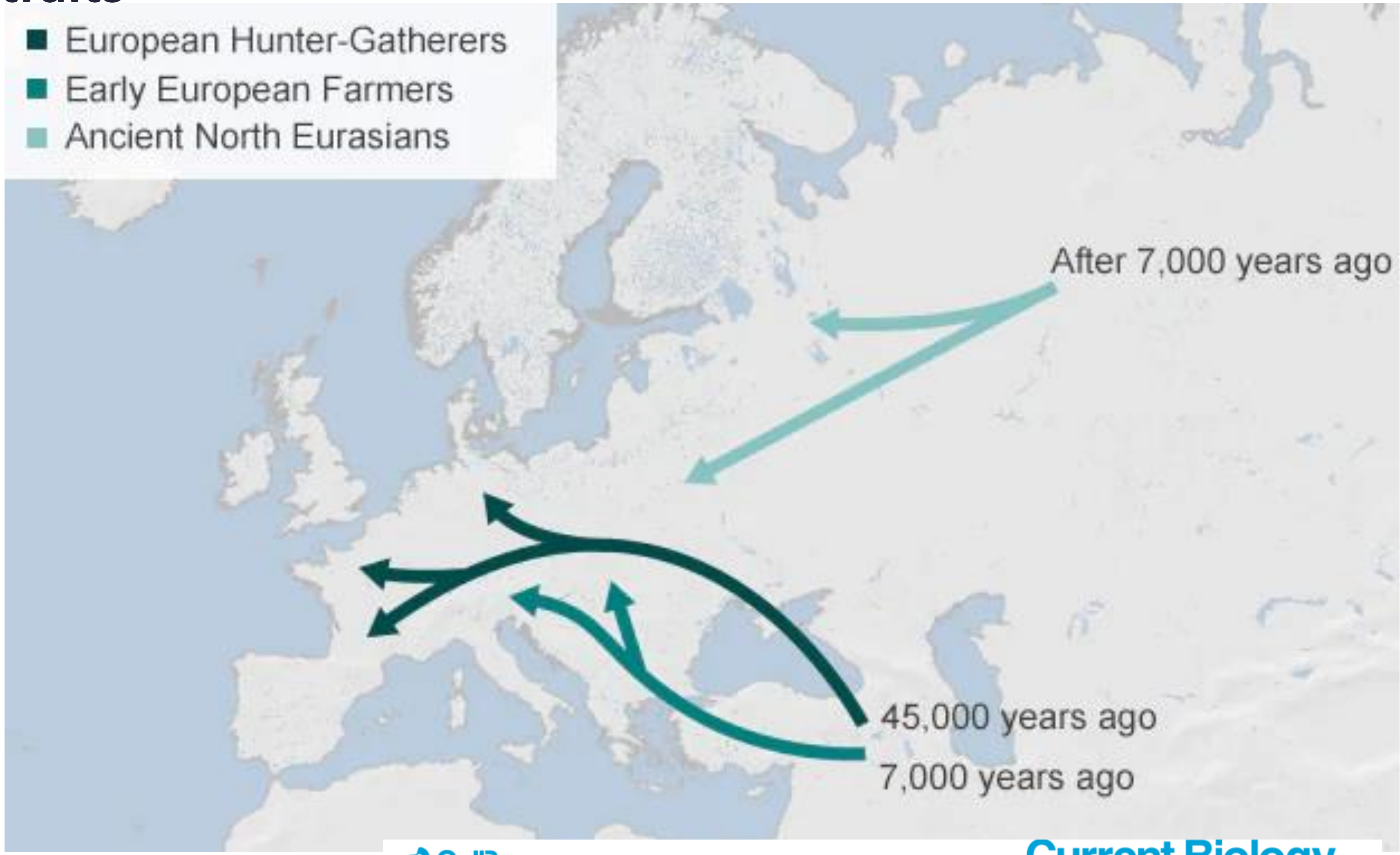


Fig. 1. Published ancient human genomes (including whole-genome sequences, exomes, and genome-wide single-nucleotide polymorphism data) by June 2021. Large dark blue circles indicate ancient individuals older than 30 kyr; medium blue circles indicate ancient individuals younger than 30 kyr and older than 10 kyr; and small light-blue circles indicate ancient individuals younger than 10 kyr.



[Liu et al., 2021]

Ancient mixing of ancestries shaped present-day European body and health traits

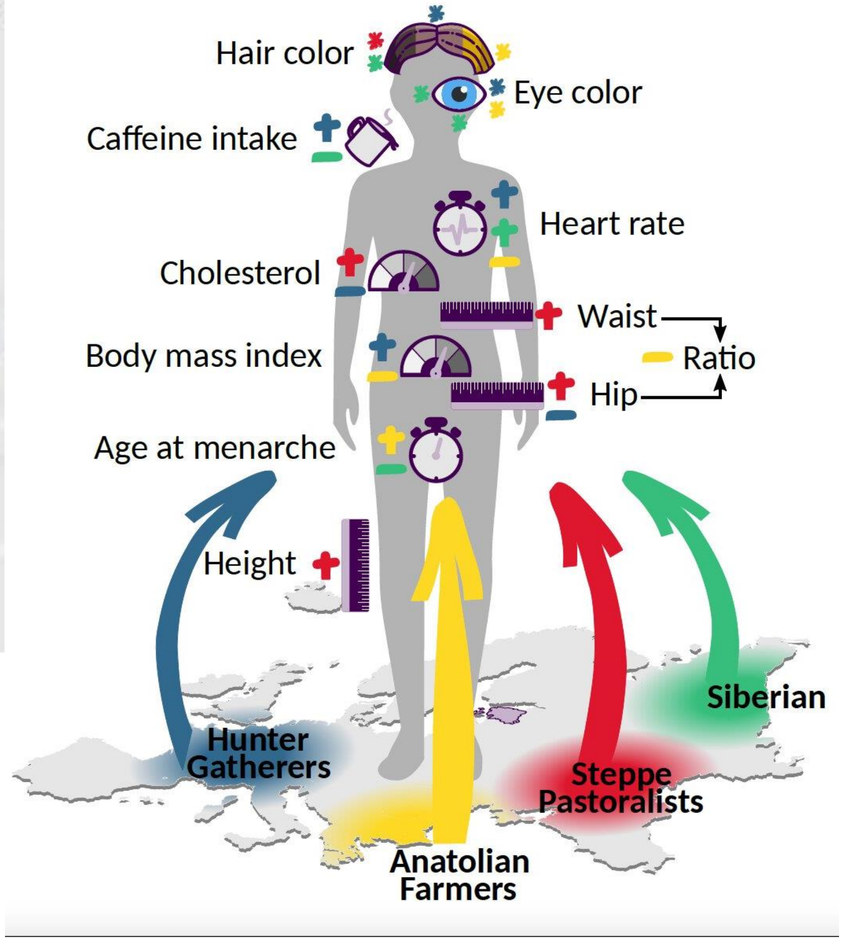


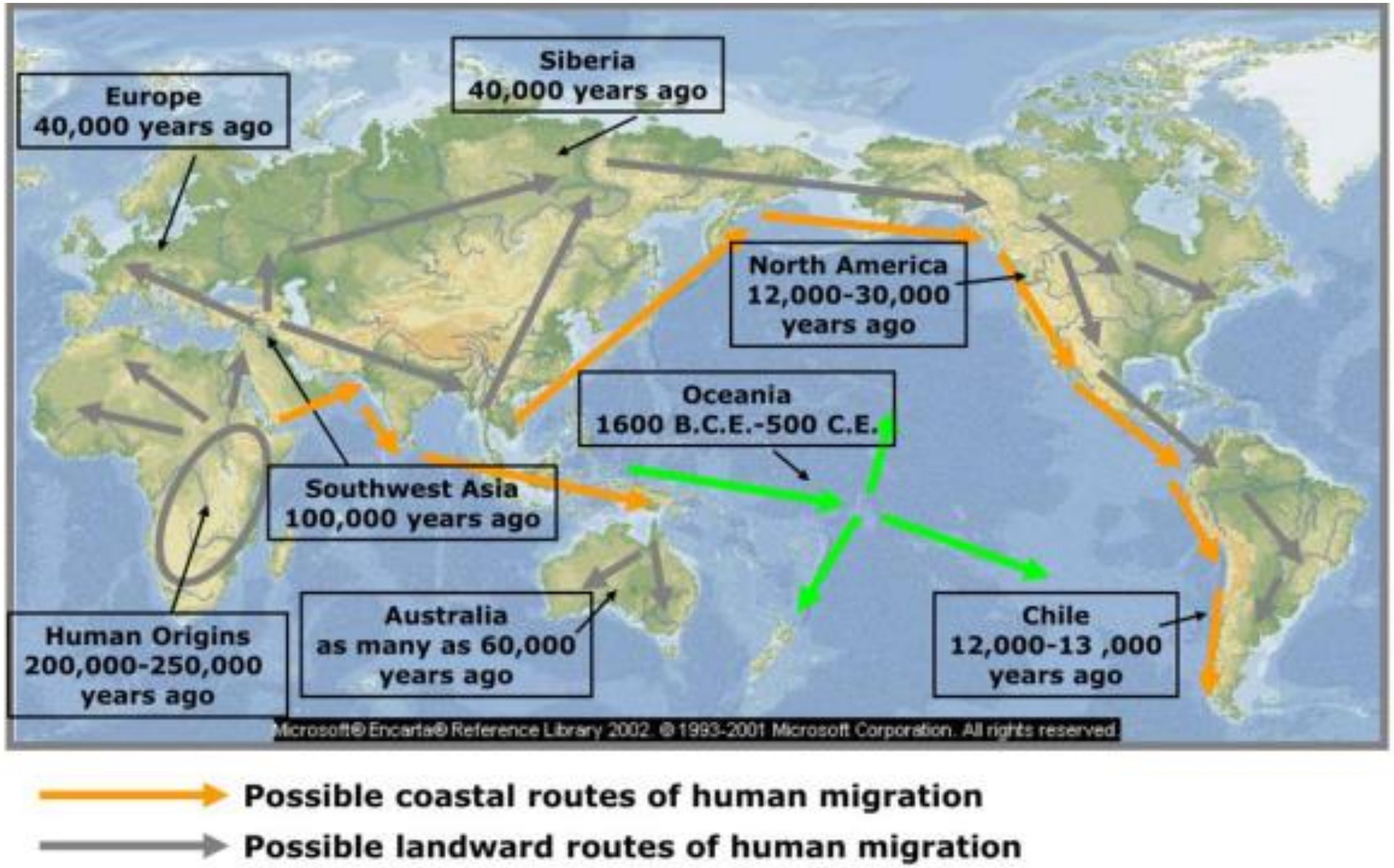
CellPress
Current Biology

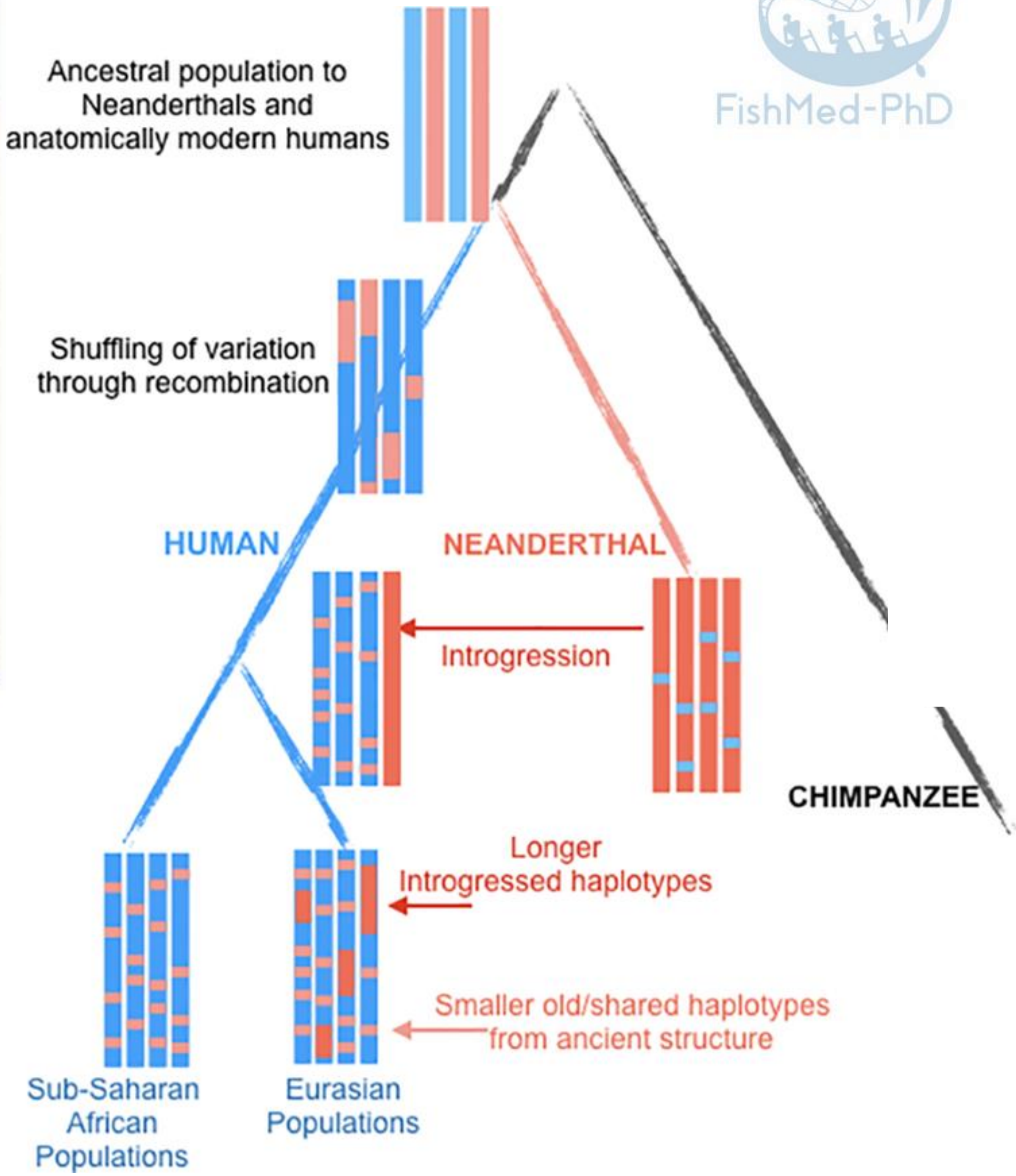
Report

Ancestral genomic contributions to complex traits in contemporary Europeans

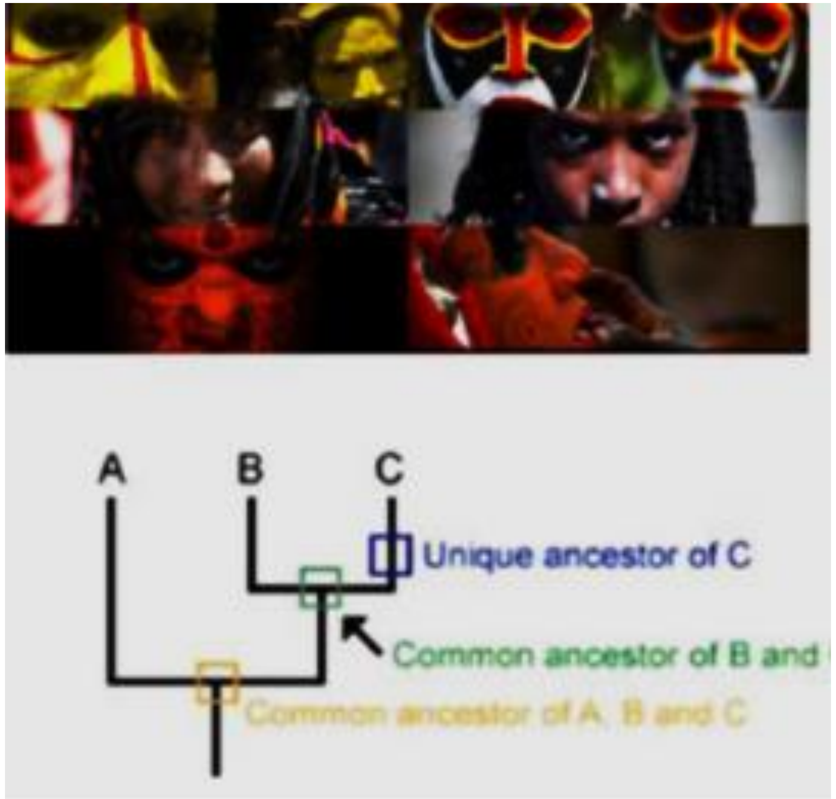
Davide Marnetto,[1,2,11,*] Vasili Pankratov,[1] Mayukh Mondal,[1] Francesco Montinaro,[1,3] Katri Pärna,[1,4] Leonardo Vallini,[5] Ludovica Molinaro,[1] Lehti Saag,[1,6] Liisa Loog,[7] Sara Montagnese,[8] Rodolfo Costa,[5,9,10] Estonian Biobank Research Team,[1] Mait Metspalu,[1] Anders Eriksson,[1] and Luca Pagani[1,5,*]

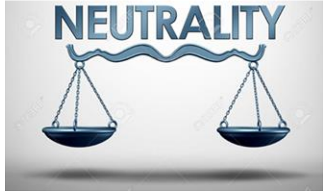


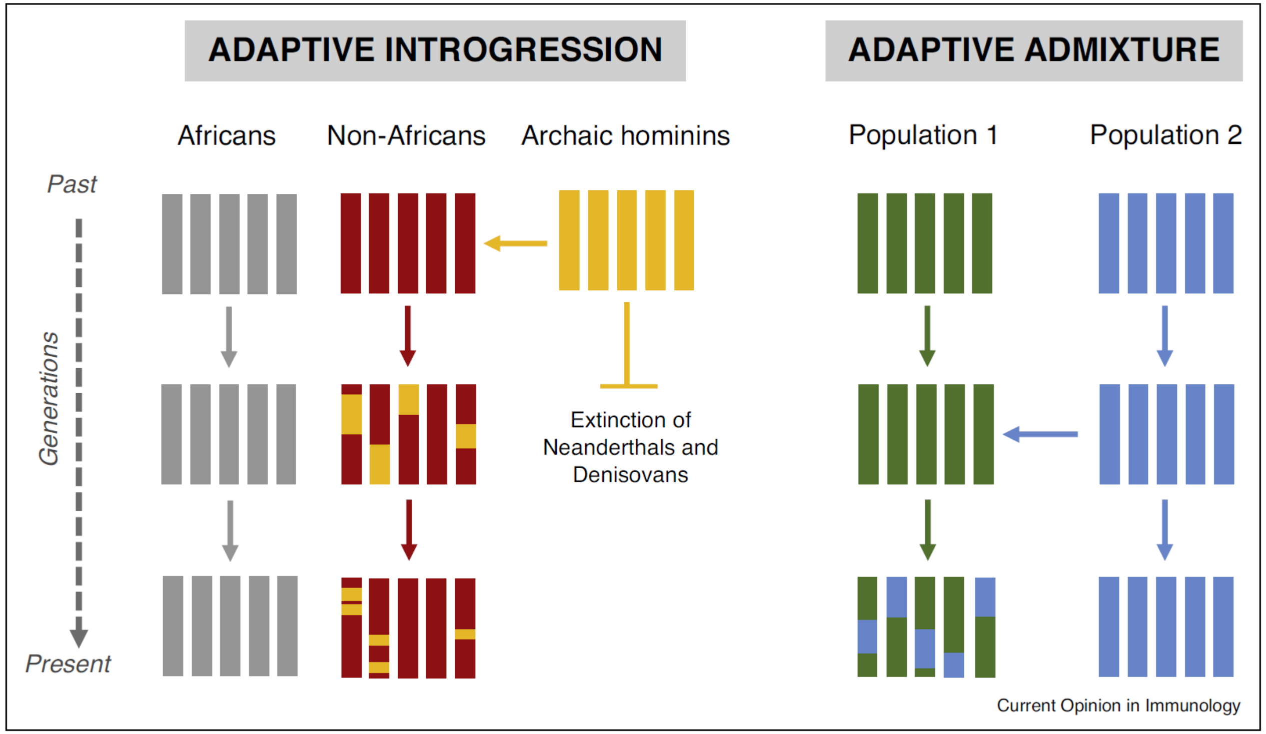

Europe
40,000 years ago
Siberia
40,000 years ago
North America
12,000-30,000
years ago
Oceania
1600 B.C.E.-500 C.E.
Southwest Asia
100,000 years ago
Australia
as many as 60,000
years ago
Chile
12,000-13 ,000
years ago
Human Origins
200,000-250,000
years ago
Microsoft® Encarta® Reference Library 2002. © 1993-2001 Microsoft Corporation. All rights reserved.
Possible coastal routes of human migration
Possible landward routes of human migration


Ancestral population to
Neanderthals and
anatomically modern humans
Shuffling of variation
through recombination
HUMAN
NEANDERTHAL
Introgression
CHIMPANZEE
Longer
Introgressed haplotypes
Smaller old/shared haplotypes
from ancient structure
Sub-Saharan
African
Populations
Eurasian
Populations

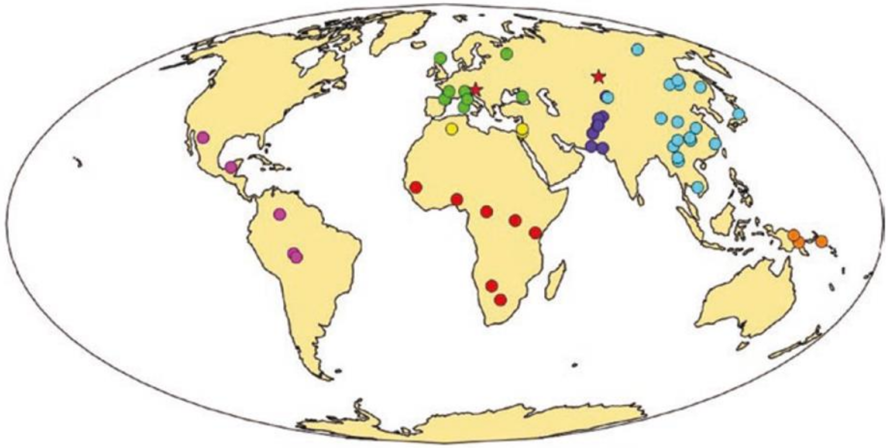
Human population genomic variability between demography and local adaptation

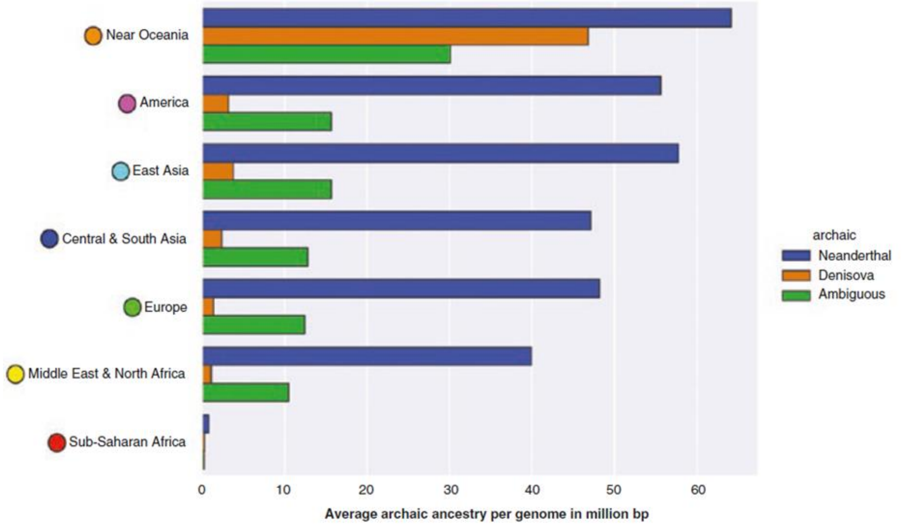




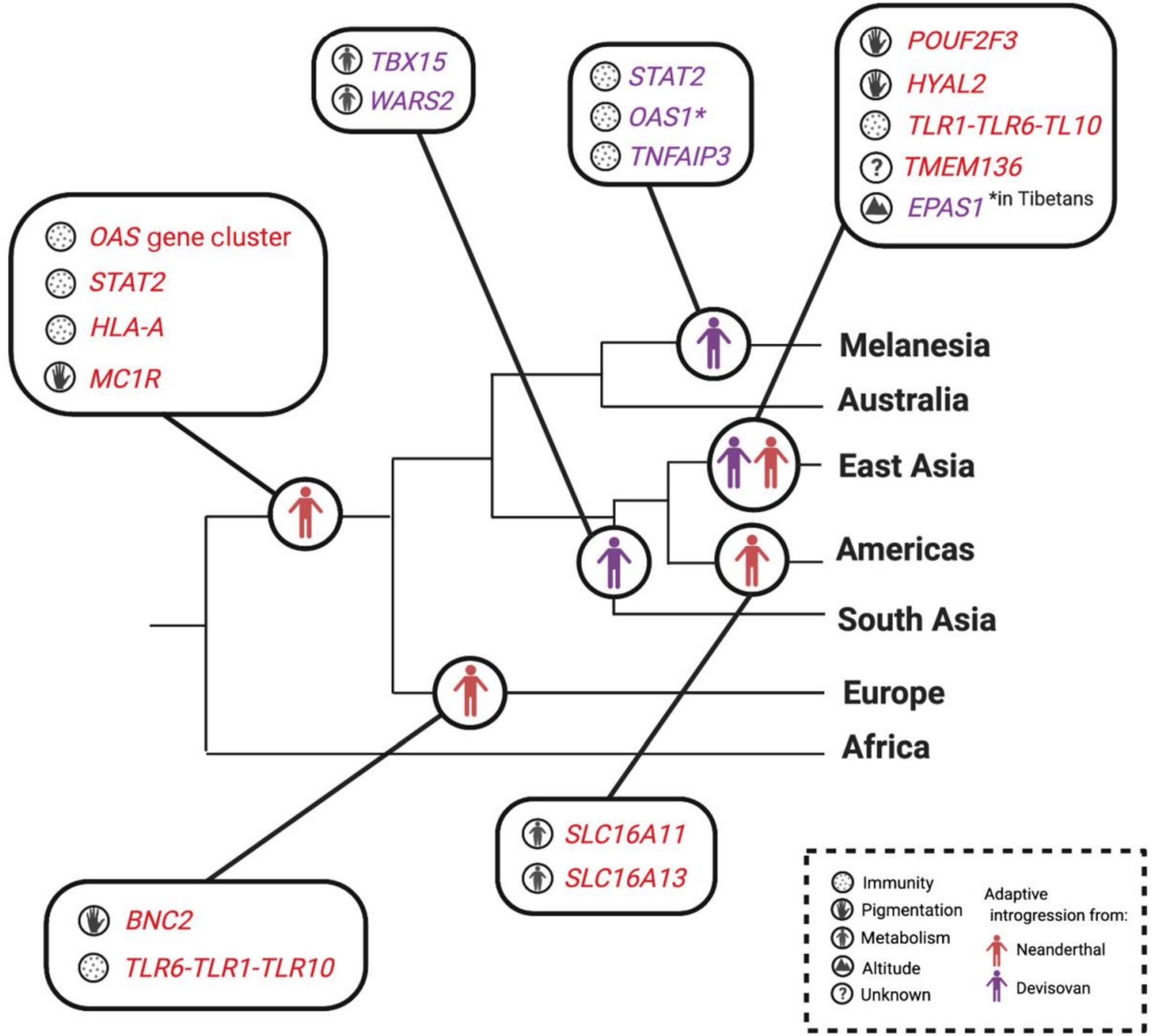


In addition to adaptive introgression, admixture within species facilitated genetic adaptation to the ever-changing world of pathogens and pollutans .



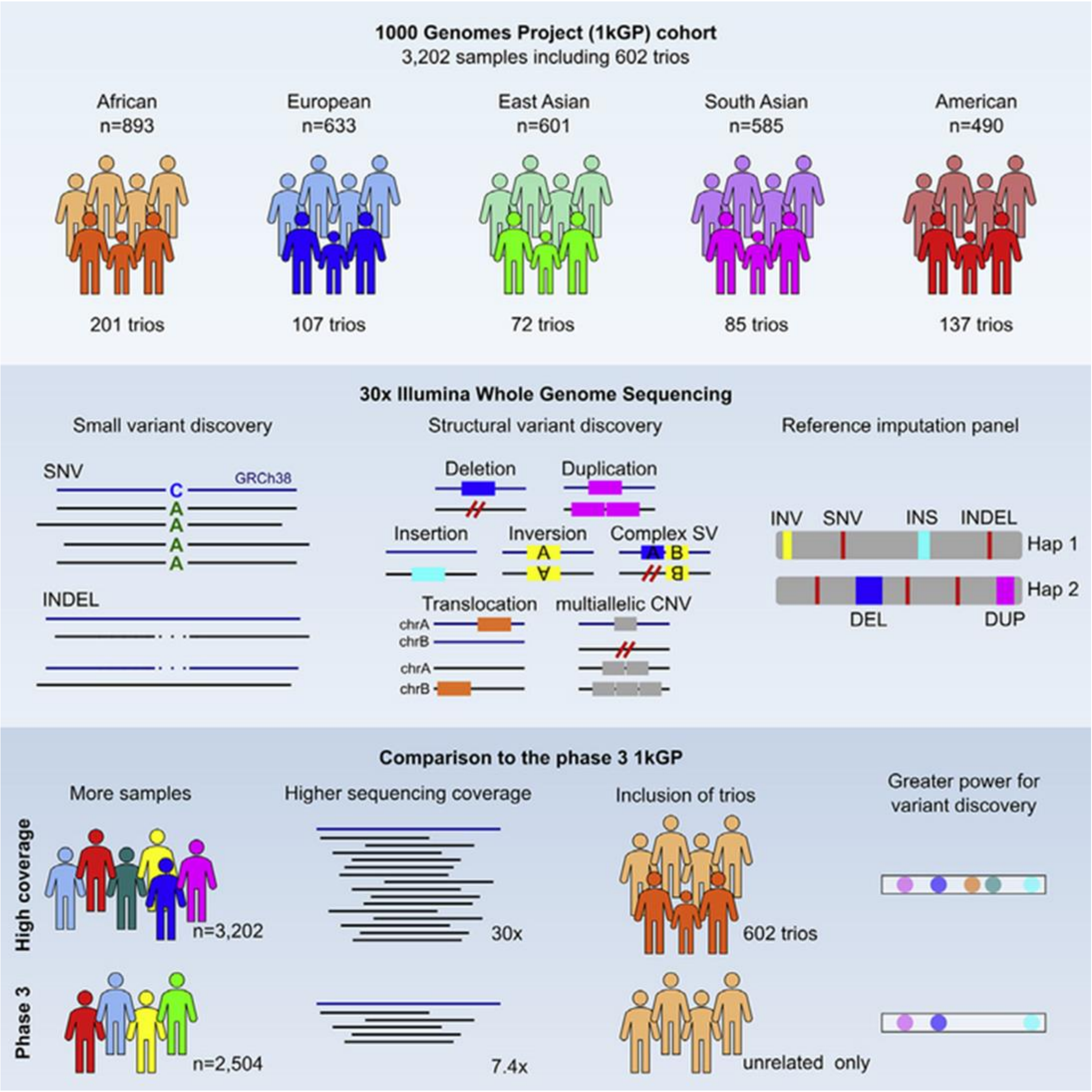


Distribution of variants of archaic hominins in modern human genomes.

