Introduction to Archaeogenetics

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MPI-SHH
SUMMER SCHOOL
2021

Doorway
to Human History

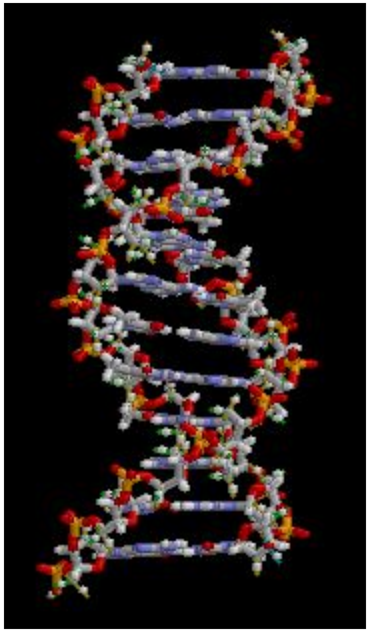
Intro to Archaeogenetics

1. What is archaeogenetics?
2. The history of archaeogenetic research
3. What are the challenges of aDNA research?
4. Laboratory methodology
5. What can we study using aDNA data?
6. How do archaeogenetics interface with archaeology and linguistics?

What is aDNA & its history?

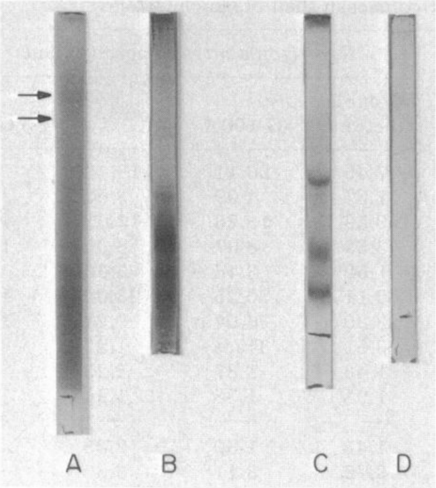
1 What is archaeogenetics?

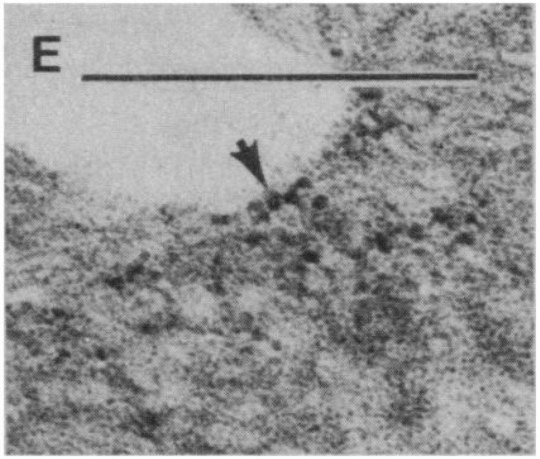
- = “arkhaios” ("ancient") + genetics ("the study of heredity")
- the study of ancient genetic material (aDNA)
- DNA = genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses
- combine knowledge of ancient and present-day genomics to understand evolution and development of species in a variety of contexts!



2.1 First evidence for ancient cell organelles

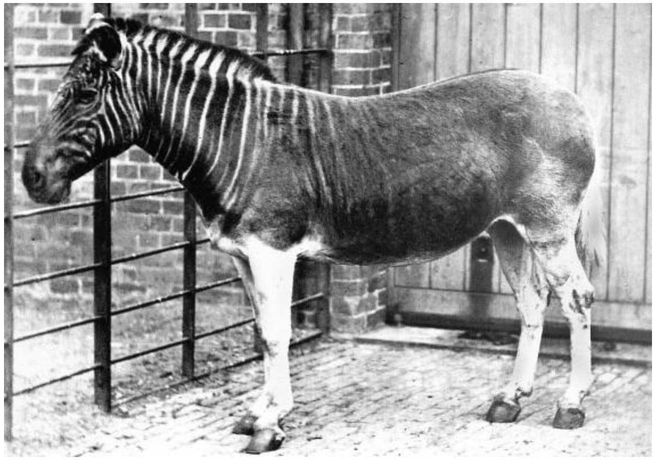
- **1972** Wyckoff: The Biochemistry of Animal Fossils
- **1976** Weiner, Lowenstam & Hood: Characterization of 80-million-year-old mollusk shell proteins *PNAS*
  - peptide bonds can last for up to 100,000,000 years in fossil shells and bones
- **1982** Poinar & Hess: Ultrastructure of 40-Million-Year-Old Insect Tissue *Science*
  - subcellular detail implying the survival of ribosomes and chromatin in insects



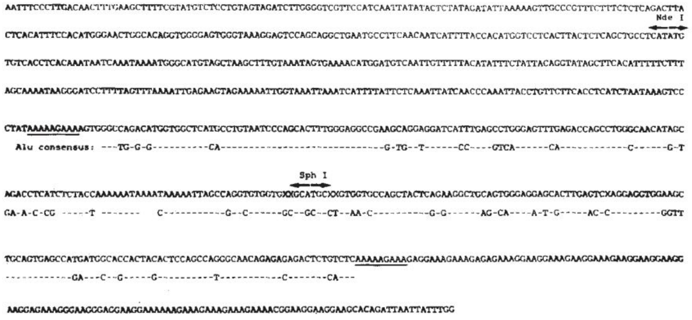


2.2 The first aDNA studies

- **1984** Higuchi, et al.: DNA Sequences from the Quagga, an Extinct Member of the Horse Family *Nature*
  - first retrieval of phylogenetically informative DNA sequences from an extinct species



- **1985** Pääbo: Molecular cloning of Ancient Egyptian mummy DNA *Nature*
  - far older DNA may be preserved in a clonable form and that nuclear DNA as well as mitochondrial DNA may persist for millenia



2.3 Early key developments

- **1983** development of **P**olymerase **C**hain **R**eaction
  - quickly became technique of choice for aDNA studies
  - eg. ancient human brain tissue, maize remains, dry skins of the extinct marsupial wolf and kangaroo rats, New Zealand moas, fossilized remains of plants and insects aged millions of years

