Evoluční medicína

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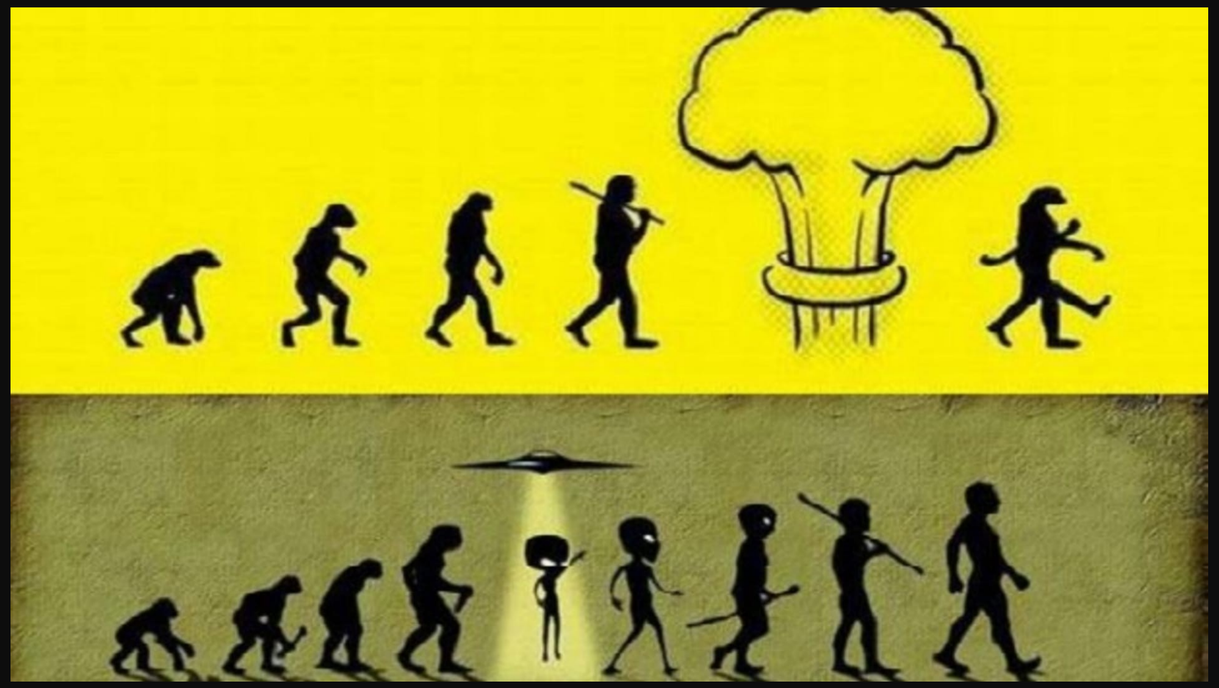
TOTALFILM
1080p
FULLHD
TRAILER CZ

Co je evoluční medicína?

- Evoluční medicína neboli darwinovská medicína je aplikací moderní evoluční teorie k pochopení zdraví a nemoci.
- Moderní biomedicínský výzkum a praxe se soustředily na molekulární a fyziologické mechanismy, které jsou základem zdraví a nemoci,
- zatímco evoluční medicína se zaměřuje na otázku, proč evoluce utvářela tyto mechanismy způsobem, který nás může zanechat náchylný k nemocem.
- Evoluční přístup vedl k důležitým pokrokům v chápání rakoviny,] autoimunitních onemocnění[a anatomie . Mezinárodní společnost pro evoluci, medicínu a veřejné zdraví koordinuje úsilí o rozvoj tohoto oboru.
- Vlastní časopis **Oxford University Press** *Evolution, Medicine* and Public Health a The Evolution and Medicine Review.



Kdy?

Začátky oboru byly těžké, ale za stěžejní publikace, která definovali nový obor jsou považována následující dvě díla:

VOLUME 66, NO. 1 MARCH 1991

THE QUARTERLY REVIEW of BIOLOGY

THE DAWN OF DARWINIAN MEDICINE

GEORGE C. WILLIAMS

Department of Ecology & Evolution, Division of Biological Sciences, State University of Stony Brook, Stony Brook, New York 11794-5245 USA

RANDOLPH M. NESSE

Department of Psychiatry, University of Michigan Medical School, Room C440, Med-Inn Bldg., 1500 E. Medical Center Dr., Ann Arbor, Michigan 48109-0840 USA

ABSTRACT

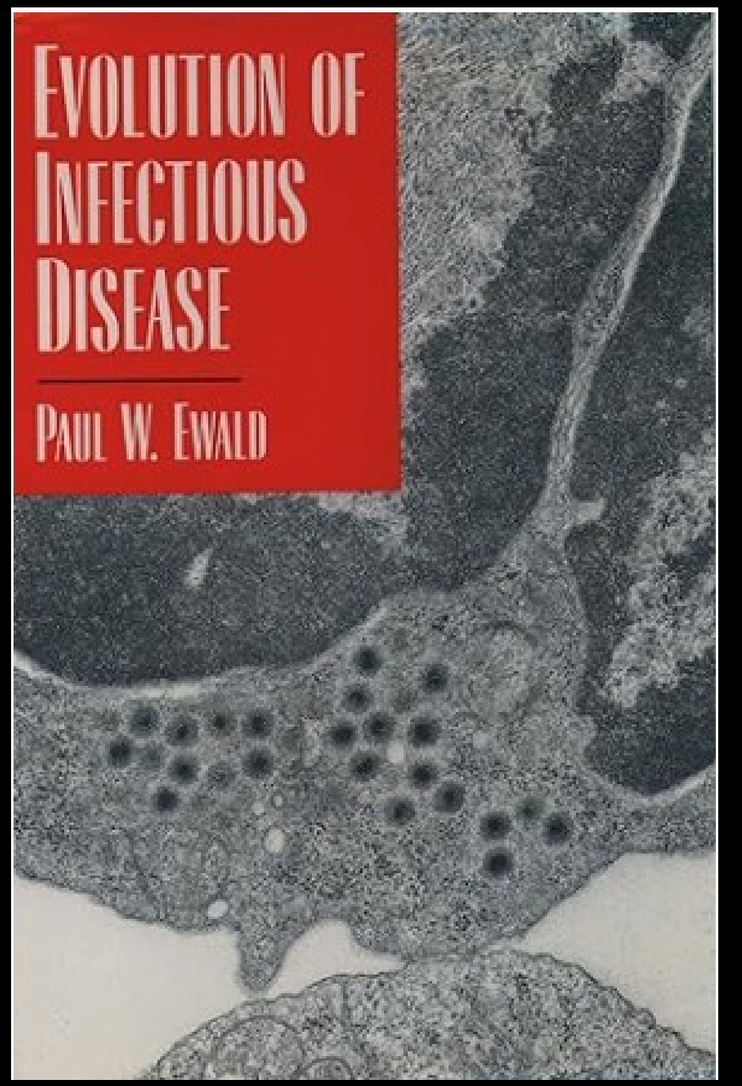
While evolution by natural selection has long been a foundation for biomedical science, it has recently gained new power to explain many aspects of disease. This progress results largely from the disciplined application of what has been called the adaptationist program. We show that this increasingly significant research paradigm can predict otherwise unsuspected facets of human biology, and that it provides new insights into the causes of medical disorders, such as those discussed below:

1. Infection. Signs and symptoms of the host-parasite contest can be categorized according to whether they represent adaptations or costs for host or parasite. Some host adaptations may have contributed to fitness in the Stone Age but are obsolete today. Others, such as fever and iron sequestration, have been incorrectly considered harmful. Pathogens, with their large populations and many generations in a single host, can evolve very rapidly. Acquisition of resistance to antibiotics is one example. Another is the recently demonstrated tendency to change virulence levels in predictable ways in response to changed conditions imposed incidentally by human activities.

2. Injuries and toxins. Mechanical injuries or stressful wear and tear are conceptually simpler than infectious diseases because they are not contests between conflicting interests. Plant-herbivore contests may often underlie chemical injury from the defensive secondary compounds of plant tissues. Nausea in pregnancy, and allergy, may be adaptations against such toxins.

3. Genetic factors. Common genetic diseases often result from genes maintained by other beneficial effects in historically normal environments. The diseases of aging are especially likely to be associated with early benefits.

4. Abnormal environments. Human biology is designed for Stone Age conditions. Modern en-



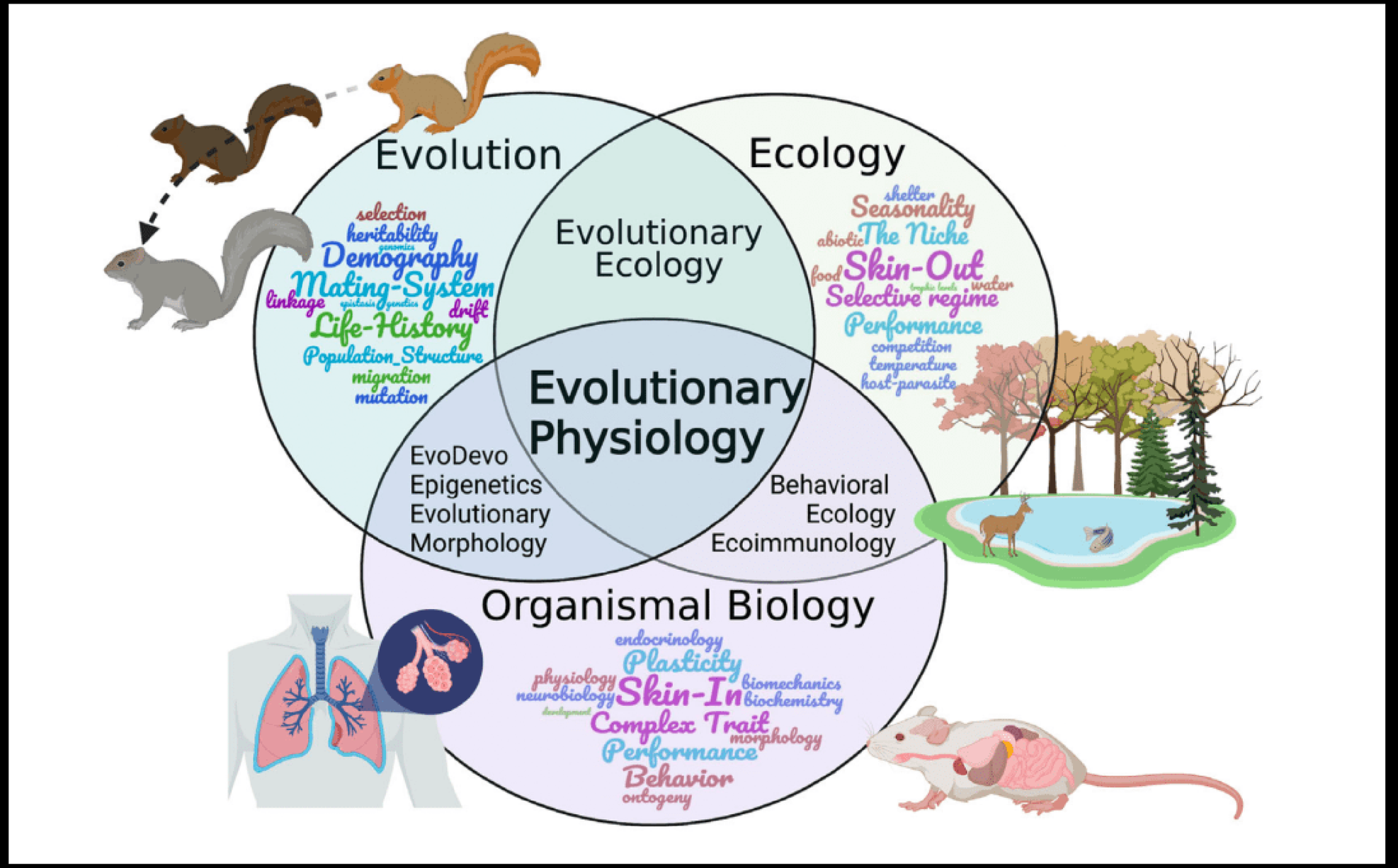
Definice evoluční medicíny

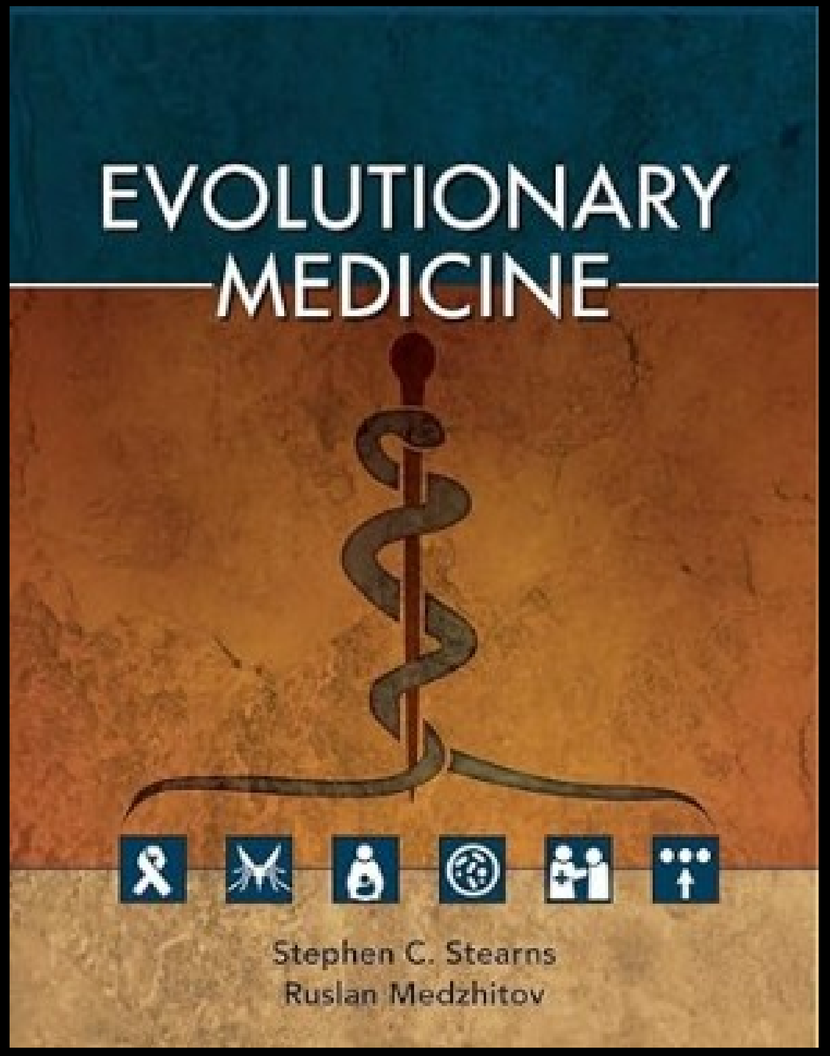
- **56 odborníků** z různých oborů (antropologové, lékaři, ošetřovatelé, biologové, paleontologové, archeologové) se dohodlo na 14 základních principech, které jsou důležité pro výuku, bádání a praxi evoluční medicíny,

- těchto **14 principů** lze dále seskupit do pěti obecných kategorií:

- **Typy vysvětlení (rámování otázek):** K úplnému biologickému pochopení vlastností, včetně těch, které zvyšují zranitelnost vůči nemocem, jsou zapotřebí jak přibližná (mechanistická), tak konečná (evoluční) vysvětlení.
- **Evoluční procesy (evoluce I):** Všechny evoluční procesy, včetně přirozeného výběru, genetického driftu, mutace, migrace a nenáhodného páření, jsou důležité pro pochopení vlastností a nemocí.
- **Reprodukční úspěch (evoluce I):** Přírodní výběr maximalizuje reprodukční úspěch, někdy na úkor zdraví a dlouhověkosti.
- **Sexuální výběr (evoluce I):** Sexuální výběr formuje rysy, které mají za následek různá zdravotní rizika mezi pohlavími.
- **Omezení (evoluce I):** Několik omezení brání schopnosti přirozeného výběru utvářet vlastnosti, které jsou hypoteticky optimální pro zdraví.
- **Kompromisy (evoluční kompromisy):** Evoluční změny v jedné vlastnosti, které zlepšují kondici, mohou být spojeny se změnami v jiných vlastnostech, které kondici snižují.
- **Teorie životní historie (evoluční kompromisy):** Vlastnosti životní historie, jako je věk při prvním rozmnožování, reprodukční délka života a rychlost stárnutí, jsou utvářeny evolucí a mají důsledky pro zdraví a nemoci.
- **Úrovně selekce (evoluce II):** Zranitelnost vůči chorobám může nastat, když má selekce protichůdné účinky na různých úrovních (např. genetické prvky, buňky, organismy, příbuzní a další úrovně).
- **Fylogeneze (evoluce II):** Sledování fylogenetických vztahů pro druhy, populace, znaky nebo patogeny může poskytnout pohled na zdraví a nemoci.