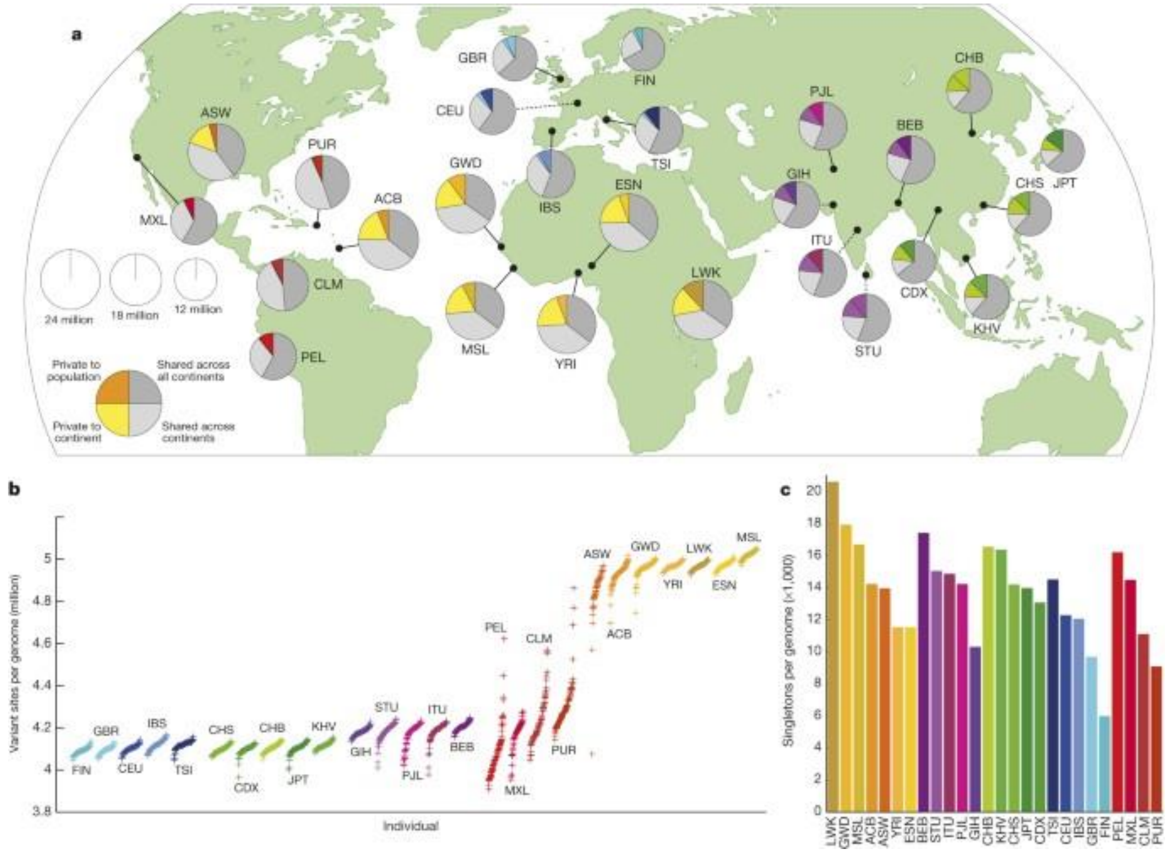


Trends in Genetics

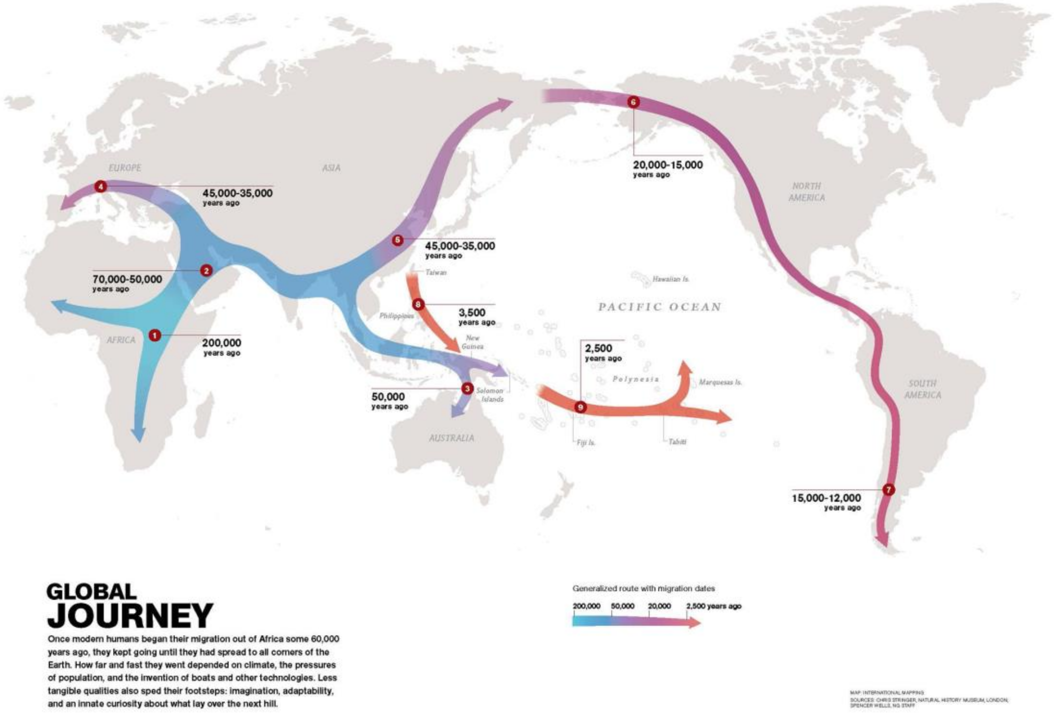
THE HUMAN GENOME VARIABILITY



The original 2,504 samples from the ***1000 Genomes Project*** *were re-sequenced and new related samples were added for generation of an improved publicly accessible whole-genome sequencing resource*



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



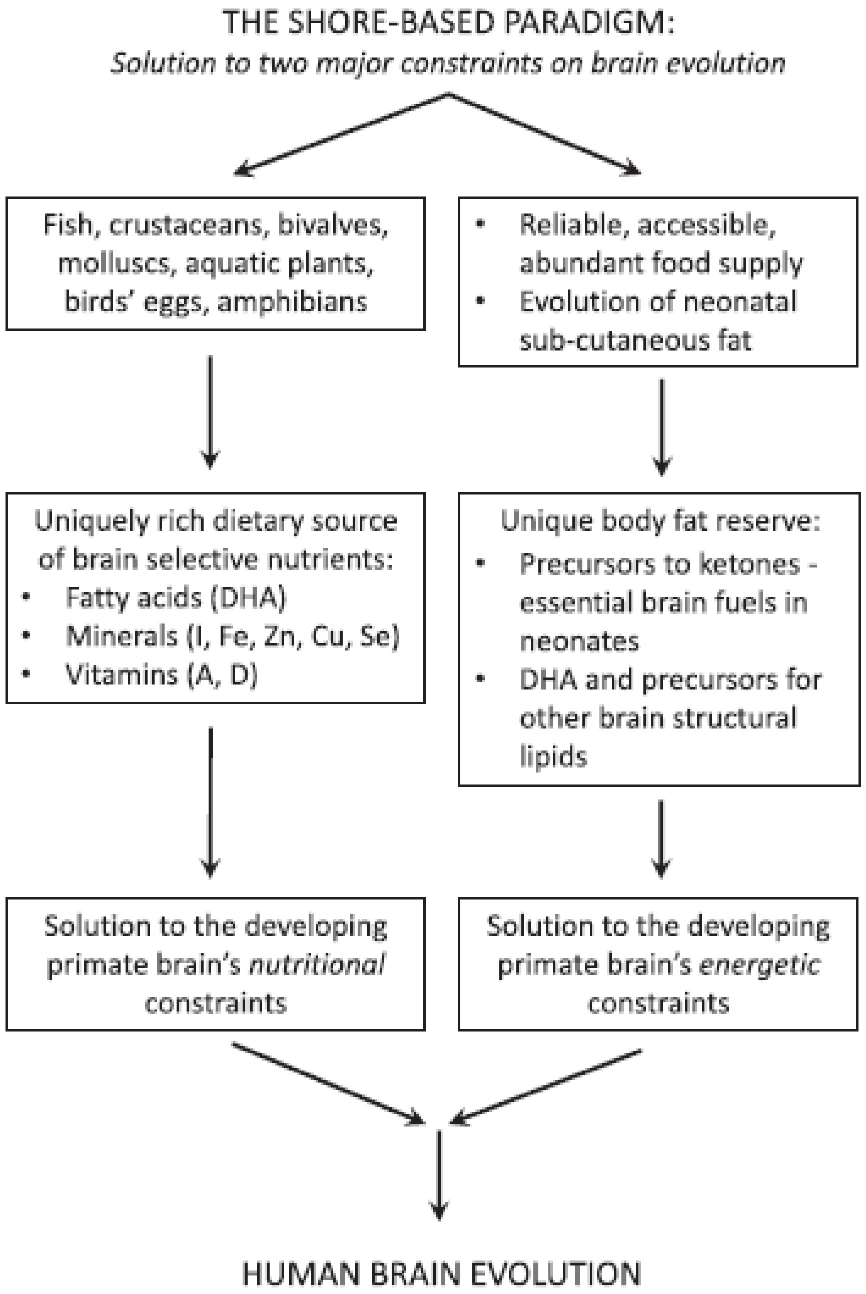
Coastal adaptations have become an important topic in discussions about the evolution and dispersal of *Homo sapiens*.

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*

↓

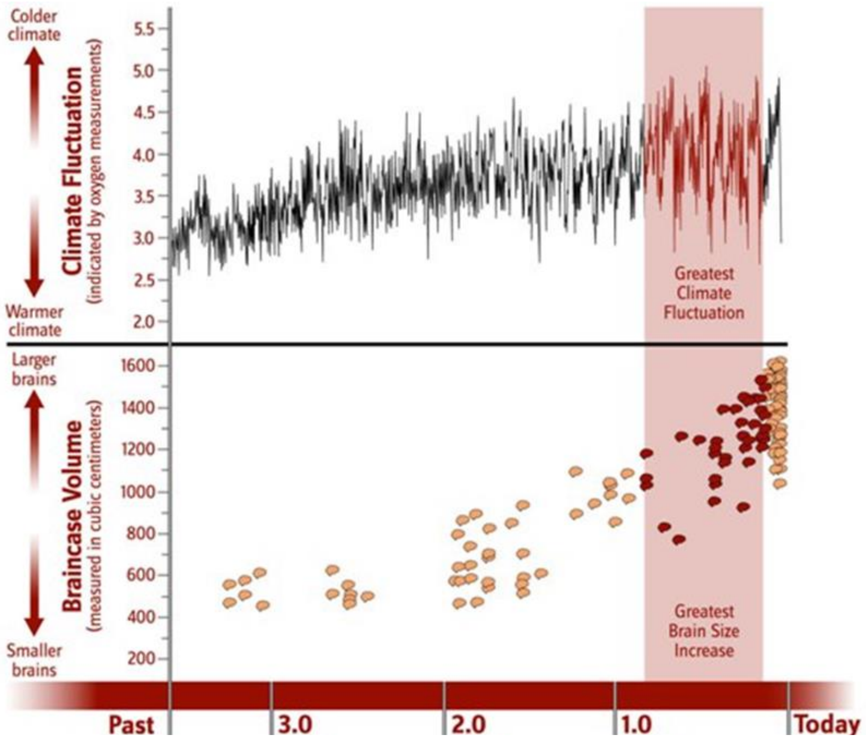
associated to the **evolution of *neonatal body fat reserves,*** which were just as important for optimal human brain development.



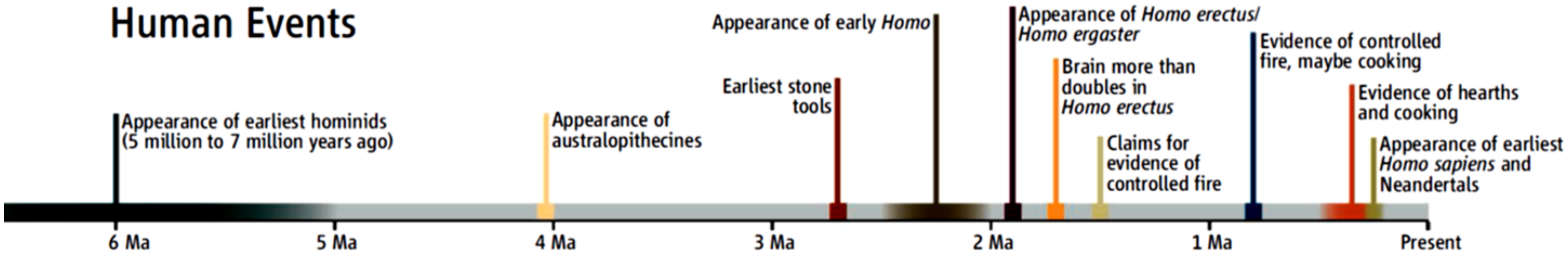
Cunnane and Crowford, 2014

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

Over the course of human evolution, **brain size tripled**

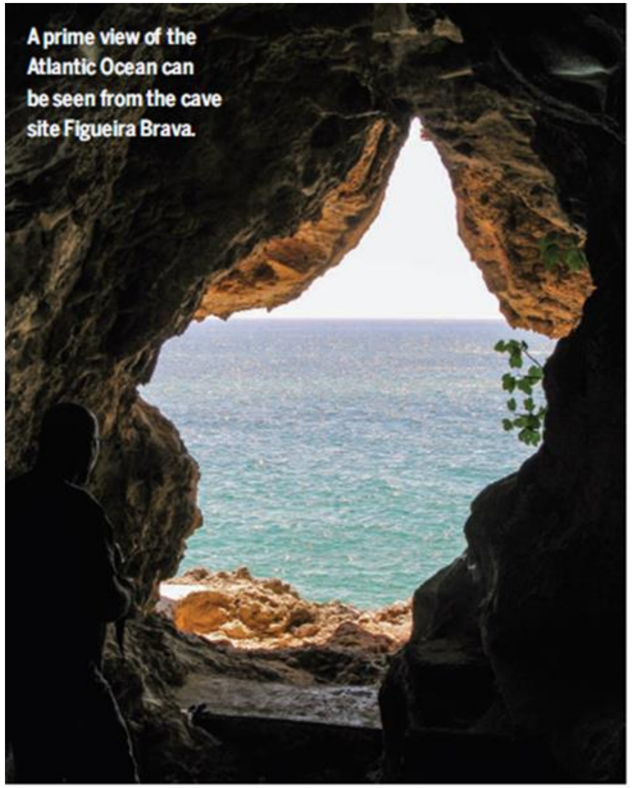


The human brain is nearly 60% fat by total weight, and that big, **powerful brain needs to be provided with certain types of fats (both saturated and unsaturated)** throughout life to provide a balance of structural integrity and fluidity to its cells.



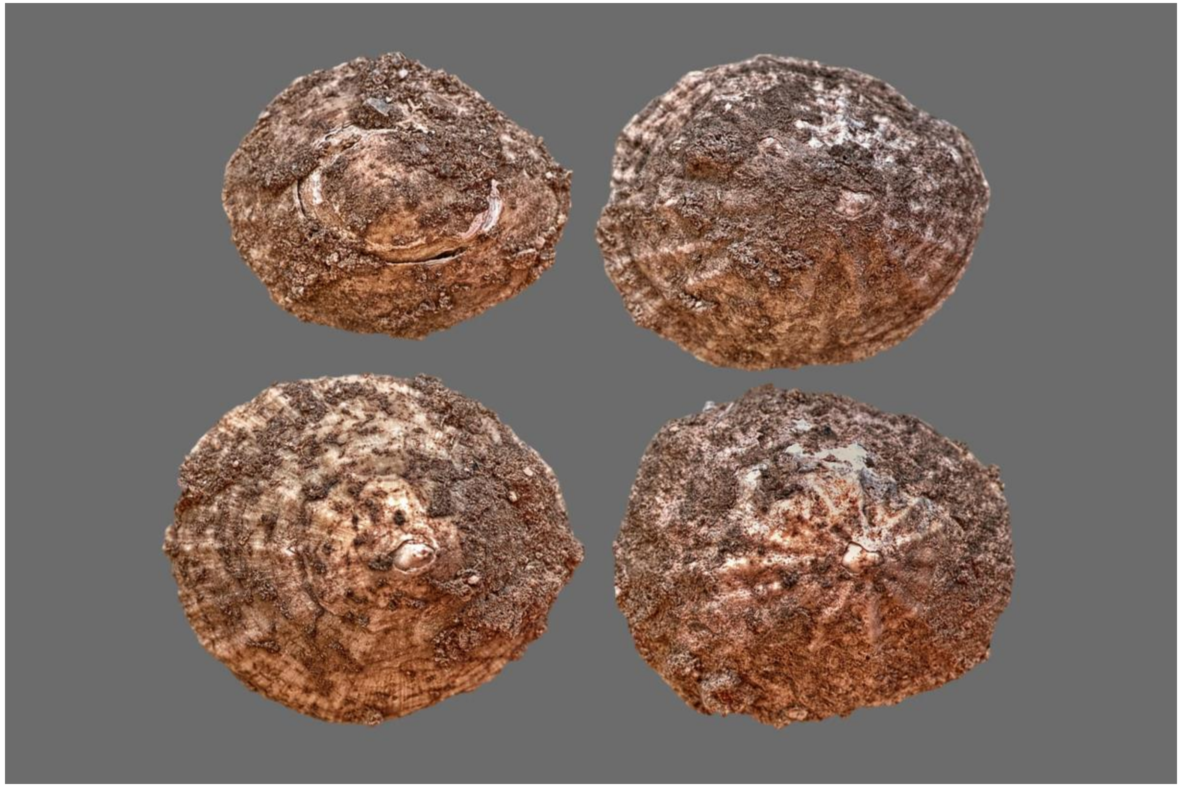
Did Neanderthal adapt to the sea in the same way as early *Homo sapiens*?

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**.



1422 27 MARCH 2020 • VOL 367 ISSUE 6485

sciencemag.org SCIENCE



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

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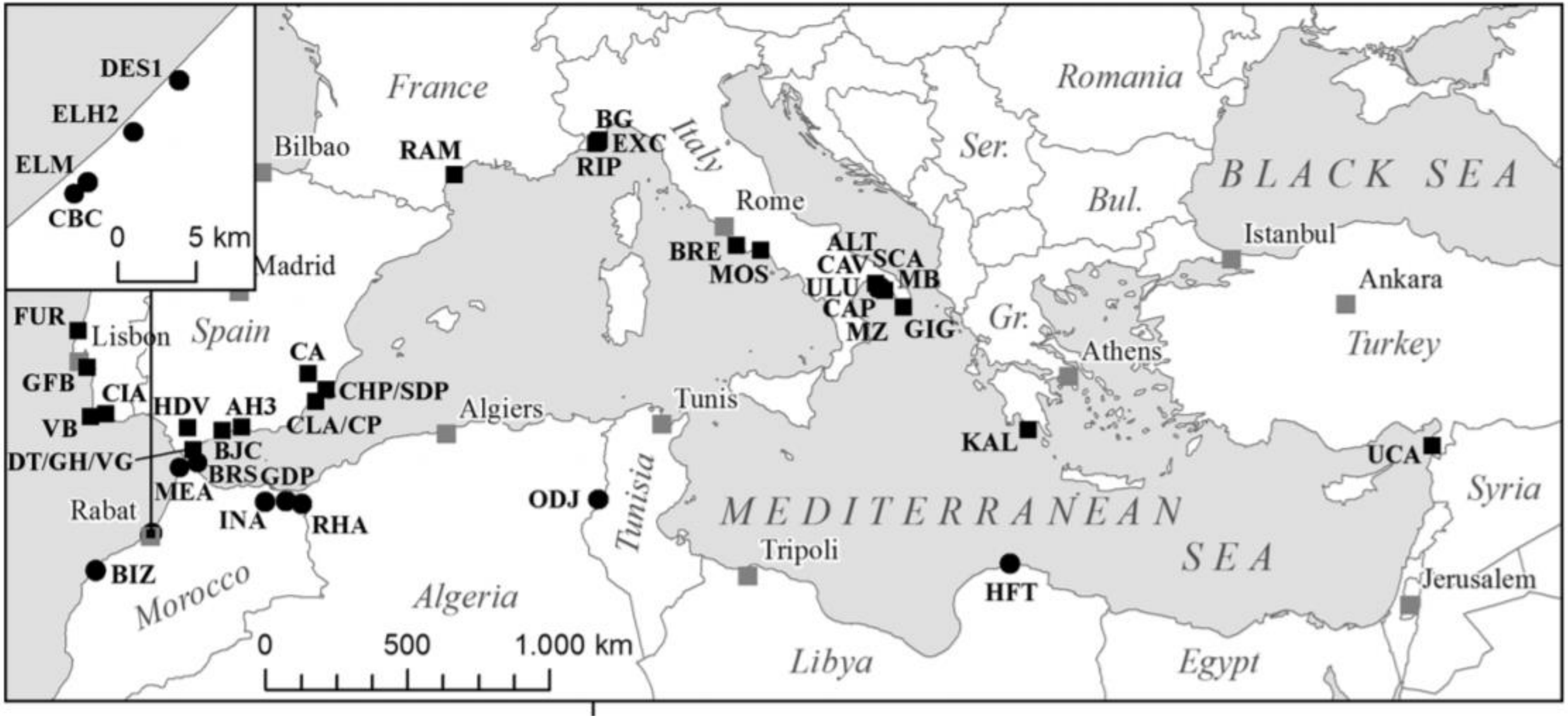
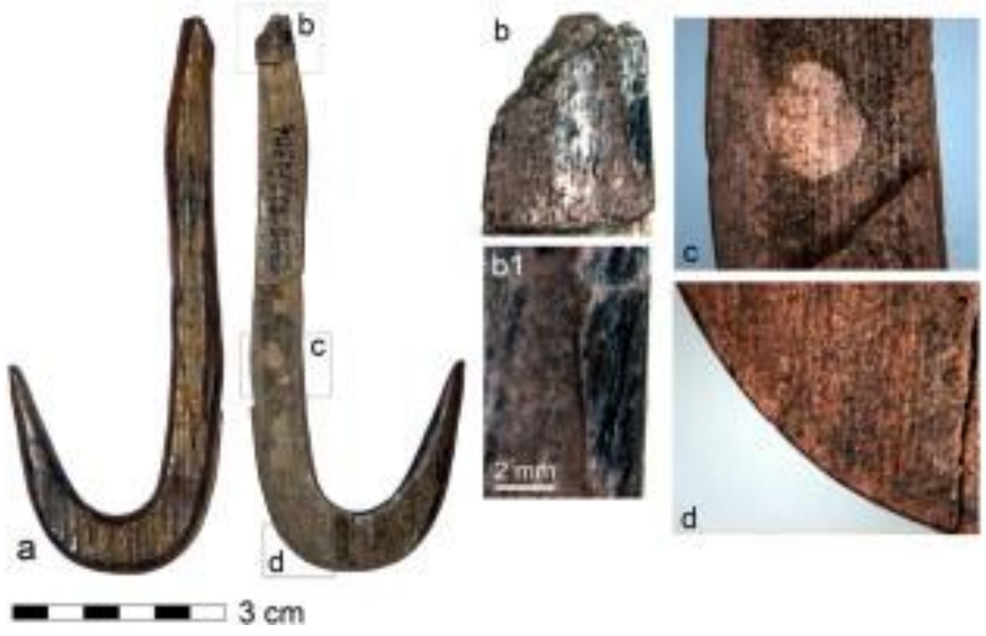


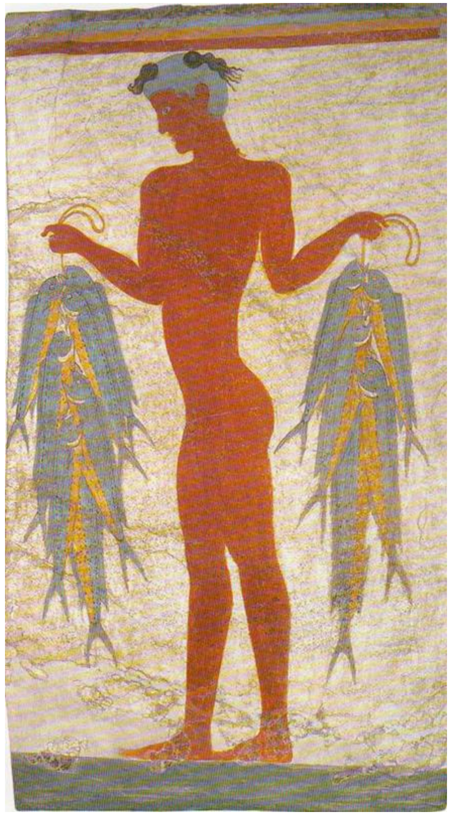
Map depicting the main sites with evidence of coastal adaptations by modern humans in north Africa (circles) and Neanderthals in Europe (rectangles).

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.



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, Greece

Aegean Talismanic seal with crab, ca. 1450 BC

Neanderthals Consumed Crabs, Other Shellfish Over 90,000 Years Ago as Evident on Cave Remains Found in Portugal

Feb 08, 2023

Many of the shells and bones were marked with black burns, which showed they were heated to over 300°C (572°F), indicating they had been roasted for the purpose of eating.

The Figueira Brava site on Portugal's coast was occupied by Neanderthals between 86,000 and 106,000 years ago.
Science

Archaeology Meets Marine Ecology: The Antiquity of Maritime Cultures and Human Impacts on Marine Fisheries and Ecosystems

Jon M. Erlandson[1] and Torben C. Rick[2]

Annu. Rev. Mar. Sci. 2010. 2:231–51

Understanding the antiquity of coastal settlement, marine fishing, and maritime migrations is difficult because global sea levels have risen ∼125 m in the past 20,000 years, drowning ancient shorelines and vast coastal landscapes. Recent efforts to better understand the importance of marine and freshwater ecosystems in human evolution have focused on different approaches and perspectives on the **antiquity of fishing societies, seafaring, and human impacts on marine ecosystems.**

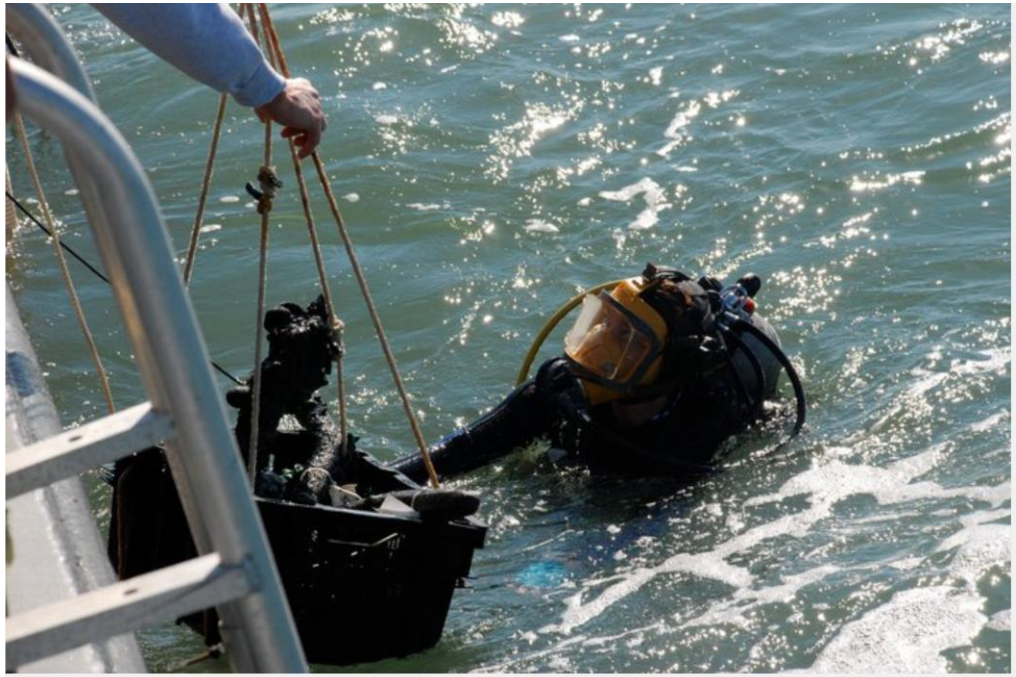
OPENQUATERNARY

Briggs, L. 2020. Ancient DNA Research in Maritime and Underwater Archaeology: Pitfalls, Promise, and Future Directions. *Open Quaternary*, 6: 3, pp. 1–14. DOI: https://doi.org/10.5334/oq.71

REVIEW

Ancient DNA Research in Maritime and Underwater Archaeology: Pitfalls, Promise, and Future Directions

Lisa Briggs



Underwater archaeologist Lisa Briggs recovering artefacts from the Queen Anne's Revenge shipwreck (Photo credit: W. Welsh)

Cytosine deamination involves the addition of an oxygen molecule and bacterial diagenesis will be significantly slowed in an anoxic environment. Moreover the 'salt effect' significantly slowed the process of depurination in high ionic environments

iScience
CellPress OPEN ACCESS

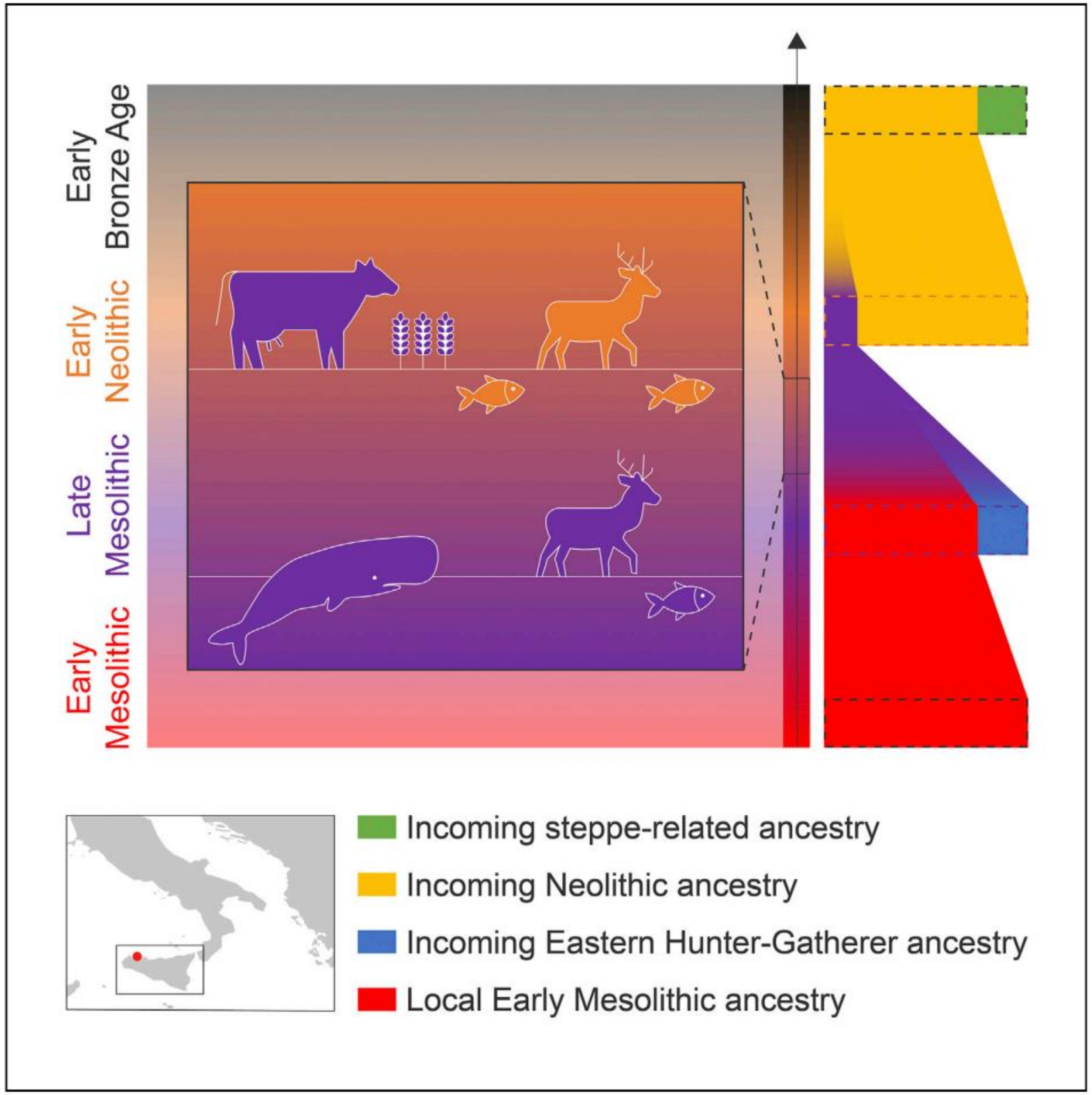
Article

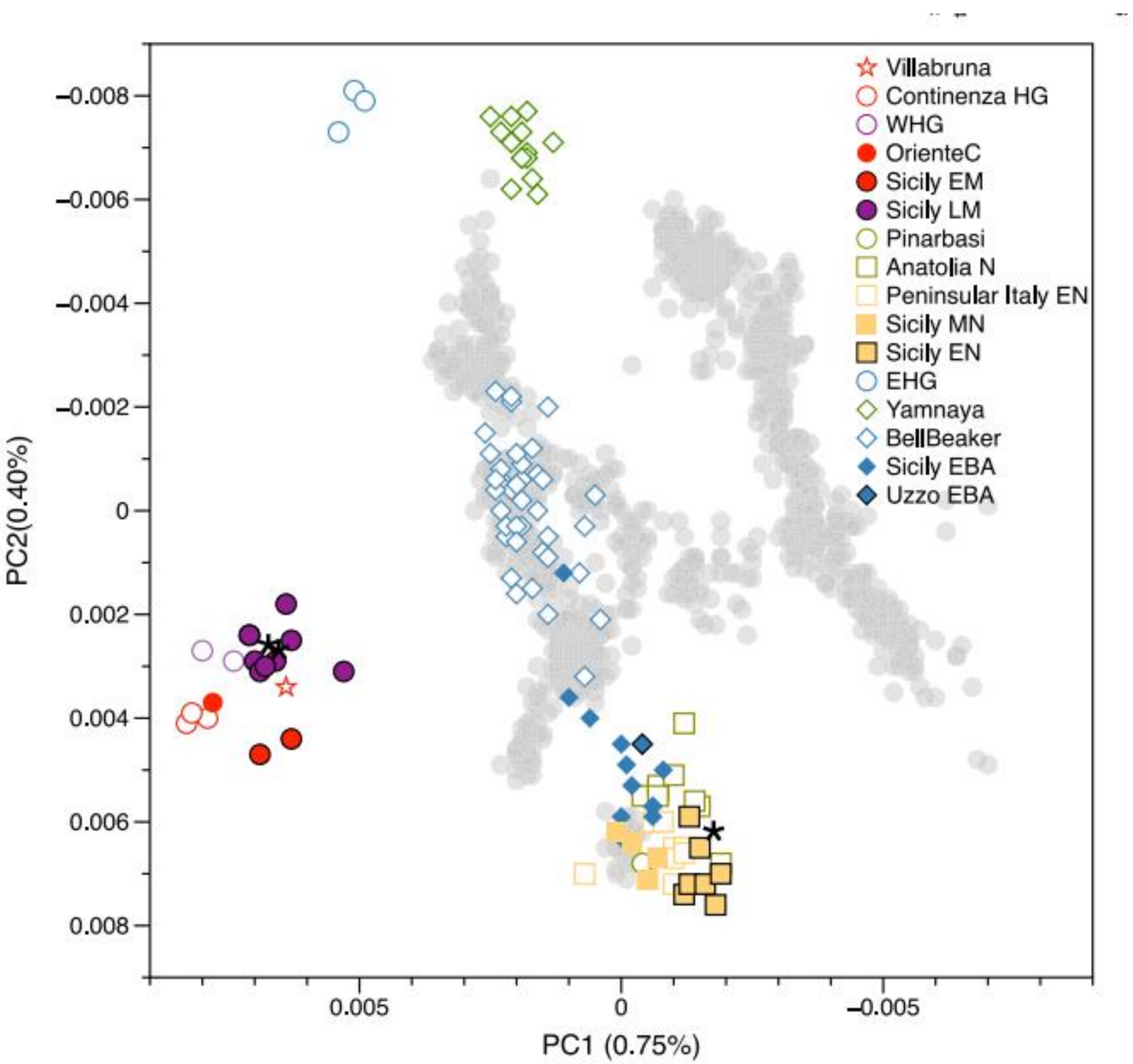
Genomic and dietary discontinuities during the Mesolithic and Neolithic in Sicily