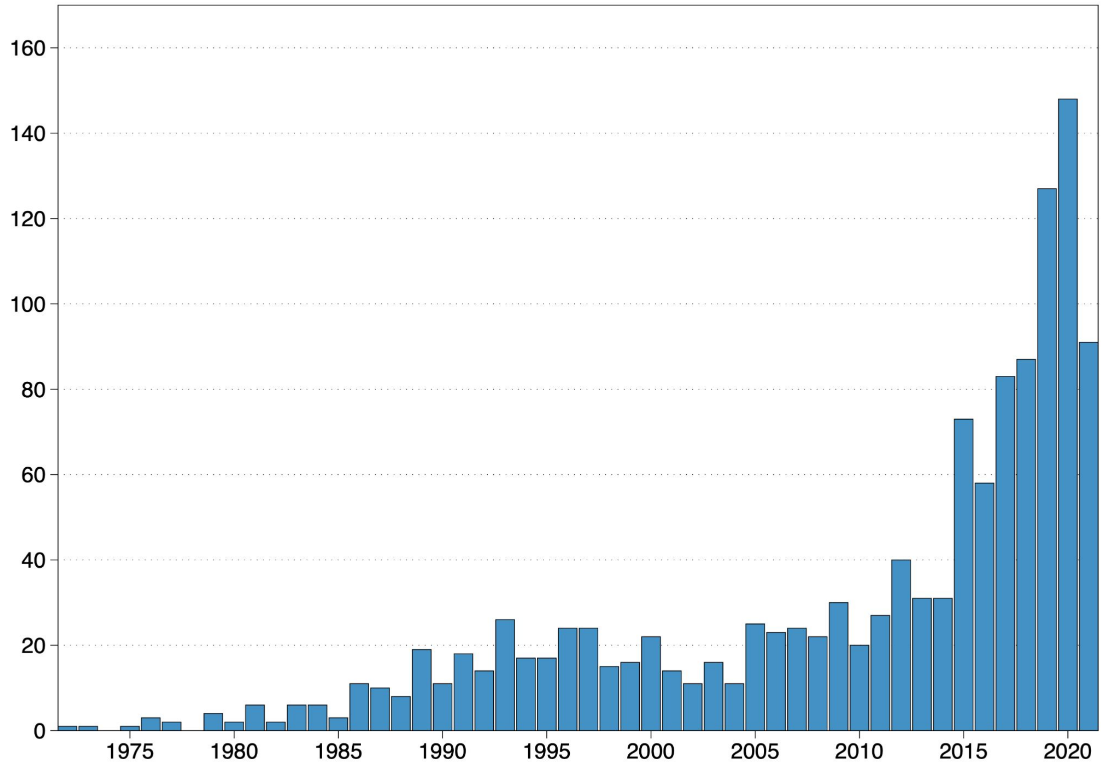
- **1989** Hagelberg, et al.: Ancient bone DNA amplified *Nature*
- **1989** Horai, et al.: DNA Amplification from Ancient Human Skeletal Remains and Their Sequence Analysis *Proc. Japan Acad.*
  - researchers were no longer limited to scarce soft-tissue remains

2.4 Human aDNA struggles

- **1993** Hagelberg & Clegg: Genetic polymorphisms in prehistoric Pacific islanders determined by analysis of ancient bone DNA *Proc. Biol. Sci.*
- **1993** Stone & Stoneking: Ancient DNA From a Pre-Columbian Amerindian Population *Am. J. Phys. Anthropol.*
- Human DNA studies became the most contentious area of ancient DNA research
- **1994** Krings, et al.: Neandertal DNA Sequences and the Origin of Modern Humans *Cell*
  - extreme safeguards against contamination, numerous controls and in two different laboratories
- **2000** Cooper & Poinar: Ancient DNA: Do It Right or Not at All *Science*
  - suggest “criteria of authenticity” (contamination, reproducibility)

2.5 aDNA "revolution"