- **Koevoluce (evoluce II):** Koevoluce mezi druhy může ovlivnit zdraví a nemoci (např. evoluční závody ve zbrojení a vzájemné vztahy, jako jsou ty, které lze vidět v mikrobiomu).
- **Plasticita (evoluce II):** Faktory prostředí mohou posunout vývojové trajektorie způsoby, které ovlivňují zdraví, a plasticita těchto trajektorií může být produktem vyvinutých adaptivních mechanismů.
- **Obrany (důvody zranitelnosti):** Mnoho příznaků a symptomů onemocnění (např. horečka) je užitečným obranným prostředkem, který může být patologický, pokud je dysregulován.
- **Nesoulad (důvody zranitelnosti):** Rizika onemocnění mohou být změněna pro organismy žijící v prostředí, které se liší od prostředí, ve kterém se vyvinuli jejich předkové.
- **Kulturní praktiky (kultura):** Kulturní praktiky mohou ovlivnit evoluci lidí a jiných druhů (včetně patogenů) způsoby, které mohou ovlivnit zdraví a nemoci (např. užívání antibiotik, porodní praktiky, strava atd.).


Evolution
selection
heritability
genomics
Demography
Mating-System
linkage
epistasis
genetics
drift
Life-History
Population_Structure
migration
mutation
Ecology
shelter
Seasonality
abiotic
The Niche
food
Skin-Out
trophic levels
water
Selective regime
Performance
competition
temperature
host-parasite
Evolutionary Ecology
Evolutionary Physiology
EvoDevo
Epigenetics
Evolutionary Morphology
Behavioral Ecology
Ecoimmunology
Organismal Biology
endocrinology
Plasticity
physiology
neurobiology
Skin-In
biomechanics
biochemistry
development
Complex Trait
morphology
Performance
Behavior
ontogeny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Stephen C. Stearns
Ruslan Medzhitov


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EVIDENCE-BASED
EVOLUTIONARY
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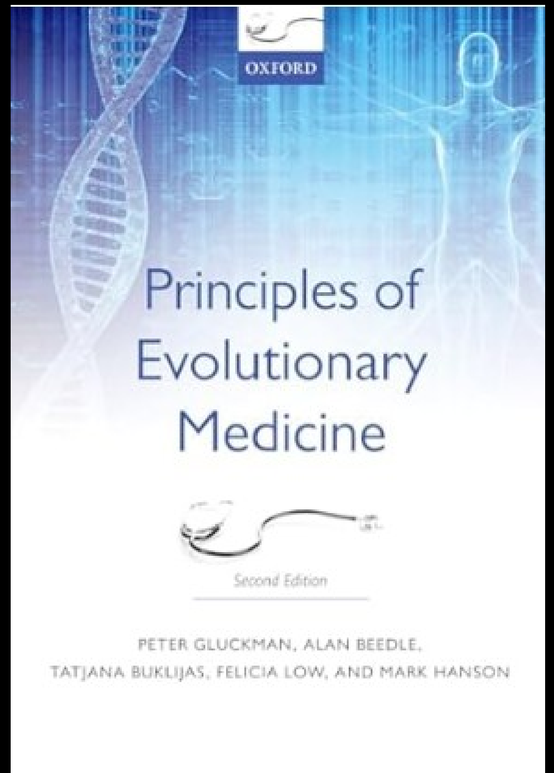
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Medicine
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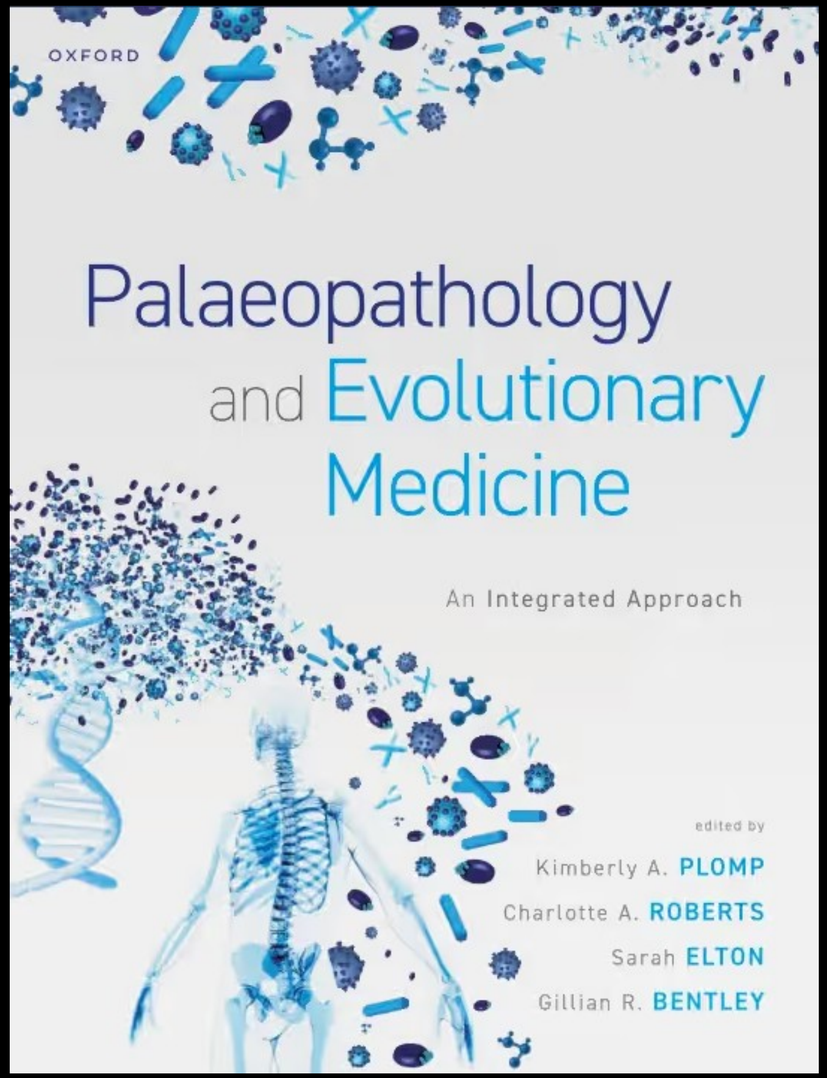
TATJANA BUKLIJAS, FELICIA LOW, AND MARK HANSON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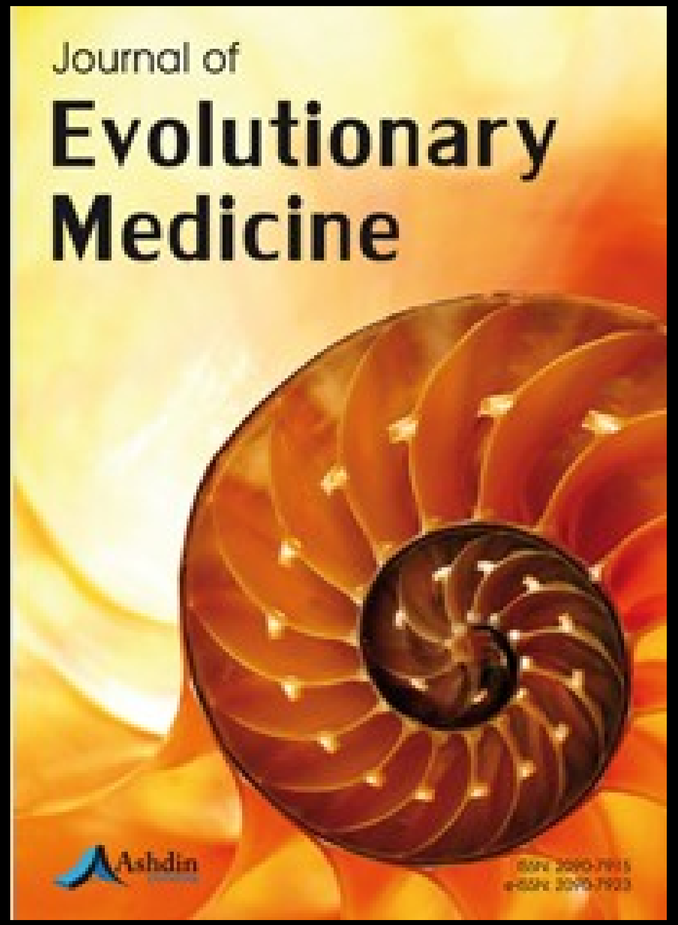

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...bridging the gap

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EVOLUTION, MEDICINE, & PUBLIC HEALTH

The Oxford Press open access journal *Evolution, Medicine & Public Health* has published eight new Clinical Briefs in 2019. They are lovely one page summaries that are perfect for teaching...or just pleasure reading.

The shapes of virulence to come
Aakash Pandey, Daniel E Dawson*Evol Med Public Health*, Volume 2019, Issue 1, 2019, Page 3, https://doi.org/10.1093/emph/eoy037

Tandem repeat disorders
Calen P Ryan*Evol Med Public Health*, Volume 2019, Issue 1, 2019, Page

About The Evolution & Medicine Review

The International Society for Evolution, Medicine, and Public Health

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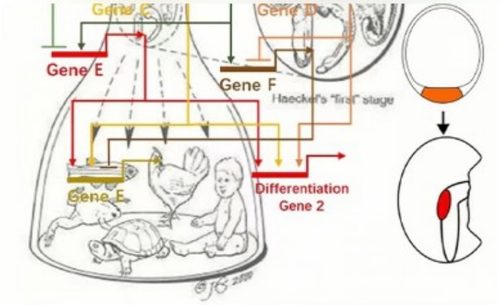
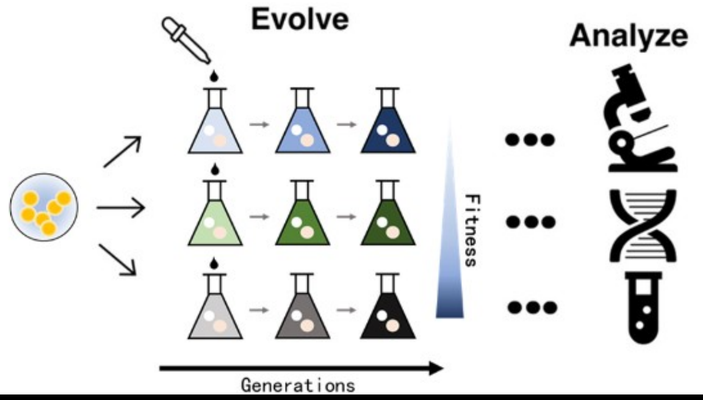
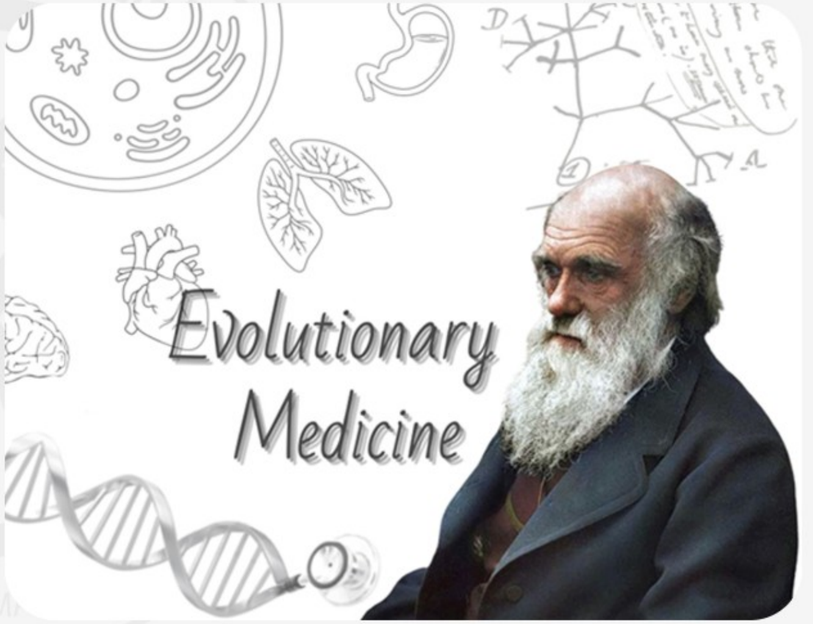


Marcoevolutionary developmental biology



Genomic evolution of major transition



Evolutionary implication on medicine

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Focus area EVOLUTIONARY MEDICINE
Focus area INFLAMMATION
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Elective: Imaging
Elective: MolOcular - Inflammatory and degenerative diseases of the eye
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Focus area EVOLUTIONARY MEDICINE

Medical Life Sciences is one of the few Master programmes worldwide with a focus on **Evolutionary Medicine**. It has been part of Medical Life Sciences form the start, and for a reason.

Diseases can be puzzling. Why certain conditions occur or how to treat them are often questions for which the answers are still pending. When regarding these questions from an evolutionary perspective, researchers often find answers.

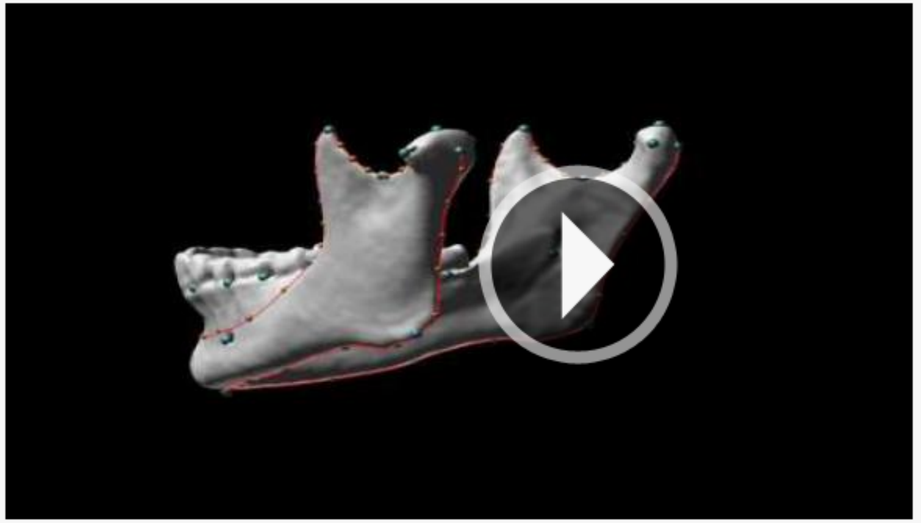
Understanding something that first seemed incomprehensible is a powerful experience. It makes progress possible and leads to new approaches, which is very important in medicine to prevent, diagnose and treat medical conditions. Evolutionary Medicine helps create opportunities to do so.

Bringing together evolution and medicine gets fascinating once you start looking at cancer, allergies, ageing, autoimmune disorders or chronic diseases: Why do we suffer from chronic conditions such as diabetes, heart disease or obesity? Why do pathogens develop drug resistance? Can we do something against it? How do our gut bacteria and diet influence our health? The more questions you try to answer, the more intriguing it gets.
You study the connections between evolution and medicine - developing hypotheses, connecting the dots and getting ready to conduct research yourself in your thesis and beyond: Evolutionary Medicine is one of the biggest drivers in today's biomedicine.

In Kiel, you are extremely well positioned for plunging into Evolutionary Medicine - or EvoMed for short:

- Medical Life Sciences has been teaching EvoMed since the programme started, with professors hosting seminars for students, running international research projects and supervising students in their thesis work. As an EvoMed student, you will be involved in research from the start.
- EvoMed lecturers are investigators in the ROOTS Cluster of Excellence. This huge interdisciplinary research project at Kiel University revolves around human societies through history. One big aspect is health. EvoMed researchers investigate how humans adapted to

Biohistory & Evolutionary Medicine Laboratory



Dr. Hila May

Our biohistory and evolutionary medicine laboratory focuses on several fields of interest:

- **Evolutionary medicine**: The impact of the "trade off" mechanism on present human health. Many parts of our body had to accommodate themselves in order to facilitate the development of our large brain and erect posture.
- **Biohistory**: Much of our history is recorded in our bones. Advanced methodologies allow us to reconstruct important events on the individual level as well as on the population level. This includes daily lifestyles, health, nutrition, inter or intra-personal violence, labor intensity, demographical structure, etc.
- **Ancient DNA**: The reconstruction of past population structure and migration. The Levant witnessed dramatic population movements and replacements during the last 15,000 years, which shaped the region's history.