He Yu,[1,19,*] Marieke S. van de Loosdrecht,[1,19] Marcello A. Mannino,[2,3,19,*] Sahra Talamo,[3,4] Adam B. Rohrlach,[1,5] Ainash Childebayeva,[1] Vanessa Villalba-Mouco,[1,6] Franziska Aron,[1] Guido Brandt,[1] Marta Burri,[1] Cäcilia Freund,[1] Rita Radzeviciute,[1] Raphaela Stahl,[1] Antje Wissgott,[1] Helen Fewlass,[3] Antonio Tagliacozzo,[7] Marcello Piperno,[8] Sebastiano Tusa,[9] Carmine Collina,[10] Vittoria Schimmenti,[11] Rosaria Di Salvo,[12] Kay Prüfer,[1,13] Cosimo Posth,[1,14,15] Jean-Jacques Hublin,[3,12] Detlef Gronenborn,[16] Didier Binder,[17] Choongwon Jeong,[1,18] Wolfgang Haak,[1,20] and Johannes Krause[1,20,21,*]

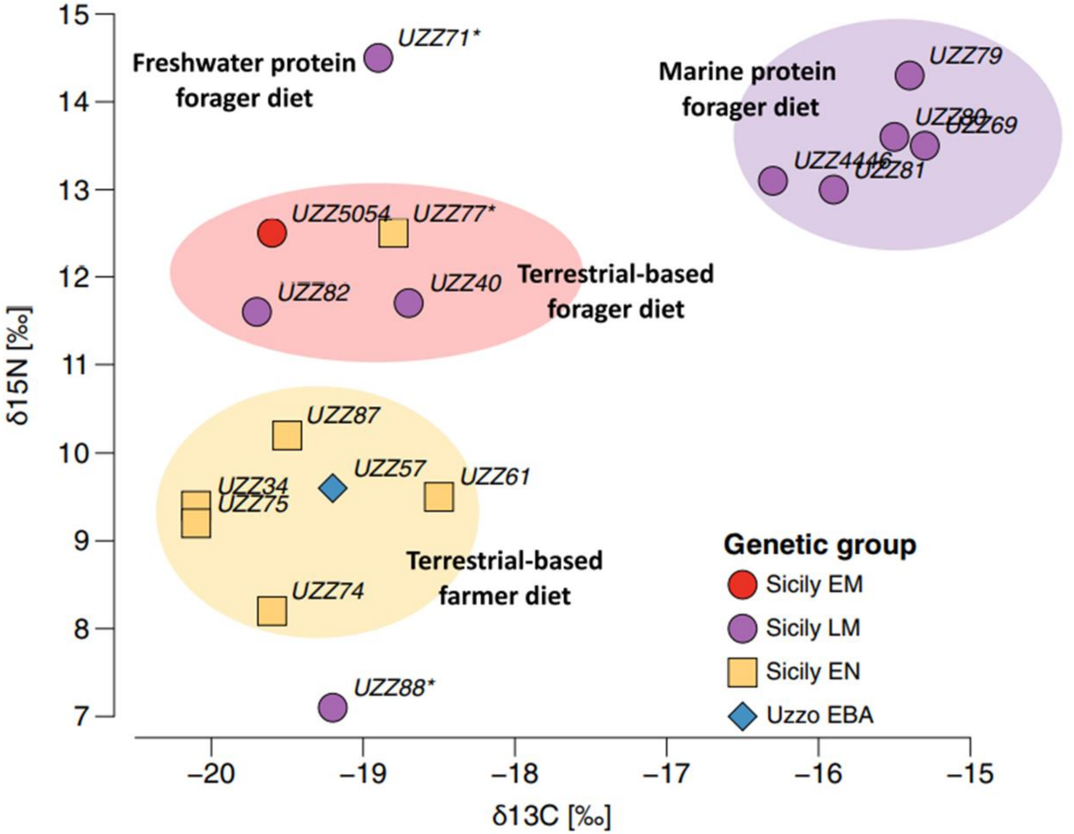
iScience 25, 104244, May 20, 2022

19 prehistoric Sicilians covering the Mesolithic to Bronze Age periods (10,700–4,100 yBP).

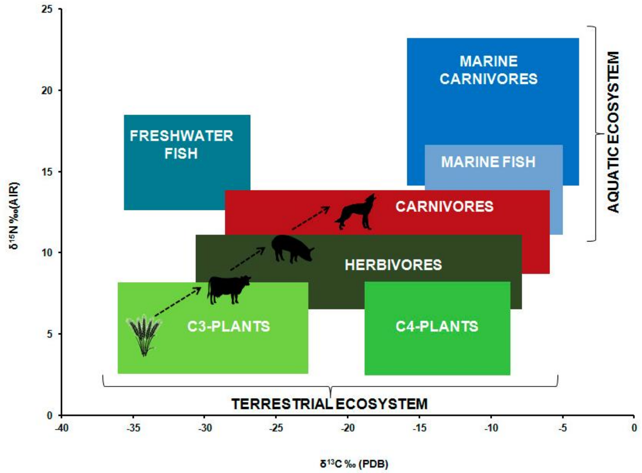




Villabruna
Continenza HG
WHG
OrienteC
Sicily EM
Sicily LM
Pinarbasi
Anatolia N
Peninsular Italy EN
Sicily MN
Sicily EN
EHG
Yamnaya
BellBeaker
Sicily EBA
Uzzo EBA
PC2(0.40%)
PC1 (0.75%)



Freshwater protein forager diet
Marine protein forager diet
Terrestrial-based forager diet
Terrestrial-based farmer diet
UZZ71*
UZZ79
UZZ80
UZZ69
UZZ4446
UZZ81
UZZ5054
UZZ77*
UZZ82
UZZ40
UZZ87
UZZ57
UZZ61
UZZ34
UZZ75
UZZ74
UZZ88*
Genetic group
Sicily EM
Sicily LM
Sicily EN
Uzzo EBA
δ15N [‰]
δ13C [‰]



MARINE CARNIVORES
FRESHWATER FISH
MARINE FISH
CARNIVORES
HERBIVORES
C3-PLANTS
C4-PLANTS
AQUATIC ECOSYSTEM
TERRESTRIAL ECOSYSTEM

Looking at the origin of fishing in Mediterranean prehistory

NEWS RELEASE 21-FEB-2023

Mediterranean hunter-gatherers relied on marine resources more than previously thought

Peer-Reviewed Publication

UNIVERSITY OF YORK

Mesolithic cemeteries in the Mediterranean, at El Collado, Valencia

The extent to which humans relied on coastal resources in the past, is key to assessing human health.

Stable isotope analyses of amino acids reveal the importance of aquatic resources to Mediterranean coastal hunter–gatherers

Maria Fontanals-Coll[1], Silvia Soncin[1,2], Helen M. Talbot[1], Matthew von Tersch[1], Juan F. Gibaja[3], André C. Colonese[4] and Oliver E. Craig[1]

PROCEEDINGS B *Proc. R. Soc. B* **290**: 20221330.

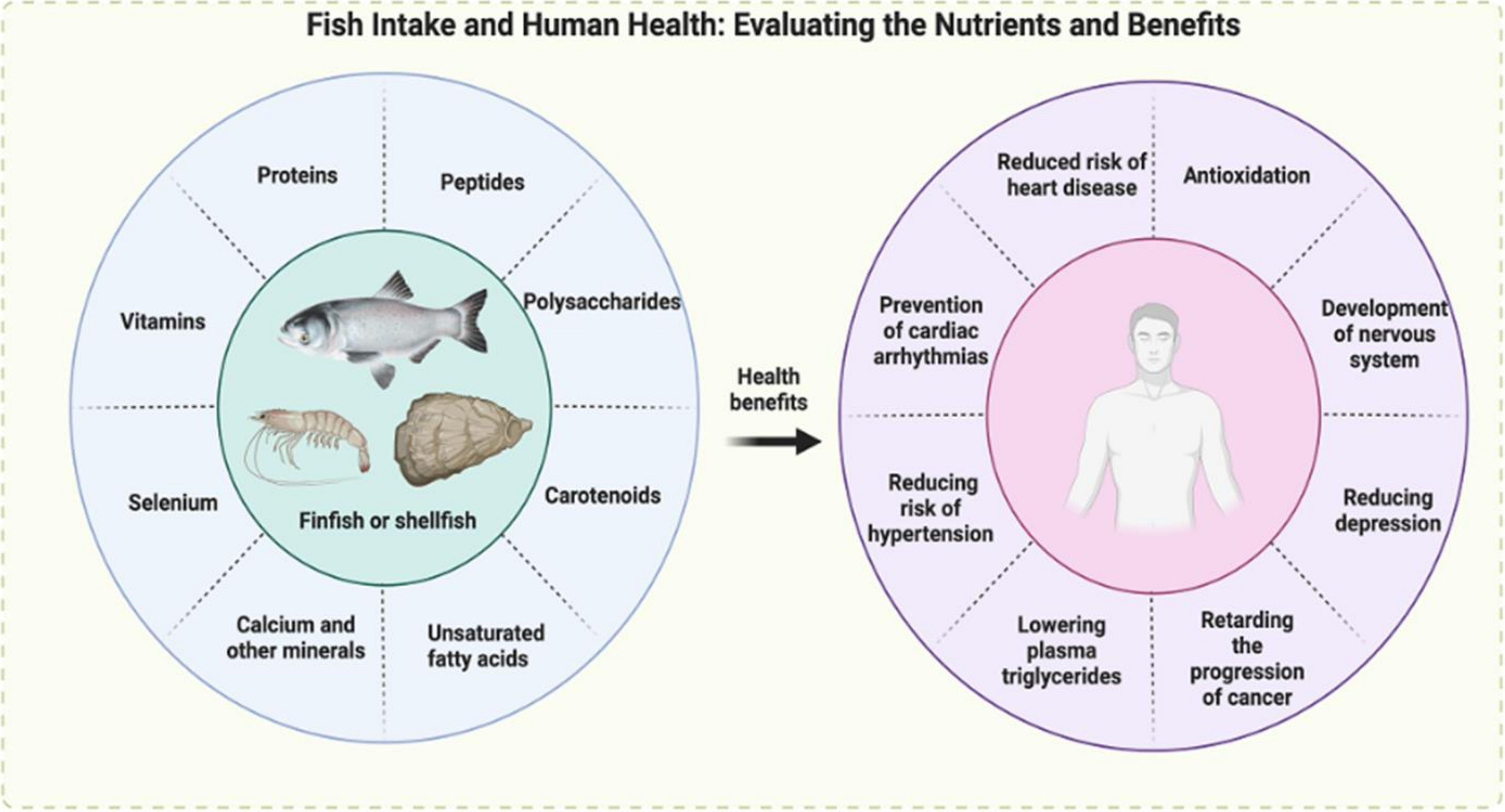
Estimation of trophic position using compound-specific isotope analysis of amino acids (CSIA-AA)

New research has revealed humans living on the Mediterranean coast 9,500 years ago may have relied more heavily on a fish diet than previously thought.

High-resolution biomolecular techniques, like compound-specific isotope analysis of individual collagen amino acids (CSIA-AA) which allows greater accuracy in discriminating between land animals and marine life.

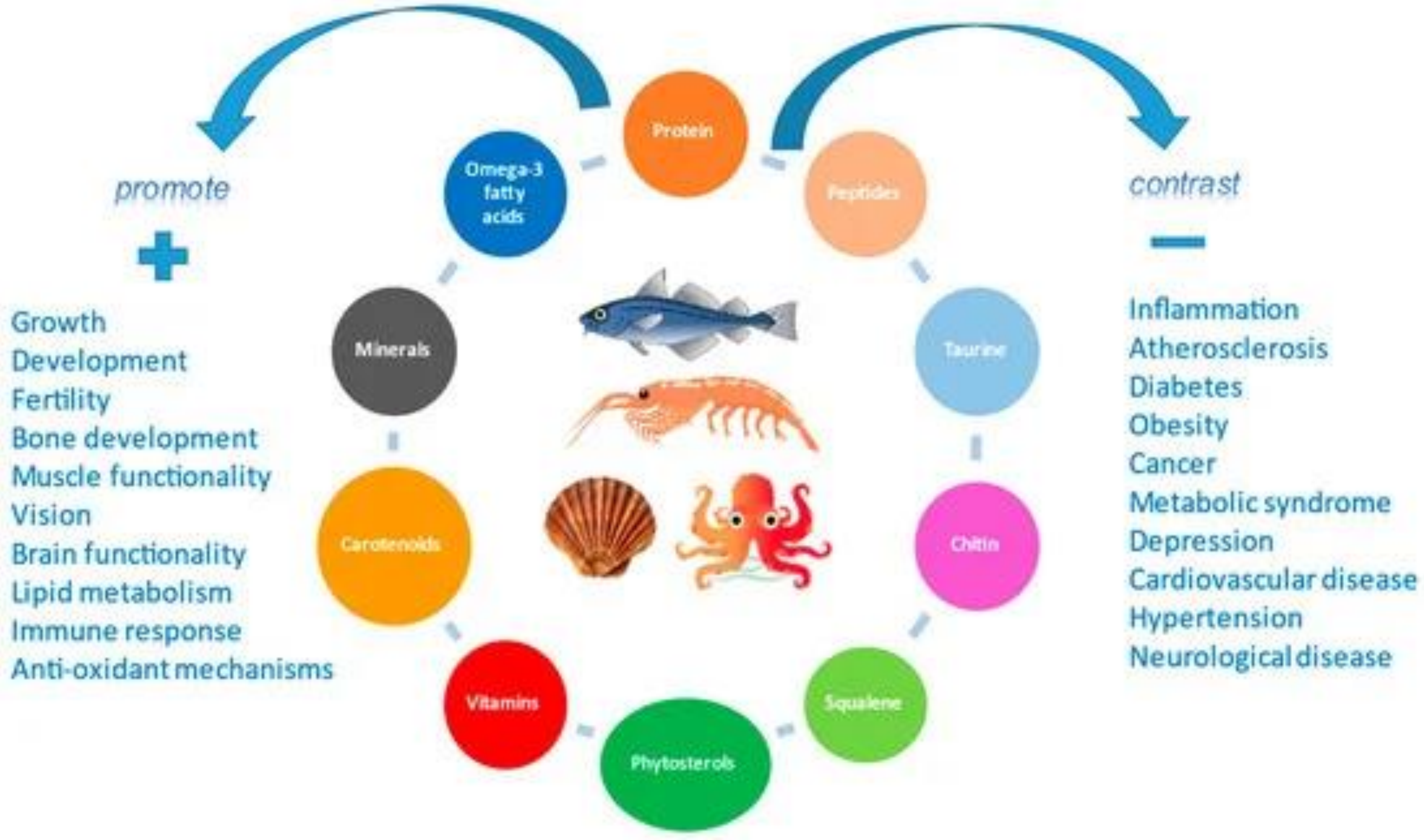
Special Issue "Fish Intake and Human Health: Evaluating the Nutrients and Benefits"

- **Fish (finfish or shellfish) are essential** to a **healthy diet**.
- Fish are the primary sources of healthy long-chain omega-3 fats and are rich in other nutrients such as vitamin D and selenium, high in protein, and low in saturated fat.
- There is strong evidence that eating fish or taking fish oil has a positive impact on the heart and blood vessels.



Fish Intake and Human Health: Evaluating the Nutrients and Benefits
Proteins
Peptides
Polysaccharides
Vitamins
Selenium
Carotenoids
Calcium and other minerals
Unsaturated fatty acids
Finfish or shellfish
Health benefits
Reduced risk of heart disease
Antioxidation
Prevention of cardiac arrhythmias
Development of nervous system
Reducing risk of hypertension
Reducing depression
Lowering plasma triglycerides
Retarding the progression of cancer

HEALTH EFFECTS



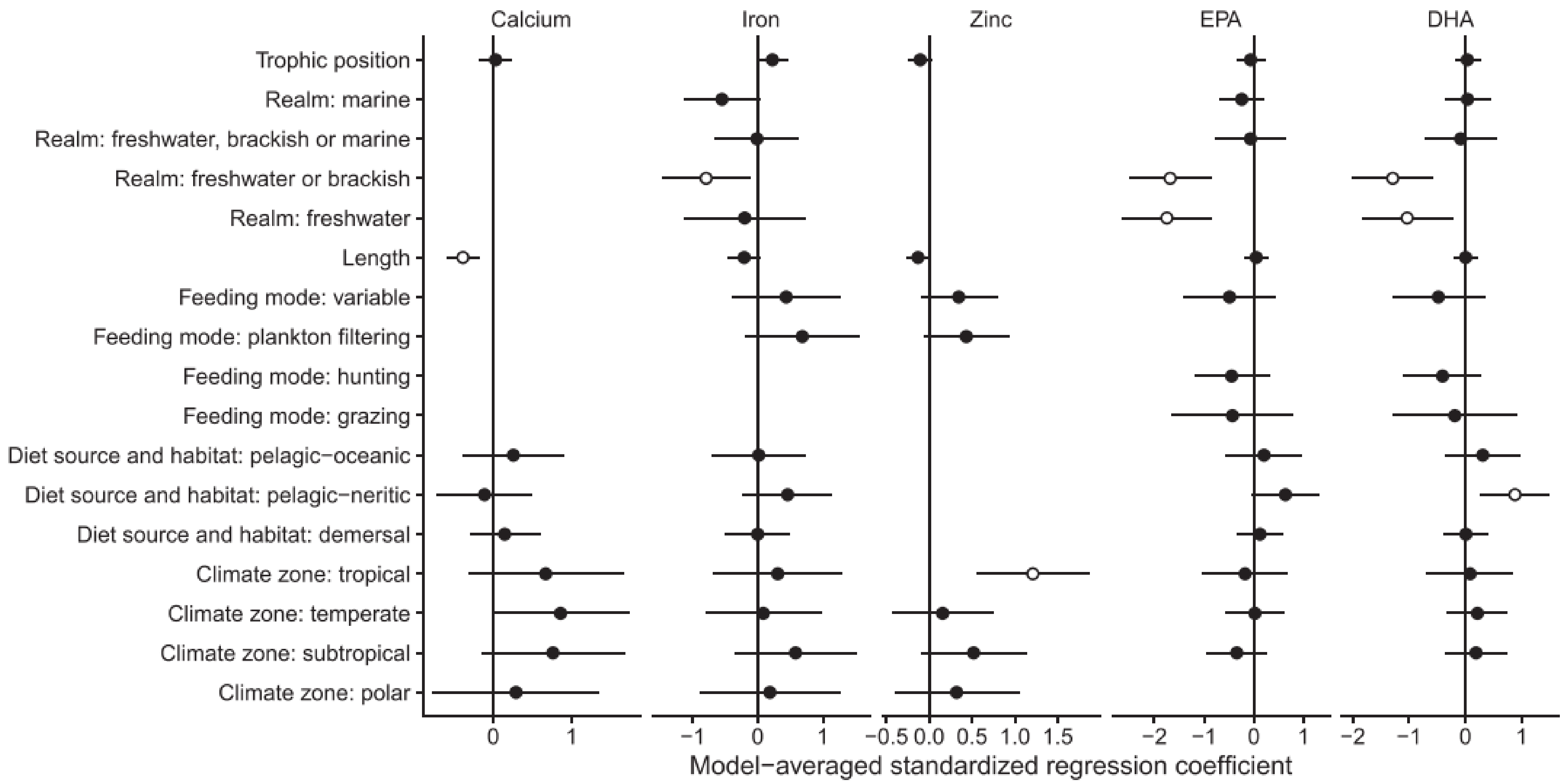
Aquatic biodiversity enhances multiple nutritional benefits to humans

Joey R. Bernhardt[a,b,1] and Mary I. O'Connor[a] PNAS 2021 Vol. 118 No. 15 e1917487118

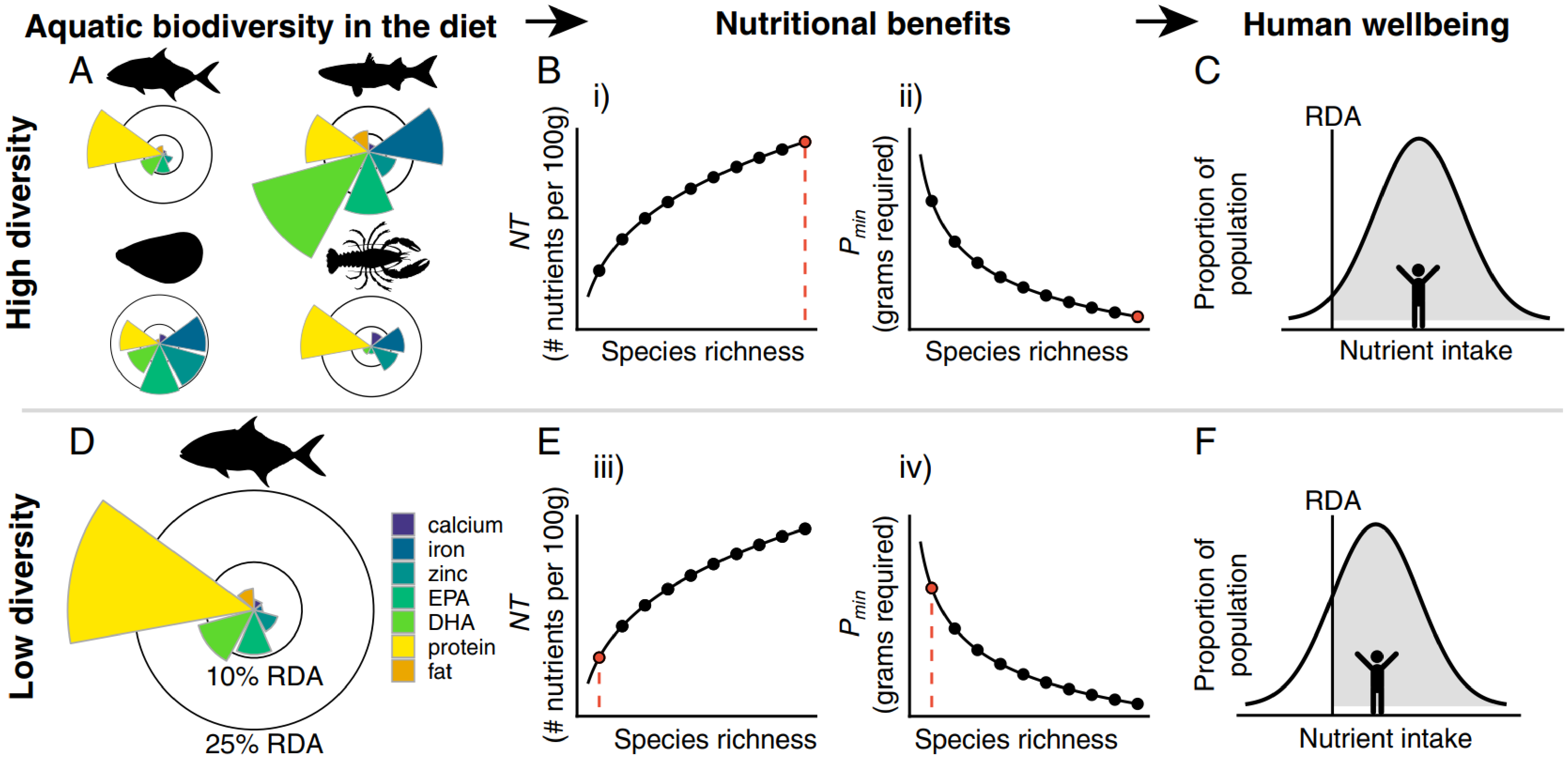
While the role of seafood is well recognized as an important source of protein in the human diet, the role of **seafood biodiversity as an important aspect of the provision of essential micronutrients** has been overlooked.

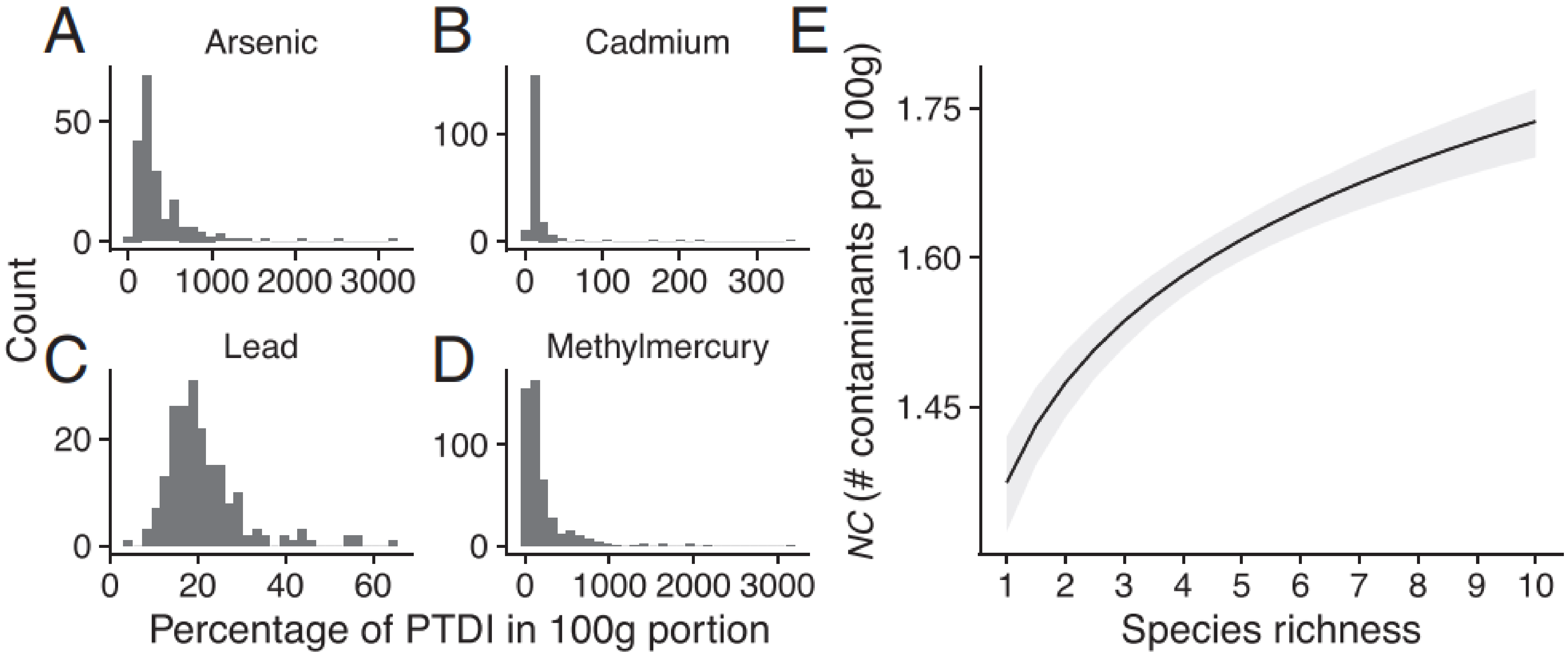
Seafood species richness improves the efficiency with which human diets can meet RDA targets by reducing the minimum portion size required

Links between the complexity of aquatic ecosystems and their capacity to produce nutritional benefits



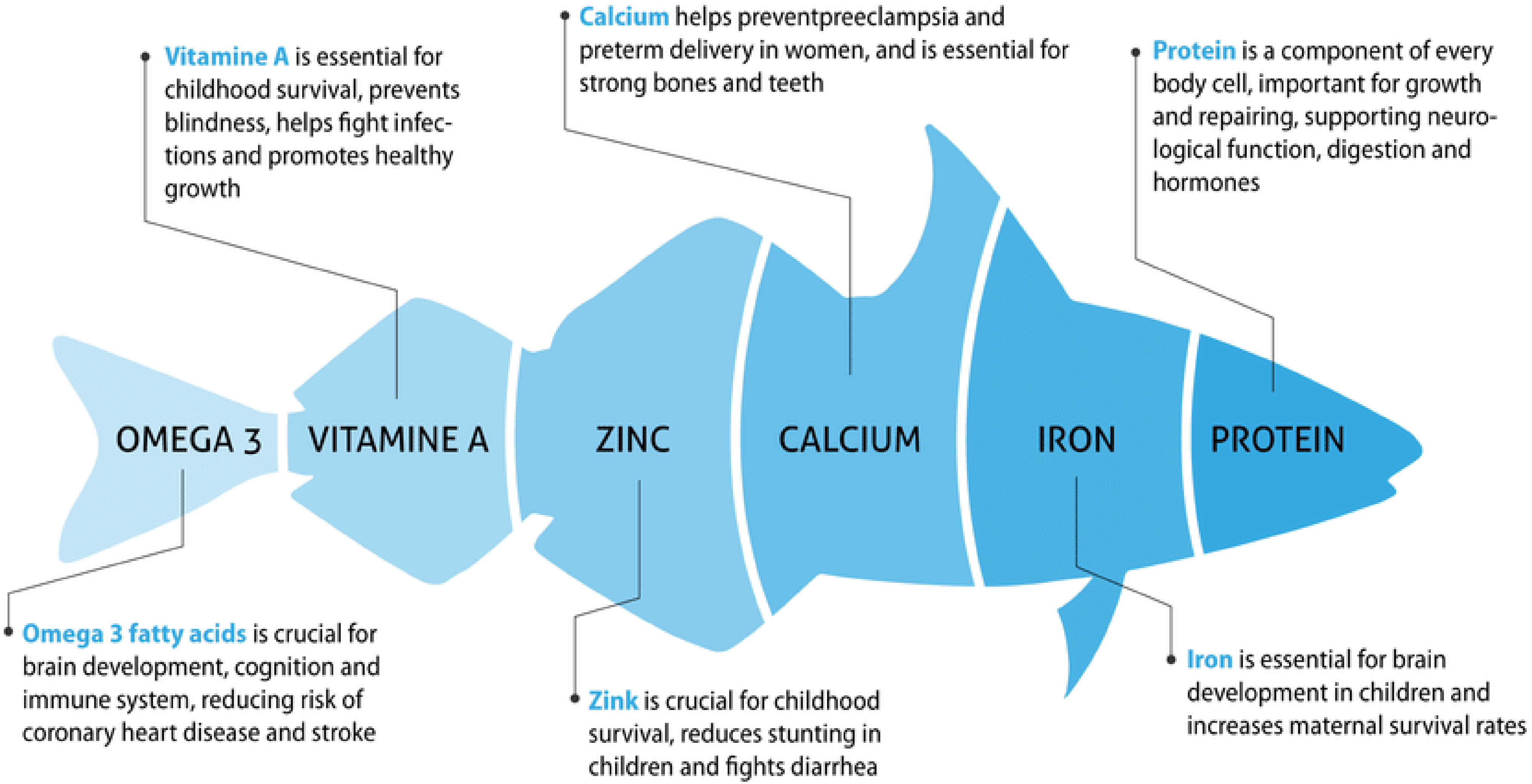
Nutrient concentrations in finfish muscle tissue vary with ecological traits in ways that differ among the essential trace elements (calcium, iron, zinc) and the essential fatty acids (EPA and DHA).