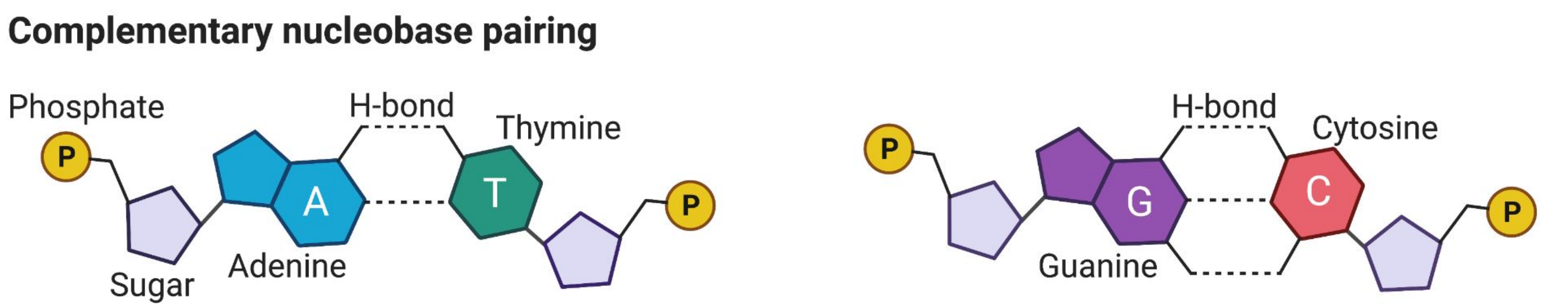
- **2005** Next-generation sequencing



PubMed results for: palaeogenetics OR archaeogenetics OR aDNA

Challenges of aDNA research

3.1 The structure of DNA



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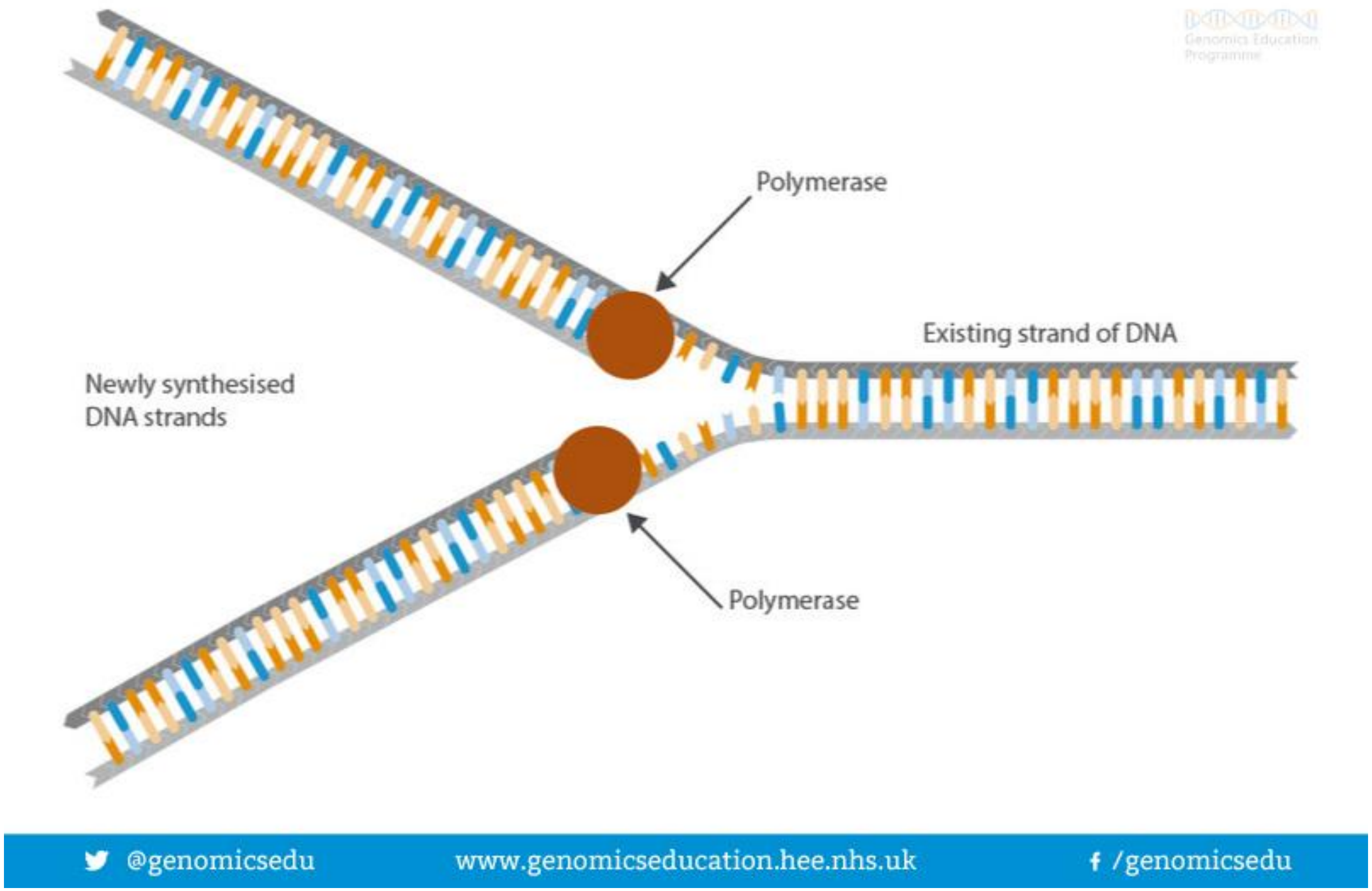
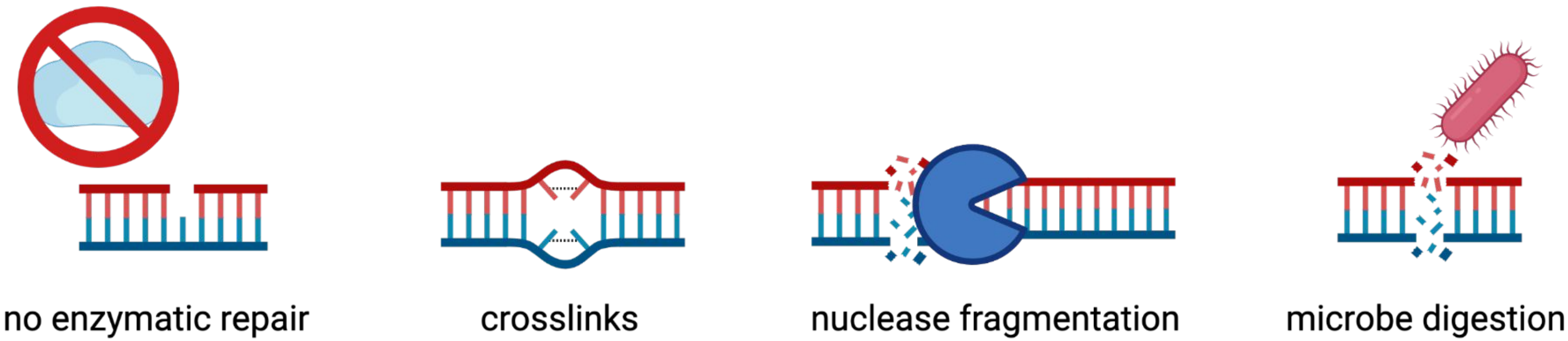
3.2 DNA replication



3.2 ancient DNA

- ancient DNA is degraded
- rate of degradation extremely variable
    - stable, cooler environments seem to facilitate DNA survival
    - depends on the microenvironment of every site
- variety of biological and chemical processes