Related Links

- Dan David Center for Human Evolution and Biohistory Research
- Shmunis Family Anthropology Institute
- Faculty of Medicine
- Department of Anatomy & Anthropology
- School of Dental Medicine
- Steinhardt Museum of Natural History
- Gitter-Smolarz Library of Life Sciences and Medicine

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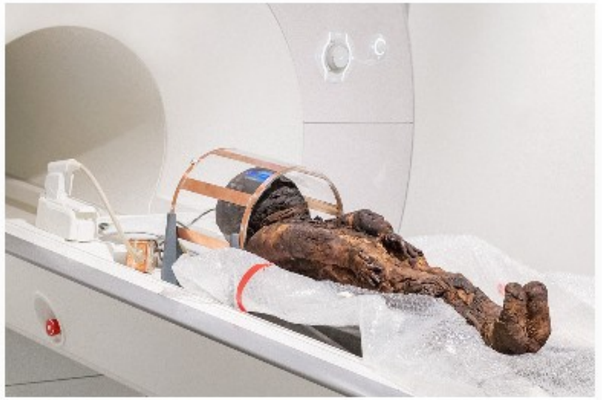

The Institute →

- → Definition of Evolutionary Medicine
- → Vision
- → Mission Statement
- → Institute's Regulations
- → Institute Structure
- → Facilities

People →

- → Directorate
- → Evolutionary Pathophysiology & Mummy Studies Group ☛ Prof. Frank Rühli, PD Patrick Eppenberger
- → Human Ecology Group ☛ Prof. Adrian Jäggi

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- → Research Groups
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- → Selected Publications
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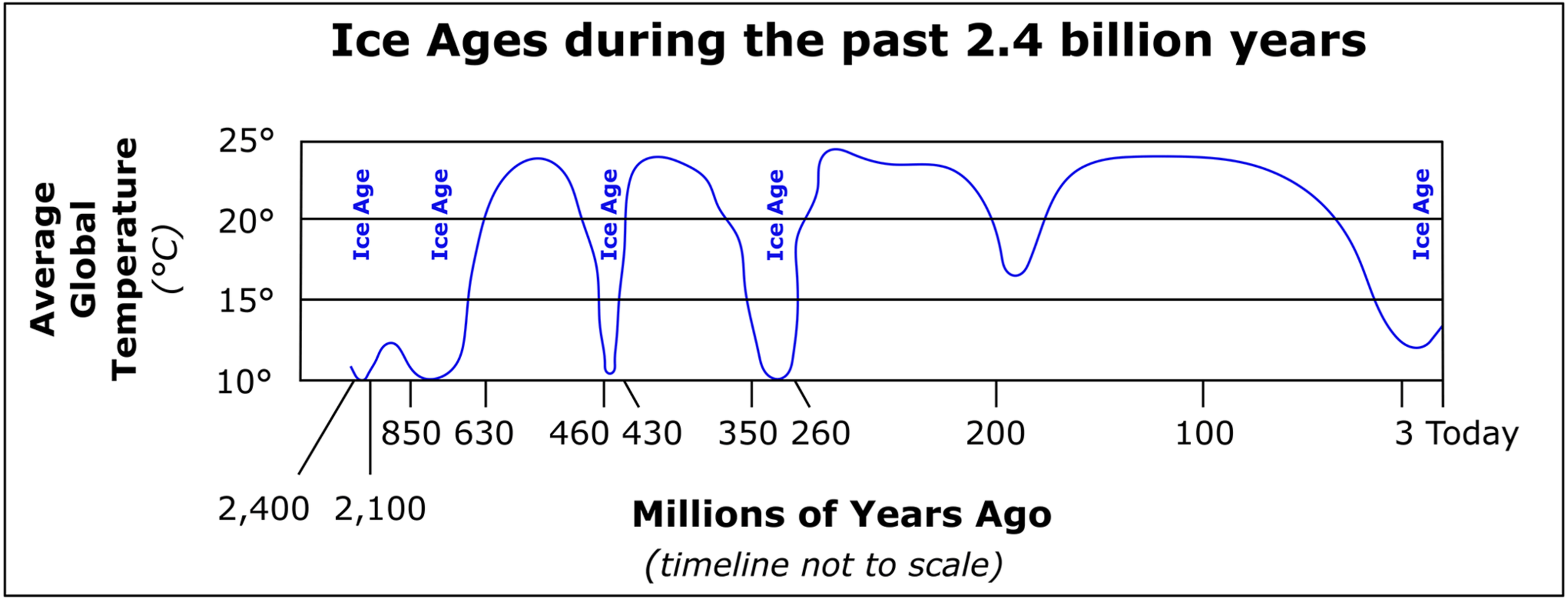
Svante Pääbo

Things to know about the geneticist who won this year's Nobel Prize in Physiology or Medicine

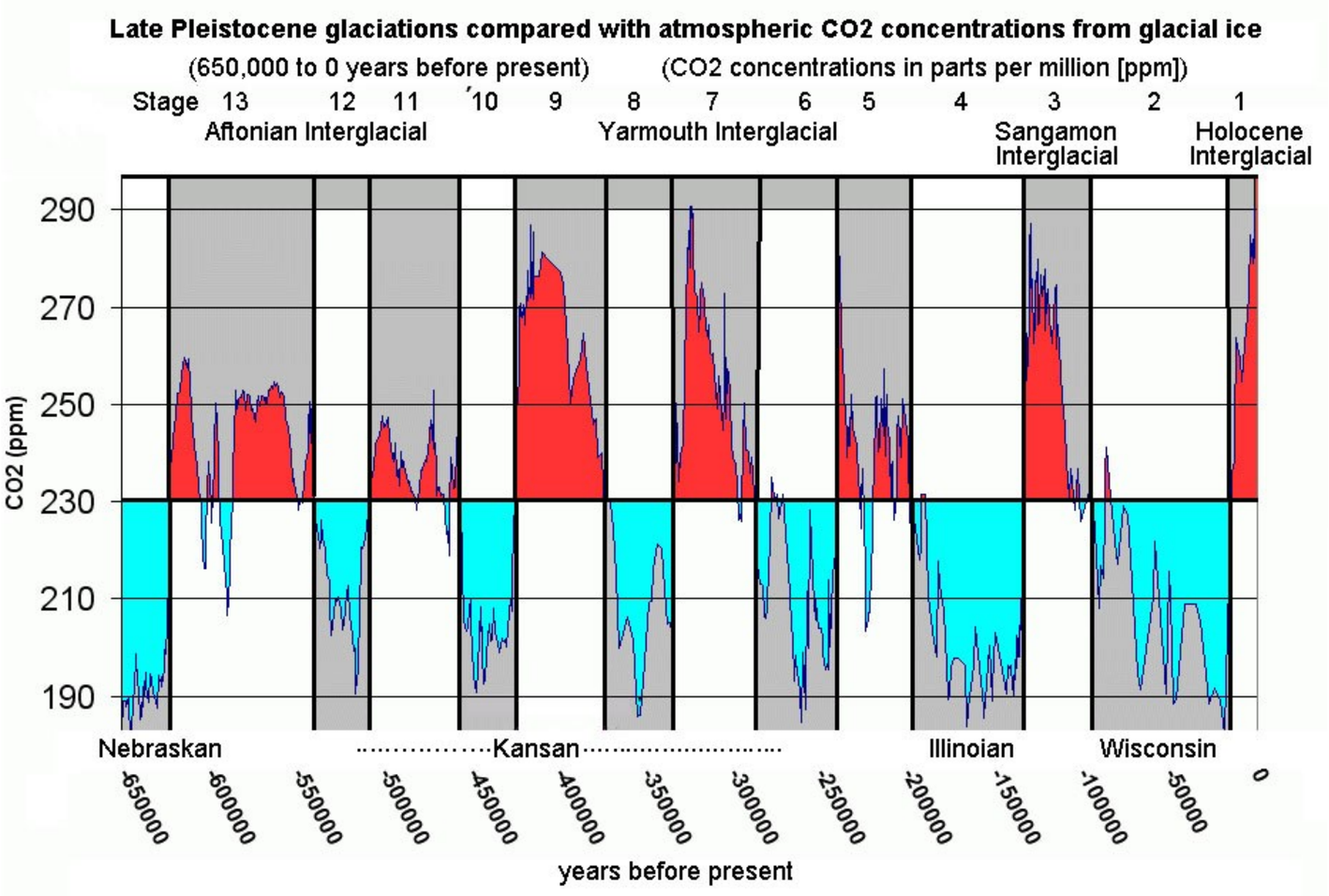
NEWS18 creative

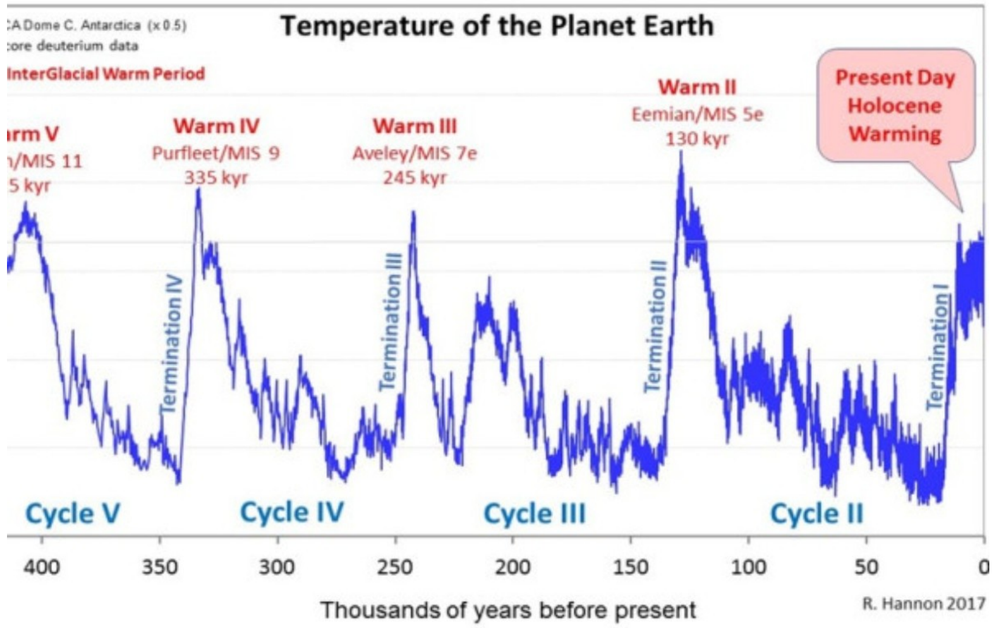
Co nám předali neandertálci

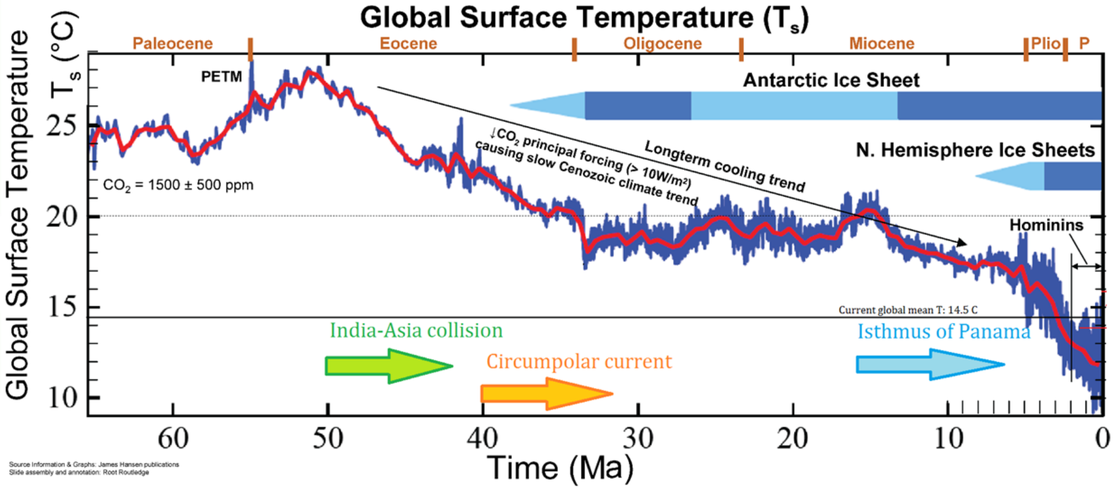
Doby ledové


Ice Ages during the past 2.4 billion years
Average Global Temperature (°C)
25°
20°
15°
10°
Ice Age
Ice Age
Ice Age
Ice Age
Ice Age
850 630
460 430
350 260
200
100
3 Today
2,400
2,100
Millions of Years Ago
(timeline not to scale)

Doby ledové


Late Pleistocene glaciations compared with atmospheric CO2 concentrations from glacial ice
(650,000 to 0 years before present)
(CO2 concentrations in parts per million [ppm])
Stage 13 12 11 10 9 8 7 6 5 4 3 2 1
Aftonian Interglacial
Yarmouth Interglacial
Sangamon Interglacial
Holocene Interglacial
CO2 (ppm)
290
270
250
230
210
190
Nebraskan
Kansan
Illinoian
Wisconsin
650000 600000 550000 500000 450000 400000 350000 300000 250000 200000 150000 100000 50000 0
years before present


A Dome C. Antarctica (x 0.5)
ore deuterium data
InterGlacial Warm Period
Temperature of the Planet Earth
rm V
/MIS 11
5 kyr
Warm IV
Purfleet/MIS 9
335 kyr
Warm III
Aveley/MIS 7e
245 kyr
Warm II
Eemian/MIS 5e
130 kyr
Present Day
Holocene
Warming
Termination IV
Termination III
Termination II
Termination I
Cycle V
Cycle IV
Cycle III
Cycle II
400 350 300 250 200 150 100 50 0
Thousands of years before present
R. Hannon 2017


Global Surface Temperature (T$_s$)
Paleocene
Eocene
Oligocene
Miocene
Plio
P
PETM
Antarctic Ice Sheet
N. Hemisphere Ice Sheets
↓CO$_2$ principal forcing (> 10W/m^2) causing slow Cenozoic climate trend
Longterm cooling trend
CO$_2$ = 1500 ± 500 ppm
Hominins
Current global mean T: 14.5 C
India-Asia collision
Circumpolar current
Isthmus of Panama
Global Surface Temperature T$_s$ (°C)
25
20
15
10
60 50 40 30 20 10 0
Time (Ma)
Source information & Graphs: James Hansen publications
Slide assembly and annotation: Rodd Routledge