Aquatic biodiversity in the diet
Nutritional benefits
Human wellbeing
A
B
C
i)
ii)
High diversity
NT (# nutrients per 100g)
Species richness
Pmin (grams required)
Species richness
RDA
Proportion of population
Nutrient intake
D
E
F
iii)
iv)
Low diversity
calcium
iron
zinc
EPA
DHA
protein
fat
10% RDA
25% RDA
NT (# nutrients per 100g)
Species richness
Pmin (grams required)
Species richness
RDA
Proportion of population
Nutrient intake

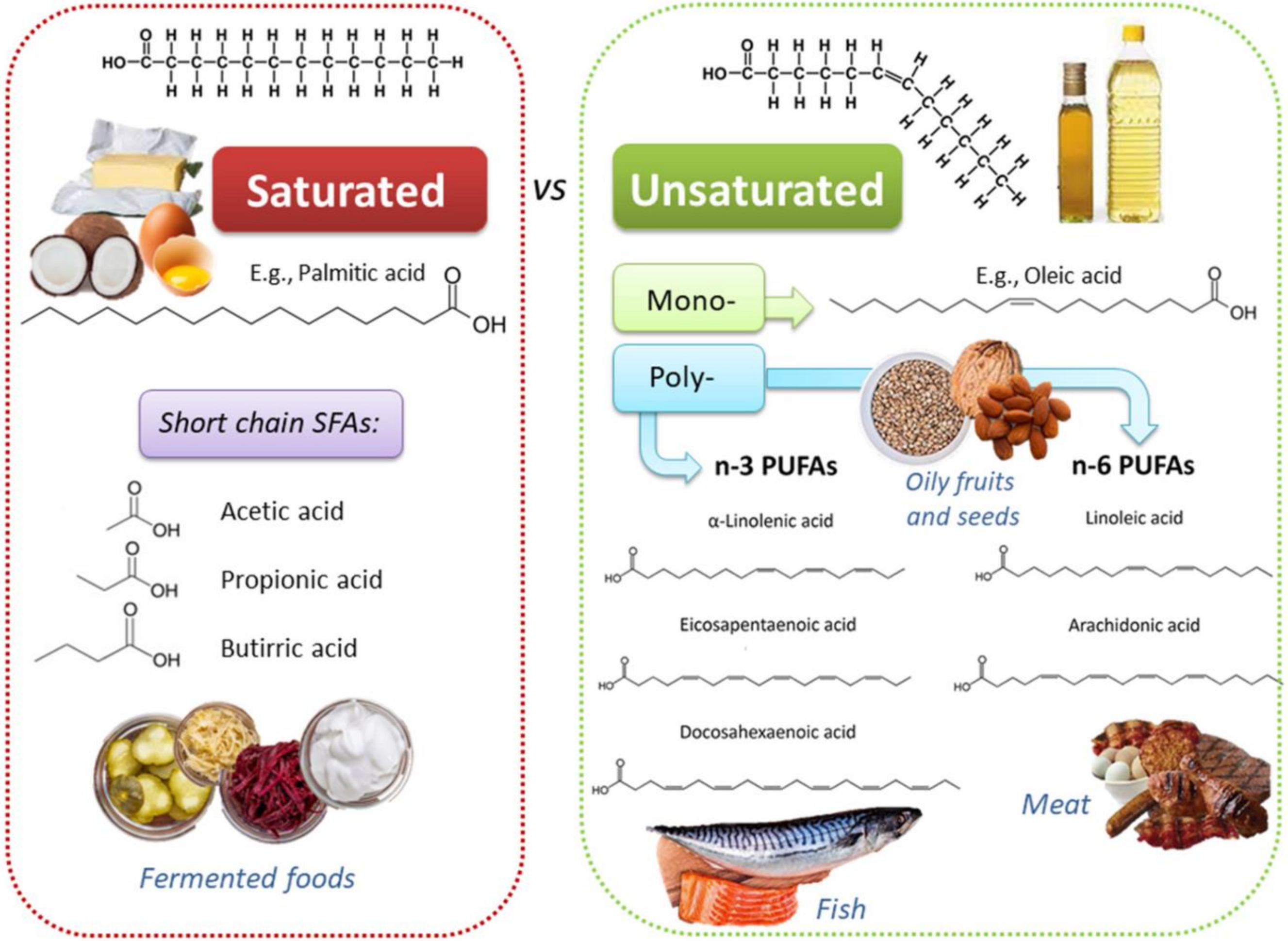


Frequency histograms of concentration of arsenic (A), cadmium (B), lead (C), and methylmercury (D) in edible muscle tissues of North American aquatic species relative to PTDI. (E) **Increasing seafood species richness increases the number of contaminants which exceed the upper tolerable limit (PTDI) in a 100 g portion (NC).**

Fish Intake, Contaminants and Human Health
Evaluating the Risks and the Benefits



Toxics: some seafood can accumulate heavy metals, dioxine, PCB, ciguatoxin and antibiotic residuals.



antioxidants MDPI

Review

Nutrigenomics of Dietary Lipids

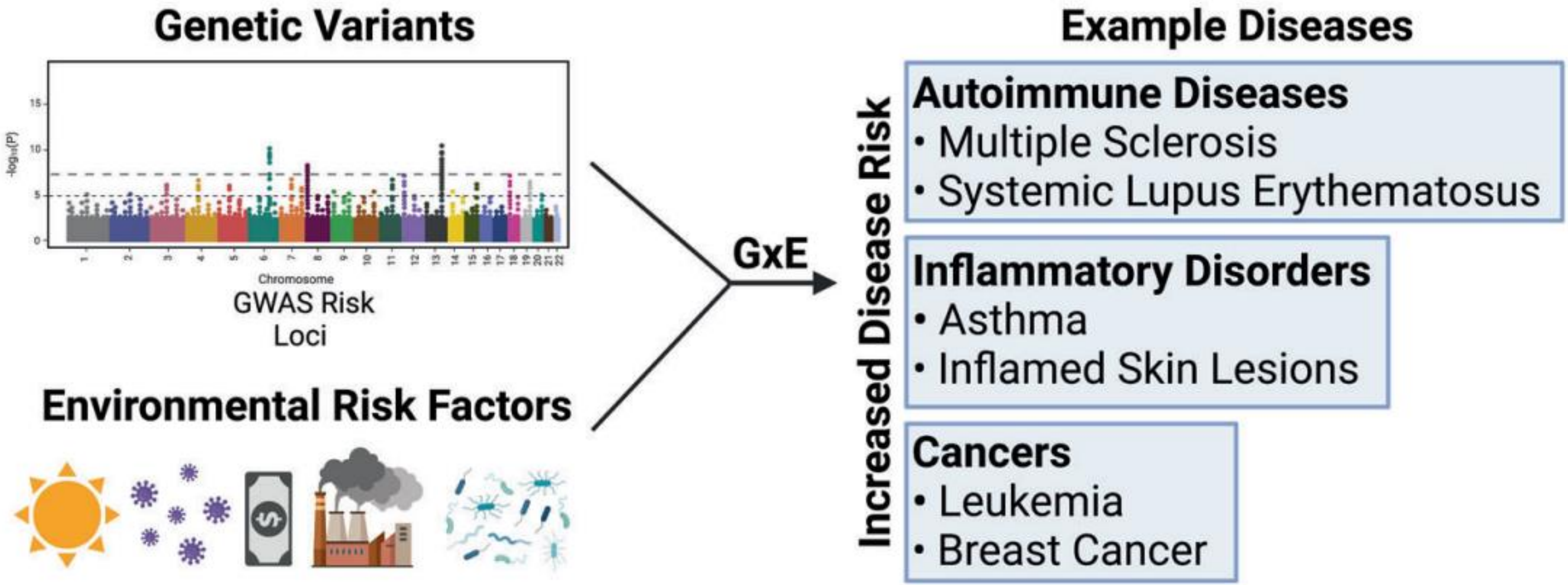
Laura Bordoni [1], Irene Petracci [2], Fanrui Zhao [2,3], Weihong Min [3], Elisa Pierella [4], Taís Silveira Assmann [5], J Alfredo Martinez [6,†] and Rosita Gabbianelli [1,*,†]

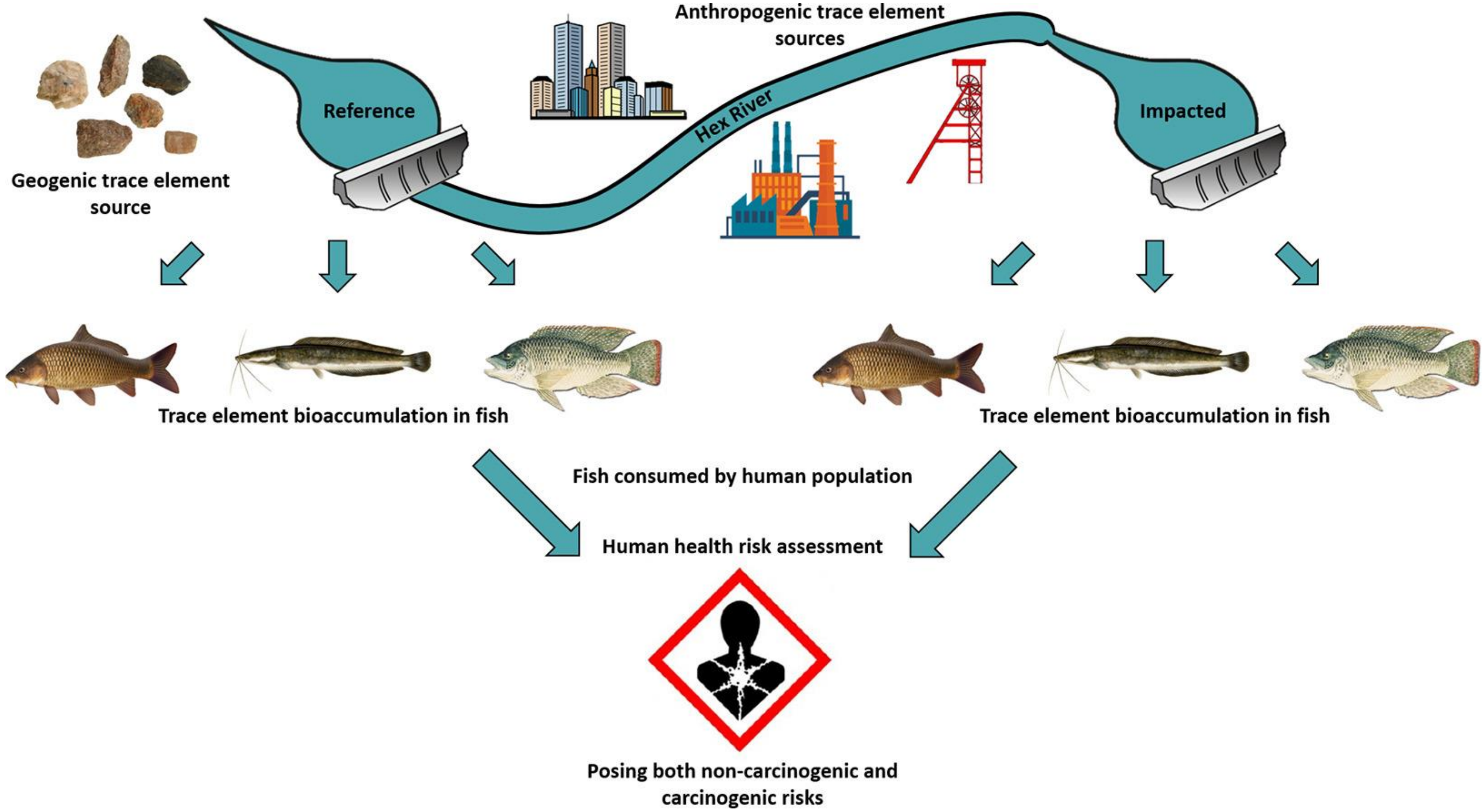
Antioxidants **2021**, *10*, 994. https://doi.org/10.3390/antiox10070994

Food has been studied not only from a chemical prospective, but also for the capacity of metabolites produced by food oxidation to modulate gene expression, directly (nutrigenomics) or by epigenetics remodeling (nutriepigenomics).

However, **inter-individual differences (i.e., the genetic variability)** **and environmental exposures** (i.e., physical activity, drug, food pesticide residues, etc.) contribute to produce a lot of effects

Gene × environment (G × E) interactions involve synergy between environmental risk factors and genetic variants.





Among the main seafood contaminants there are organochlorine pesticides, organotin compounds, phthalates, brominated flame retardants, polyflourinated compounds, polycyclic aromatic hydrocarbons (PAH), dioxins, dioxin-like PCBs and non-dioxin-like PCBs, heavy metals (mercury, cadmium, lead) and arsenic

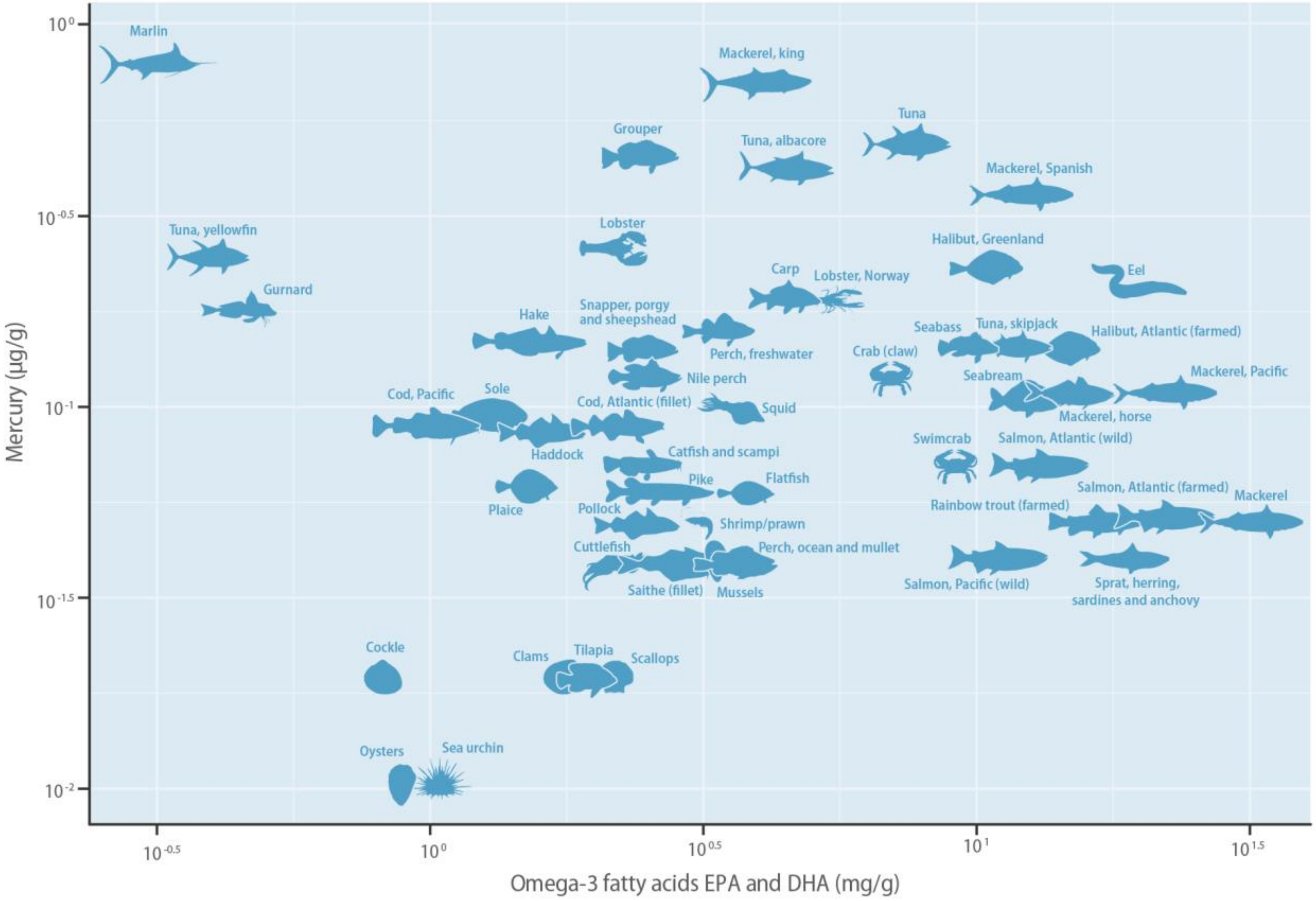
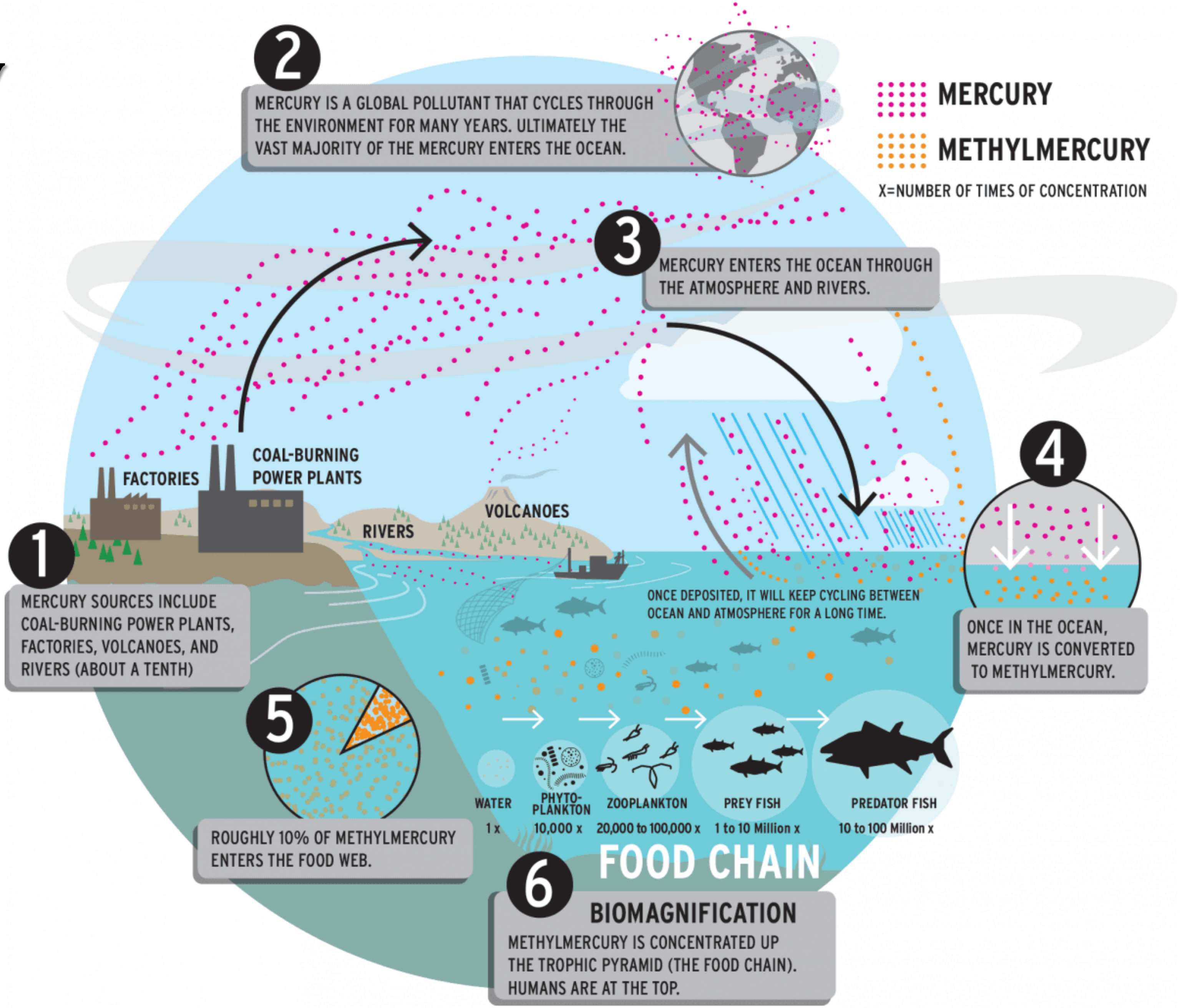


Fig 7. Illustration of omega-3 fatty acids and Mercury (Hg) in various seafood (From [68])

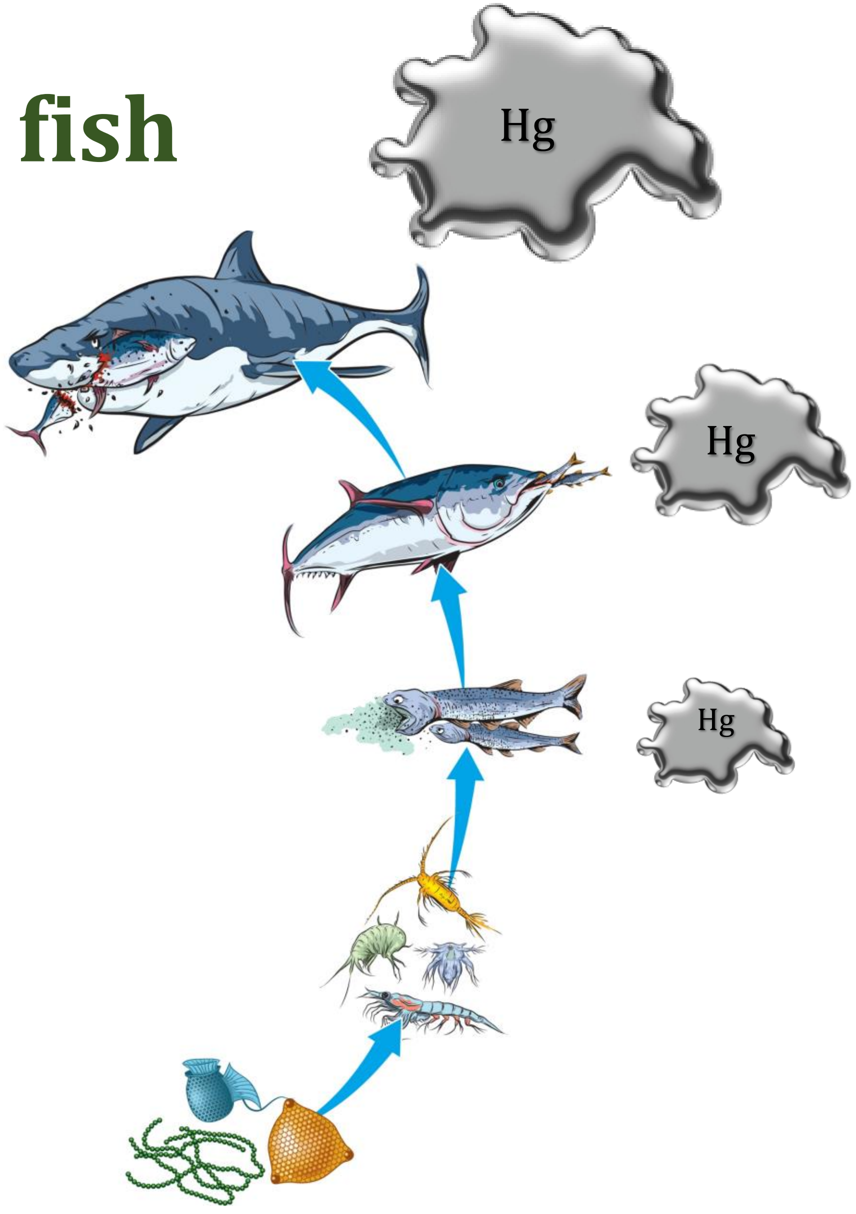
Global mercury (Hg) cicle



FishMed-PhD

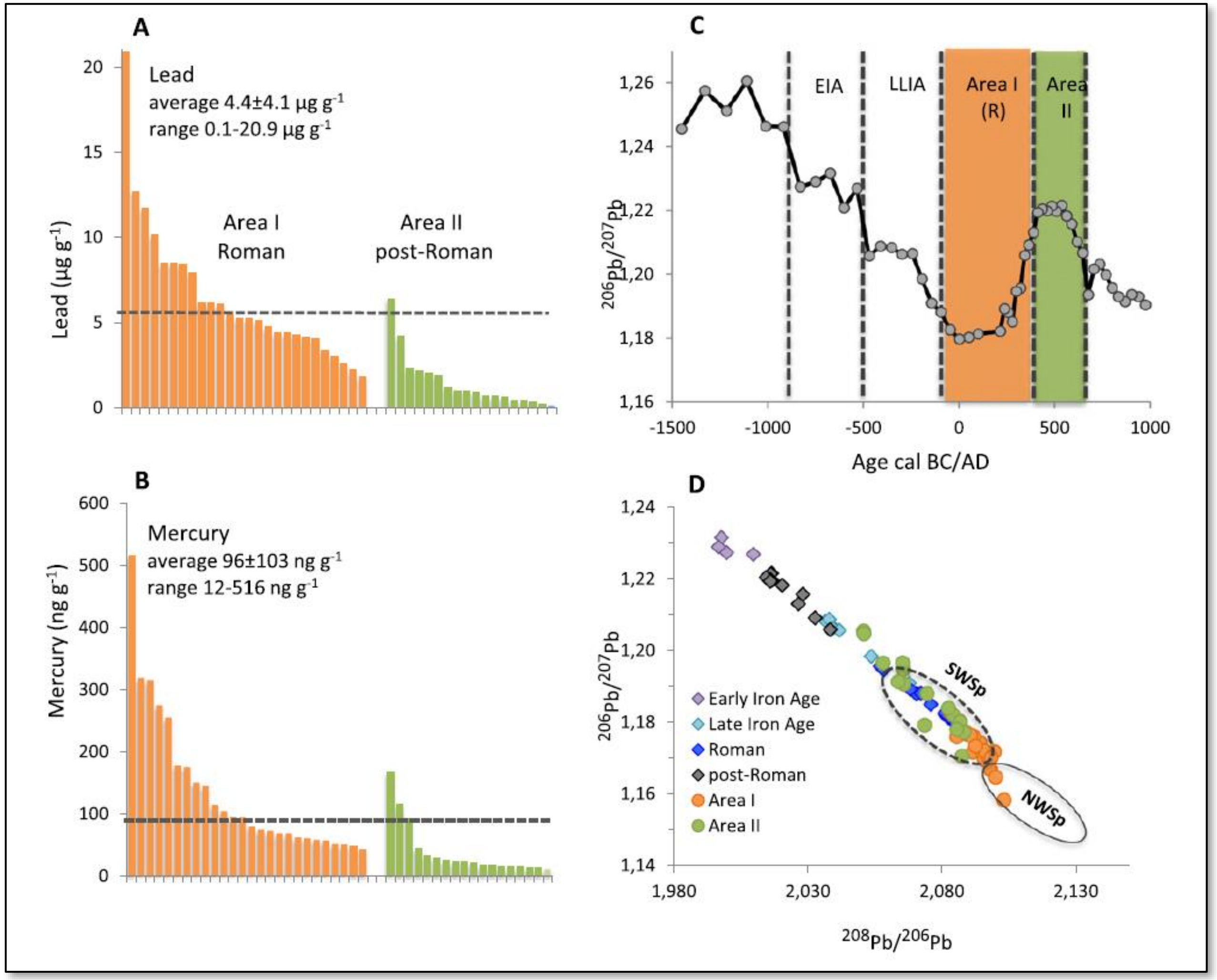
Mercury concentration in fish increases with:

- Trophic level
- Size
- Age
- Demersal habitat



FishMed-PhD

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



Skeletons are an archive reflecting contaminant exposure.

Lanzada, NWSpain. Roman inhabitants of this settlement incorporated two times more mercury and lead into their bones than post-Romans inhabiting the same site, independent of sex or age.