- fragmentation and damage

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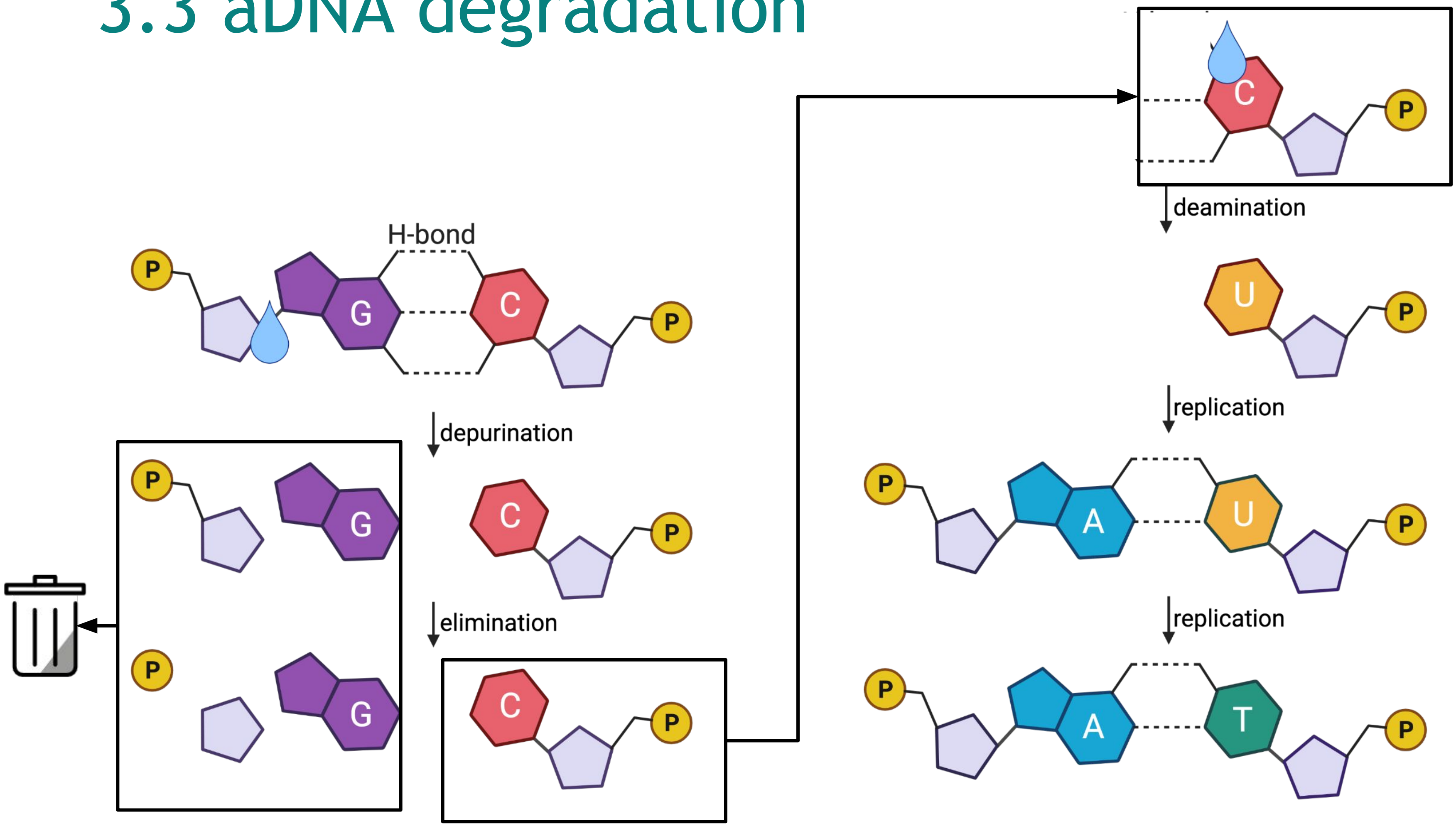
Hofreiter et al. (2001)
Briggs et al. (2007)
Allentoft et al. (2012)
Sawyer et al. (2012)
Dabney et al. (2013)
Key et al. (2017)
Kistler et al. (2017)

3.3 aDNA degradation



- strand breaks (fragmentation)
- C-to-T transitions

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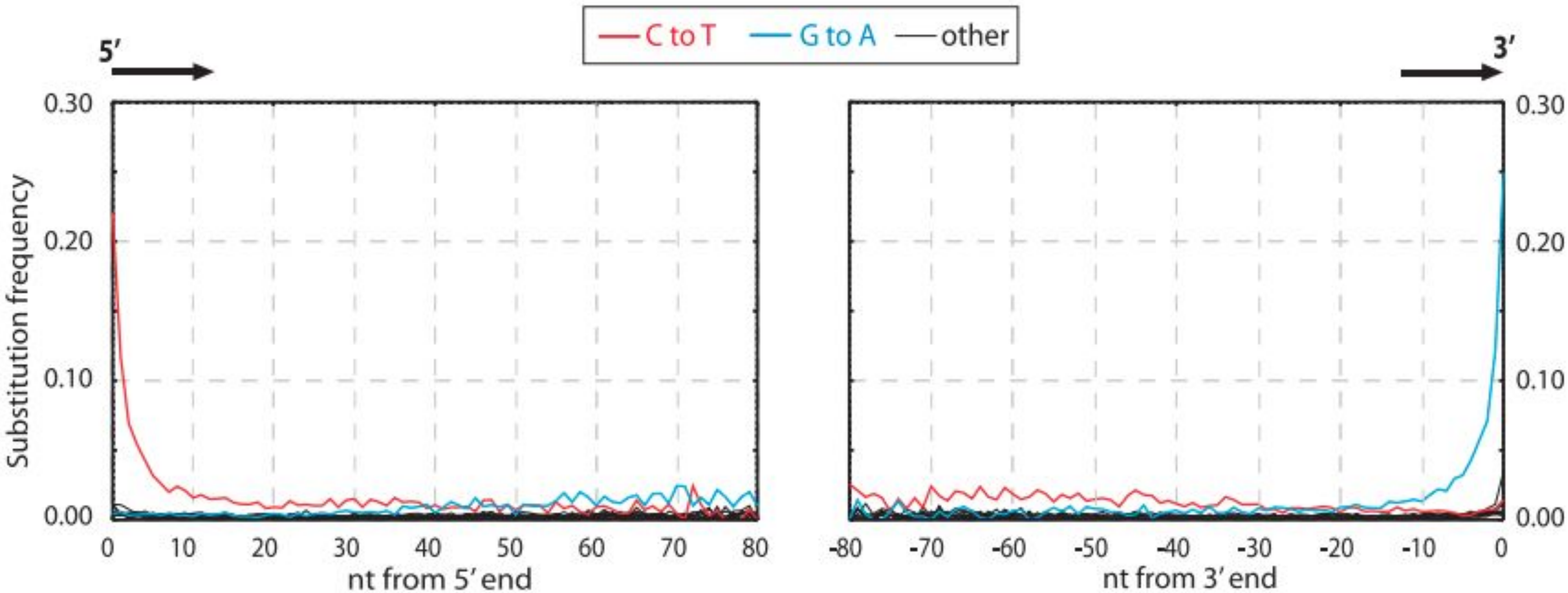
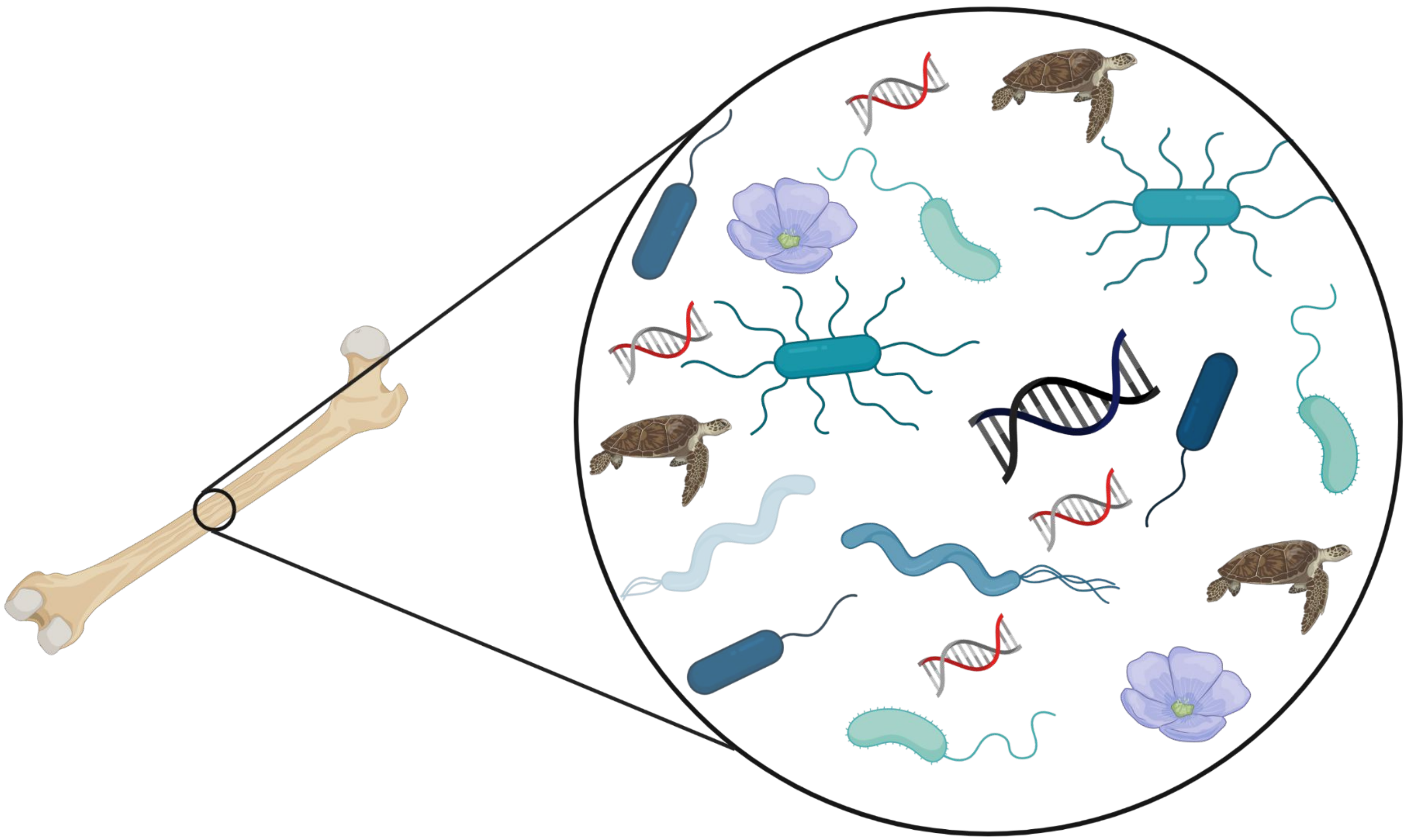
3.4 aDNA “damage pattern”