Doby ledové

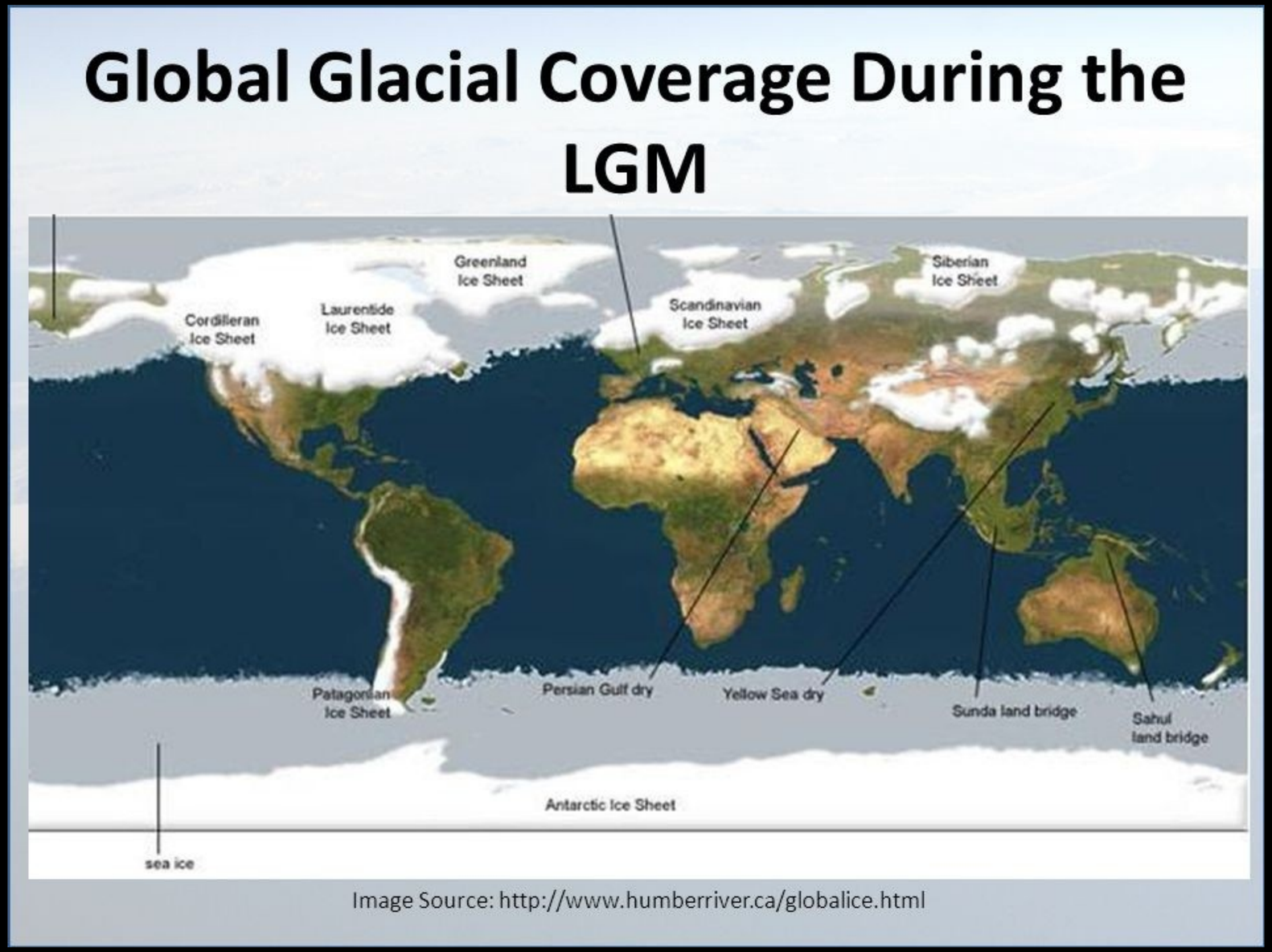
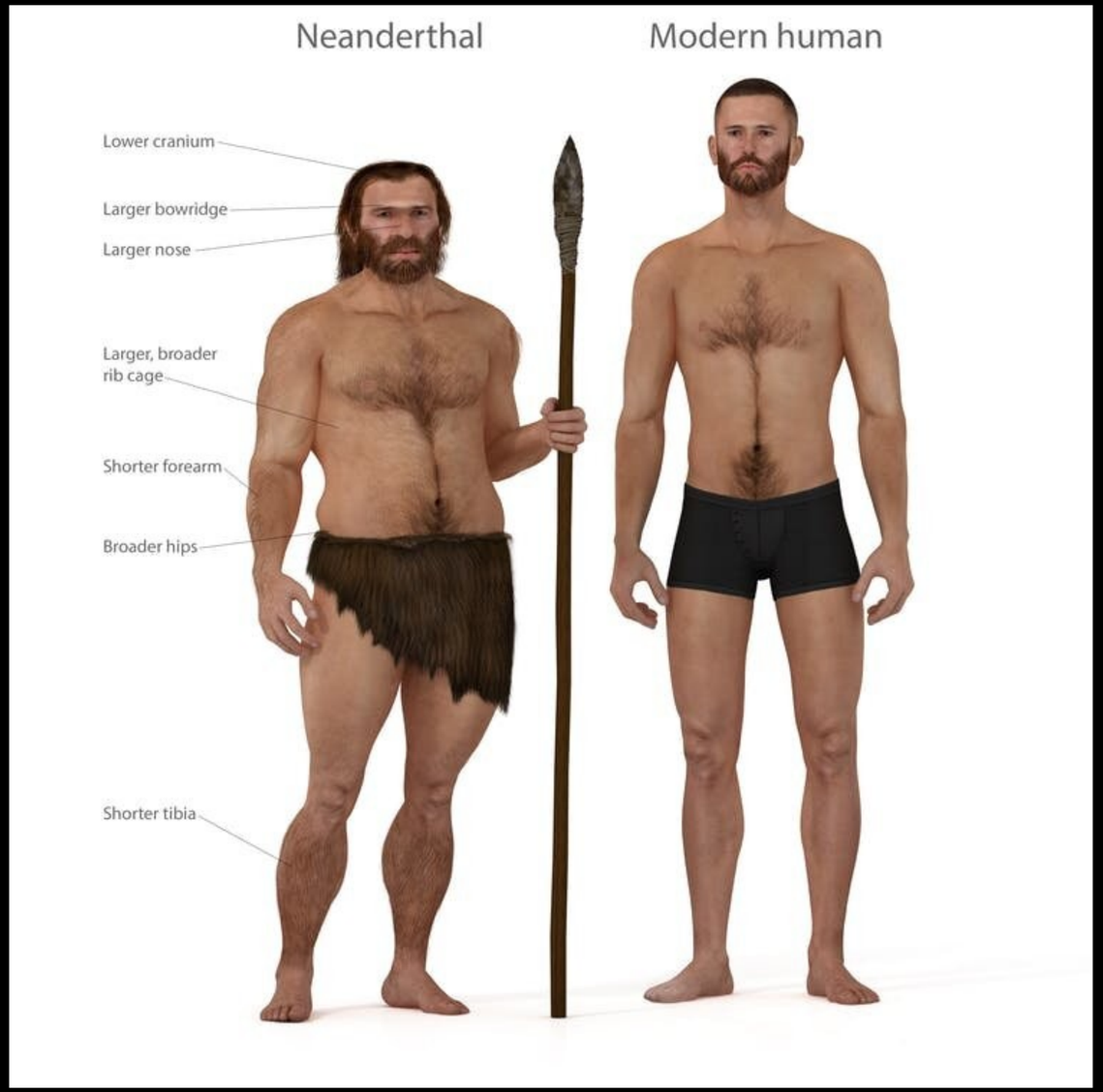
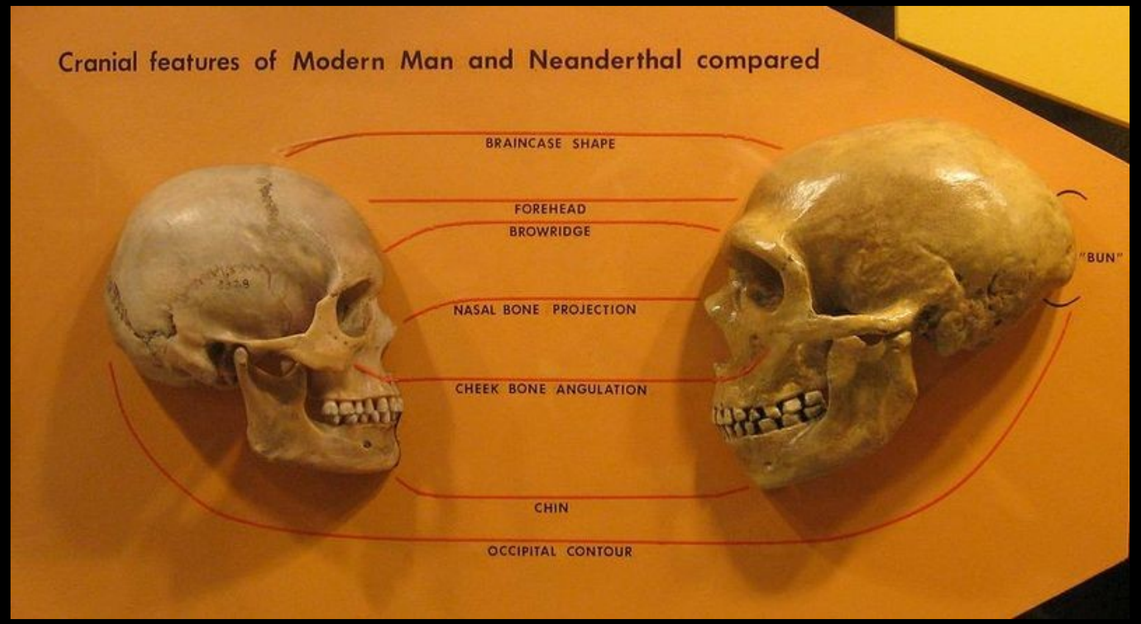
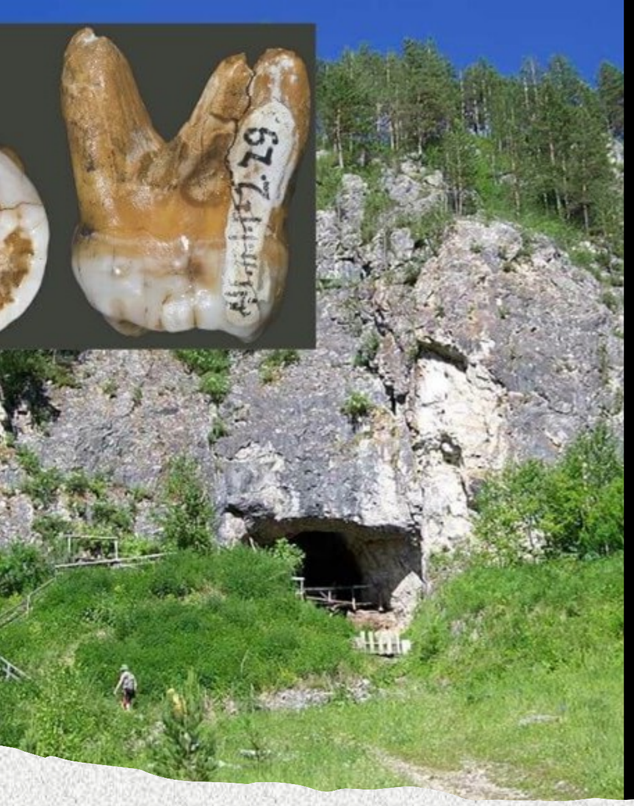


Image Source: http://www.humberriver.ca/globalice.html

Člověk neandertálský – *Homo neanderthalesis*

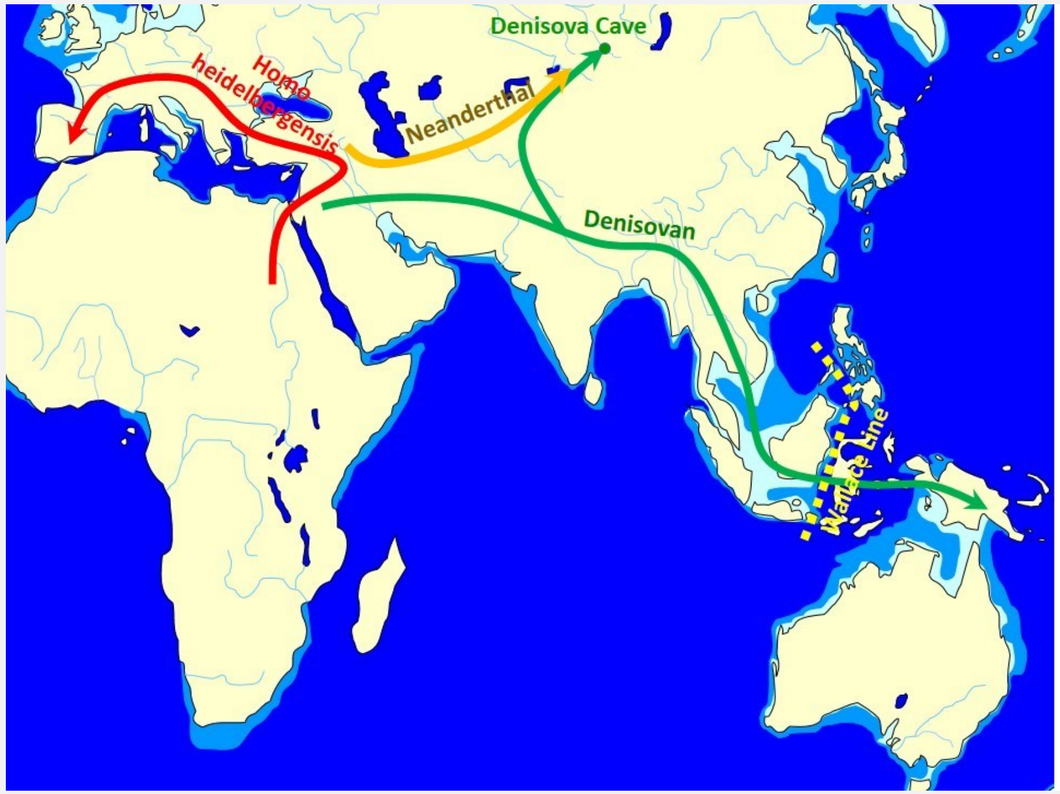

Neanderthal
Modern human
Lower cranium
Larger bowridge
Larger nose
Larger, broader rib cage
Shorter forearm
Broader hips
Shorter tibia

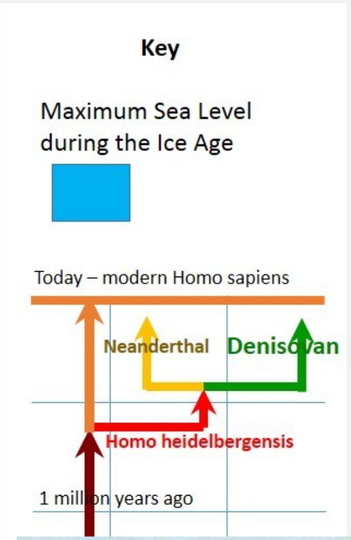

Cranial features of Modern Man and Neanderthal compared
BRAINCASE SHAPE
FOREHEAD
BROWRIDGE
"BUN"
NASAL BONE PROJECTION
CHEEK BONE ANGULATION
CHIN
OCCIPITAL CONTOUR