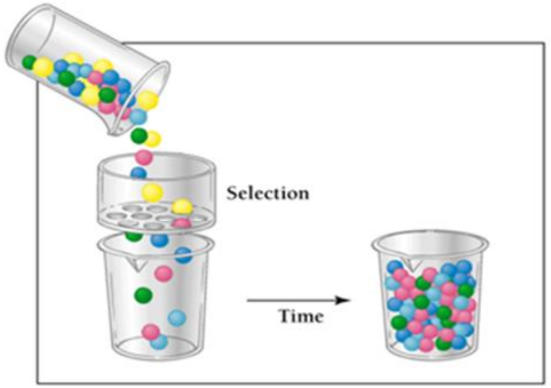
SIGNALS OF ADAPTATION

- The **genetic bases of adaptation are complex** and characterized by successive and contradictory selective forces acting on the same genes through changing conditions.
- the general approach to prove adaptive explanations: identify a **geographically differentiated heritable trait in indigenous populations.**

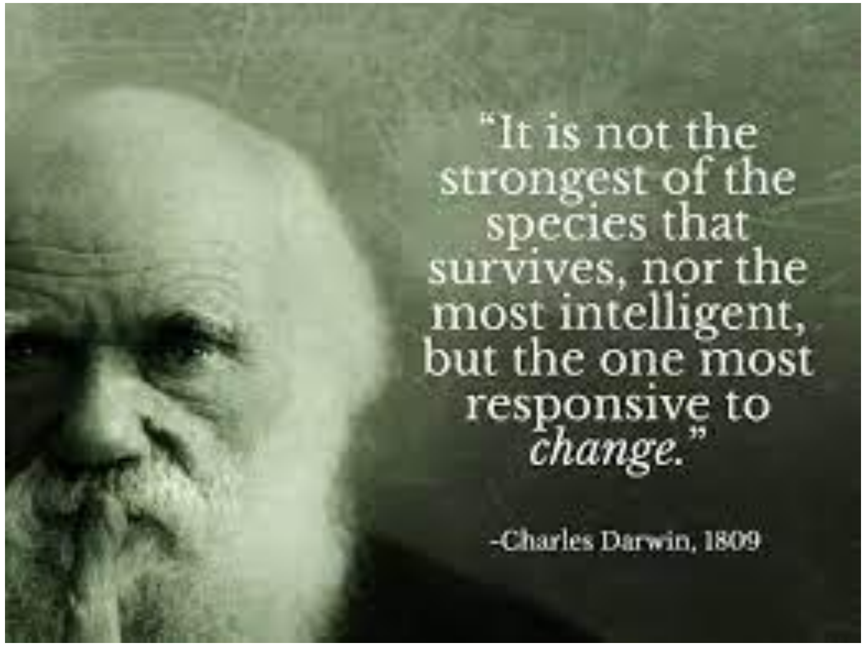
FishMed-PhD

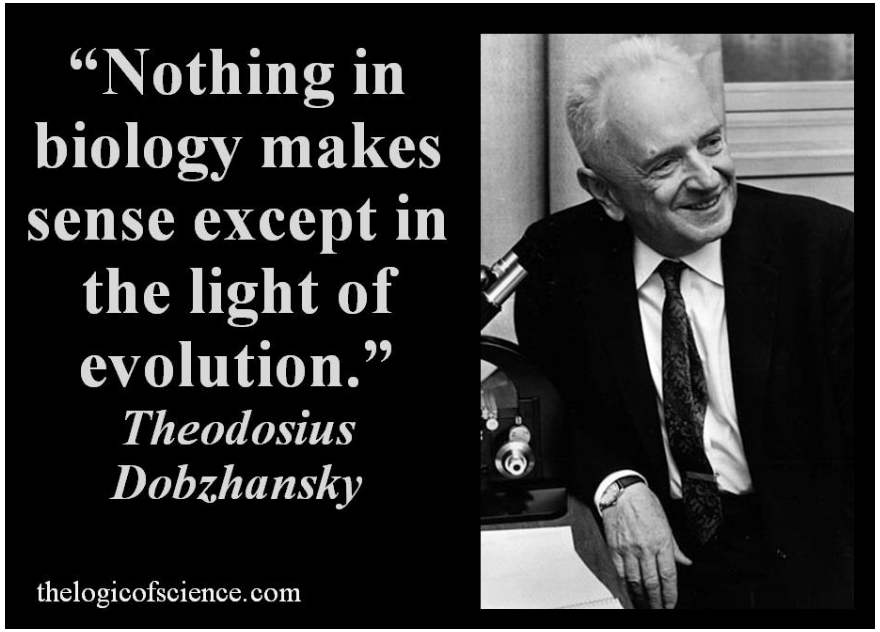
Shaping diversity:

Selection



Differential reproduction of genotypes in succeeding generations



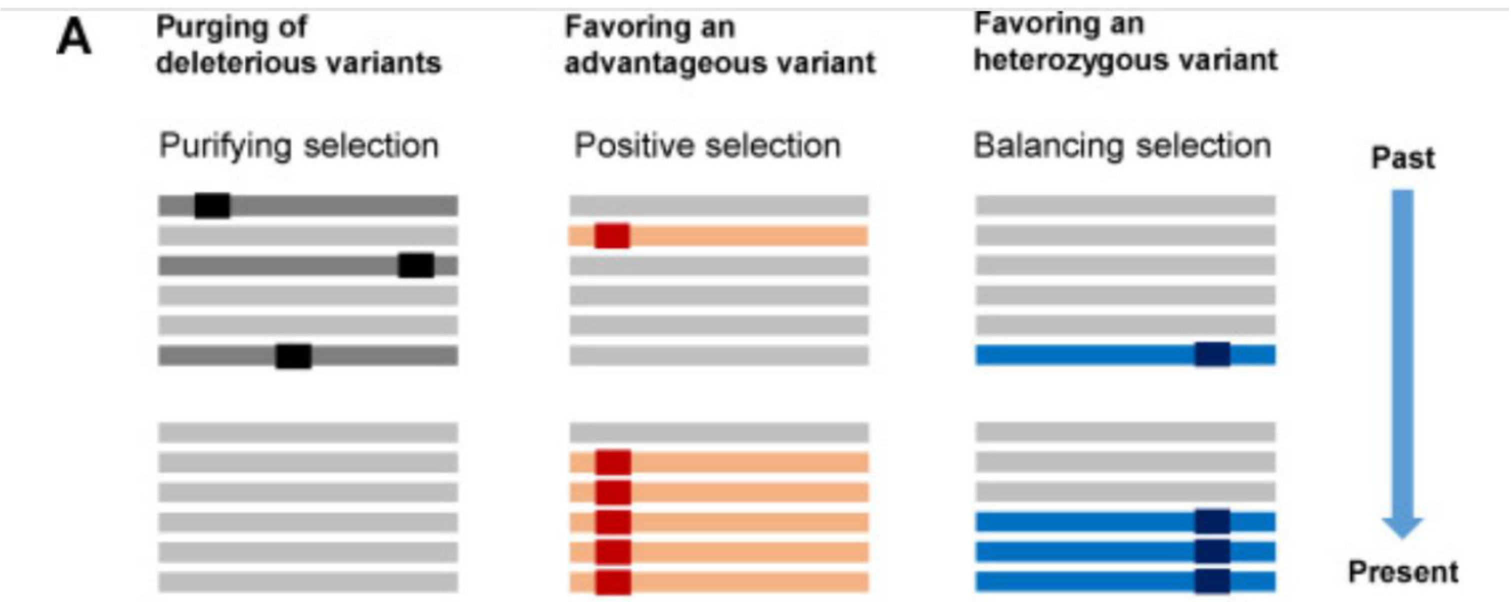


Aspects of selection signatures depend on type, age and strength of selection events.

Natural selection acts in **at least three modes**:

- **positive,**
- **purifying** (also called stabilizing or negative, eliminating a damaging allele) and
- **balancing selection** (including heterozygote advantage and frequency-dependent selection).

Each of these selection modes is a response to the external pressure, and each **operates to change allele frequencies**; yet, each leaves a specific mark on genome variation and architecture.



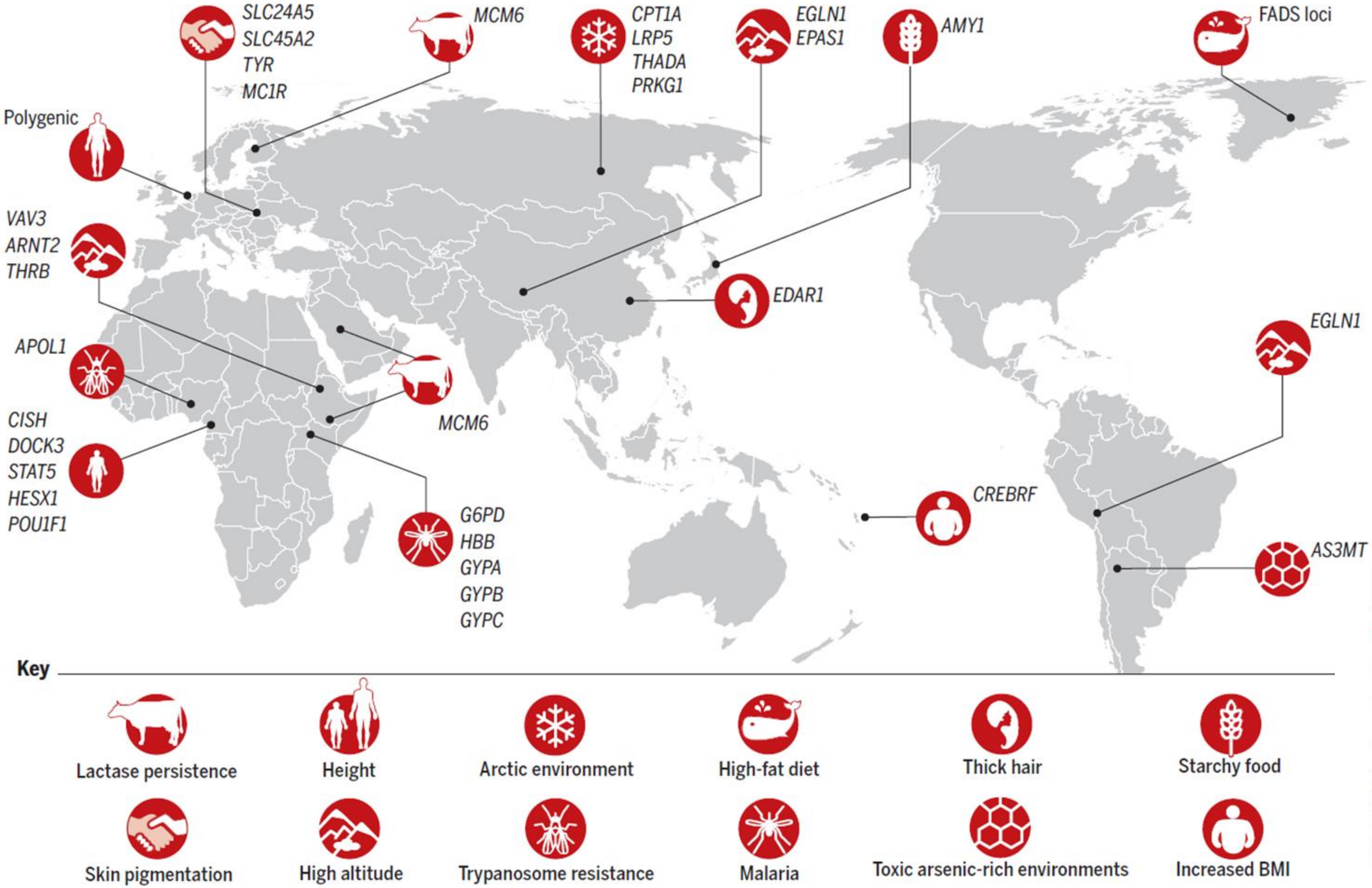


Fig. 1. Examples of human local adaptations, each labeled by the phenotype and/or selection pressure, and the genetic loci under selection. [Adapted from (*13*)]

REVIEW

Going global by adapting local: A review of recent human adaptation

Shaohua Fan,[1*] Matthew E. B. Hansen,[1*] Yancy Lo,[1,2*] Sarah A. Tishkoff[1,3†]

The spread of modern humans across the globe has led to genetic adaptations to diverse local environments. Recent developments in genomic technologies, statistical analyses, and expanded sampled populations have led to improved identification and fine-mapping of genetic variants associated with adaptations to regional living conditions and dietary practices. Ongoing efforts in sequencing genomes of indigenous populations, accompanied by the growing availability of "-omics" and ancient DNA data, promises a new era in our understanding of recent human evolution and the origins of variable traits and disease risks.

FADS CLUSTER

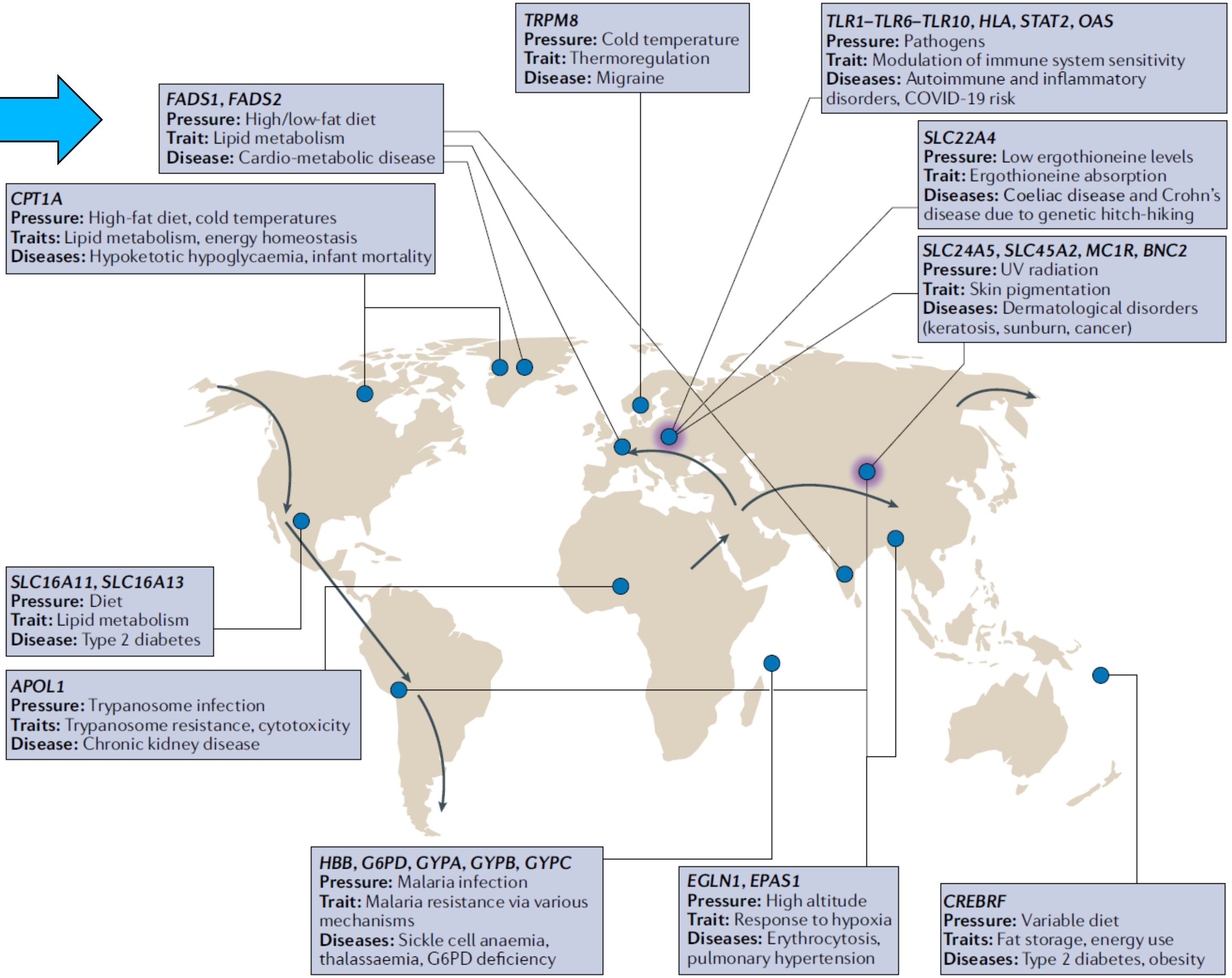
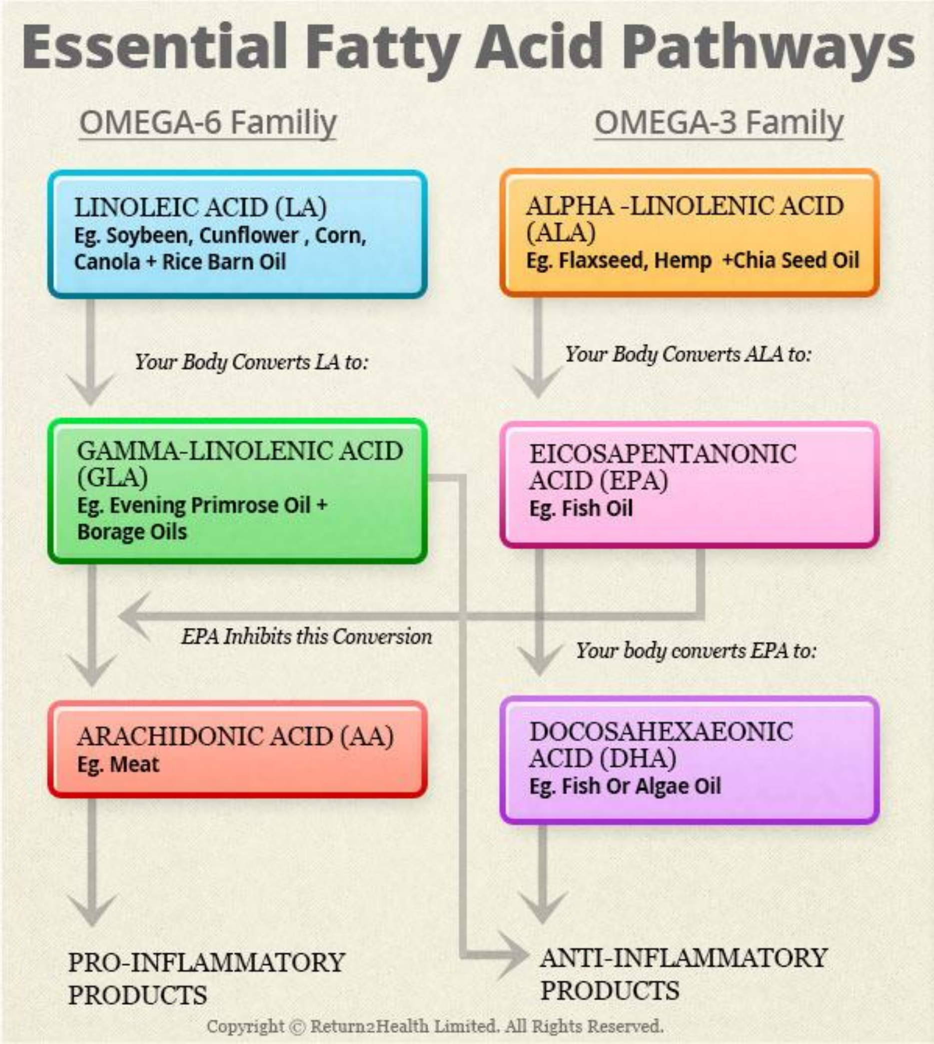


Fig. 2 | **Recent adaptation has produced evolutionary trade-offs that lead to disease in some environments.** Representative genes that have experienced local adaptive evolution over the past 100,000 years as humans moved across the globe. We focus on adaptations that also produced the potential for disease due to trade-offs or mismatches with modern environments. For each, we list the evolutionary pressure, the trait(s) influenced and the associated disease(s). The approximate regions where the adaptations occurred are indicated by blue circles. Arrows represent the expansion of human populations, and purple shading represents introgression events with archaic hominins. Supplementary Table S1 presents more details and references. COVID-19, coronavirus disease 2019; G6PD, glucose-6-phosphate dehydrogenase; UV, ultraviolet.

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

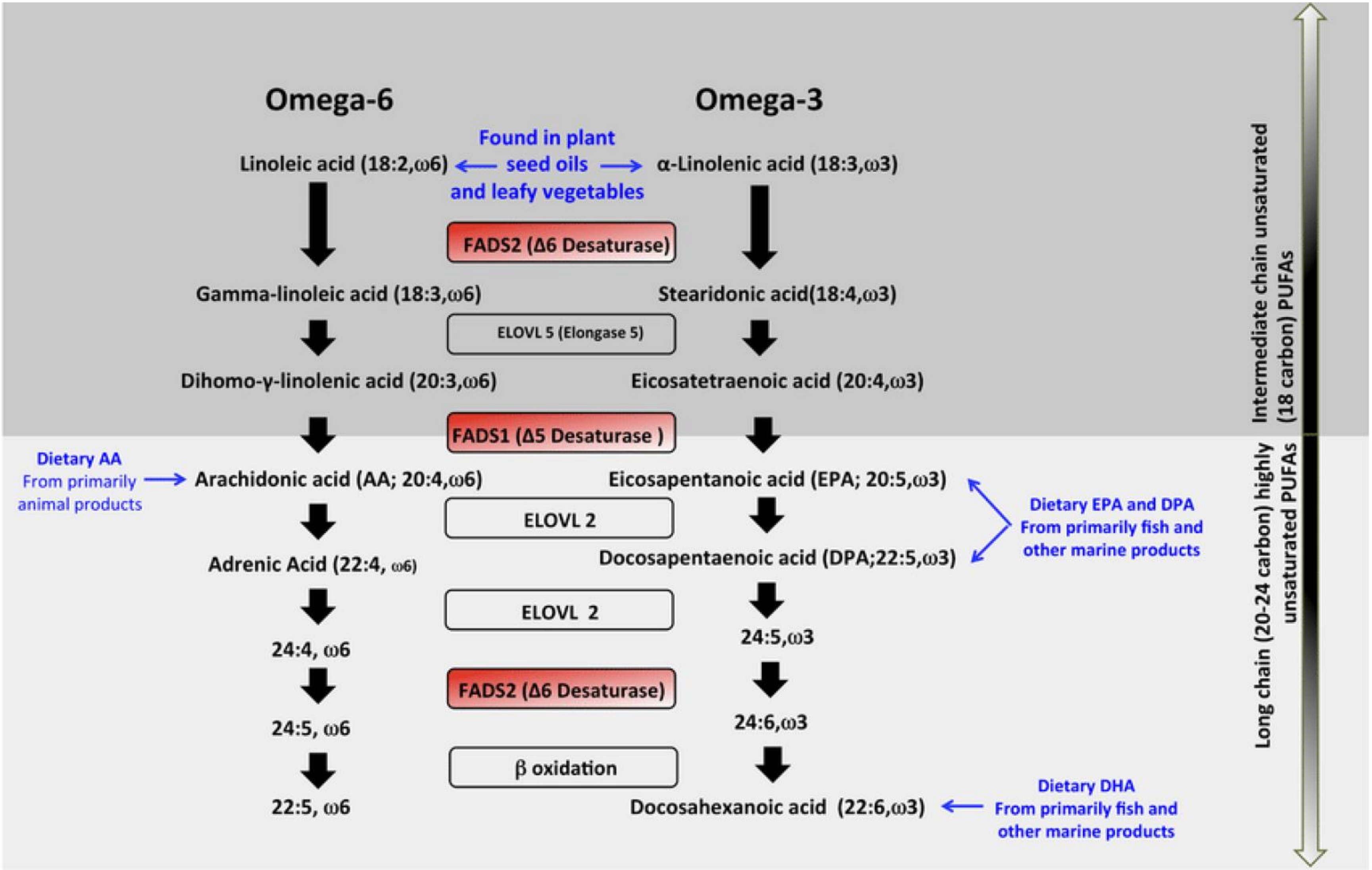
- a balance existed during the long evolutionary history of genus *Homo;*
- ***essential to humans*** *in the sense that they* ***cannot be synthesized de novo*** *but need to be supplied through* ***dietary intake****;*
- lack of the converting enzyme, omega-3 desaturase (omega-6 to omega-3 fatty acids);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

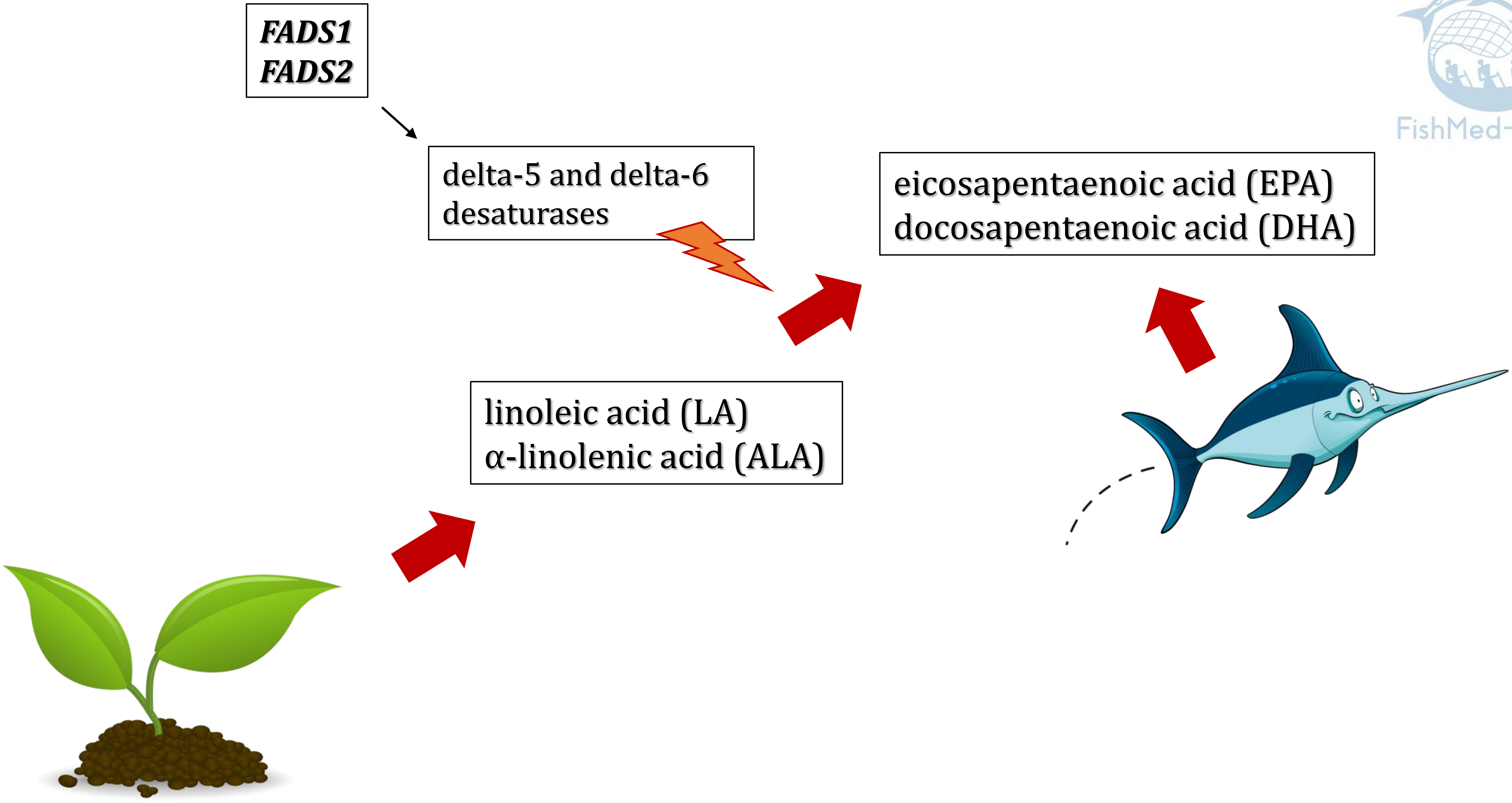
The rate-limiting steps of this process are catalyzed by fatty acid desaturase FADS 1 and 2

FADS GENES - LCPUFA METABOLISM

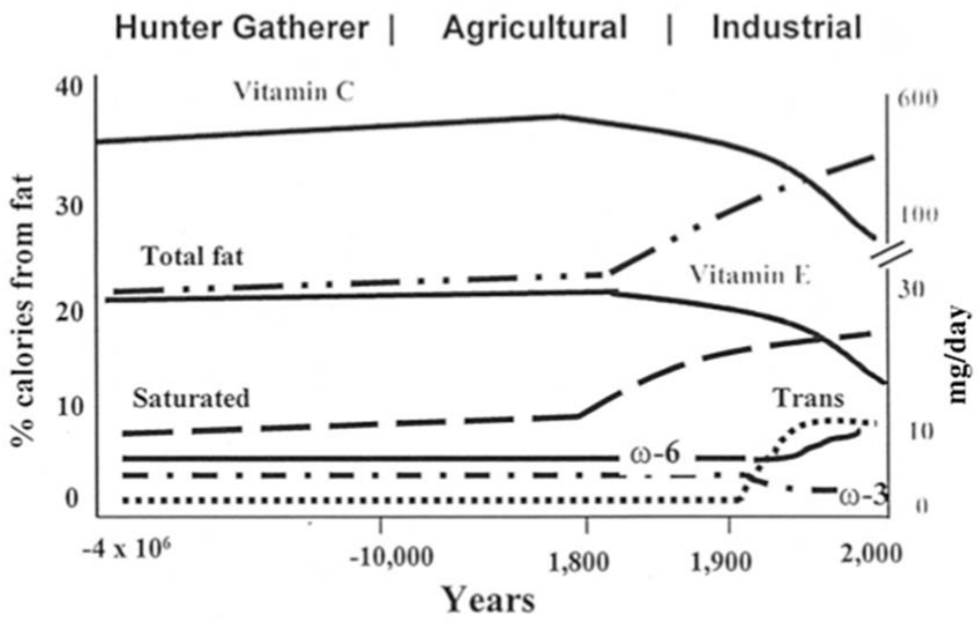


Omega-6 and omega-3 **long chain polyunsaturated fatty acids** (LCPUFAs) and their metabolites:

- ❑ 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**


FADS1
FADS2
delta-5 and delta-6 desaturases
linoleic acid (LA)
α-linolenic acid (ALA)
eicosapentaenoic acid (EPA)
docosapentaenoic acid (DHA)

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).

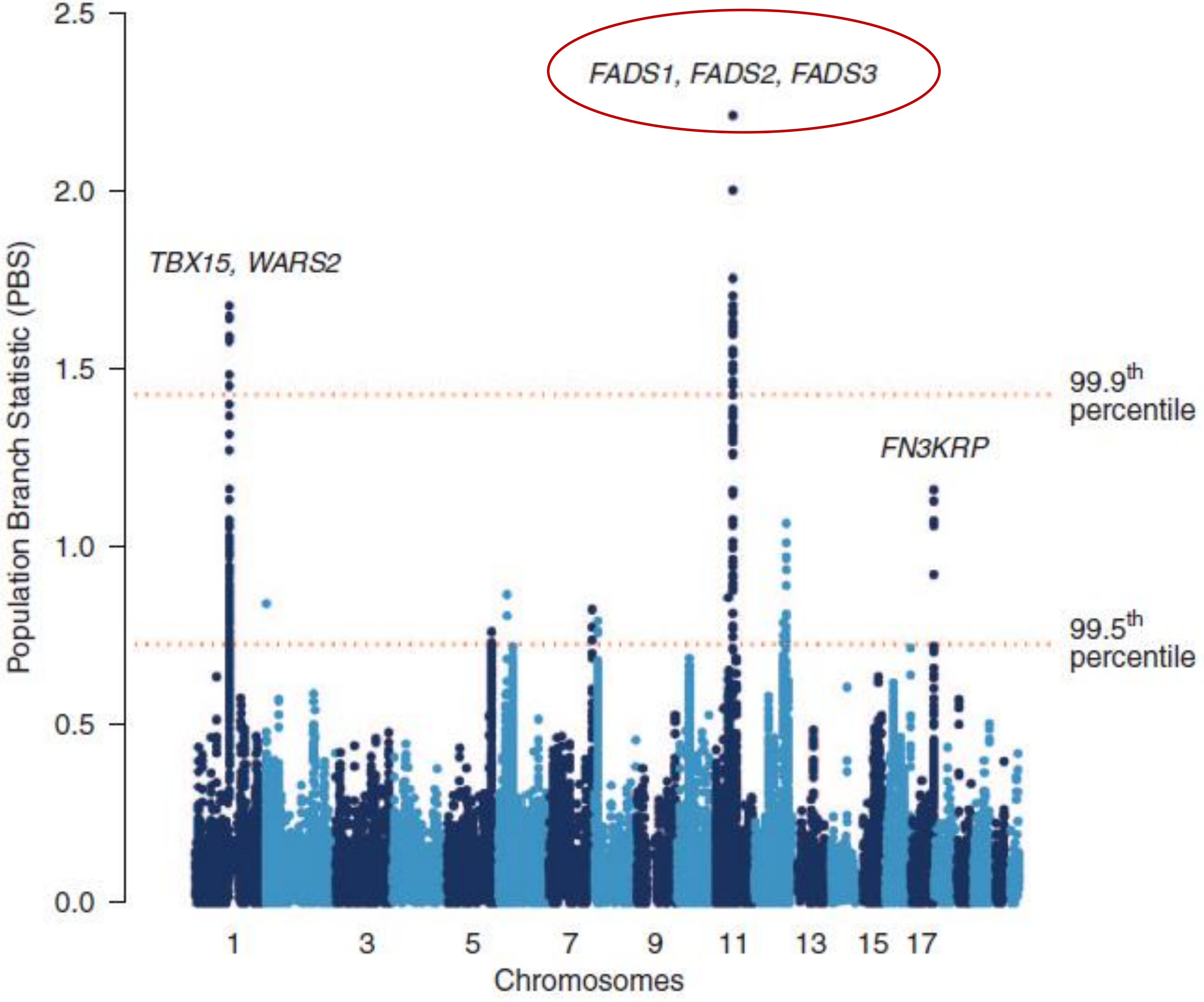


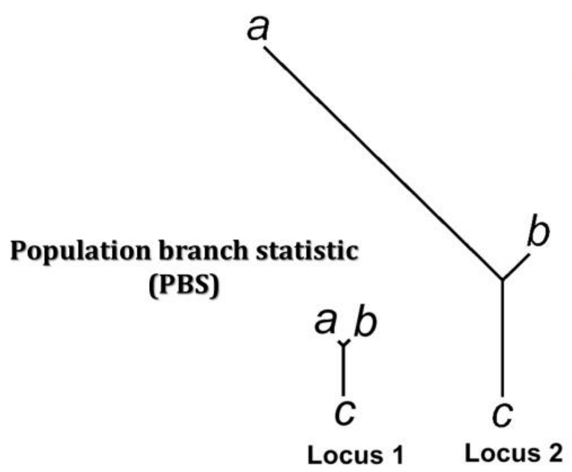
Rapid dietary changes over short periods of time have occurred **over the past 100–150 years** → totally new phenomenon in human evolution.