Briggs et al. (2007)

3.5 Contamination



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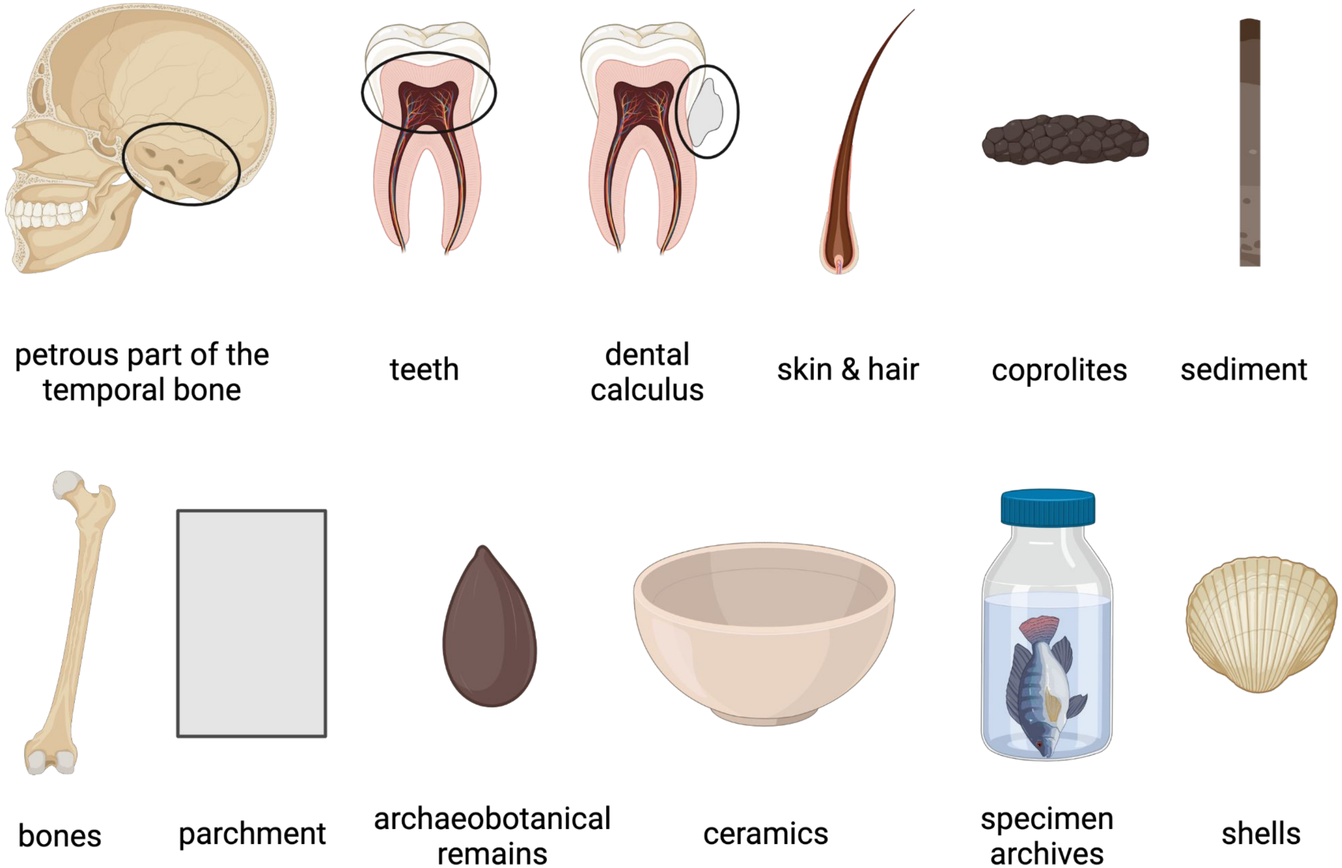
Laboratory methodology