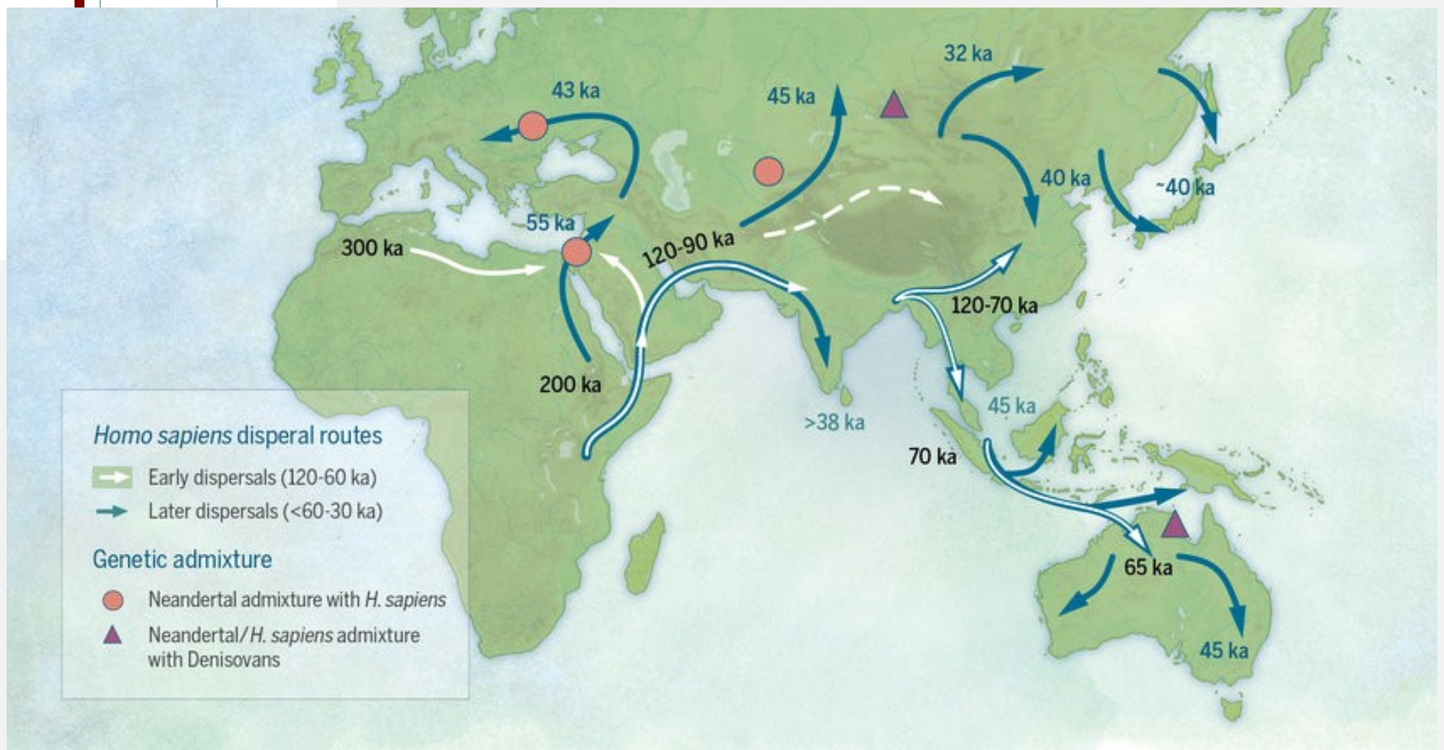


Homo denisoviensis

Migrace moderního člověka







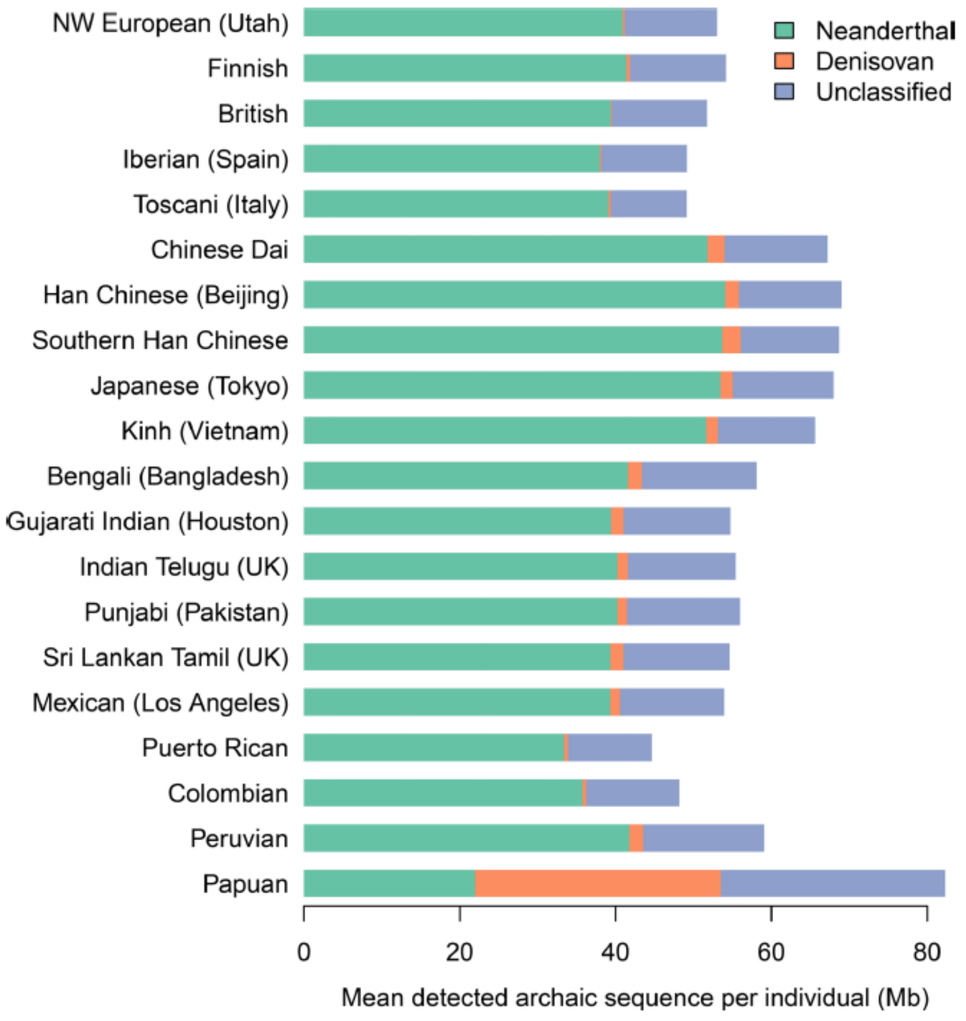
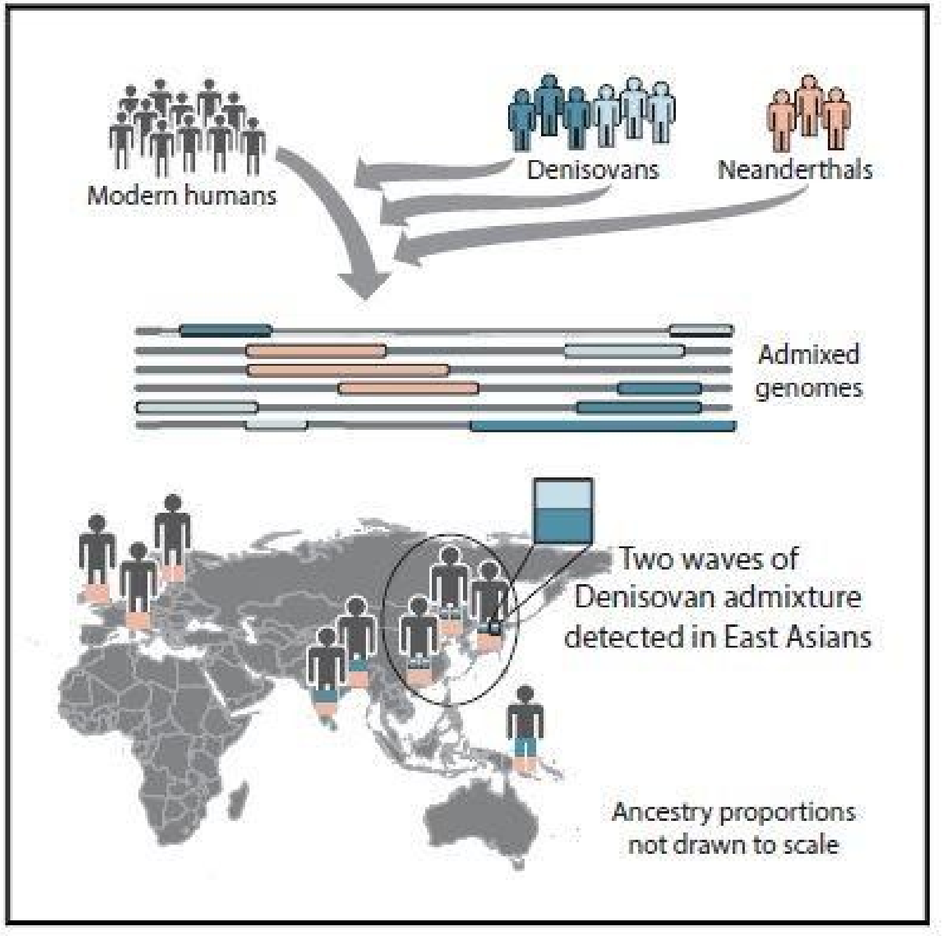
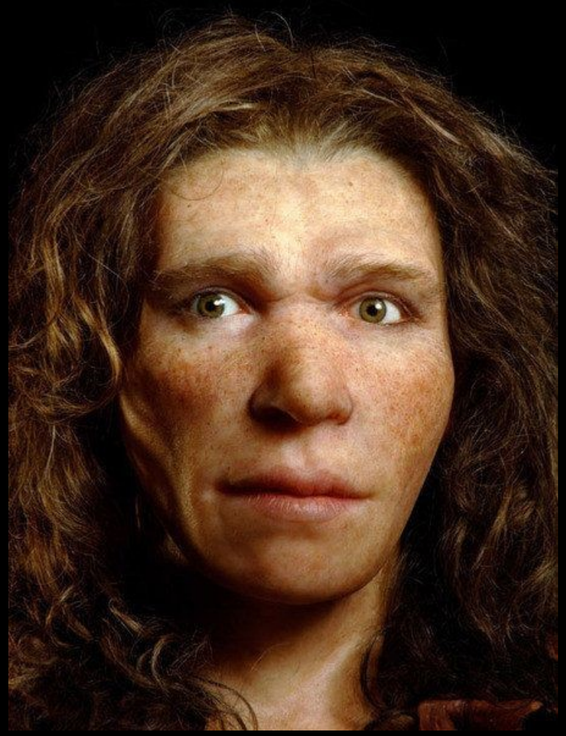


Figure 5. Mean amounts of detected introgressed material per individual, classified by affinity to the Altai Neanderthal and Altai Denisovan genomes

Definitions of the affinity groups are given in Methods. Unclassified material includes segments that are too short to be confidently classified into an affinity group, as well as longer segments that have low levels of affinity to the archaic genomes.



Adaptace neandertálců na klima v Evropě a co jsme po nich zdědili



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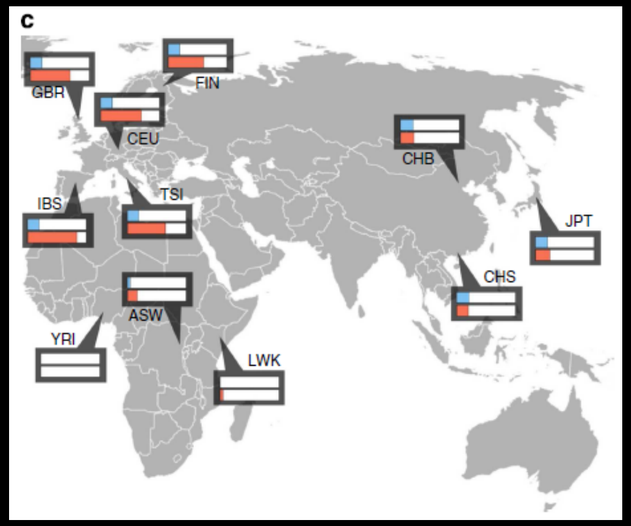
The phenotypic legacy of admixture between modern humans and Neanderthals

Corinne N. Simonti[1], Benjamin Vernot[2], Lisa Bastarache[3], Erwin Bottinger[4], David S. Carrell[5], Rex L. Chisholm[6], David R. Crosslin[2,5], Scott J. Hebbring[7], Gail P. Jarvik[2,5], Iftikhar J. Kullo[8], Rongling Li[9], Jyotishman Pathak[10], Marylyn D. Ritchie[11,12], Dan M. Roden[13,14], Shefali S. Verma[11], Gerard Tromp[15,16], Jeffrey D. Prato[3], William S. Bush[17], Joshua M. Akey[†,2], Joshua C. Denny[†,1,3,13], and John A. Capra[1,3,18,19,*]



nature COMMUNICATIONS

ARTICLE

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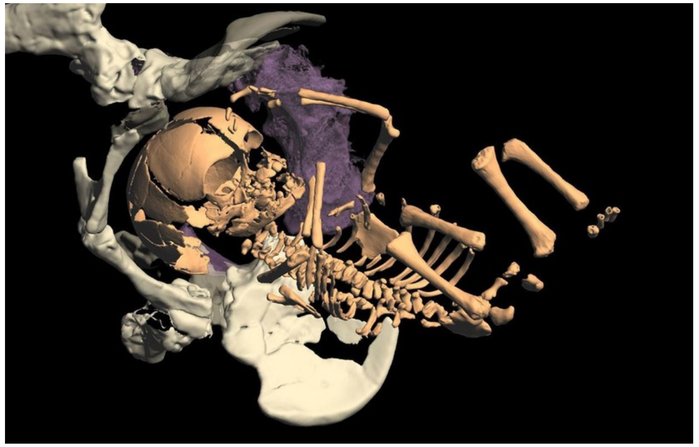
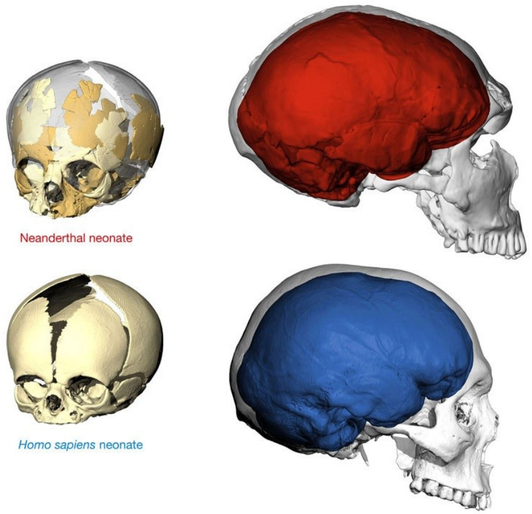
Neanderthal ancestry drives evolution of lipid catabolism in contemporary Europeans

Ekaterina E. Khrameeva[1,2], Katarzyna Bozek[1,3], Liu He[1], Zheng Yan[1], Xi Jiang[1], Yuning Wei[1], Kun Tang[1], Mikhail S. Gelfand[2,4], Kay Prufer[3], Janet Kelso[3], Svante Paabo[3], Patrick Giavalisco[5], Michael Lachmann[3] & Philipp Khaitovich[1,3]

Tuková tkáň

Víc dětí a méně potratů





The Neandertal Progesterone Receptor

Hugo Zeberg [ID],*,1,2 Janet Kelso,[1] and Svante Pääbo*,1,3
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Current Biology

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Report

A Neanderthal Sodium Channel Increases Pain Sensitivity in Present-Day Humans

Hugo Zeberg,[1,2,6,*] Michael Dannemann,[1] Kristoffer Sahlholm,[2,3] Kristin Tsuo,[1] Tomislav Maricic,[1] Victor Wiebe,[1] Wulf Hevers,[1] Hugh P.C. Robinson,[2,4] Janet Kelso,[1] and Svante Pääbo[1,5,*]

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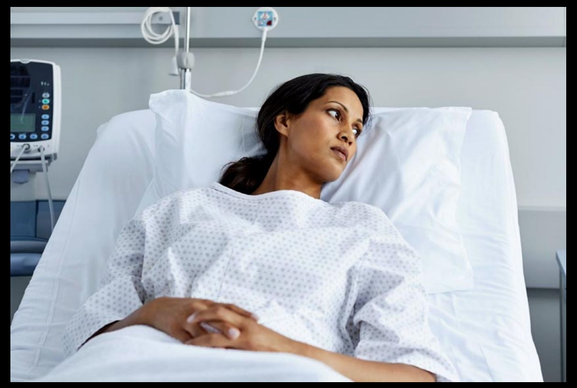
Evidence that RNA viruses drove of adaptive introgression between Neanderthals and modern humans

David Enard[1,2,*] and Dmitri A Petrov[3]



Article

The major genetic risk factor for severe COVID-19 is inherited from Neanderthals

https://doi.org/10.1038/s41586-020-2818-3
Received: 3 July 2020
Accepted: 22 September 2020
Published online: 30 September 2020
Check for updates

Hugo Zeberg[1,2]✉ & Svante Pääbo[1,2]✉

A recent genetic association study[1] identified a gene cluster on chromosome 3 as a risk locus for respiratory failure after infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A separate study (COVID-19 Host Genetics Initiative)[2] comprising 3,199 hospitalized patients with coronavirus disease 2019 (COVID-19) and control individuals showed that this cluster is the major genetic risk factor for severe symptoms after SARS-CoV-2 infection and hospitalization. Here we show that the risk is conferred by a genomic segment of around 50 kilobases in size that is inherited from Neanderthals and is carried by around 50% of people in south Asia and around 16% of people in Europe.

Check for updates

A genomic region associated with protection against severe COVID-19 is inherited from Neandertals

Hugo Zeberg[a,b,1] and Svante Pääbo[a,c,1]

[a]Department of Evolutionary Genetics, Max Planck Institute for Evolutionary Anthropology, D-04103 Leipzig, Germany; [b]Department of Neuroscience, Karolinska Institutet, SE-17177 Stockholm, Sweden; and [c]Human Evolutionary Genomics Unit, Okinawa Institute of Science and Technology, Okinawa 904-0495, Japan

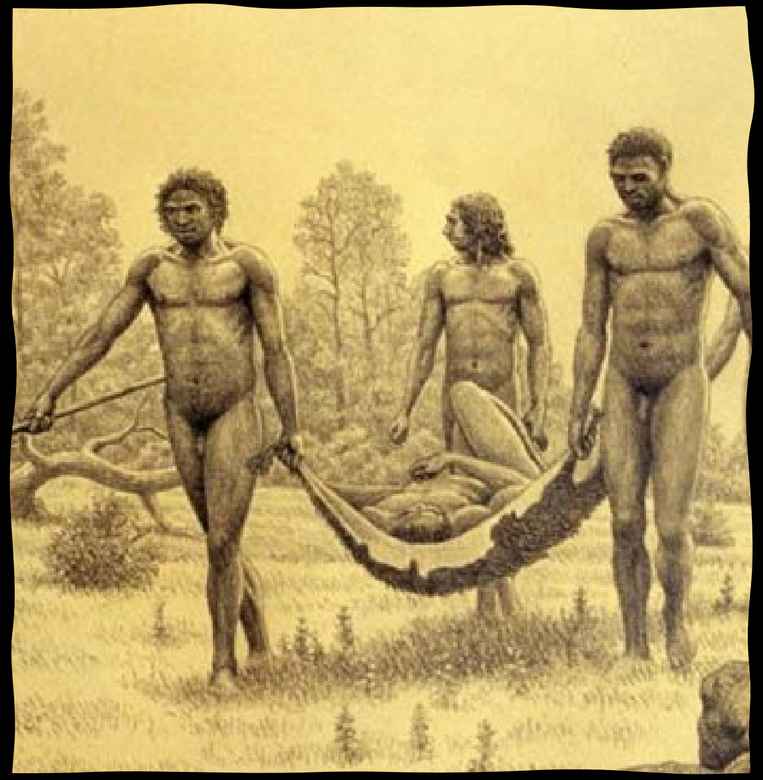
Contributed by Svante Pääbo, January 22, 2021 (sent for review December 21, 2020; reviewed by Tobias L. Lenz and Lluis Quintana-Murci)

LETTER

Altitude adaptation in Tibetans caused by introgression of Denisovan-like DNA

Emilia Huerta-Sánchez[1,2,3]*, Xin Jin[1,4]*, Asan[1,5,6]*, Zhuoma Bianba[7]*, Benjamin M. Peter[2], Nicolas Vin
Xin Yi[1,5,6], Mingze He[1,8], Mehmet Somel[9], Peixiang Ni[1], Bo Wang[1], Xiaohua Ou[1], Huasang[1], Jiangbai Luo
Kui Li[11], Guoyi Gao[12], Ye Yin[1], Wei Wang[1], Xiuqing Zhang[1,13,14], Xun Xu[1], Huanming Yang[1,15,16], Yingrui Li[1], Ji
Jun Wang[1,15,17,18,19] & Rasmus Nielsen[1,2,20,21]

Vyhubili jsme neandertálce? Ne!