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

Omega-6/Omega-3 ratios in different populations

Urbanization and **industrialization** processes change the ratio



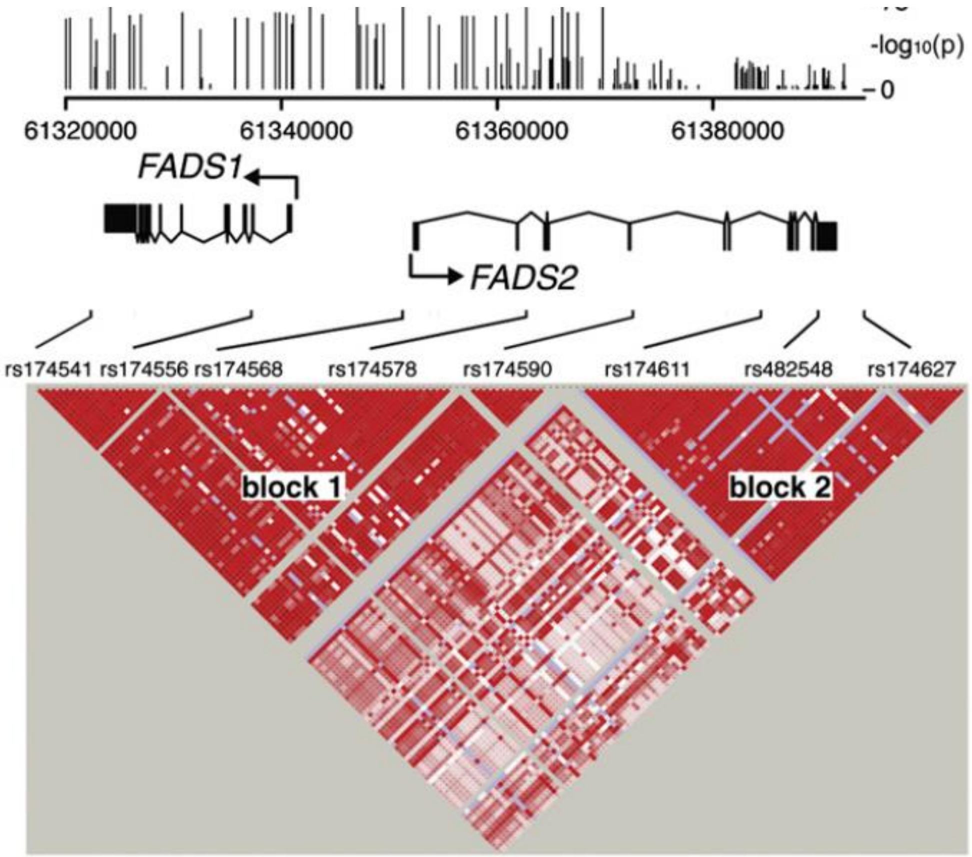


Fumagalli et al., 2015. Greenlandic Inuit show genetic signatures of diet and climate adaptation

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.

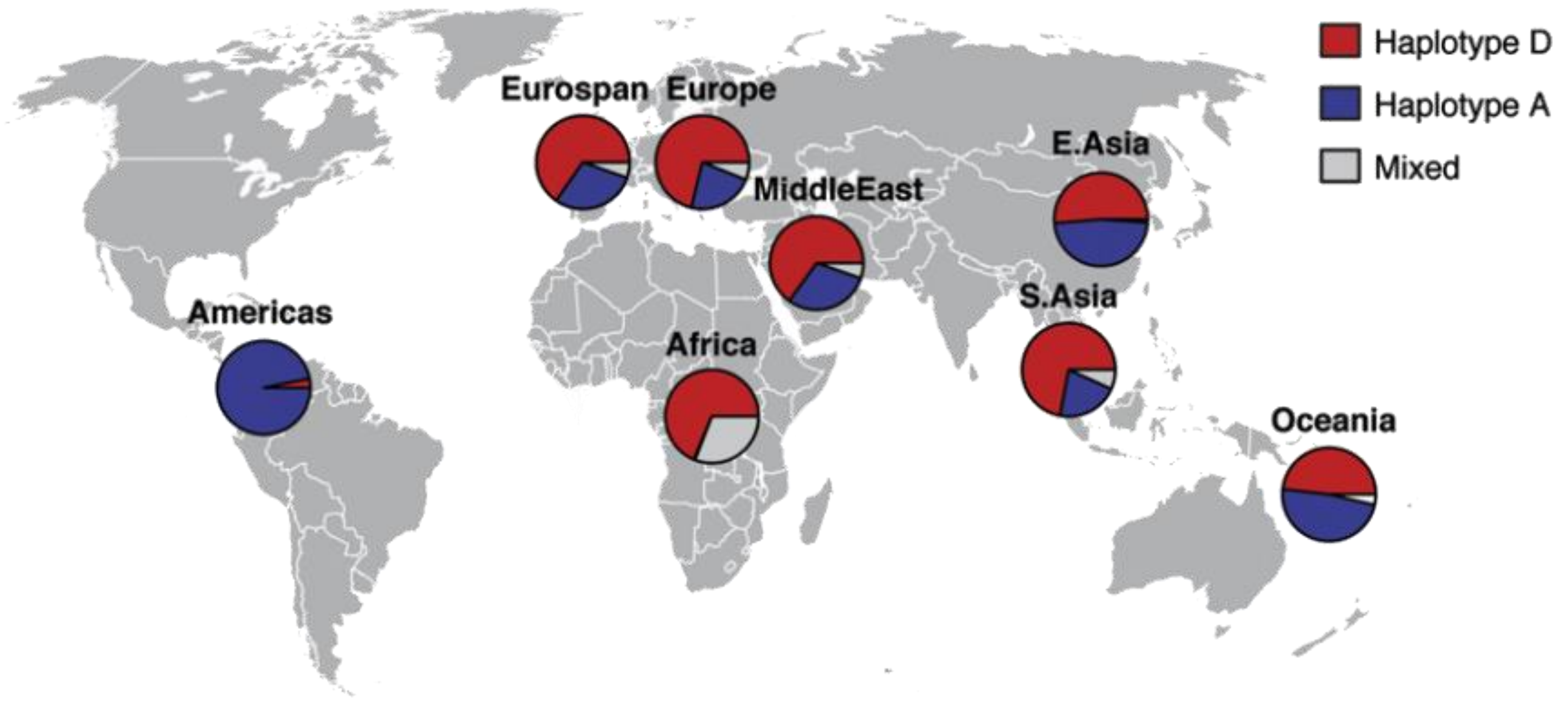
LD and HAPLOTYPE BLOCK

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



LD BLOCK 1: FADS1 + 1° half of FADS2

HAPLOTYPE A

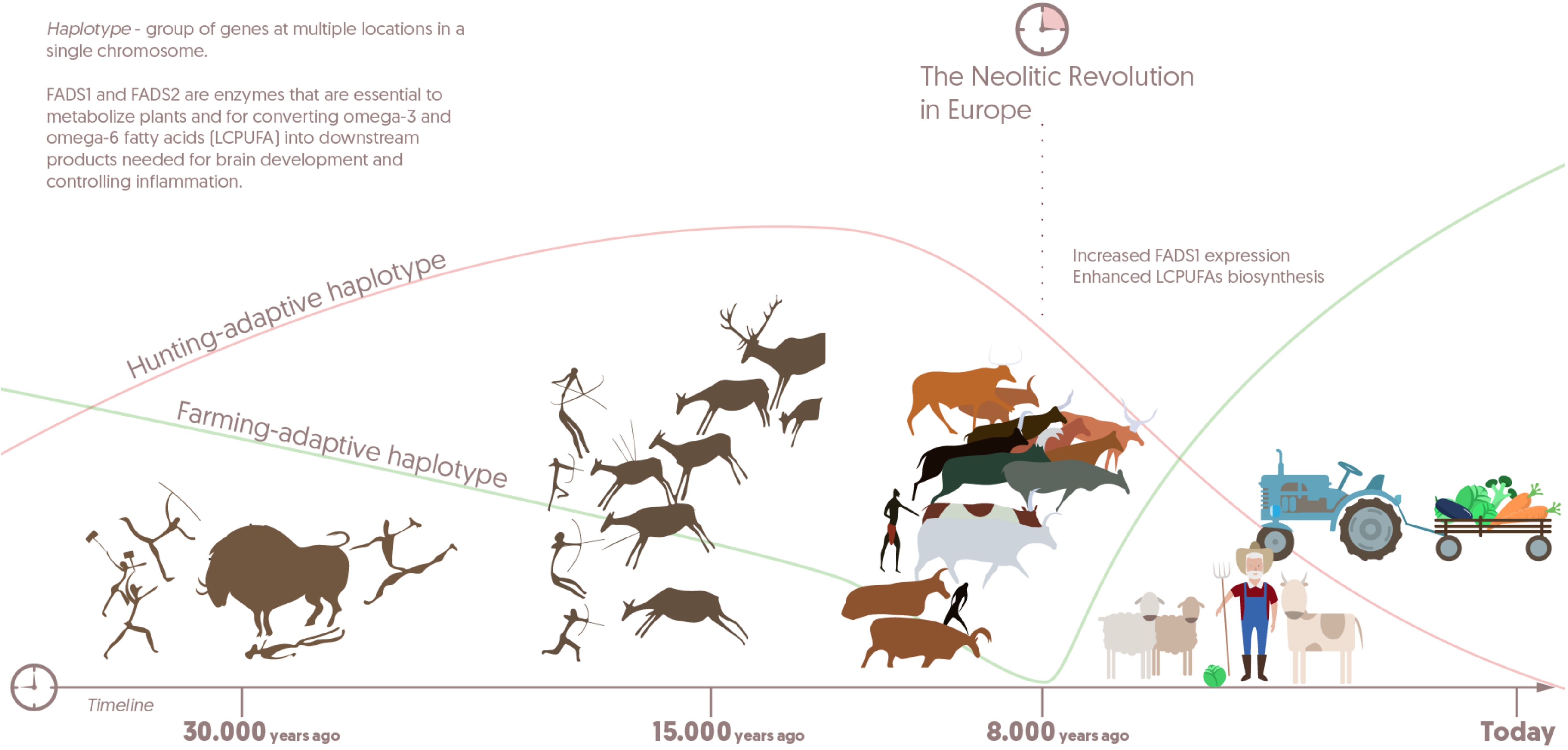


HAPLOTYPE D

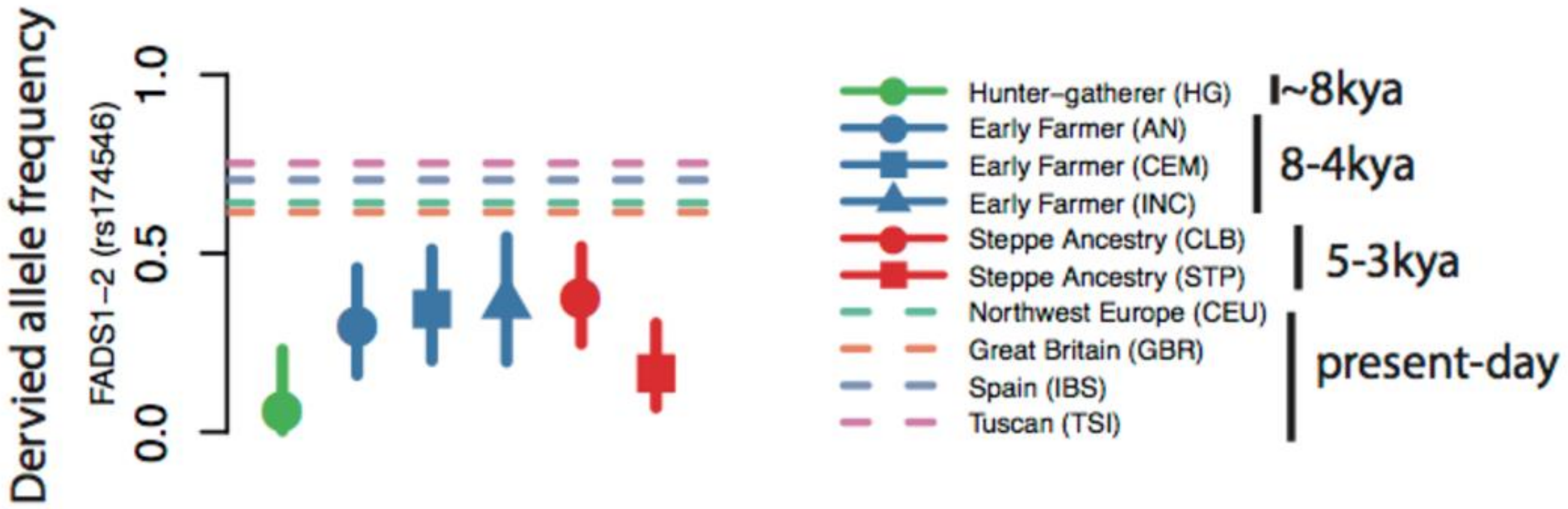
(increased FADS1 activity and is hypothesized to be an adaptation to a diet relatively low in PUFA, whereas haplotype A is hypothesized to be advantageous in a PUFA-rich environment).

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.



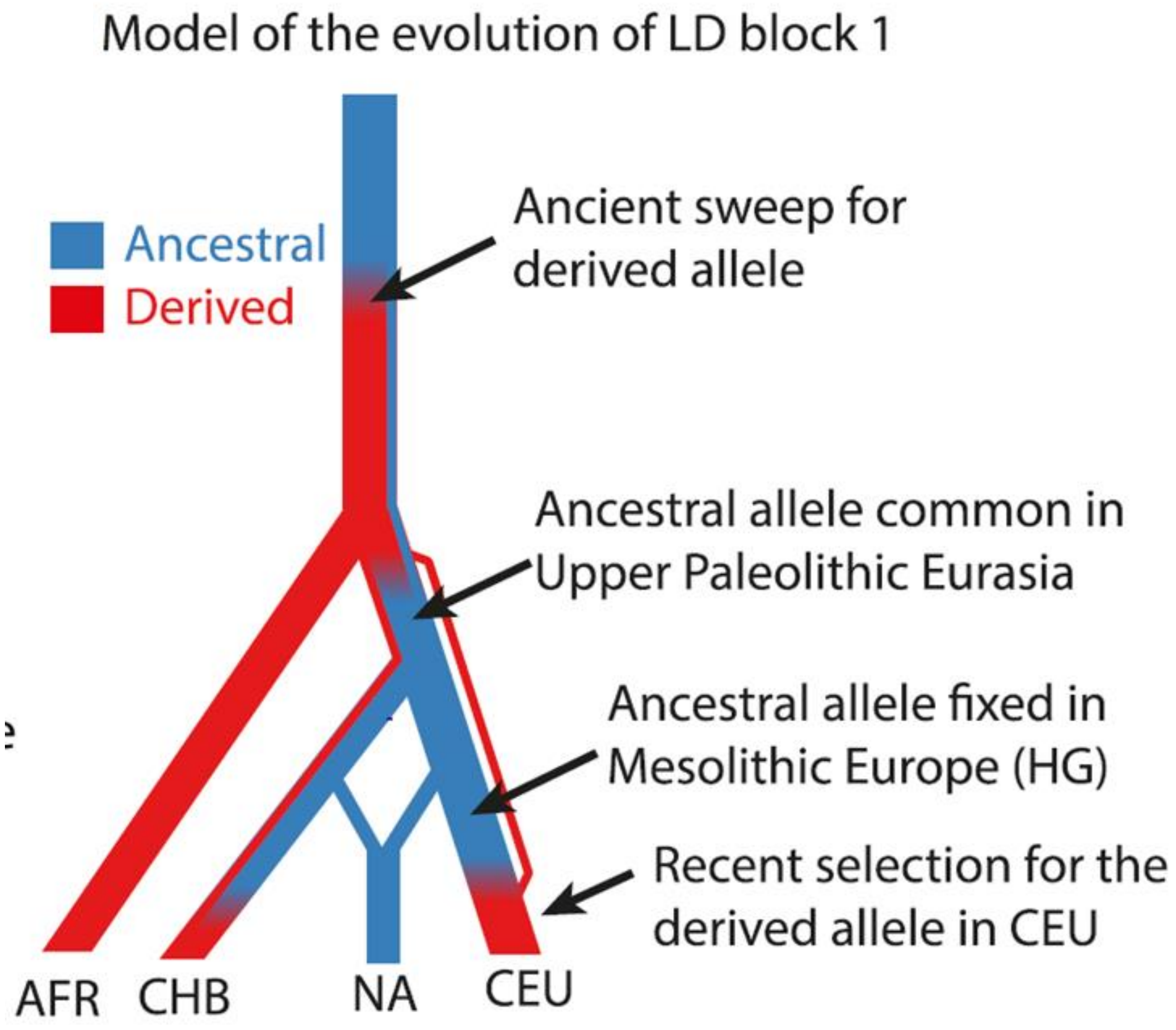
Selection has targeted **different alleles in the FADS genes in Europe than it has in South Asia or Greenland.**



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%.**

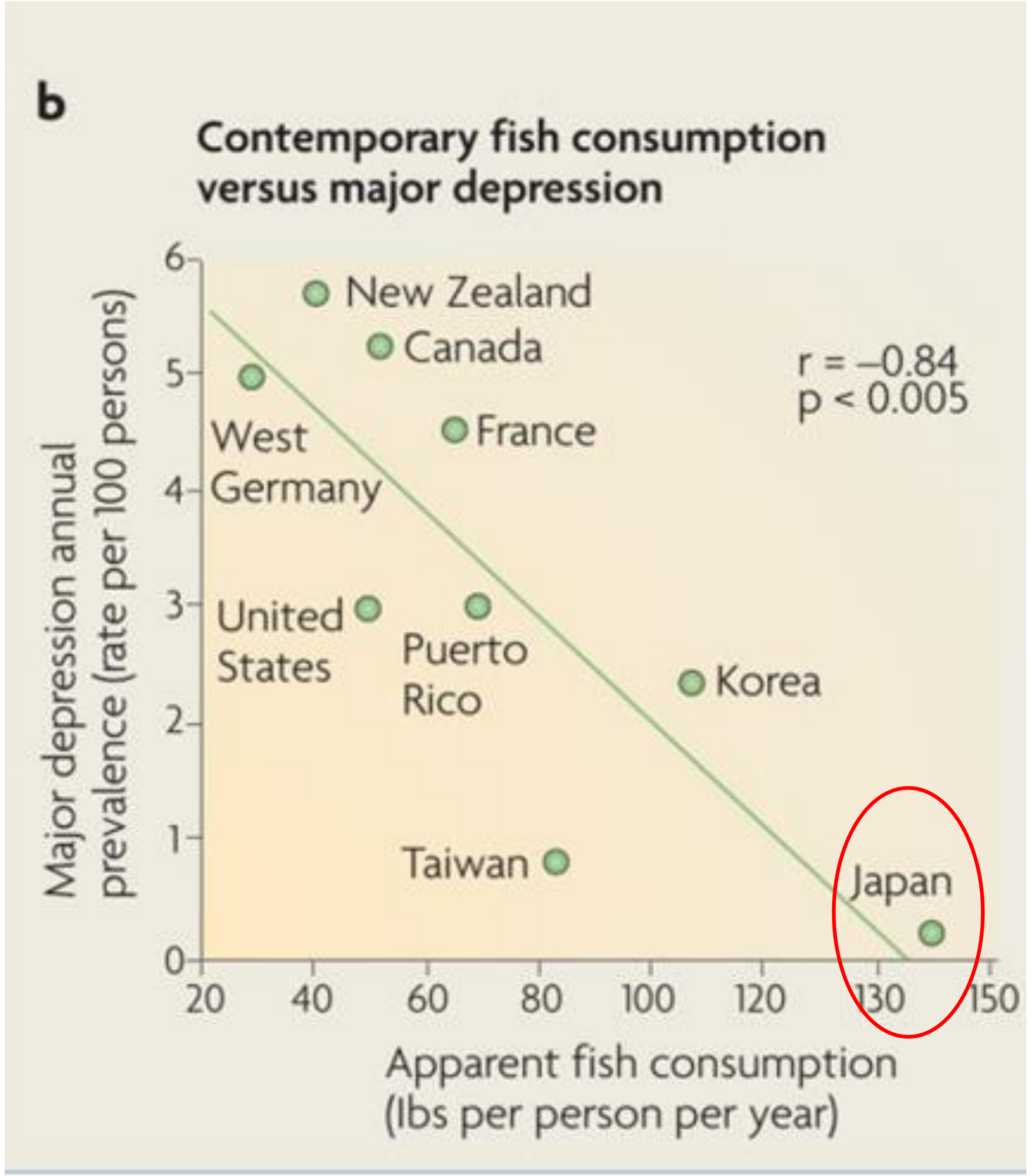
The trajectory of the derived haplotype in East Asian populations is less clear. It is common today in East Asia (40%), and the locus does exhibit a signal of selection in East Asian populations. But, with **limited ancient DNA evidence, it is unclear whether this represents recent selection or ancient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

Conclusions FADS genes:



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.



MAJOR DEPRESSION AND FISH CONSUMPTION

Igarashi et al. Genes & Nutrition (2019) 14:21
https://doi.org/10.1186/s12263-019-0646-6

Genes & Nutrition

RESEARCH Open Access

Identification of the 12q24 locus associated with fish intake frequency by genome-wide meta-analysis in Japanese populations

Maki Igarashi[1,2], Shun Nogawa[3], Kaoru Kawafune[3], Tsuyoshi Hachiya[3,4], Shoko Takahashi[3], Huijuan Jia[1], Kenji Saito[1,3] and Hisanori Kato[1*]

Table 2 Lead variants associated with fish intake frequency

SNP	Chr	Position	Gene(s)	EA	NEA	EAF	Beta	SE (beta)	$P_{association}$	I^2	$P_{heterogeneity}$
rs11758482	6	2,438,231	*GMDS–C6orf195*	G	A	0.405	0.110	0.024	3.8×10^{-6}	49.8	0.05
rs12003047	9	25,527,621	*IZUMO3–TUSC1*	C	T	0.015	0.431	0.097	8.7×10^{-6}	53.3	0.04
rs11066015	12	112,168,009	*ACAD10*	A	G	0.265	– 0.174	0.027	5.4×10^{-11}	0.0	0.65
rs1201914	20	59,274,641	*CDH26–CDH4*	G	A	0.452	– 0.117	0.023	4.8×10^{-7}	0.0	0.49

SNP single nucleotide polymorphism, *Chr* chromosome, *EA* effect allele, *NEA* non-effect allele, *EAF* effect allele frequency, *SE* standard error
Chromosomal positions are according to the human genome assembly version GRCh37/hg19

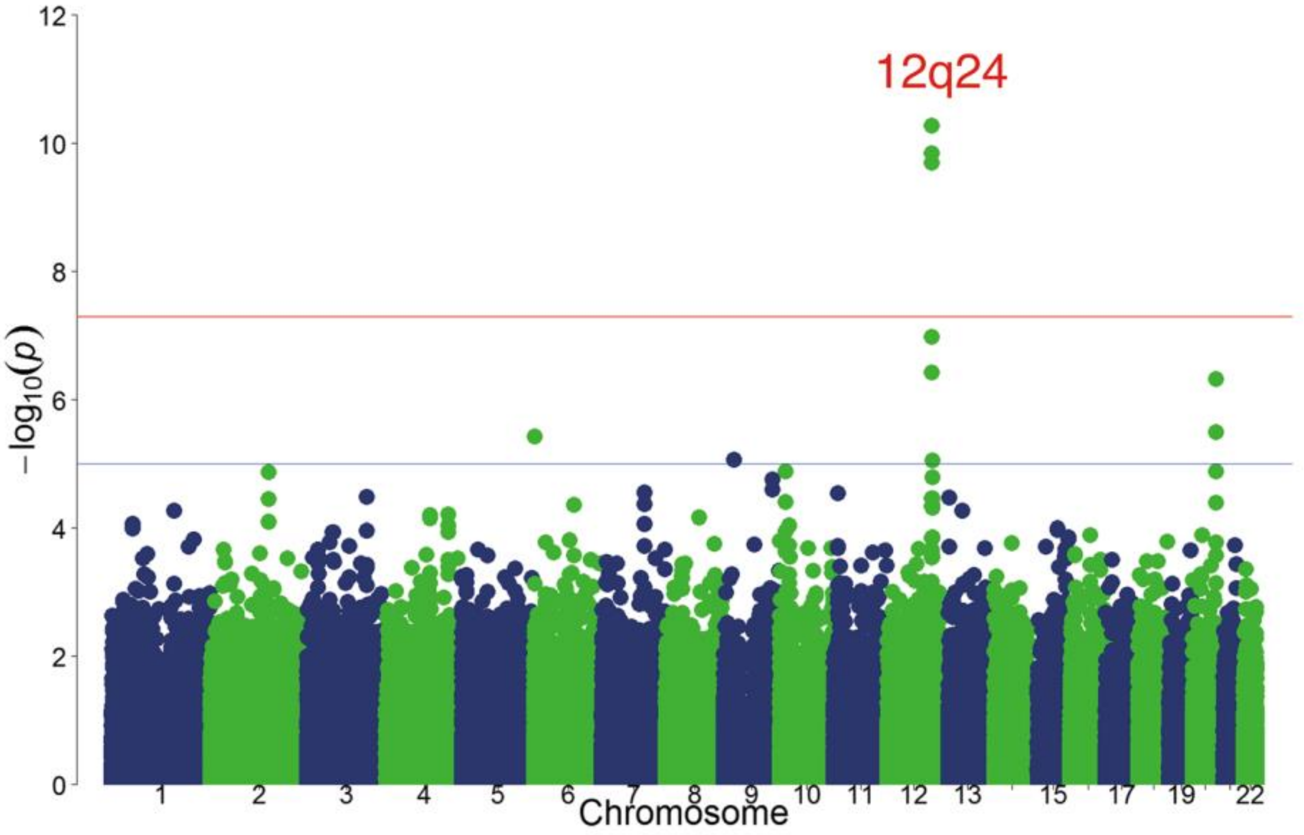


Fig. 2 Genome-wide meta-analysis of fish intake frequency. The *x*-axis represents chromosomal positions, and the *y*-axis represents $-\log_{10} P$ values. The red and blue horizontal lines indicate the genome-wide significance ($P = 5 \times 10^{-8}$) and suggestive significance ($P = 5 \times 10^{-5}$) levels, respectively

The association between the 12q24 locus and fish intake frequency was attenuated by adjusting for alcohol consumption or alcohol intake frequency, indicating that the 12q24 locus influences fish intake frequency via drinking habits

The 12q24 locus is an approximately 2-Mb region with a strong LD, and it has been reported to widely influence metabolic traits.

In the 12q24 locus**, rs671** is a SNP that is **located in the ALDH2 gene** and causes an amino acid substitution.

The rs671 minor allele reduces the degradation of acetaldehyde, a toxic intermediate metabolite of alcohol, and thus results in reduced alcohol consumption.

nutrients

Review

Genetic Biomarkers of Metabolic Detoxification for Personalized Lifestyle Medicine

Lucia Aronica [1,2,*], Jose M. Ordovas [3,4,5], Andrey Volkov [6], Joseph J. Lamb [7], Peter Michael Stone [7,8,9,10], Deanna Minich [8,11], Michelle Leary [12], Monique Class [8,13], Dina Metti [7], Ilona A. Larson [1], Nikhat Contractor [14], Brent Eck [1] and Jeffrey S. Bland [15]

Nutrients **2022**, *14*, 768. https://doi.org/10.3390/nu14040768

Common genetic variants within genes involved in Phase I/Phase II detox reactions associated with **variability of response to foods or nutrients that modulate detox metabolism.**

Phase I Detox Enzymes		
CYP1A2		
Effect allele	Allele frequency	Effects on enzymatic function
rs762551-C Strength of evidence: Convincing (A).		C-allele carriers produce an enzyme variant with 62–70% lower activity and are less inducible by xenobiotics. Low CYP1A activity can result in decreased clearance of toxins, a lower 2/16-alpha hydroxyestrone ratio, and a higher risk of certain cancers. Consequently, lower production of reactive detoxification intermediates may reduce oxidative stress.
CYP1B1		
Effect allele	Allele frequency	Effects on enzymatic function
rs1056836-C Strength of evidence: Possible (C).		Individuals with the CC genotype tend to have higher enzymatic activity than G-allele carriers, which may result in greater activation of toxicants, greater production of 4-hydroxy estrogens, and greater oxidative damage. The effects of this SNP are affected by age, ethnicity, and menopausal status.

Phase II detox enzymes

GSTM1

Effect allele	Allele frequency	Effects on enzymatic function
GSTM1 deletion *GSTT1* deletion Strength of evidence: Probable (B).	  * -: deletion; +: present	Individuals carrying *GSTM1* or *GSTT1* double deletions (-/- genotype) may have a decreased ability to detoxify environmental toxicants, carcinogens, and products of oxidative stress. Gene deletions are more frequent among Caucasian and Asian populations and less frequent in African populations. Different segmental deletions have different frequencies in the population and between different ethnicities.

COMT

Effect allele	Allele frequency	Effects on enzymatic function
rs4680-A Strength of evidence: Probable (B).		The A allele (Met) produces an enzyme with 40 % lower activity than that encoded by the G allele (Val). A-allele carriers may have a decreased ability to degrade neurotransmitters, estrogen, and various xenobiotics. This may result in increased sensitivity to environmental toxicants, a higher risk of developing neuropsychiatric disorders, and impaired estrogen metabolism.

UGT1A1

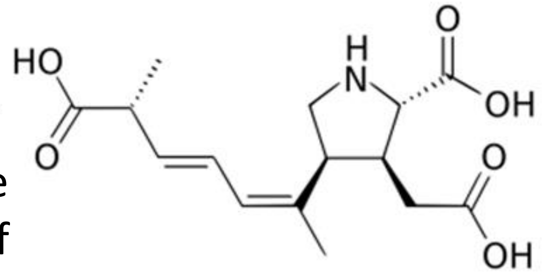
Effect allele	Allele frequency	Effects on enzymatic function
rs3064744-TA Strength of evidence: Possible (C).		Individuals carrying two insertion alleles (TA/TA genotype) may have a lower enzymatic activity than those carrying at most one copy of the deletion allele (-). This may result in increased toxicity in response to certain drugs (acetaminophen) and to a benign cardio-protective condition known as Gilbert syndrome, characterized by increased serum levels of total and unconjugated bilirubin.

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.

TWO DIFFERENT ALLELE EFFECT

GSS →

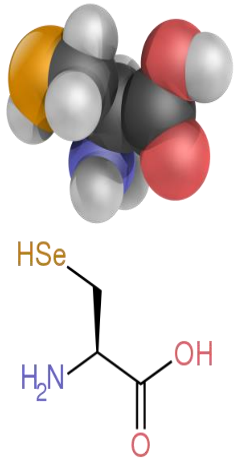


it encodes for an enzyme, glutathione synthetase, that is involved in the synthesis of glutathione, to which mercury is conjugated before being eliminated.

Glutathione synthetase is a potent antioxidant

Minor allele (G) ↘ **Decreased expression of *GSS*** ↘ **Reduced MeHg elimination**

SEPP1



Selenoprotein P plasma 1

SEPP1 encodes a selenoprotein, which fights the oxidative stress created by mercury by binding the toxicant directly via a selenocysteine residue

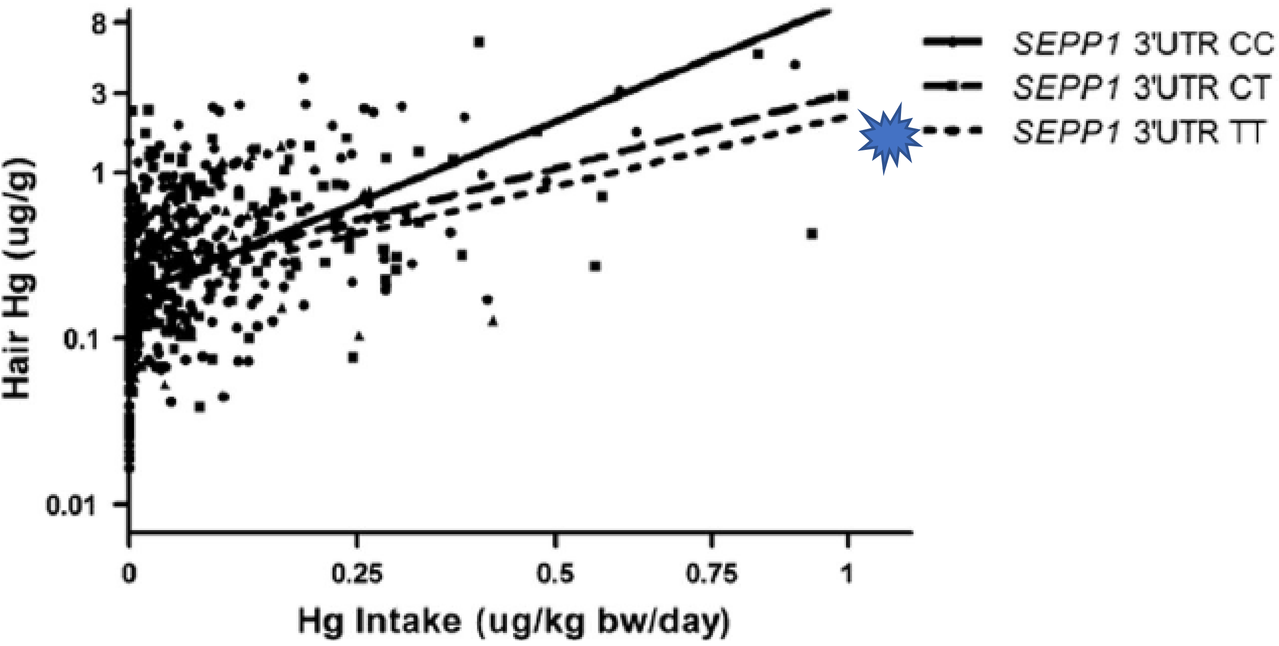
SEPP1 3'UTR T allele is linked to greater SEPP1 expression and mercury binding capacity.