4.1 Sources of aDNA



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Rasmussen et al. (2010)
Gamba et al. (2015)
Pinhasi et al. (2015)
Pedersen et al. (2015)

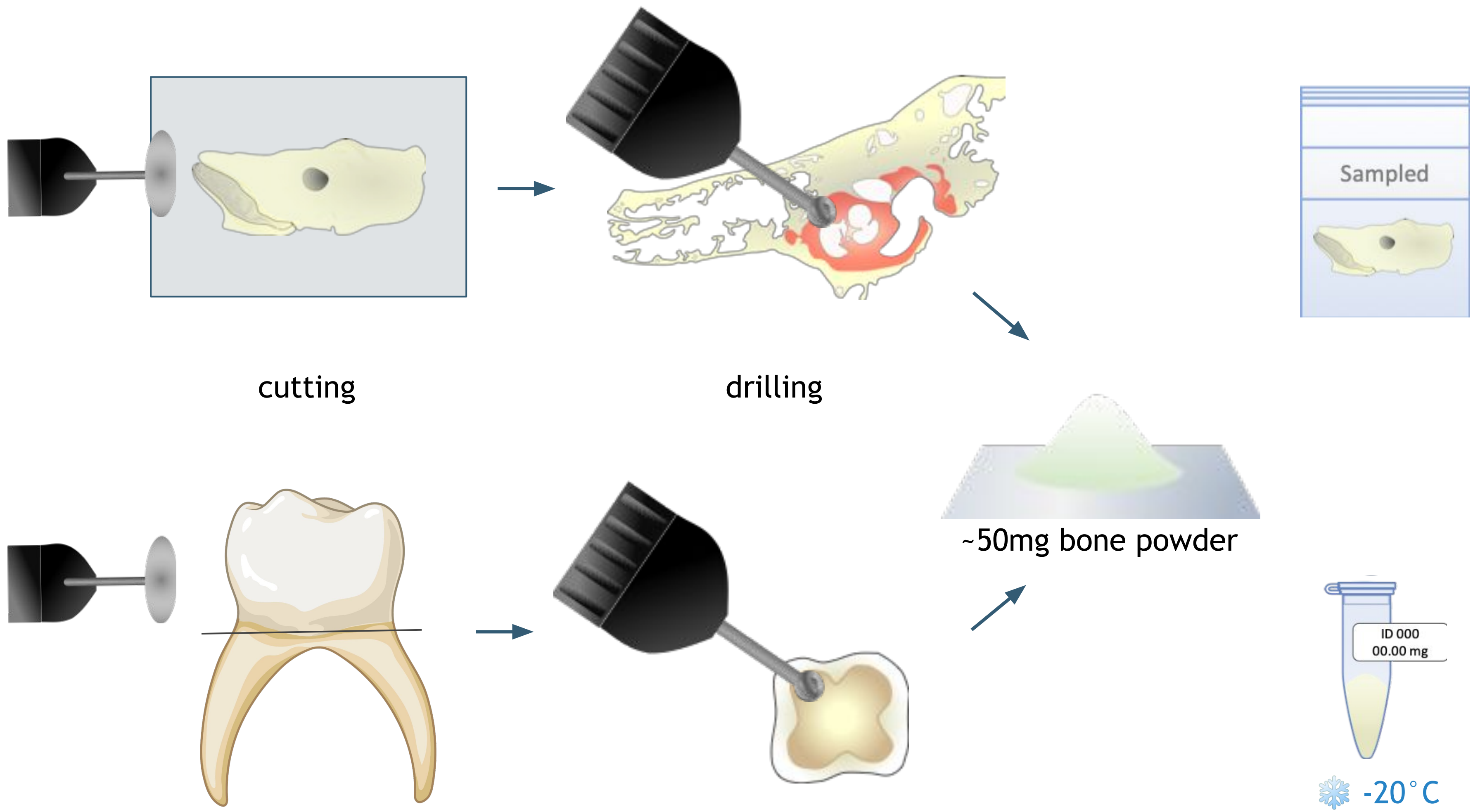
Warinner et al. (2015)
Green & Speller (2017)
Parker et al. (2020)

4.2 Clean room protocol

- dedicated space for only aDNA work & protective lab gear
- decontamination of all used materials (UV & bleach)
- blanks & positive controls

Key et al. (2017)

4.3 Sample preparation



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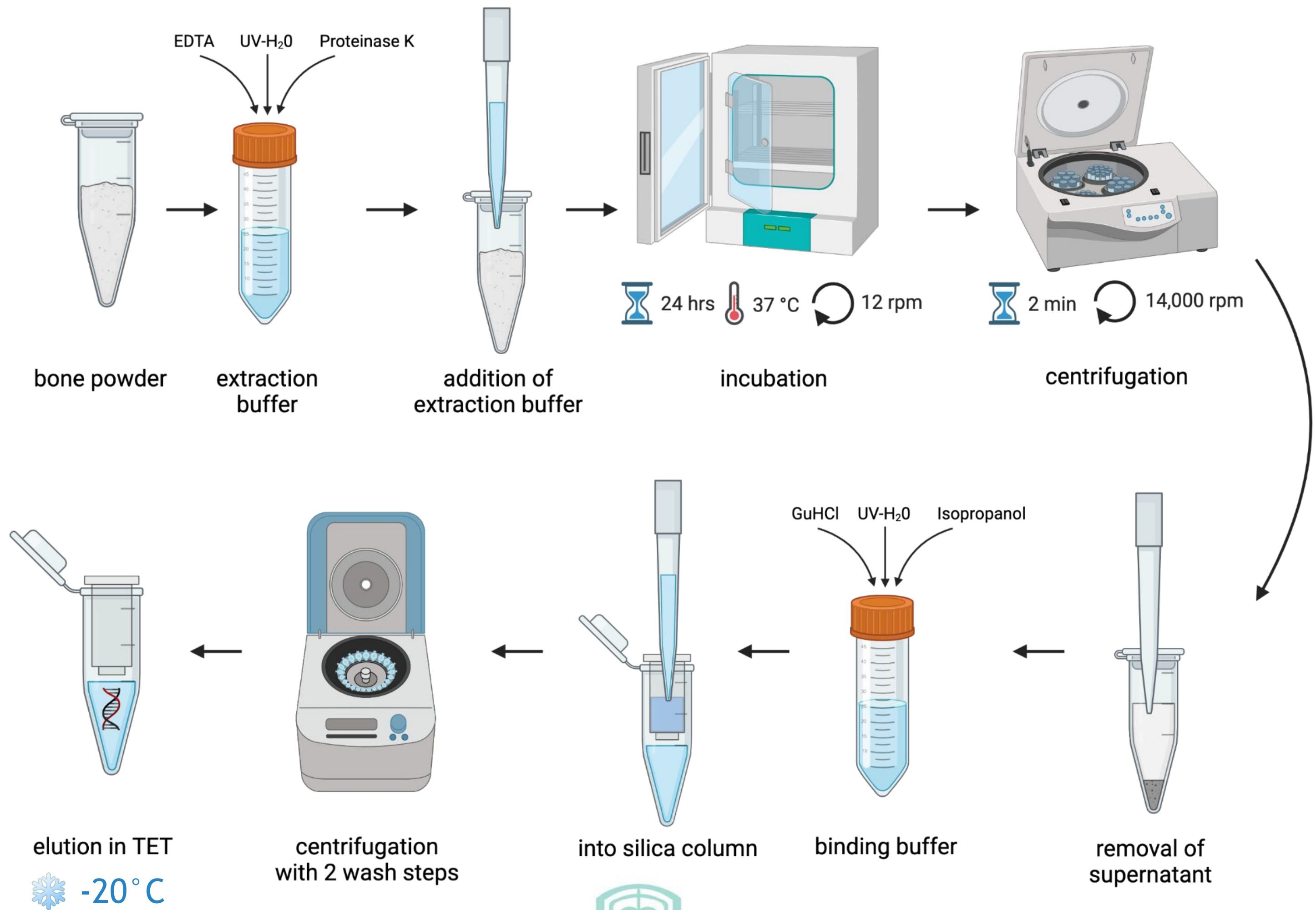
Gamba et al. (2015)
Pinhasi et al. (2015)