Homo heidelbergensis

L'anthropologie 124 (2020) 102797

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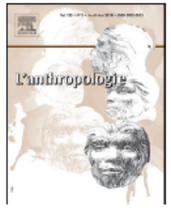

Original article

Hibernation in hominins from Atapuerca, Spain half a million years ago☆

Hibernation des hominidés d'Atapuerca, en Espagne, il y a un demi-million d'années

Antonis Bartsiokas [a,*], Juan-Luis Arsuaga [b,c]

[a] *Department of History and Ethnology, Democritus University of Thrace, 69100 Komotini, Greece*
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Hibernation
Atapuerca
Chronic Kidney Disease (CKD)

ABSTRACT

Both animal hibernation and human renal osteodystrophy are characterized by high levels of serum parathyroid hormone. To test the hypothesis of hibernation in an extinct human species, we examined the hominin skeletal collection from Sima de los Huesos, Cave Mayor, Atapuerca, Spain, for evidence of hyperparathyroidism after a thorough review of the literature. We studied the morphology of the fossilized bones by using macrophotography, microscopy

Výživa paleolitických lidí

Tzv. „lovci mamutů“ byli ekonomicky závislí na sobech (již domestikace spolu se psem, pes pomáhal hlídat stáda sobů) a malé zvěři (zajíci, lišky, bělokur, atd.), na mamutech závislí nebyli, mamut byl uloven 1-2 za/rok, ale kosti mamutů jsou nejnápadnější a dle nich získali své jméno (E. Štorch).
Ze sobů využívali vše, včetně mléka samic.

nature ecology & evolution

Article

https://doi.org/10.1038/s41559-024-02382-z

Isotopic evidence of high reliance on plant food among Later Stone Age hunter-gatherers at Taforalt, Morocco

Received: 19 June 2023

Accepted: 1 March 2024

Published online: 29 April 2024

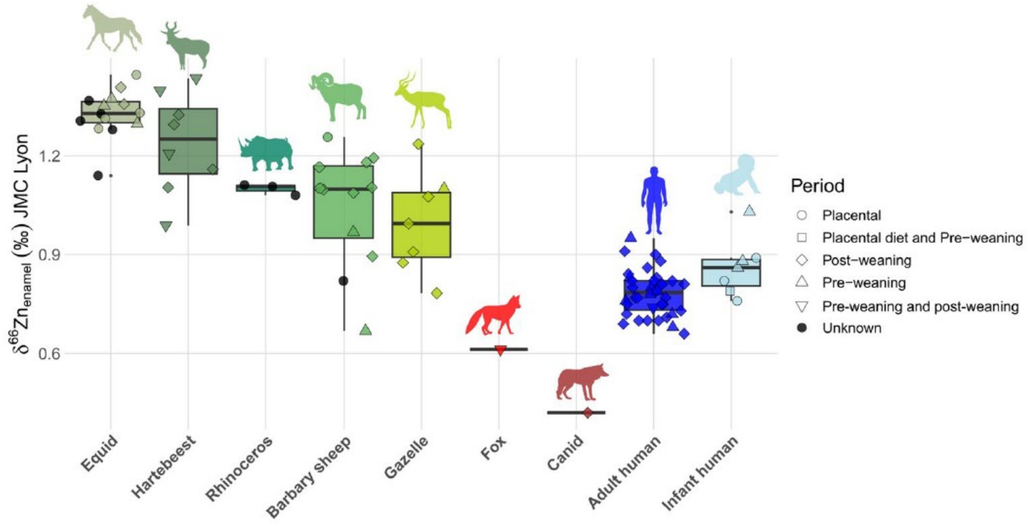
Check for updates

Zineb Moubtahij[1,2], Jeremy McCormack[1,3], Nicolas Bourgon[1,4], Manuel Trost[1], Virginie Sinet-Mathiot[1,5,6], Benjamin T. Fuller[2], Geoff M. Smith[1,7], Heiko Temming[1], Sven Steinbrenner[1], Jean-Jacques Hublin[1,8], Abdeljalil Bouzouggar[9,10], Elaine Turner[11] & Klervia Jaouen[1,2]

The transition from hunting-gathering to agriculture stands as one of the most important dietary revolutions in human history. Yet, due to a scarcity of well-preserved human remains from Pleistocene sites, little is known about the dietary practices of pre-agricultural human groups. Here we present the isotopic evidence of pronounced plant reliance among Late Stone Age hunter-gatherers from North Africa (15,000–13,000 cal BP), predating the advent of agriculture by several millennia. Employing a comprehensive multi-isotopic approach, we conducted zinc (δ^{66}Zn) and strontium ($^{87}Sr/^{86}Sr$) analysis on dental enamel, bulk carbon ($\delta^{13}C$) and nitrogen ($\delta^{15}N$) and sulfur ($\delta^{34}S$) isotope analysis on dentin and bone collagen, and single amino acid analysis on human and faunal remains from Taforalt (Morocco). Our results unequivocally demonstrate a substantial plant-based component in the diets of these hunter-gatherers. This distinct dietary pattern challenges the prevailing notion of high reliance on animal proteins among pre-agricultural human groups. It also raises intriguing questions surrounding the absence of agricultural development in North Africa during the early Holocene. This study underscores the importance of investigating dietary practices during the transition to agriculture and provides insights into the complexities of human subsistence strategies across different regions.

While the term 'Neolithic' remains ambiguous and this period occurred at different times worldwide, it generally implies the domestication of wild animals and plants, as well as the adoption of sedentary settlements[1,2]. The transition from hunting-gathering economies to agriculture-based ones, also known as Neolithization, is one of the most important dietary revolutions in human history[3,4]. Beyond being a revolution, a progressive intensification of plant consumption is believed to have begun long before domestication in the Neolithic[1,5]. Evidence of an early shift to grain-based resources is demonstrated by the discovery of a substantial archaeobotanical assemblage in the Upper Palaeolithic site of Ohalo II, in the Near East, dated to approximately 23,000 cal BP[5] (Fig. 1). This transformation intensified with the Natufians, a hunter-gatherer group that inhabited the Near East during the Late Pleistocene and the beginning of the Holocene (14,600–11,500 cal BP)[6]. A shift towards an increased reliance on plant foods occurred during this period[6–8], probably driven by several factors, including the depletion of large game species and the availability of a wider range of edible plants in the environment, which led to the

A full list of affiliations appears at the end of the paper. e-mail: zinebmoubtahij3@gmail.com



Hobitky z neolitu


H1
H2
H3
H4


OSTROŽSKÁ
LHOTA 2025
BRODSKÉ
OBJEKT H2

Nanismus

Nejstarší nález

Paleolit – Calábrie-Itálie (10 000 let BP)

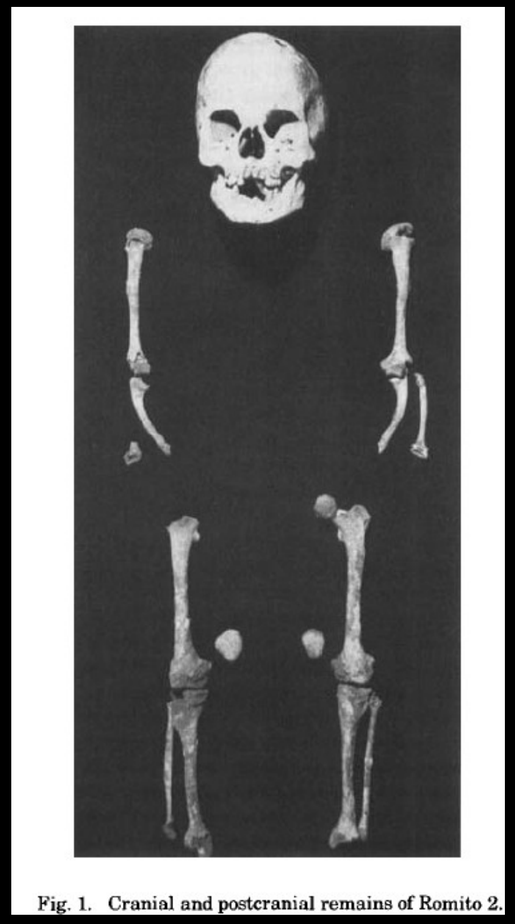
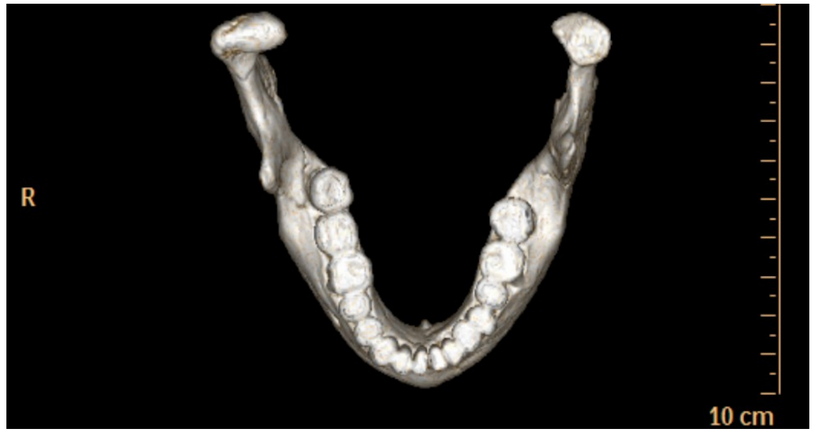
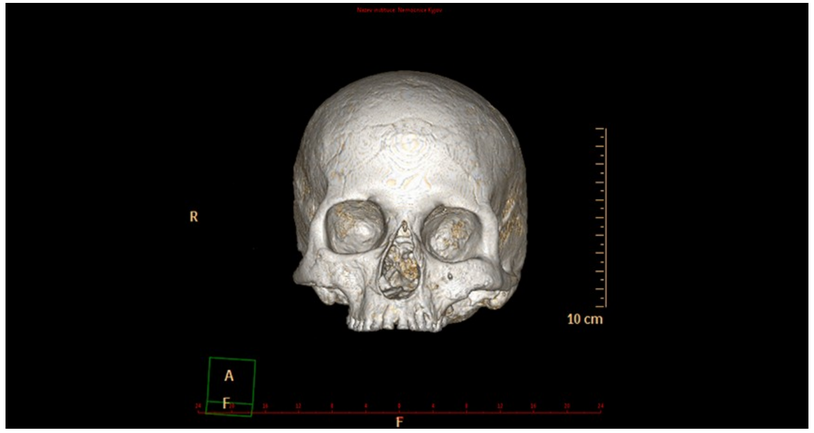
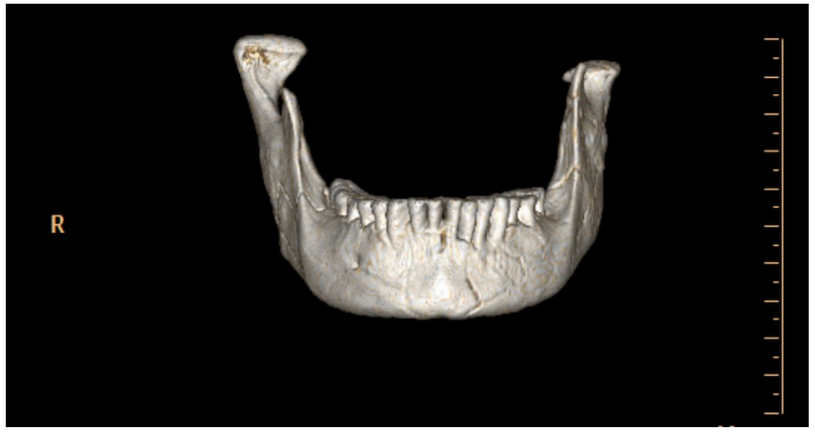


Fig. 1. Cranial and postcranial remains of Romito 2.

Žena s křivou tváří







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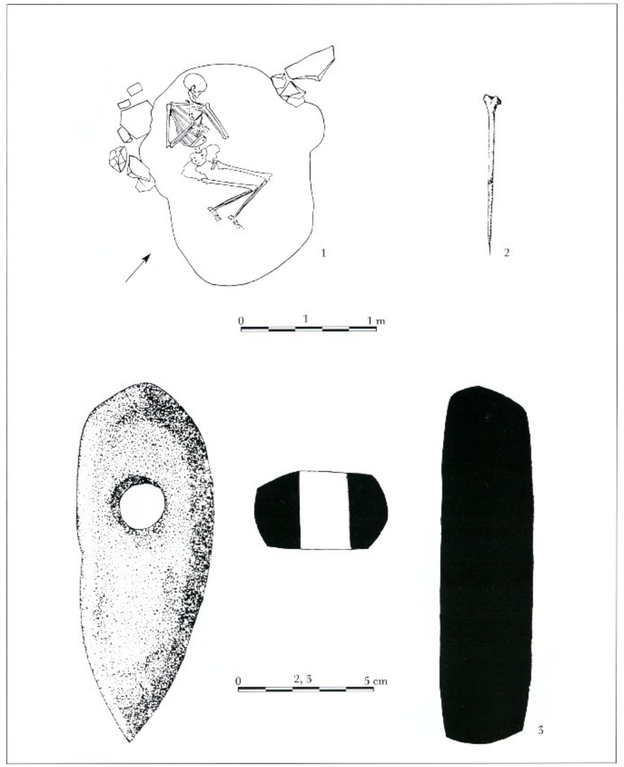
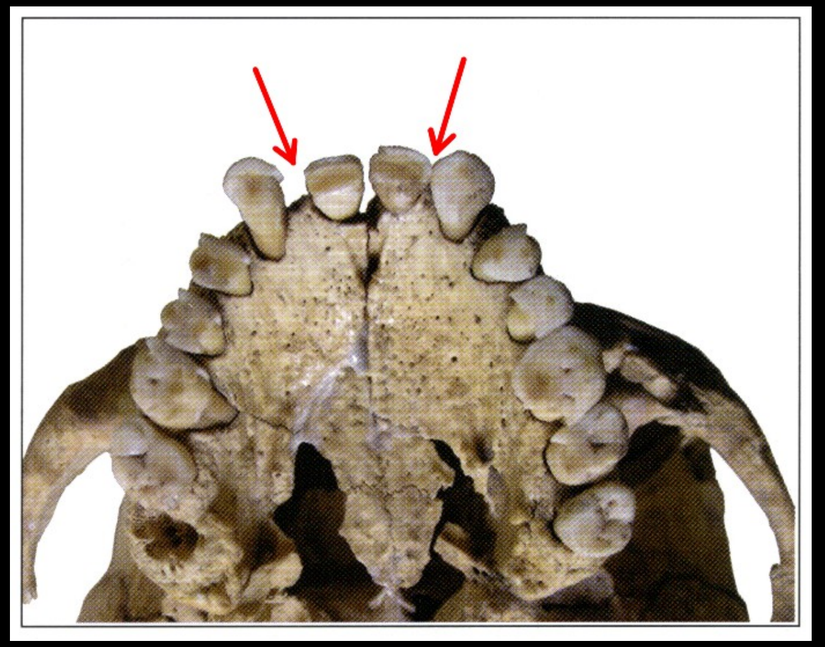


Neznámá z Hlinska u Přerova

KLIPPEL-FEILŮV SYNDROM

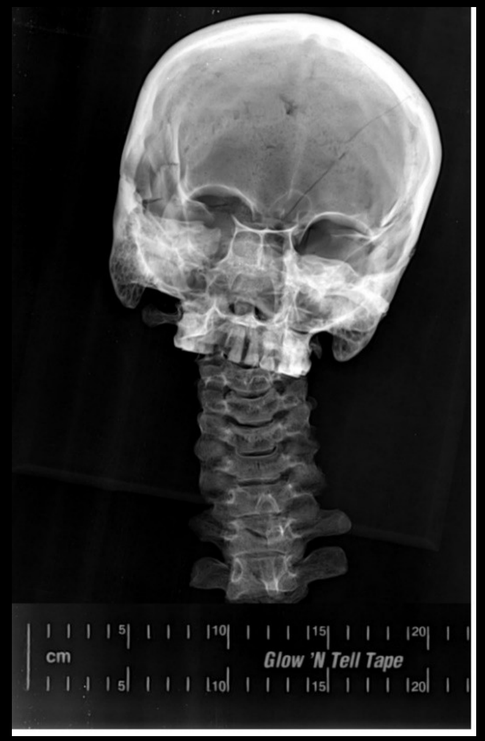
Srůst krčních obratů C1 a C2

Horní čelist s absencí obou druhých řezáků

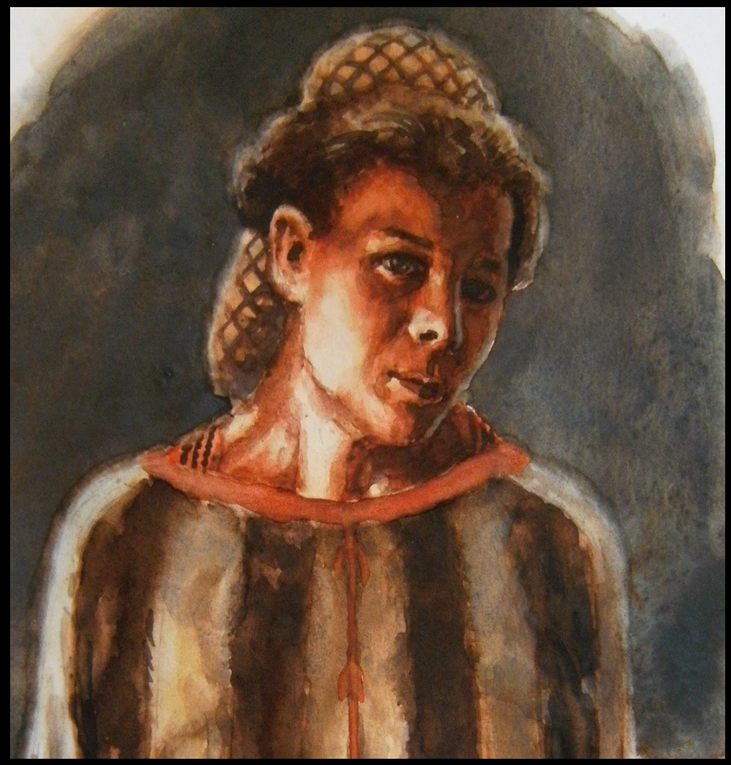


KLIPPEL-FEILŮV SYNDROM

Rentgenový snímek

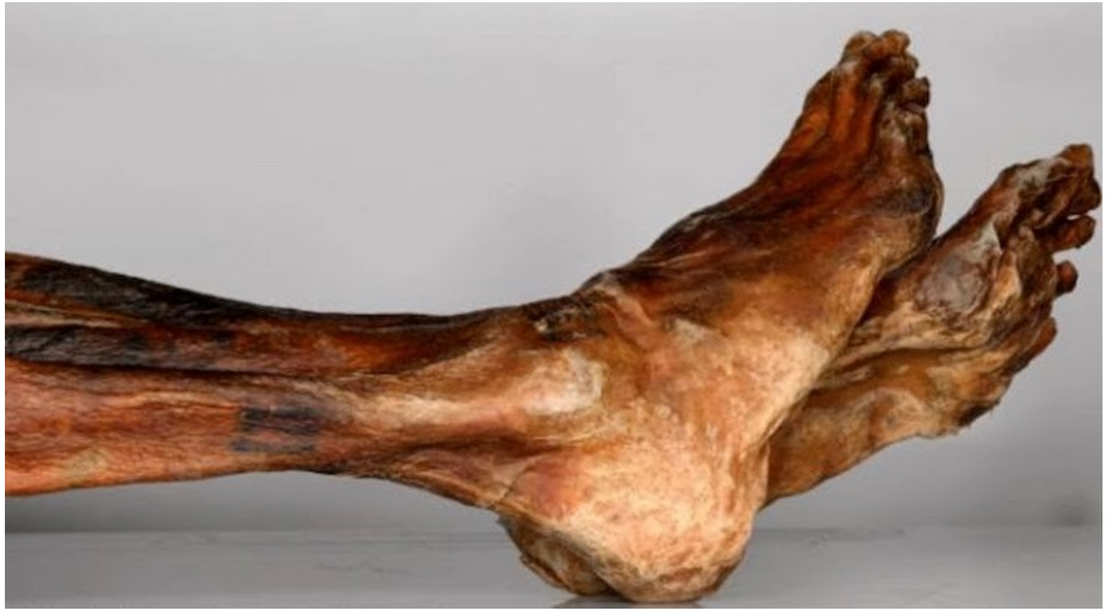


Kresebná rekonstrukce



Model hlavy Zachycující sklon hlavy na levou stranu

Ötzi

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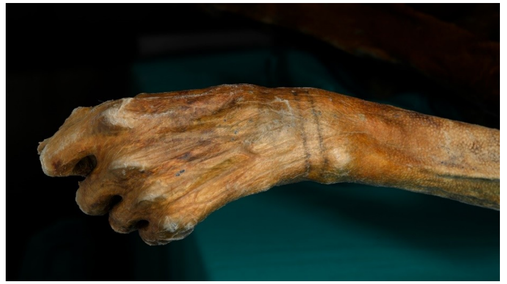