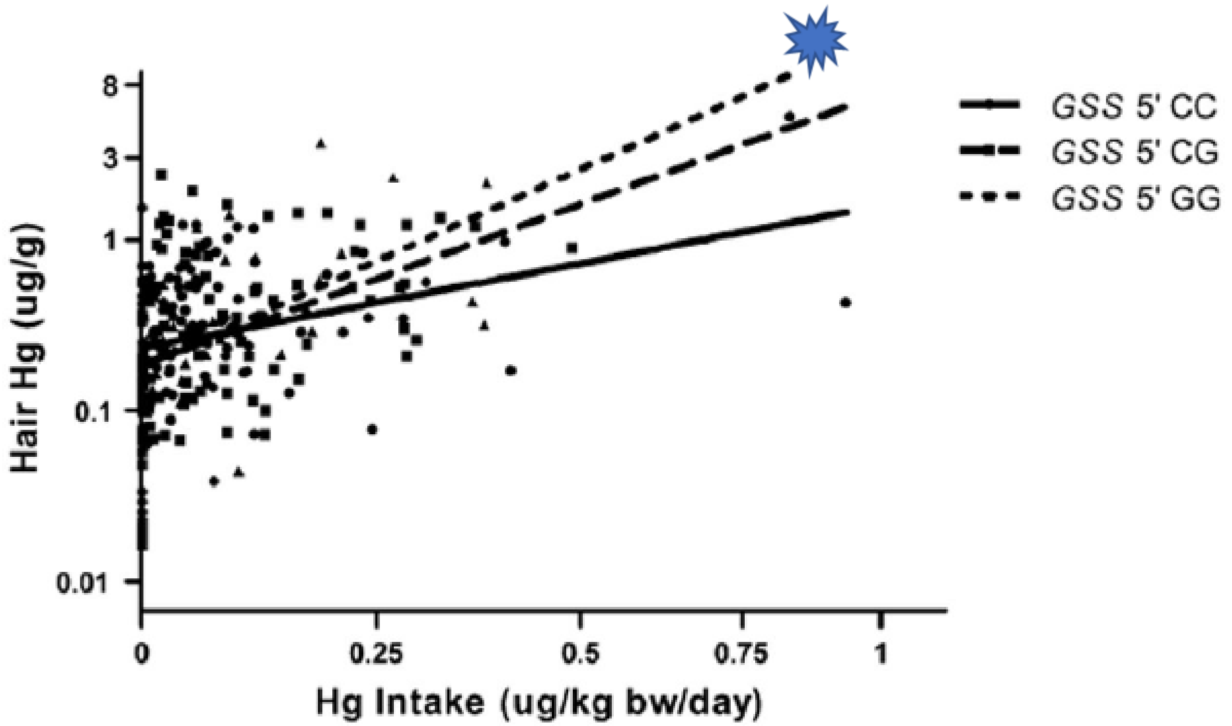
1) Fish consumption as estimated by a self-administered survey was the best predictor of measured hair mercury level

TaqMan SNP Genotyping Assay

2) Regression model:

GSS 5' minor allele was associated with increasing hair mercury concentration per unit of fish mercury





lower hair mercury per unit of intake from fish consumption

FishMed-PhD

Two examples from traditional Fishing Community

FS is a defined group of people **who share identity and** interact each other to perform activities along the fisheries value chain based on experiential knowledge accumulated over time and passed along generations.

Traditions represent a set of practices developed by repetition over time and regulated by shared values, beliefs, accepted rules, and negotiated across different levels and consist of the cultural background and identity of specific groups of people who exercise them. Traditional usually refers to cultural continuity transmitted in the form of social attitudes, beliefs, principles, and conventions of behavior and practice derived from historical experience.

Ttaditional Communities of Brazilian Amazon

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

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

The only source of mercury exposure was the intake of contaminated fish

Questionnaires on sociodemographic, lifestyle, and health information

+

7-day recall food consumption frequency questionnaire

Blood sample collection

Genomic analysis

+

Mercury level measurements

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

Authors genotyped two glutathione-related genes, *GSTM1* and *GCLC*

Multiplex PCR

GSTM1

GCLC

glutathione S-transferase

enzyme that catalysed the conjugation of glutathione to methylmercury

glutamate-cysteine ligase

encodes one of the two subunits that constitute glutamate-cysteine ligase, the first rate-limiting enzyme of glutathione synthesis

RESULTS

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

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

Functional *GSTM1* *is* related to lower methylmercury-conjugating activity, lower methylmercury excretion, and a higher methylmercury retention.

Moreover, also persons carrying at least one T allele for *GCLC* had significant 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.

Seychelles population with a diet rich in fish. Over 80% of Seychellois women eat fish daily, and the median fish meals per week during pregnancy is 12.

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

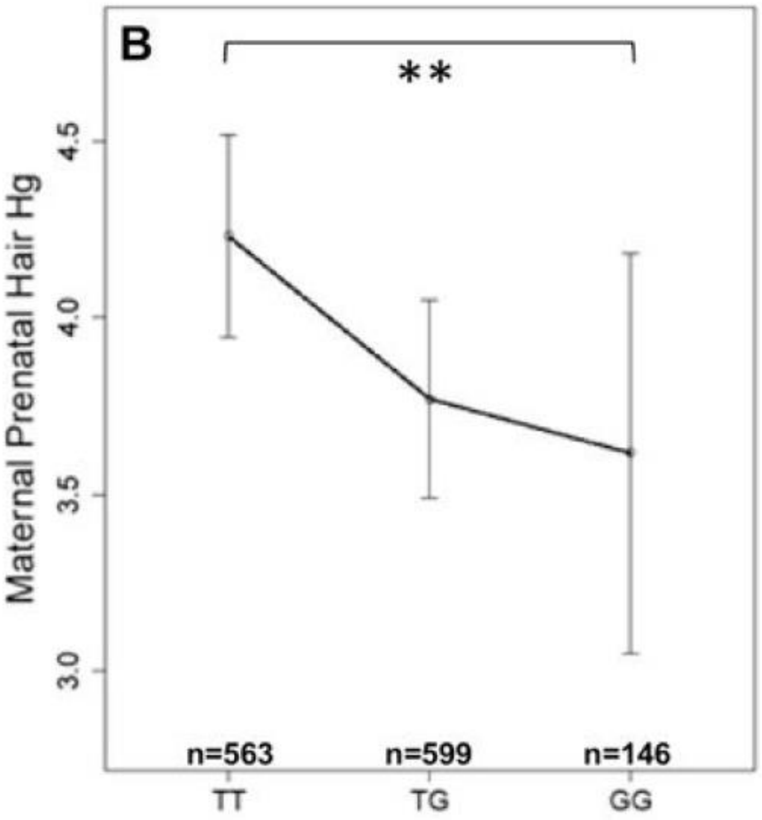
TaqMan SNP Genotyping Assay

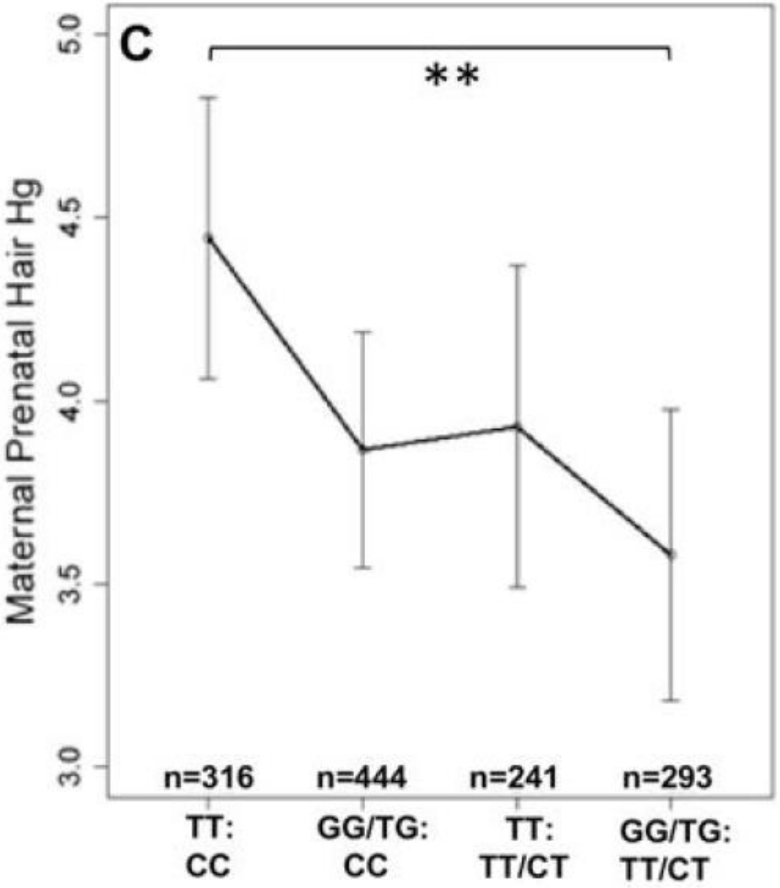
- GCLC → Glutamate-Cysteine Ligase Catalytic Subunit
- GSTP1 → Glutathione S-transferase

Pyrosequencing

- GCLM → Glutamate-Cysteine Ligase Modifier Subunit

GCLC **– rs761142 TT homozygotes showed higher hair Hg levels**





GCLC GCLM **– rs761142 TT and rs41303970 CC homozygotes showed higher hair Hg levels**

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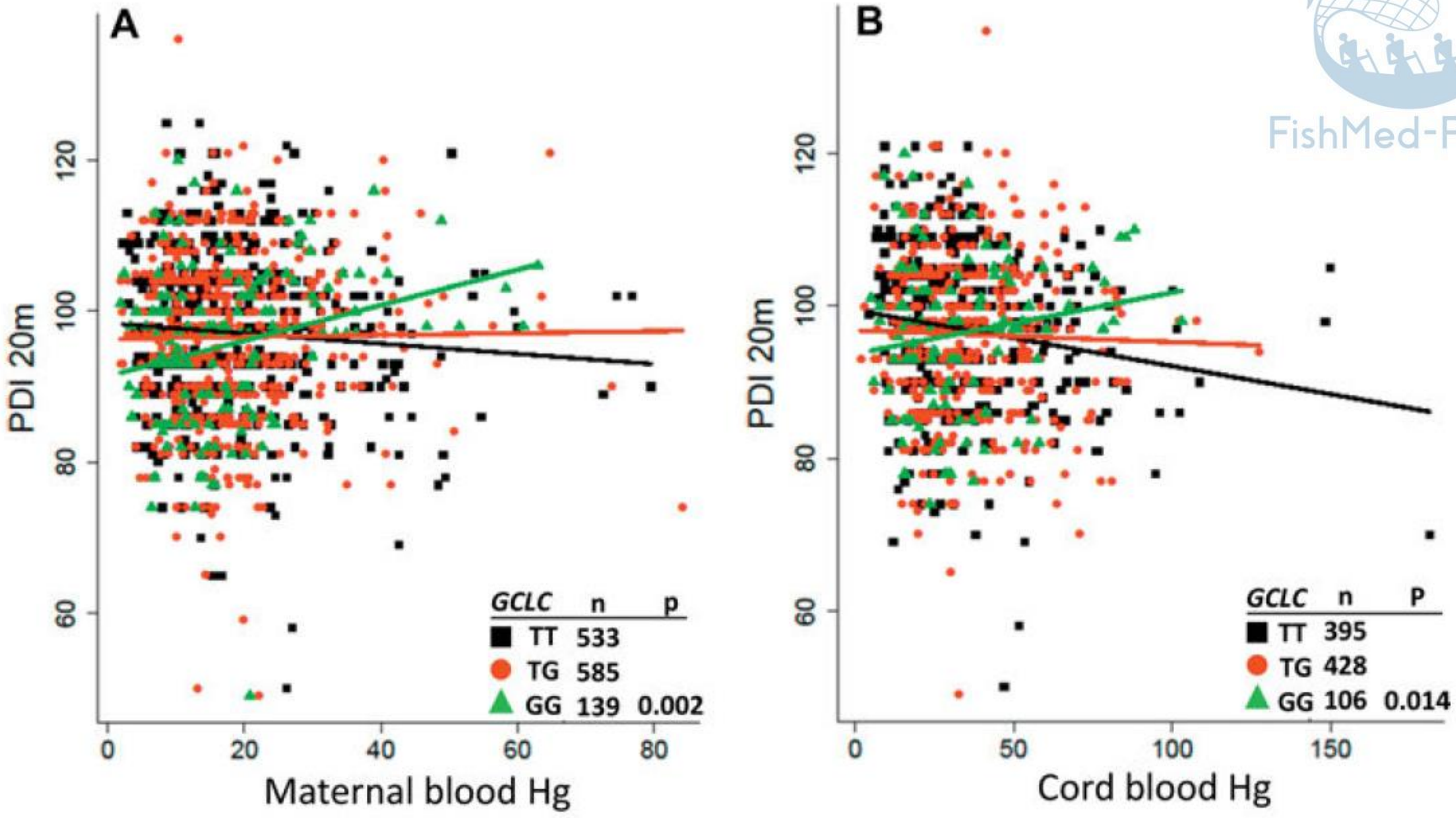
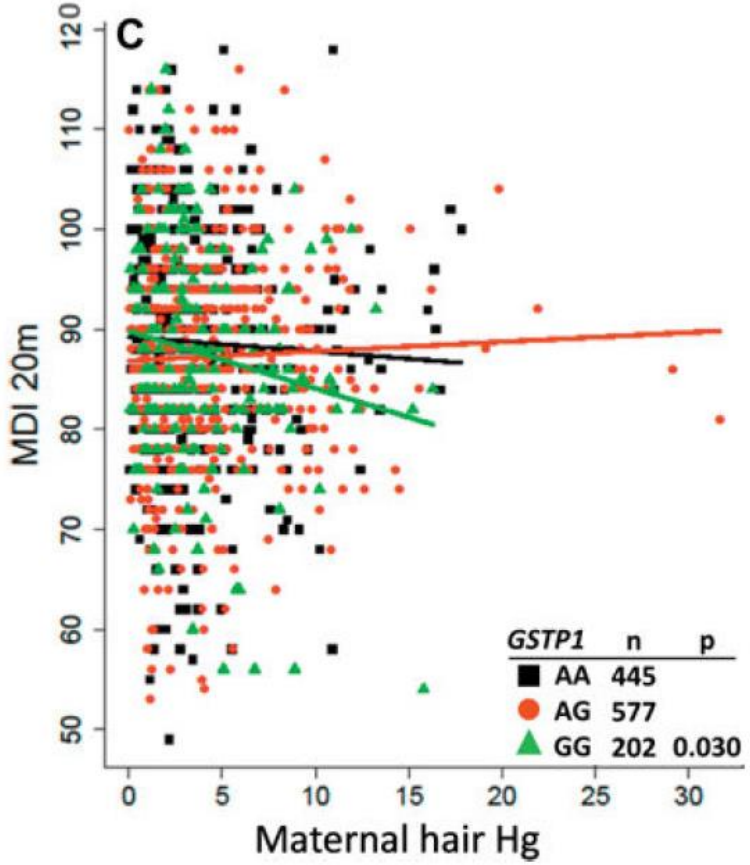
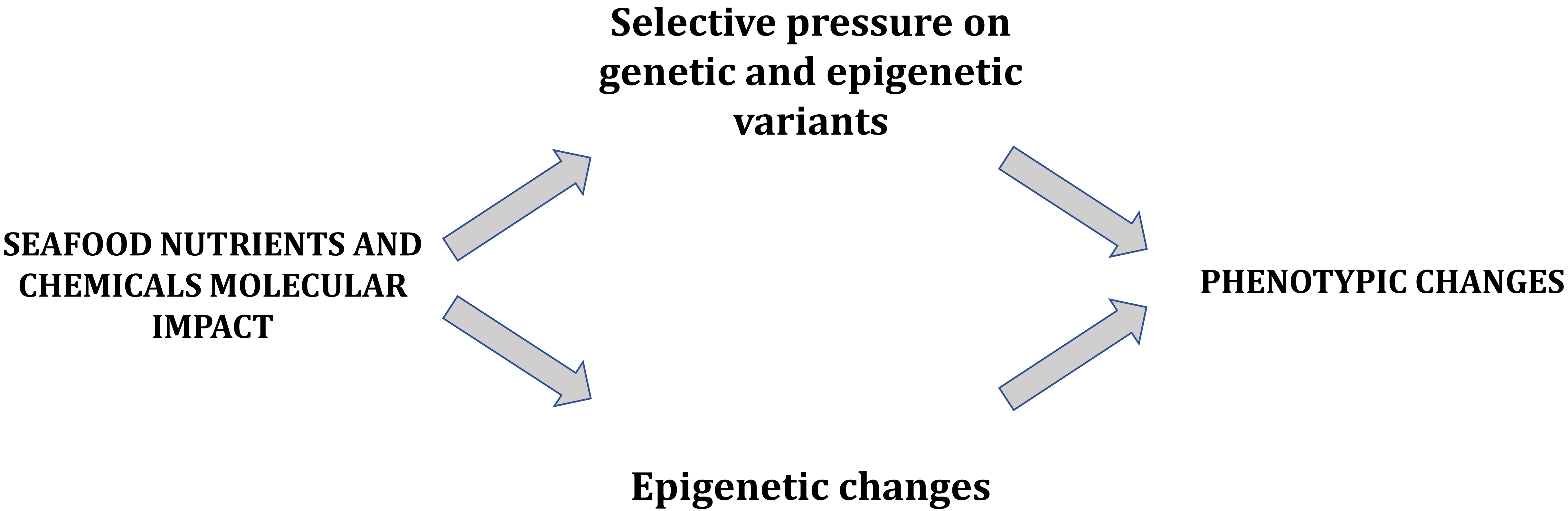
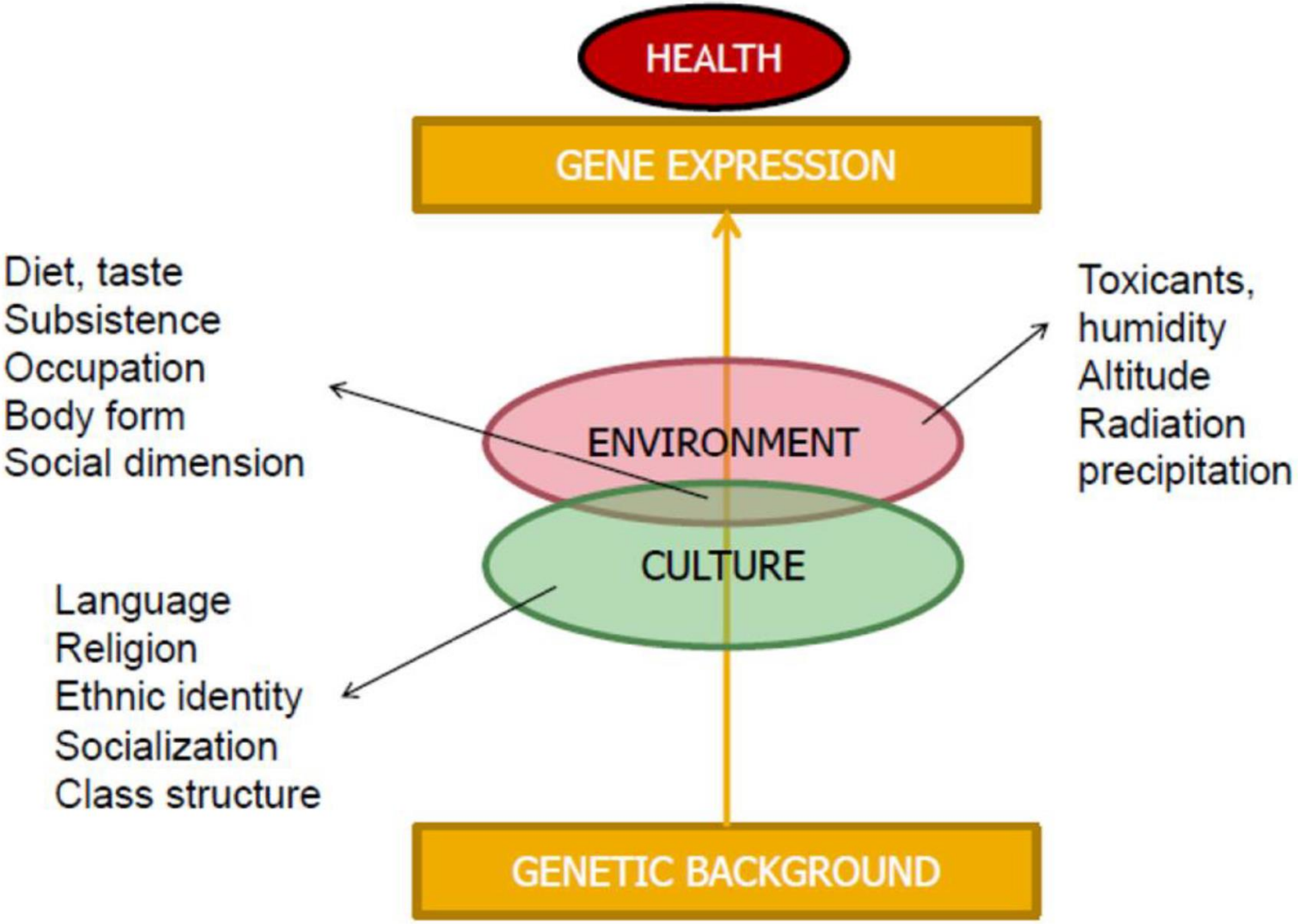
Increasing Hg in maternal and cord blood was associated with lower PDI among GCLC rs761142 TT carriers





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

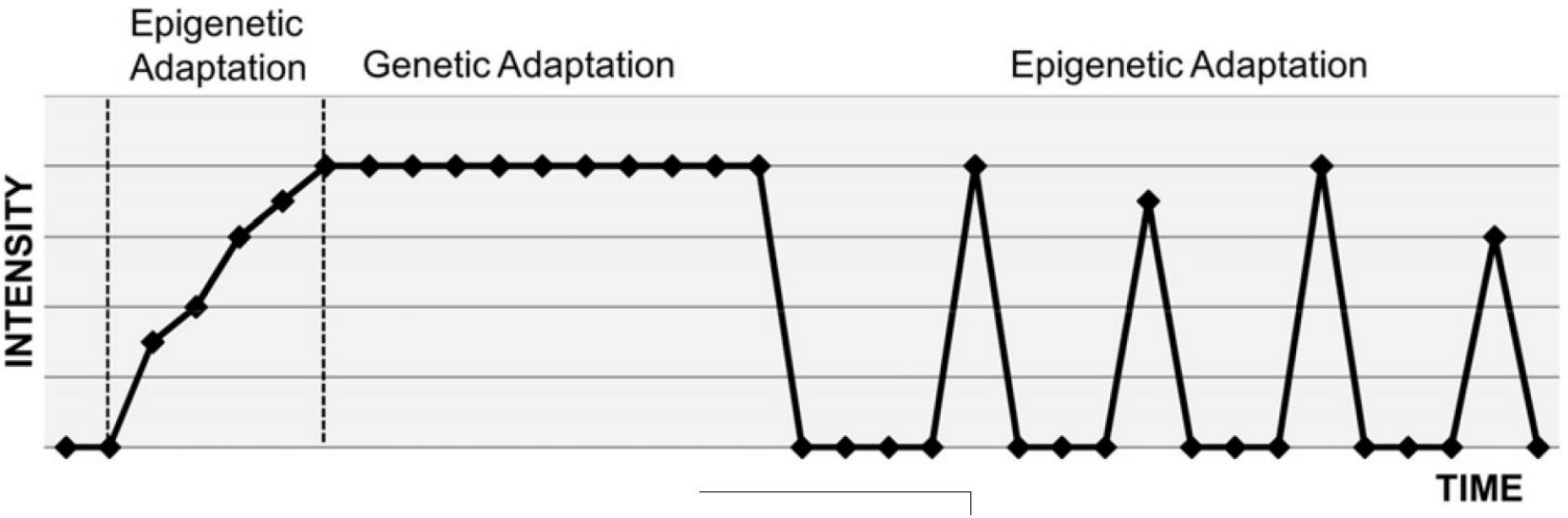

Selective pressure on genetic and epigenetic variants
SEAFOOD NUTRIENTS AND CHEMICALS MOLECULAR IMPACT
PHENOTYPIC CHANGES
Epigenetic changes


HEALTH
GENE EXPRESSION
Diet, taste
Subsistence
Occupation
Body form
Social dimension
ENVIRONMENT
Toxicants,
humidity
Altitude
Radiation
precipitation
CULTURE
Language
Religion
Ethnic identity
Socialization
Class structure
GENETIC BACKGROUND

EPIGENETIC SIDE OF HUMAN ADAPTATION

"When natural selections 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)

STIMULUS (such as diet, pathogens, climate)



Review Paper

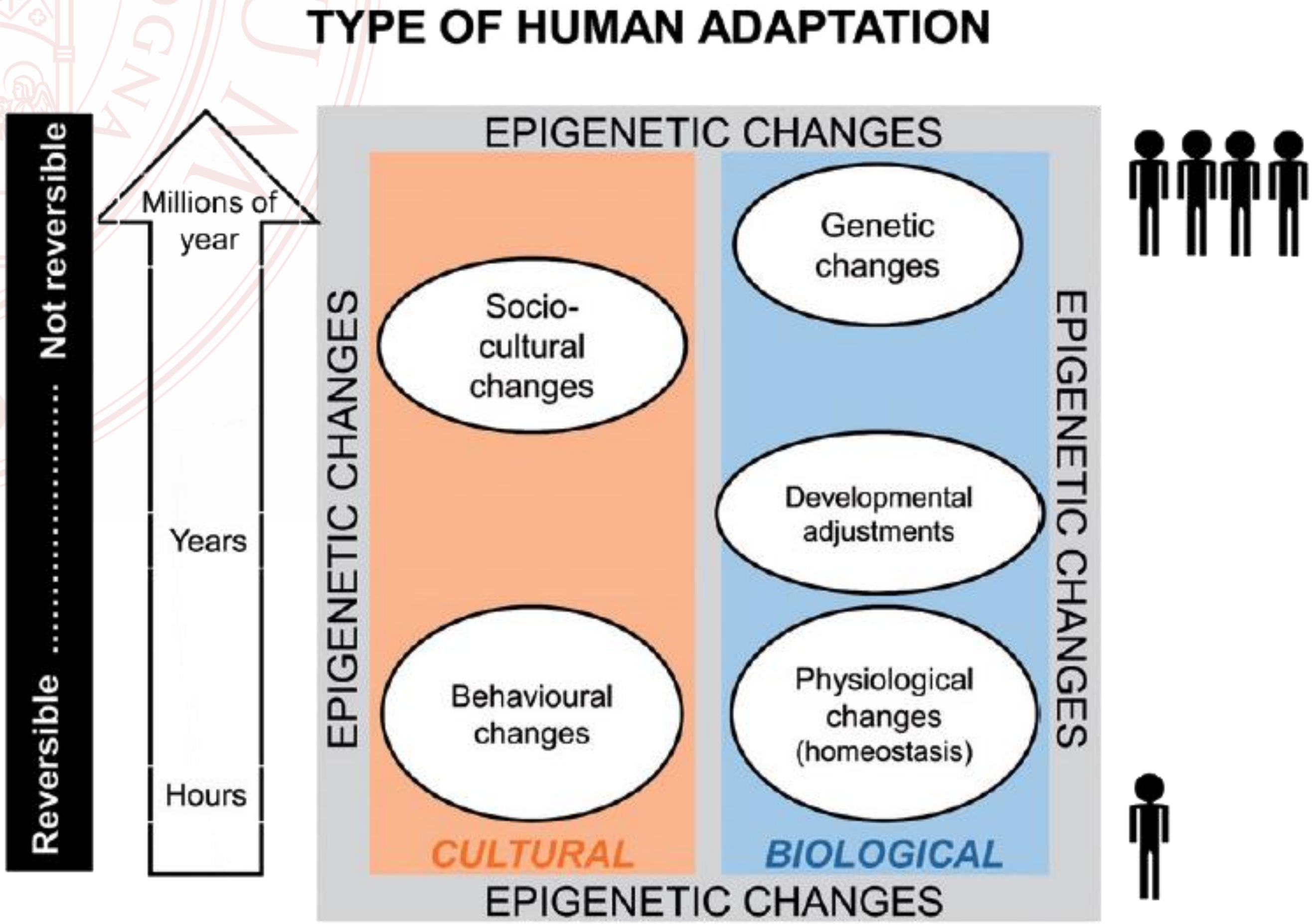
The epigenetic side of human adaptation: hypotheses, evidences and theories

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

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

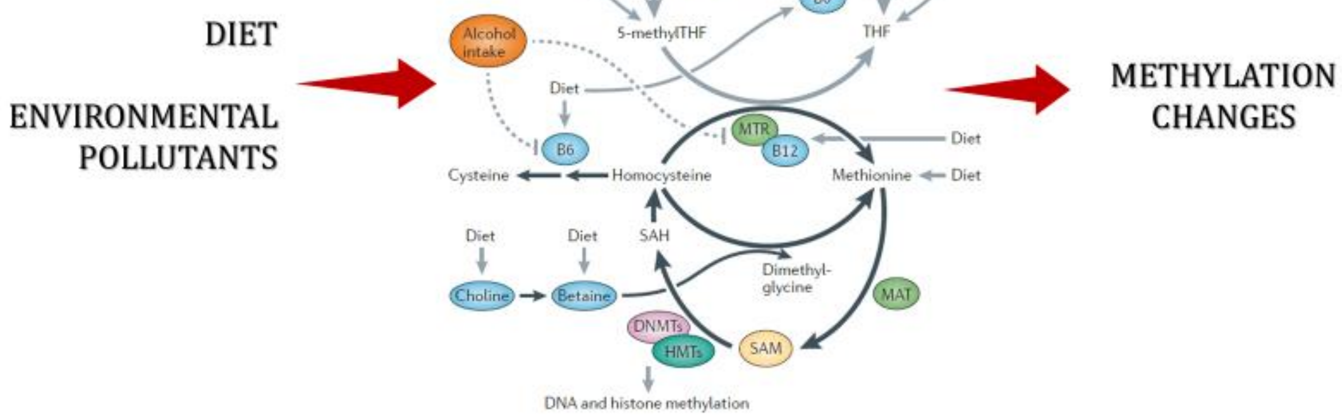
Epigenetics mechanisms could represent “medium-term” strategies to cope with a demanding environmental condition



Epigenetic changes → Gene expression changes

A common type of epigenetic modification is called DNA methylation. DNA methylation involves the attachment of small chemical groups called methyl groups (each consisting of one carbon atom and three hydrogen atoms) to DNA building blocks

Synthesis of methylation enzymes



Methylation variability across human populations

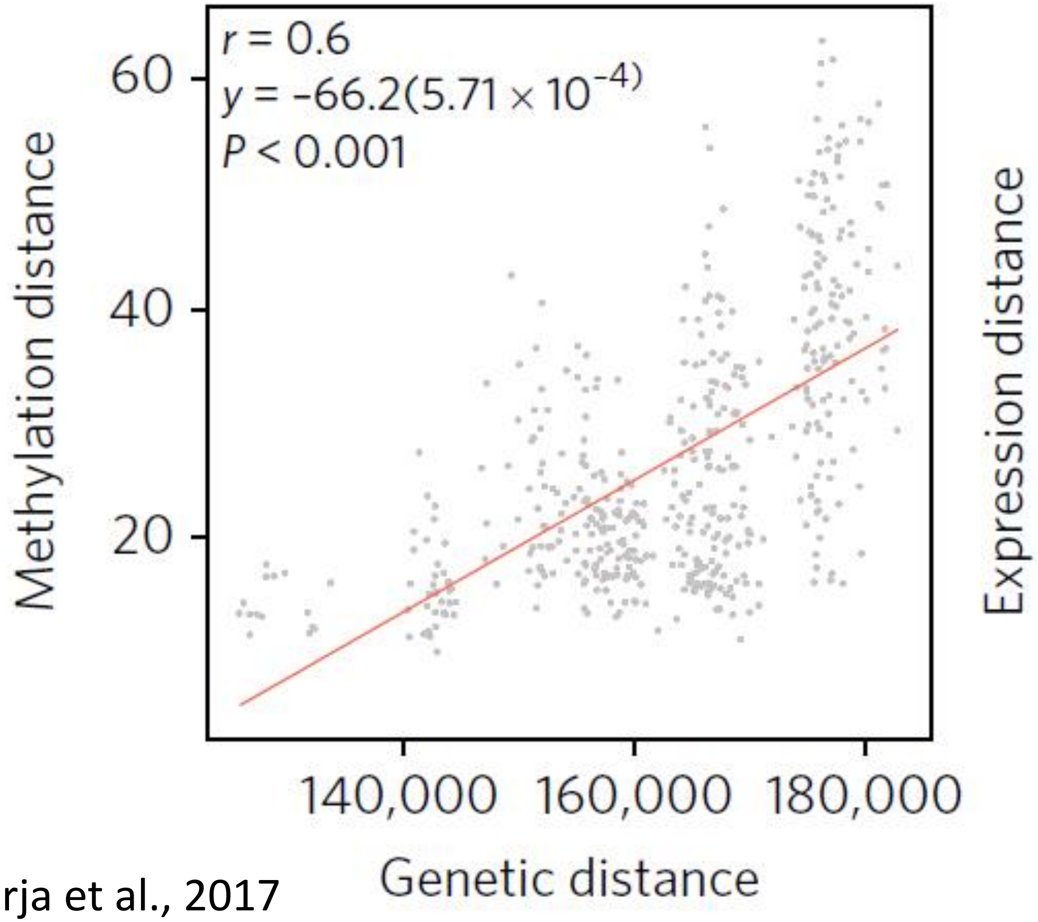
Environment

- Diet
- UVA exposure
- Pathogens load

...