4.4 DNA extraction



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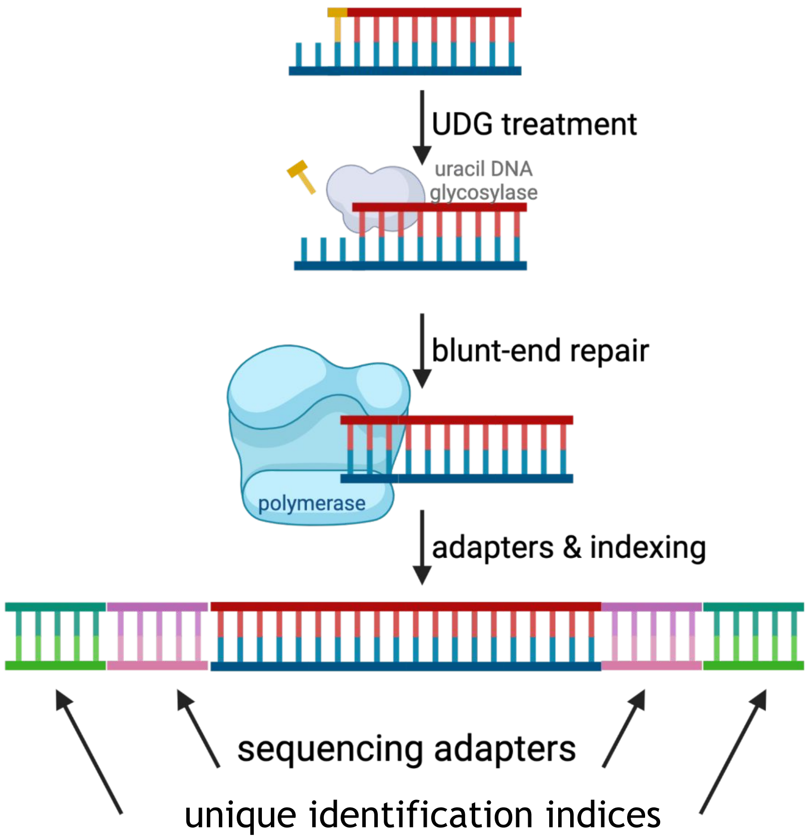
Dabney et al. (2013)

4.5 Library preparation



automated liquid-handling workstation

~3 work days

~9 hours

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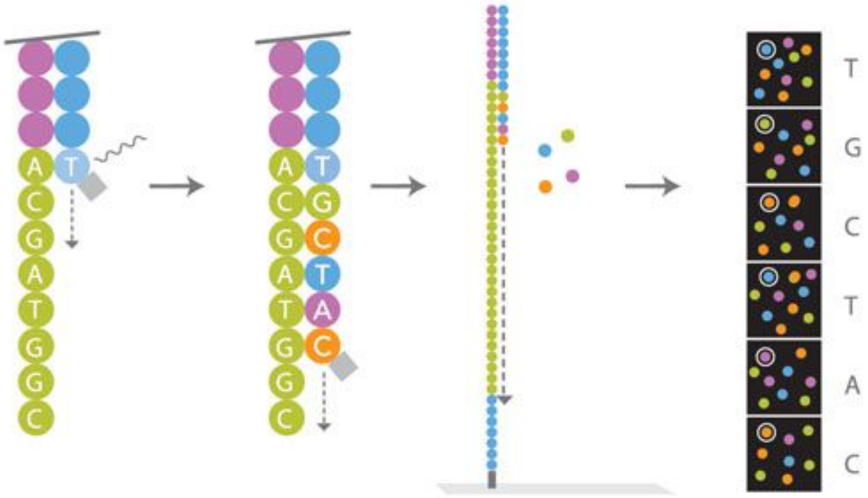
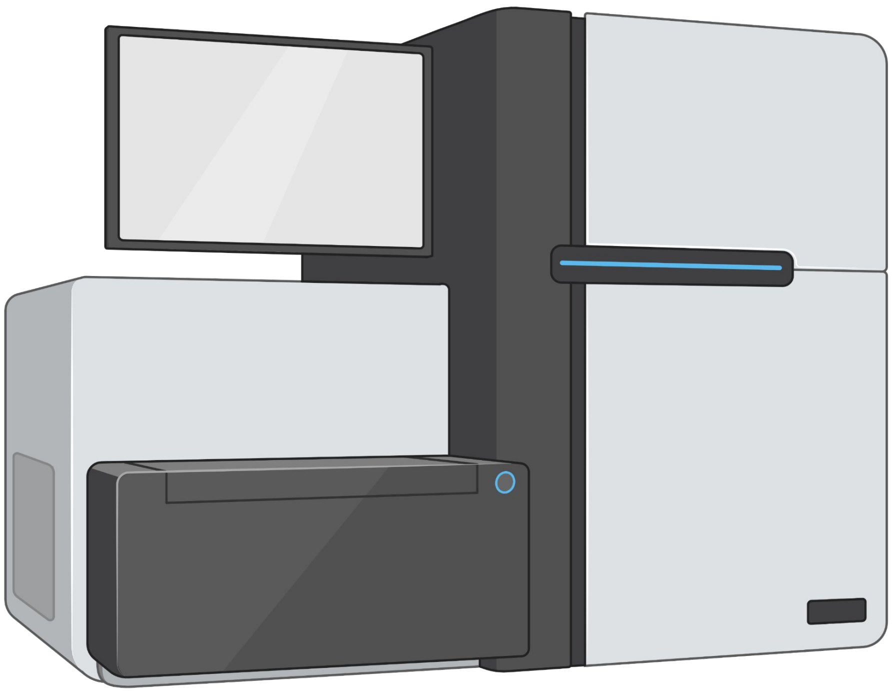
Meyer & Kircher (2010)
Kircher et al. (2012)
Rohland et al. (2015)
Gansauge et al. (2020)