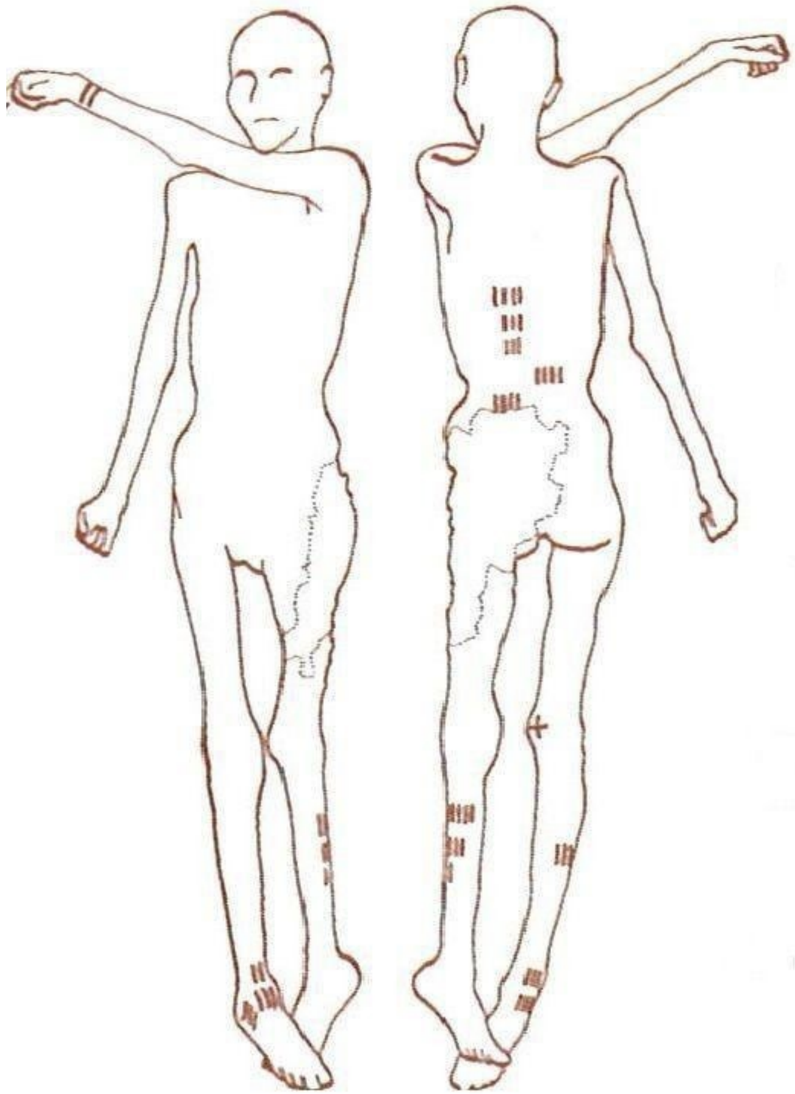

European Journal of Archaeology 2024, page 1 of 22

Chalcolithic Tattooing: Historical and Experimental Evaluation of the Tyrolean Iceman's Body Markings

Aaron Deter-Wolf[1*], Benoît Robitaille[2], Danny Riday[3], Aurélien Burlot[4] and Maya Sialuk Jacobsen[5]

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[2]*Independent Researcher, Québec Canada*
[3]*The Temple Tattoo; Tamahere, New Zealand*
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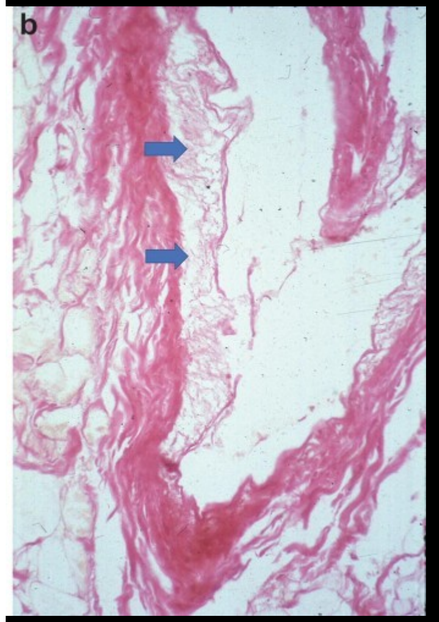
**Author for correspondence: Aaron.Deter-Wolf@tn.gov*

The Tyrolean ice mummy known as Ötzi presents some of the earliest direct evidence of tattooing in the human past. Despite decades of study, it remains unclear how the Iceman's tattoos were created and what tools and methods were used. Popular discussions of the Iceman describe his tattoos as having been made by incision, first cutting the skin and then rubbing in pigment from the surface. The authors review the scholarly literature on the Iceman's tattoos and summarize ethnographic, historic, and anthropological research on global patterns of tattooing to contextualize the Iceman's marks within pre-electric tattooing traditions. The results of recent experimental tattooing studies are then compared to the physical signature of the Iceman's marks to evaluate existing claims and provide informed hypotheses as to how those tattoos were created.

Keywords: tattoo, Iceman, Chalcolithic, experimental archaeology, Tyrol, Ötzi



Slavná mumie Icemana známá jako Ötzi byla podle nedávných studií geneticky náchylná ke kardiovaskulárním chorobám. Nejen, že tato genetická predispozice byla prokazatelná u 5000 let staré ledové mumie, objevil se již také příznak v podobě arteriosklerózy.

Není cukr jako cukr

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RESEARCH ARTICLE

Songbirds avoid the oxidative stress costs of high blood glucose levels: a comparative study

Csongor I. Vágási[1,*], Orsolya Vincze[1,2], Marie Adámková[3,4], Tereza Kauzálová[3], Ádám Z. Lendvai[5], Laura I. Pătraş[6], Janka Pénzes[1], Péter L. Pap[1,‡], Tomáš Albrecht[3,7,‡] and Oldřich Tomášek[3,4,‡]

ABSTRACT

Chronically high blood glucose levels (hyperglycaemia) can compromise healthy ageing and lifespan at the individual level. Elevated oxidative stress can play a central role in hyperglycaemia-induced pathologies. Nevertheless, the lifespan of birds shows no species-level association with blood glucose. This suggests that the potential pathologies of high blood glucose levels can be avoided by adaptations in oxidative physiology at the macroevolutionary scale. However, this hypothesis remains unexplored. Here, we examined this hypothesis using comparative analyses controlled for phylogeny, allometry and fecundity based on data from 51 songbird species (681 individuals with blood glucose data and 1021 individuals with oxidative state data). We measured blood glucose at baseline and after stress stimulus and computed glucose stress reactivity as the magnitude of change between the two time points. We also measured three parameters of non-enzymatic antioxidants (uric acid, total antioxidants and glutathione) and a marker of oxidative lipid damage (malondialdehyde). We found no clear evidence for blood glucose concentration being correlated with either antioxidant or lipid damage levels at the macroevolutionary scale, as opposed to the hypothesis postulating that high blood glucose levels entail oxidative costs. The only exception was the moderate evidence for species with a stronger stress-induced increase in blood glucose concentration evolving moderately lower investment into antioxidant defence (uric acid and glutathione). Neither baseline nor stress-induced glucose levels were associated with oxidative physiology. Our findings support the hypothesis that birds evolved adaptations preventing the (glyc)oxidative costs of high blood glucose observed at the within-

KEY WORDS: Antioxidants, Glucose, Hyperglycaemia, Lipid peroxidation, Phylogenetic comparison, Physiological ecology

INTRODUCTION

Living organisms use chemical energy to sustain their vital functions, with carbohydrates, lipids and proteins as the main metabolic energy substrates. Among carbohydrates, glucose has a prominent role in metabolism as it fulfils multiple metabolic functions. Besides being an important energy carrier, it is a vital precursor in the synthesis of a wide variety of other important biomolecules, including fatty, amino and nucleic acids, cholesterol, glycoproteins and glycolipids (Braun and Sweazea, 2008; Sweazea, 2022). The mere existence of several regulatory mechanisms that control glucose metabolism both at baseline conditions and during perturbations (e.g. stress response) provides evidence for the biological significance of glucose homeostasis (Braun and Sweazea, 2008). Deregulation of glucose homeostasis induces metabolic stress with a plethora of deleterious health consequences (Picard et al., 2014).

Birds have outstandingly high blood glucose levels in normal physiological state, on average two to four times higher than that of similar-sized mammals (Braun and Sweazea, 2008; Holmes et al., 2001; Satoh, 2021). Only frugivorous and nectarivorous bats with a sugar-rich diet can have blood glucose values comparable to those of some birds (Kelm et al., 2011; Peng et al., 2017). Constitutively high blood glucose in birds is evolutionarily coupled with athletic capacity, high metabolic rate and elevated body temperature (Satoh, 2021). Moreover, avian blood glucose levels coevolve positively

Původ rakoviny mléčné žlázy u lidí psů a koček

BRCA

BRCA (**BR**east **CA**ncer) jsou tumor supresorové geny. V organismu se nachází ve dvou typech *BRCA1* a *BRCA2*. Produkty těchto genů se účastní kontroly buněčného cyklu a **oprav poškozené DNA**. Mutace zvyšuje riziko vzniku nádorových onemocnění, zejména prsu a vaječníků.

Genetický podklad [upravit | editovat zdroj]

BRCA1 se nachází na dlouhém raménku chromozomu 17 a má 22 exonů. Produktem je velký protein pBRCA1 (220 kDa). *BRCA2* je lokalizován na chromozomu 13q. Produktem je polypeptid pBRCA2 velký 384 kDa.[1] Proteiny pBRCA1 a pBRCA2 se nachází v **jádře**. Obsahují vazebné domény, které jim umožňují interagovat s dalšími proteiny. Prokázanou interakcí je vazba s produktem genu **RAD51**.

Princip působení [upravit | editovat zdroj]

Na poškození DNA zareaguje produkt genu *AT*. Proteinkinasa ATM spustí fosforylační kaskádu, během níž se fosforyluje protein *pBRCA1*. Ten následně interaguje s proteinem **pRAD51**, který se účastní oprav **dvouřetězcových zlomů** DNA procesem **homologní rekombinace**. Protein pBRCA2 také interaguje s tímto komplexem. Jeho úlohou je transportovat pRAD51 do místa poškození.

Mutace [upravit | editovat zdroj]

Mutace v genech *BRCA1* a *BRCA2* se v rodinách dědí autosomálně dominantně s vysokou penetrancí. Frekvence v populaci je přibližně 1:800.[2] Dědičné mutace v těchto genech jsou odpovědné za **HBC** (*hereditary breast cancer syndrome*) a **HBOC** (*hereditary breast/ovarian cancer syndrome*). V populaci je abnormalitami v genech způsobeno 3–5 % malignit prsu. Mutace v genech BRCA se podílí při vývoji přibližně u 2/3 hereditárních nádorů.[3] Detekované mutace mají rozmanité důsledky.[1]

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Chapter 11 MAMMARY GLAND TUMORS

Mammary tumors, at least in dogs and to a certain extent in cats, have many similarities to breast neoplasms in women. In human breast neoplasms, a highly invasive and treatment-resistant protein, responsible for malignant evolution, has been identified. This protein, called ***stromelysin-3 (ST3)*** appears in the case of malignant tumors, having extremely high levels, and is not found in cultured malignant tumor cells, but is detected around the tumor. So, the healthy cells adjacent to the tumor, having the property to change the extracellular matrix, the stroma, favoring the invasion of metastatic cells, produce it. It seems that cancer cells produce substances that cause healthy cells to produce ST3. Attempts are made to obtain anti-ST3 drugs [25].

Mammary gland tumors are frequent in dogs and cats, appearing extremely sporadically in other domestic animals. In **bitches,** the incidence of mammary tumors is estimated at 50% of all neoplasms in this species, of which approximately 60% are benign and 40% malignant [8]. The mean onset age for mammary tumors is between 10 and 11 years. Incidence is higher in certain breeds, such as: Poodle, English Spaniel, Brittany Spaniel, English Setter, Pointer, Fox Terrier, Boston Terrier and Cocker Spaniel; incidence is lower in Chihuahua and Boxer breeds [6].

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Mammary Tumor

Mammary tumors are neoplasms of epithelial and/or myoepithelial cells of the mammae.
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Biology and Diseases of Mice

Mark T. Whary DVM, PhD, DACLAM, ... Stephen W. Barthold DVM, PhD, Diplomate ACVP, in Laboratory Animal Medicine (Third Edition), 2015

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Review > Breast Dis. 2007;28:7-21. doi: 10.3233/bd-2007-28102.

Comparative pathology of mammary gland cancers in domestic and wild animals

Linda Munson [1], Anneke Moresco

Affiliations + expand

PMID: 18057539 DOI: 10.3233/bd-2007-28102

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Abstract

Mammary cancer occurs among all taxonomic groups, and comparing the disease in animals with breast cancer in women could greatly improve our understanding of the relevant risk factors and genetic profiles for this disease. Differences in cancer prevalence between carnivores and herbivores and between captive and wild carnivores are striking and support the hypotheses that diet and reproductive history are major risk factors. Domestic dogs and cats have a high prevalence of mammary tumors, and the majority of tumors in cats are aggressive cancers. Many domestic dogs and cats are prevented from breeding, resulting in their being exposed to recurrent estrogen peaks followed by high persistent levels of progesterone. Therefore progesterone appears to be a significant risk factor for cancer development. Supporting this suspicion is the observation that most mammary cancers in zoo cats are in those treated with the potent synthetic progestin contraceptive, melengestrol acetate. The more common morphologic types of mammary cancer in canids and felids include tubulopapillary, solid, cribriform, comedo and anaplastic carcinomas. Dogs also develop complex carcinomas, which likely evolve from the complex adenomas or mixed tumors that are so common in this species and are promoted by exogenous progesterone treatment. Among zoo felids, jaguars are at higher risk for mammary cancer and also have a high prevalence of ovarian

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Published online 2010 Sep 29. doi: 10.1128/JCM.01157-10

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PMID: 20881168

Mouse Mammary Tumor Virus-Like Nucleotide Sequences in Canine and Feline Mammary Tumors

Wei-Li Hsu,[1,†] Hsing-Yi Lin,[2,†] Shyan-Song Chiou,[1] Chao-Chin Chang,[1] Szu-Pong Wang,[1] Kuan-Hsun Lin,[2] Songkhla Chulakasian,[2] Min-Liang Wong,[2] and Shih-Chieh Chang[2,3,*]

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ABSTRACT

Go to:

Mouse mammary tumor virus (MMTV) has been speculated to be involved in human breast cancer. Companion animals, dogs, and cats with intimate human contacts may contribute to the transmission of MMTV between mouse and human. The aim of this study was to detect MMTV-like nucleotide sequences in canine and feline mammary tumors by nested PCR. Results showed that the presence of MMTV-like env and LTR sequences in canine malignant mammary tumors was 3.49% (3/86) and 18.60% (16/86), respectively. For feline malignant mammary tumors, the presence of both env and LTR sequences was found to be 22.22% (2/9). Nevertheless, the MMTV-like LTR and env sequences also were detected in normal mammary glands of dogs and cats. In comparisons of the MMTV-like DNA sequences of our findings to those of NIH 3T3 (MMTV-positive murine cell line) and human breast cancer cells, the sequence similarities ranged from 94 to 98%. Phylogenetic analysis revealed that intermixing among sequences identified from tissues of different hosts, i.e., mouse, dog, cat, and human, indicated the MMTV-like DNA existing in these hosts. Moreover, the env transcript was detected in 1 of the 19 MMTV-positive samples by reverse transcription-PCR. Taken together, our study provides evidence for the existence and expression of MMTV-like sequences in neoplastic and normal mammary glands of dogs and cats.

viruses | MDPI

Review

The Viral Origin of Human Breast Cancer: From the Mouse Mammary Tumor Virus (MMTV) to the Human Betaretrovirus (HBRV)

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Abstract: A Human Betaretrovirus (HBRV) has been identified in humans, dating as far back as about 4500 years ago, with a high probability of it being acquired by our species around 10,000 years ago, following a species jump from mice to humans. HBRV is the human homolog of the MMTV (mouse mammary tumor virus), which is the etiological agent of murine mammary tumors. The hypothesis of a HMTV (human mammary tumor virus) was proposed about 50 years ago, and has acquired a solid scientific basis during the last 30 years, with the demonstration of a robust link with breast cancer and with PBC, primary biliary cholangitis. This article summarizes most of what is known about MMTV/HMTV/HBRV since the discovery of MMTV at the beginning of last century, to make evident both the quantity and the quality of the research supporting the existence of HBRV and its pathogenic role. Here, it is sufficient to mention that scientific evidence includes that viral sequences have been identified in breast-cancer samples in a worldwide distribution, that the complete proviral genome has been cloned from breast cancer and patients with PBC, and that saliva contains HBRV, as a possible route of inter-human infection. Controversies that have arisen concerning results obtained from human tissues, many of them outdated by new scientific evidence, are critically discussed and confuted.