Could methylation changes contribute to human adaptation?

Genetic background



Carja et al., 2017

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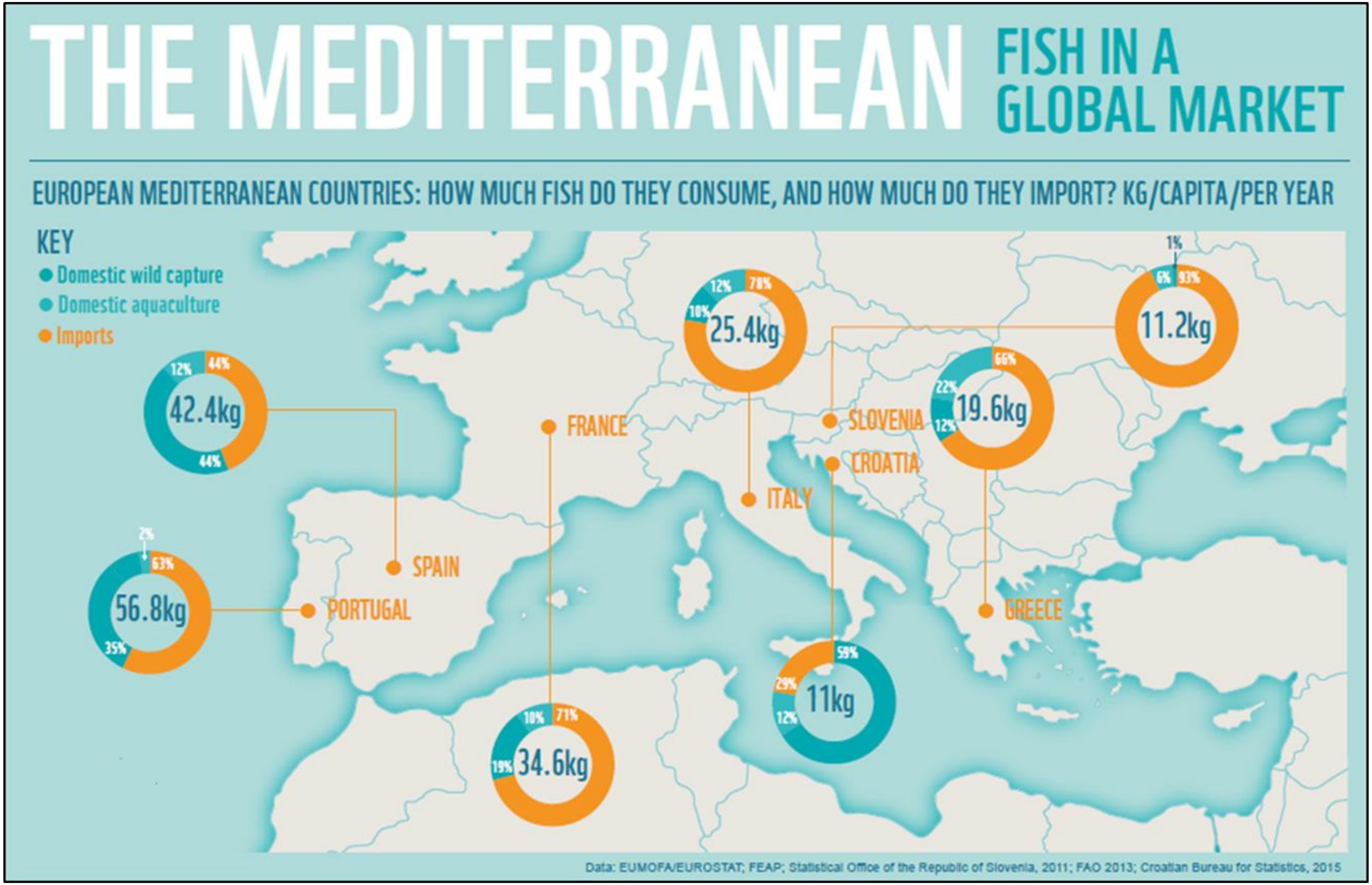
THE MEDITERRANEAN
FISH IN A GLOBAL MARKET
EUROPEAN MEDITERRANEAN COUNTRIES: HOW MUCH FISH DO THEY CONSUME, AND HOW MUCH DO THEY IMPORT? KG/CAPITA/PER YEAR
KEY
Domestic wild capture
Domestic aquaculture
Imports
42.4kg
12%
44%
44%
SPAIN
56.8kg
2%
63%
35%
PORTUGAL
FRANCE
34.6kg
10%
71%
19%
25.4kg
12%
78%
10%
ITALY
11.2kg
1%
6%
93%
SLOVENIA
19.6kg
66%
22%
12%
CROATIA
11kg
59%
29%
12%
GREECE
Data: EUMOFA/EUROSTAT; FEAP; Statistical Office of the Republic of Slovenia, 2011; FAO 2013; Croatian Bureau for Statistics, 2015

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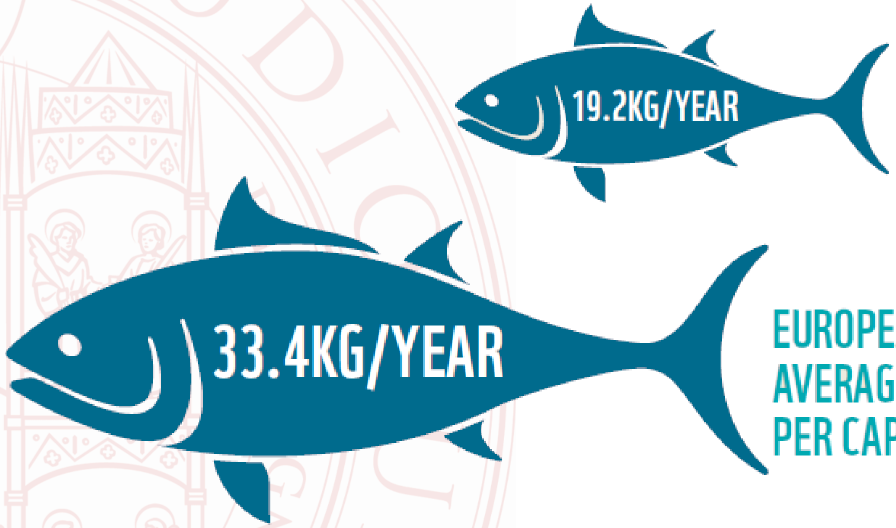
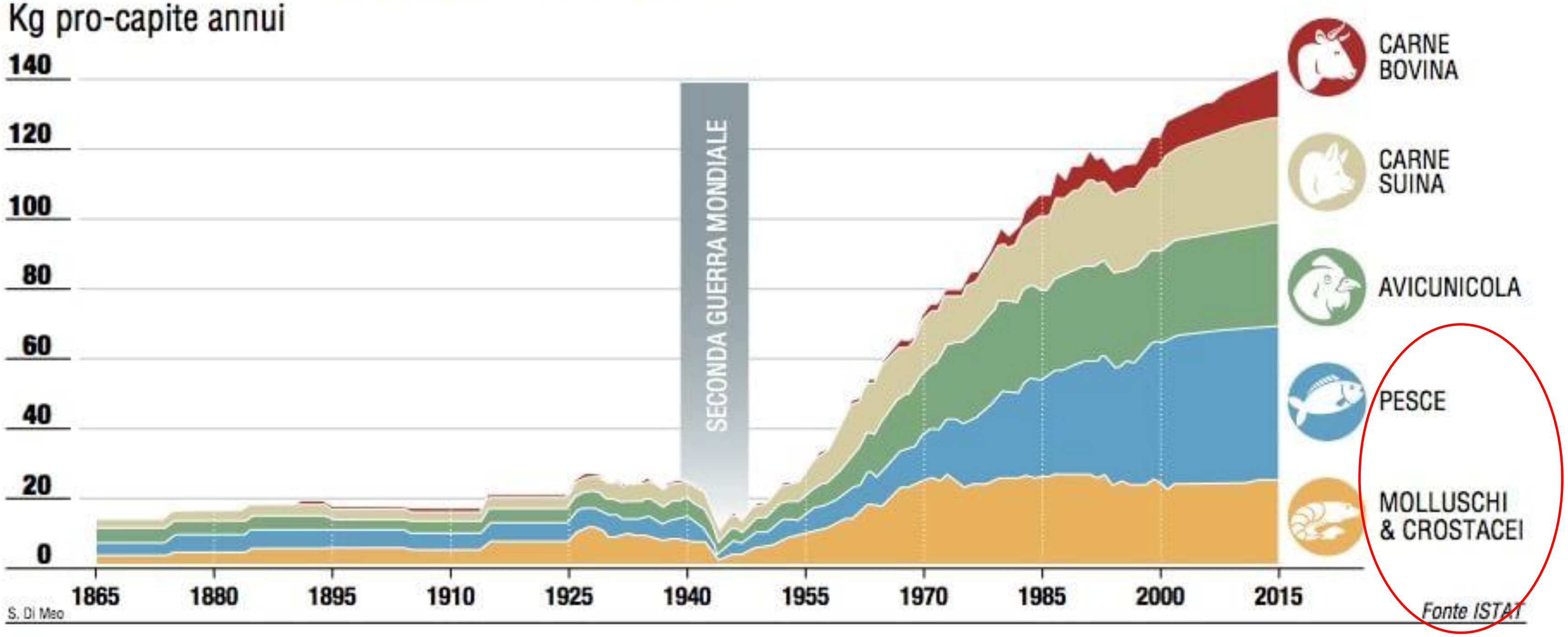


GLOBAL AVERAGE FISH CONSUMPTION PER CAPITA

EUROPEAN MEDITERRANEAN AVERAGE FISH CONSUMPTION PER CAPITA

I CONSUMI DI CARNE E PESCE IN ITALIA

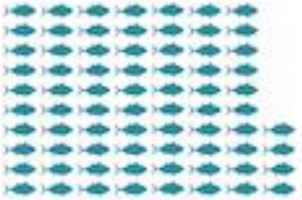


A global estimate of seafood consumption by coastal Indigenous peoples

Andrés M. Cisneros-Montemayor, Daniel Pauly,
Lauren V. Weatherdon, and Yoshitaka Ota, 2016.

Coastal Indigenous peoples:

74 kg per capita

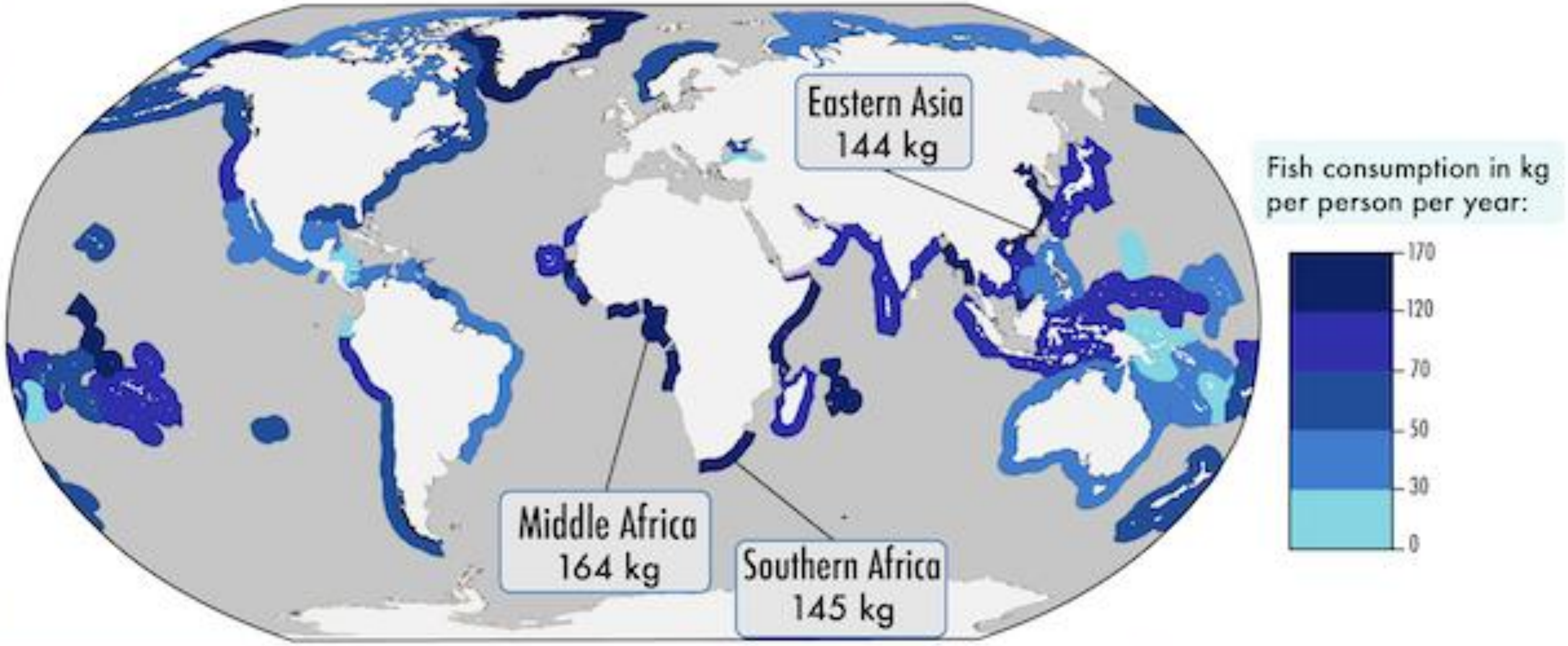


Global average:

19 kg per capita

Coastal Indigenous Peoples database:

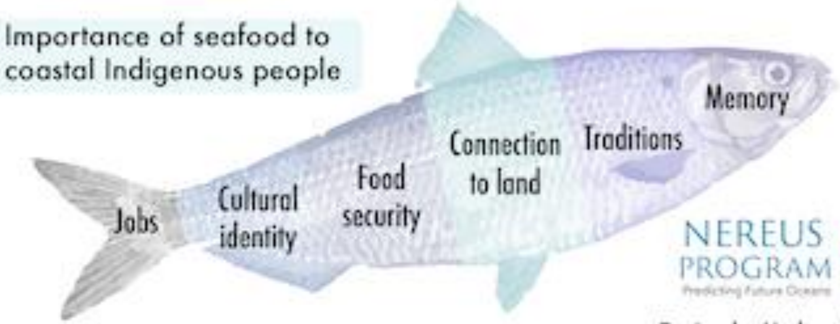
More than **1900** communities identified & **600** ethnic groups.



2.1 million metric tonnes

Coastal Indigenous people's consumption of seafood per year

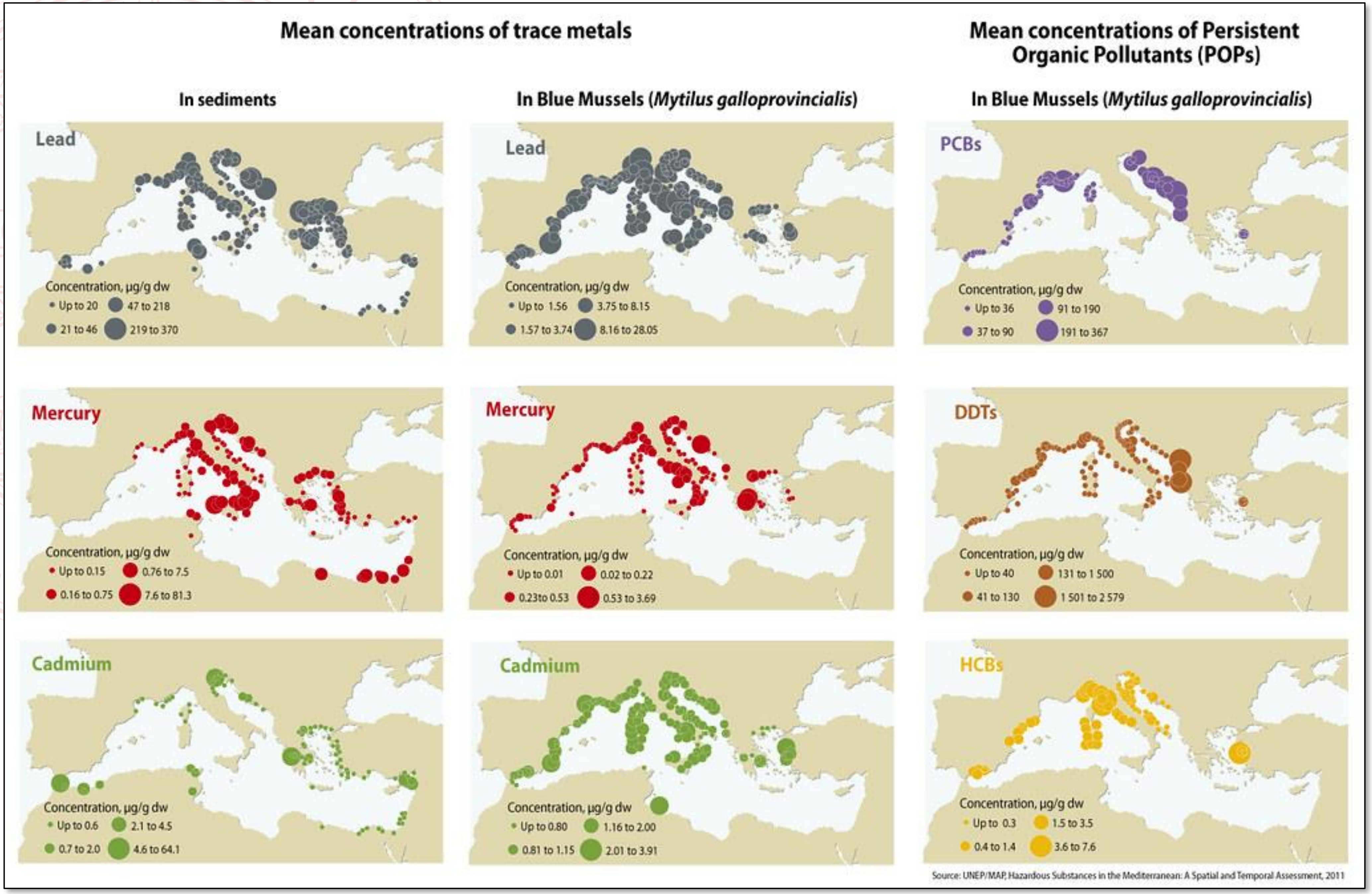
Importance of seafood to coastal Indigenous people



NEREUS PROGRAM Predicting Future Oceans

THE NIPPON FOUNDATION

Design by Lindsay Lafreniere


Mean concentrations of trace metals
Mean concentrations of Persistent Organic Pollutants (POPs)
In sediments
In Blue Mussels (Mytilus galloprovincialis)
In Blue Mussels (Mytilus galloprovincialis)
Lead
Concentration, µg/g dw
Up to 20
21 to 46
47 to 218
219 to 370
Lead
Concentration, µg/g dw
Up to 1.56
1.57 to 3.74
3.75 to 8.15
8.16 to 28.05
PCBs
Concentration, µg/g dw
Up to 36
37 to 90
91 to 190
191 to 367
Mercury
Concentration, µg/g dw
Up to 0.15
0.16 to 0.75
0.76 to 7.5
7.6 to 81.3
Mercury
Concentration, µg/g dw
Up to 0.01
0.23to 0.53
0.02 to 0.22
0.53 to 3.69
DDTs
Concentration, µg/g dw
Up to 40
41 to 130
131 to 1 500
1 501 to 2 579
Cadmium
Concentration, µg/g dw
Up to 0.6
0.7 to 2.0
2.1 to 4.5
4.6 to 64.1
Cadmium
Concentration, µg/g dw
Up to 0.80
0.81 to 1.15
1.16 to 2.00
2.01 to 3.91
HCBs
Concentration, µg/g dw
Up to 0.3
0.4 to 1.4
1.5 to 3.5
3.6 to 7.6
Source: UNEP/MAP, Hazardous Substances in the Mediterranean: A Spatial and Temporal Assessment, 2011

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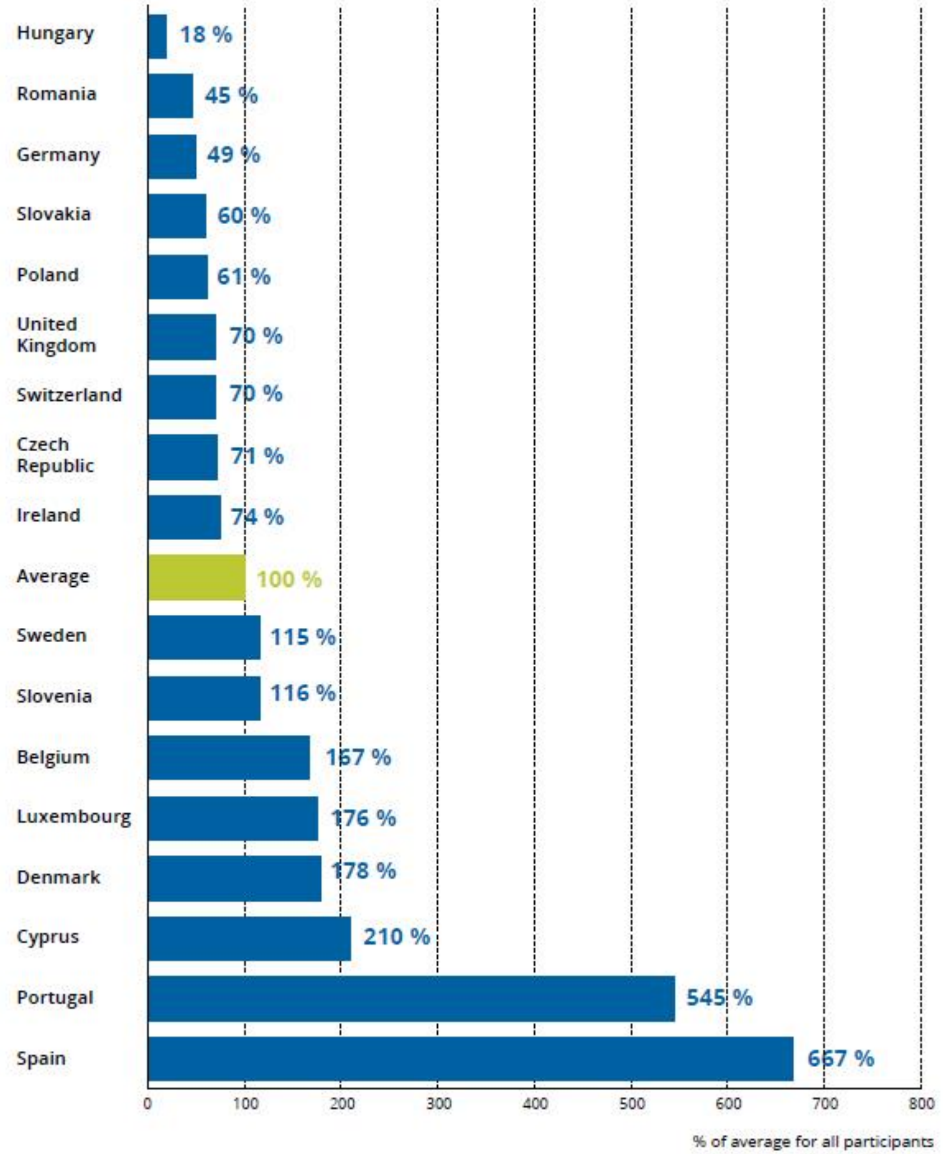
Mercury levels in hair of mothers as a percentage of the Europe-wide average

Mediterranean countries



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

Received: 16 November 2017 | Revised: 21 April 2018 | Accepted: 27 April 2018
DOI: 10.1111/faf.12295

ORIGINAL ARTICLE

WILEY FISH and FISHERIES

FishMed-PhD

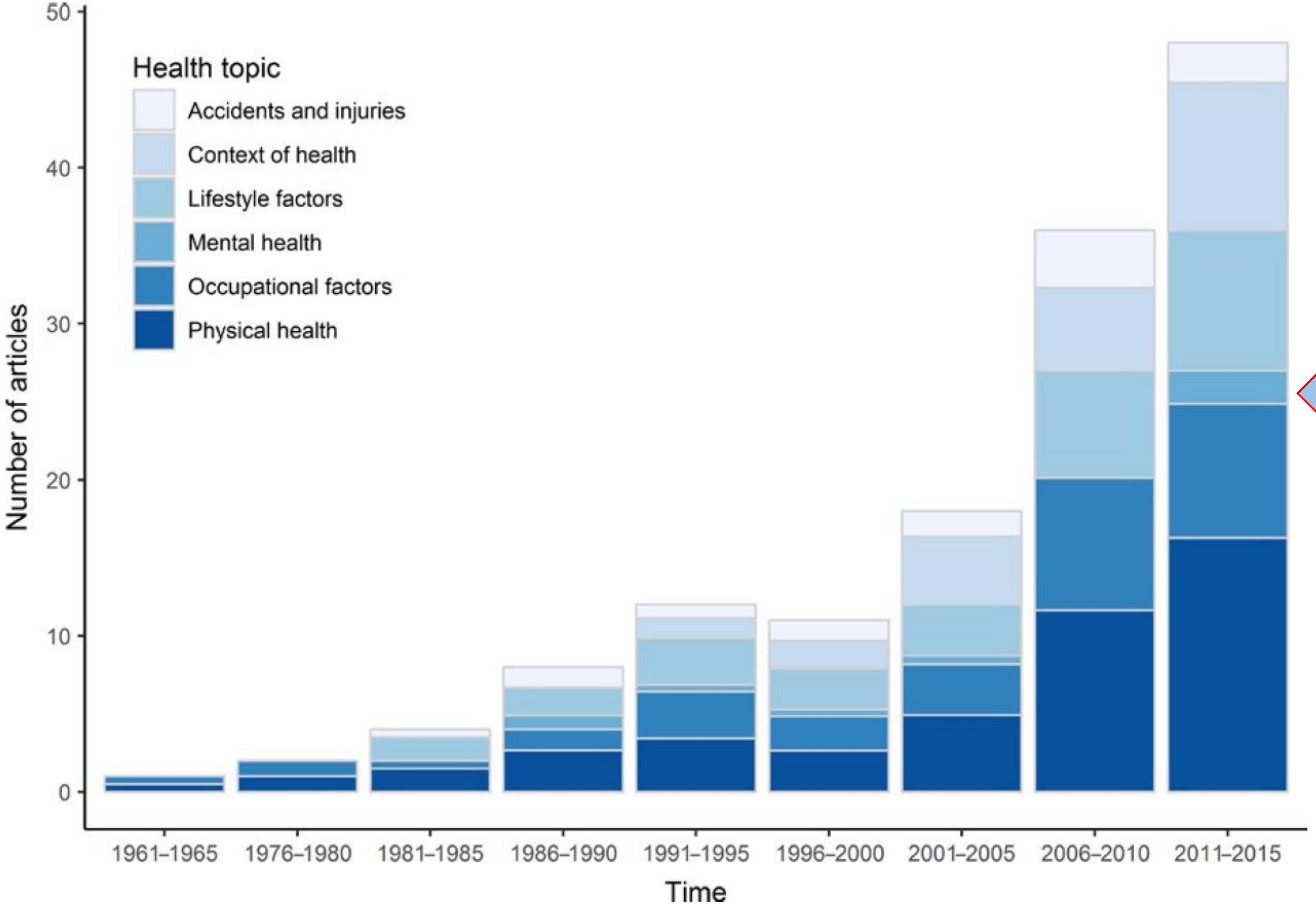
Health in fishing communities: A global perspective

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.**



mental health

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Take home message

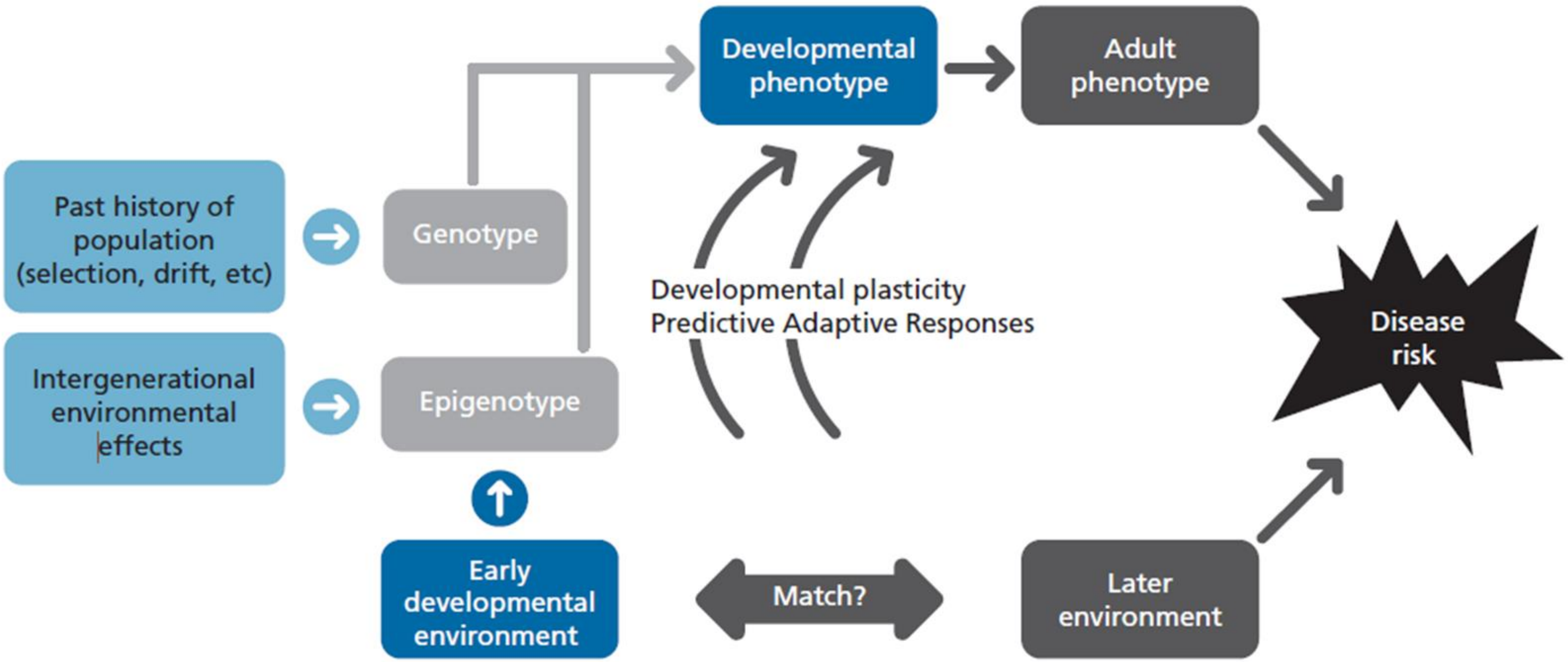

Figure 4.4 Disease risk in adulthood is influenced by a complex interplay between an organism's early developmental environment, later environment, intergenerational effects, and its evolutionary history. These factors shape the genetic and epigenetic repertoires to contribute to a particular developmental 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.

Thank you for your attention

aDNALab, Department of Cultural Heritage

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