Keywords: HBRV; MMTV; HMTV; human Betaretrovirus; mouse mammary tumor virus; human mammary tumor virus; breast cancer; PBC; primary biliary cholangitis; etiology

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Citation: Bevilacqua, G. The Viral Origin of Human Breast Cancer: From the Mouse Mammary Tumor Virus (MMTV) to the Human Betaretrovirus (HBRV). *Viruses* **2022**, *14*, 1704. https://doi.org/10.3390/v14081704

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Review

Canine Mammary Cancer: State of the Art and Future Perspectives

Eliza Vazquez [1], Yulia Lipovka [1], Alejandro Cervantes-Arias [2], Adriana Garibay-Escobar [1], Michelle M. Haby [1], Felisbina Luisa Queiroga [3,*] and Carlos Velazquez [1,*]

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Simple Summary: Mammary tumors are the most frequent neoplasia in female dogs. They develop spontaneous cancer and share several biological, clinical, pathological and molecular characteristics with cancer diagnosed in humans. Mammary cancer is also one of the leading causes of death in both species. This review provides a detailed description of the histological, molecular and clinical aspects of mammary cancer in canines; it discusses risk factors and currently available diagnostic and treatment options, as well as remaining challenges and unanswered questions.

Abstract: Mammary cancer is the most frequently diagnosed neoplasia in women and non-spayed female dogs and is one of the leading causes of death in both species. Canines develop spontaneous mammary tumors that share a significant number of biological, clinical, pathological and molecular characteristics with human breast cancers. This review provides a detailed description of the histological, molecular and clinical aspects of mammary cancer in canines; it discusses risk factors and currently available diagnostic and treatment options, as well as remaining challenges and unanswered questions. The incidence of mammary tumors is highly variable and is impacted by biological, pathological, cultural and socioeconomic factors, including hormonal status, breed, advanced age, obesity and diet. Diagnosis is mainly based on histopathology, although several efforts have been made to establish a molecular classification of canine mammary tumors to widen the spectrum of treatment options, which today rely heavily on surgical removal of tumors. Lastly, standardization of clinical study protocols, development of canine-specific biological tools, establishment of adequate dog-specific disease biomarkers and identification of targets for the development of new therapies that could improve survival and have less adverse effects than chemotherapy are among the remaining challenges.

Keywords: mammary cancer; canine; molecular classification; diagnosis; treatment

MUNI MED

Trimethylamine N-oxide (TMAO)

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Marine fish may be biochemically constrained from inhabiting the deepest ocean depths

Paul H. Yancey[a,1], Mackenzie E. Gerringer[a,b], Jeffrey C. Drazen[b], Ashley A. Rowden[c], and Alan Jamieson[d]

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Edited by George N. Somero, Stanford University, Pacific Grove, CA, and approved February 7, 2014 (received for review November 23, 2013)

No fish have been found in the deepest 25% of the ocean (8,400–11,000 m). This apparent absence has been attributed to hydrostatic pressure, although direct evidence is wanting because of the lack of deepest-living species to study. The common osmolyte trimethylamine *N*-oxide (TMAO) stabilizes proteins against pressure and increases with depth, going from 40 to 261 mmol/kg in teleost fishes from 0 to 4,850 m. TMAO accumulation with depth results in increasing internal osmolality (typically 350 mOsmol/kg in shallow species compared with seawater's 1,100 mOsmol/kg). Preliminary extrapolation of osmolalities of predicted isosmotic state at 8,000–8,500 m may indicate a possible physiological limit, as greater depths would require reversal of osmotic gradients and, thus, osmoregulatory systems. We tested this prediction by capturing five of the second-deepest known fish, the hadal snailfish (*Notoliparis kermadecensis*; Liparidae), from 7,000 m in the Kermadec Trench. We found their muscles to have a TMAO content of 386 ± 18 mmol/kg and osmolality of 991 ± 22 mOsmol/kg. These data fit previous extrapolations and, combined with new osmolalities from bathyal and abyssal fishes, predict isosmotic state at 8,200 m. This is previously unidentified evidence that biochemistry could constrain the depth of a large, complex taxonomic group.

might limit a species' depth range, as proteins adapted to a particular pressure range do not work well at other pressures. Even with such adaptations, many proteins from deep species still retain significant levels of pressure sensitivity in vitro (9, 11–14). Recently, another mechanism for pressure adaptation has been hypothesized involving "piezolytes" (11, 15): small organic solutes that counteract the effects of pressure on proteins, potentially allowing proteins to work over greater depth ranges but possibly also constraining species depths if regulation of these solutes is limited (11, 13–17). Piezolytes are solutes first discovered as organic osmolytes (intracellular chemical effectors that prevent osmotic water loss). Most marine invertebrates are osmoconformers with internal osmolalities about the same as seawater, about 1,100 mOsmol/kg at 35 ppt; however, whereas extracellular fluids are dominated by NaCl, cells accumulate organic osmolytes to achieve osmotic balance. In many shallow-living marine invertebrate taxa, these osmolytes are neutral amino acids such as glycine and taurine and methylamines such as trimethylamine *N*-oxide (TMAO) (18).

Inorganic ions are not elevated intracellularly above basal levels to serve as osmolytes because they perturb macro-

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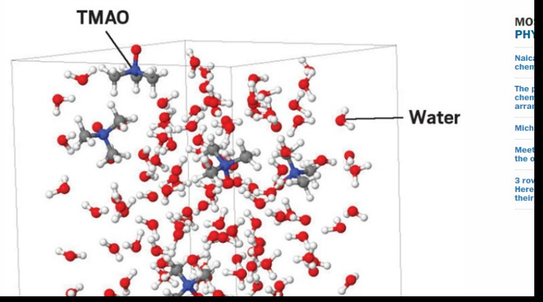
Trimethylamine *N*-oxide fortifies hydrogen bonds in water

by Emily Harwitz, special to C&EN

October 25, 2022



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CKJ Review

CKJ REVIEW

The dietary source of trimethylamine N-oxide and clinical outcomes: an unexpected liaison

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ABSTRACT

The profile of gut microbiota can vary according to host genetic and dietary characteristics, and be influenced by disease state and environmental stressors. The uremic dysbiosis results in a loss of biodiversity and overgrowth of microorganisms that may cause elevation of metabolic solutes such as trimethylamine N-oxide (TMAO), inducing pathogenic effects on its host. In patients with chronic kidney disease (CKD), TMAO levels are elevated because of a decreased clearance and an increased production from the uremic gut dysbiosis with a disrupted intestinal barrier and elevated enzymatic hepatic activity. Dietary precursors of TMAO are abundant in animal-derived foods such as red meat, egg yolk and other full-fat dietary products. TMAO is also found naturally in fish and certain types of seafood, with the TMAO content highly variable according to the depth of the sea where the fish is caught, as well as processing and storage. Although evidence points towards TMAO as being an important link to vascular damage and adverse cardiovascular outcomes, the evidence in CKD patients has not been consistent. In this review we discuss the potential dietary sources of TMAO and its actions on the intestinal microbiome as an explanation for the divergent results. We

ASN

Circulating trimethylamine *N*-oxide in association with diet and cardiometabolic biomarkers: an international pooled analysis

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ABSTRACT

Background: Trimethylamine *N*-oxide (TMAO), a diet-derived, gut microbial-host cometabolite, has been linked to cardiometabolic diseases. However, the relations remain unclear between diet, TMAO, and cardiometabolic health in general populations from different regions and ethnicities.

Objectives: To examine associations of circulating TMAO with dietary and cardiometabolic factors in a pooled analysis of 16 population-based studies from the United States, Europe, and Asia.

Methods: Included were 32,166 adults (16,269 white, 13,293 Asian, 1247 Hispanic/Latino, 1236 black, and 121 others) without cardiovascular disease, cancer, chronic kidney disease, or inflammatory bowel disease. Linear regression coefficients (β) were computed for standardized TMAO with harmonized variables. Study-specific results were combined by random-effects meta-analysis. A false discovery rate <0.10 was considered significant.

Results: After adjustment for potential confounders, circulating TMAO was associated with intakes of animal protein and saturated fat ($\beta = 0.124$ and 0.058, respectively, for a 5% energy increase) and with shellfish, total fish, eggs, and red meat ($\beta = 0.370$, 0.151, 0.081, and 0.056, respectively, for a 1 serving/d increase). Plant protein and nuts showed inverse associations ($\beta = -0.126$ for a 5% energy increase from plant protein and −0.123 for a 1 serving/d increase of nuts). Although the animal protein–TMAO association was consistent across populations, fish and shellfish associations were stronger in Asians ($\beta = 0.285$ and 0.578), and egg and red meat associations were more prominent in Americans ($\beta = 0.153$ and 0.093). Besides, circulating TMAO was positively associated with creatinine ($\beta = 0.131$ SD increase in log-TMAO), homocysteine ($\beta = 0.065$), insulin ($\beta = 0.048$), glycated hemoglobin ($\beta = 0.048$), and glucose ($\beta = 0.023$), whereas it was inversely associated with HDL cholesterol ($\beta = -0.047$) and blood pressure ($\beta = -0.030$). Each TMAO-biomarker association remained significant after further adjusting for creatinine and was robust in subgroup/sensitivity analyses.

Conclusions: In an international, consortium-based study, animal protein was consistently associated with increased circulating TMAO, whereas TMAO associations with fish, shellfish, eggs, and red meat varied among populations. The adverse associations of TMAO with certain cardiometabolic biomarkers, independent of renal function, warrant further investigation. *Am J Clin Nutr* 2021;113:1145–1156.

Keywords: trimethylamine *N*-oxide, diet, biomarker, cardiovascular disease, Consortium of Metabolomics Studies

Introduction

The gut microbiota and its metabolites are increasingly recognized as playing important roles in human nutrition and

Gut microbiota–derived metabolite trimethylamine-N-oxide and multiple health outcomes: an umbrella review and updated meta-analysis

Doudou Li,[1] Ying Lu,[1] Shuai Yuan,[1,2] Xiaxia Cai,[3] Yuan He,[4] Jie Chen,[1] Qiong Wu,[5] Di He,[5] Aiping Fang,[6] Yacong Bo,[7] Peige Song,[8] Debby Bogaert,[9] Kostas Tsilidis,[10,11] Susanna C Larsson,[2,12] Huanling Yu,[3] Huilian Zhu,[6] Evropi Theodoratou,[13,14] Yimin Zhu,[5] and Xue Li[1]

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ABSTRACT

Background: Trimethylamine-N-oxide (TMAO) is a gut microbiota–derived metabolite produced from dietary nutrients. Many studies have discovered that circulating TMAO concentrations are linked to a wide range of health outcomes.

Objectives: This study aimed to summarize health outcomes related to circulating TMAO concentrations.

Methods: We searched the Embase, Medline, Web of Science, and Scopus databases from inception to 15 February, 2022 to identify and update meta-analyses examining the associations between TMAO and multiple health outcomes. For each health outcome, we estimated the summary effect size, 95% prediction CI, between-study heterogeneity, evidence of small-study effects, and evidence of excess-significance bias. These metrics were used to evaluate the evidence credibility of the identified associations.

Results: This umbrella review identified 24 meta-analyses that investigated the association between circulating TMAO concentrations and health outcomes including all-cause mortality, cardiovascular diseases (CVDs), diabetes mellitus (DM), cancer, and renal function. We updated these meta-analyses by including a total of 82 individual studies on 18 unique health outcomes. Among them, 14 associations were nominally significant. After evidence credibility assessment, we found 6 (33%) associations (i.e., all-cause mortality, CVD mortality, major adverse cardiovascular events, hypertension, DM, and glomerular filtration rate) to present highly suggestive evidence.

Conclusions: TMAO might be a novel biomarker related to human health conditions including all-cause mortality, hypertension, CVD, DM, cancer, and kidney function. Further studies are needed to investigate whether circulating TMAO concentrations could be an intervention target for chronic disease. This review was registered at www.crd.york.ac.uk/prospero/ as CRD42021284730. *Am J Clin Nutr* 2022;116:230–243.

Keywords: umbrella review, updated meta-analyses, trimethylamine-N-oxide, TMAO, all-cause mortality, cardiovascular disease, hypertension, diabetes mellitus

Introduction

Trimethylamine-N-oxide (TMAO) is a gut microbiota metabolite derived from phosphatidylcholine, choline, betaine, and L-carnitine, which are abundant in seafoods, dairy products, egg yolks, muscle, and organ meats (1, 2). These nutrients can be hydrolyzed by trimethylamine (TMA) lyase from gut flora to form the TMAO precursor TMA, which is further oxidized by hepatic flavin monooxygenases to form TMAO (2, 3). A multitude of studies have discovered that circulating TMAO concentrations are linked to a wide range of health outcomes, including cardiovascular and cerebrovascular diseases (4–6), type 2 diabetes mellitus (DM) (7), hypertension (8), renal dysfunction (9, 10), cancer, and mortality (11, 12). The relations between

 Am J Clin Nutr 2022;116:230–243. Printed in USA.

TMAO je produktem oxidace trimethylaminu, běžný produkt metabolitu trimethylových kvartérních amoniových sloučenin, jako je cholin , trimethylglycin a L-karnitin

toxins

MDPI

Review

Trimethylamine *N*-Oxide: The Good, the Bad and the Unknown

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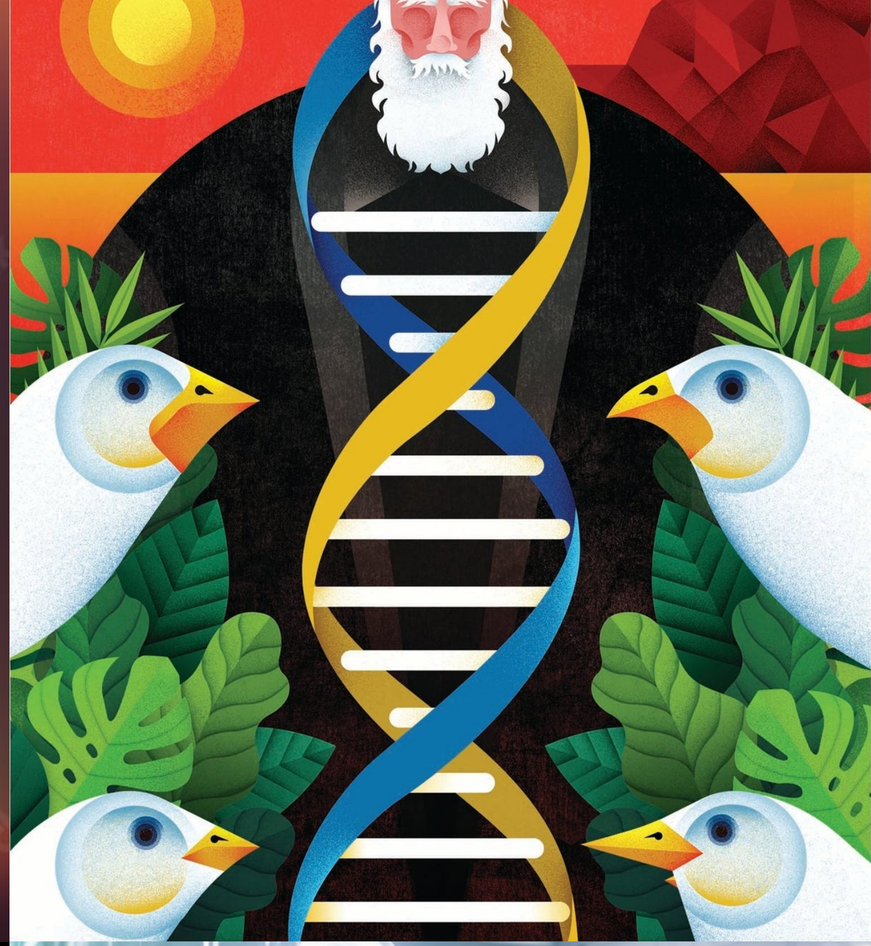
Abstract: Trimethylamine *N*-oxide (TMAO) is a small colorless amine oxide generated from choline, betaine, and carnitine by gut microbial metabolism. It accumulates in the tissue of marine animals



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