4.6 Sequencing





See “G7W: Intro to NGS processing” tomorrow at 11:00 (CEST) for more details

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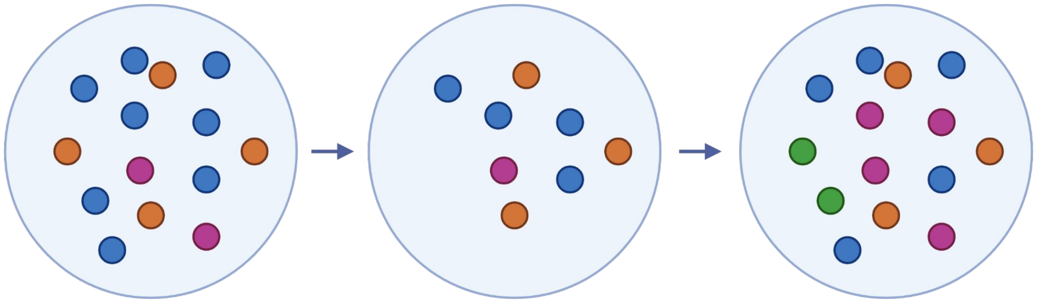
What do we study with aDNA?

5.1 Population Genetics

- Population genetics studies genetic differences within and across populations, and the dynamics of how populations evolve
- processes such as natural selection, genetic drift, mutation and gene flow/admixture
- ancient DNA → comparisons between genetic variation at different time points to infer past demographic processes



→ G2L
Intro to PopGen
tomorrow @ 3.30 pm

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5.2 PopGen - Extinct Hominins

Neanderthals (*Homo [sapiens] neanderthalensis*)

- occupied parts of Eurasia between ca. 400,000 - 30,000 yrs
- morphological comparisons → direct ancestors of AMHs OR genetic contribution to AMHs OR complete replacement
- early mtDNA studies: outside human variation
- nuclear DNA: minor contribution to non-Africans (1.5 - 2.5%) & indications of positive & purifying selection

Krings et al. (1997)
Green et al. (2010)
Prüfer et al. (2014) & (2017)

5.2 PopGen - Extinct Hominins

Denisovans

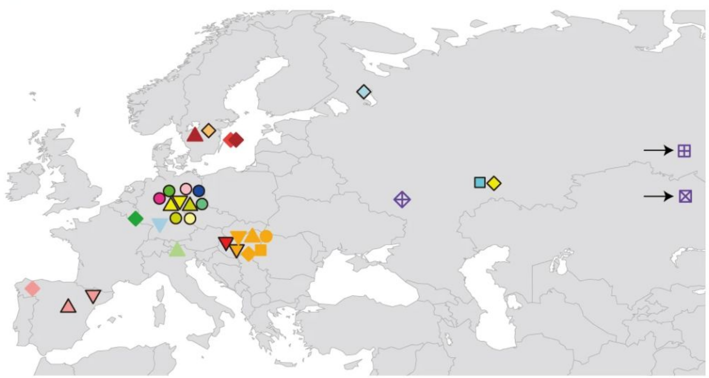
- individual bones recovered from Denisova Cave, Siberia & Tibet dated ~160,000 yrs
- common origin with Neanderthals
- contribution to Near Oceanians (~3%), East/South Asians & Native Americans (~0.2%)
- regional differences in introgressed sequences
- some evidence for divergent Denisovan ancestries in Papuans

Reich et al. (2010)

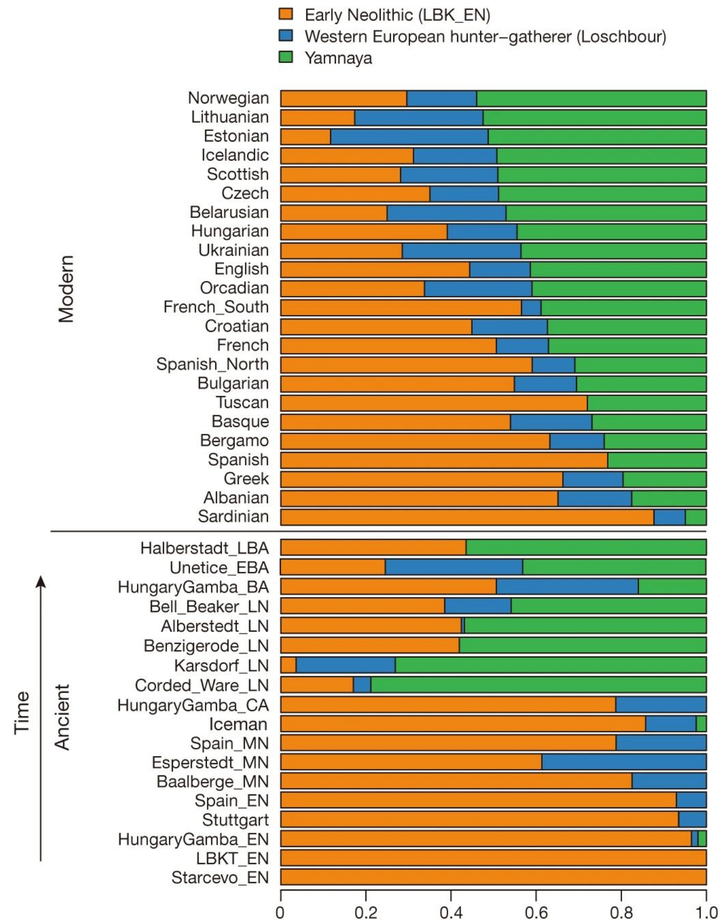
Reich et al. (2010) & (2011)
Meyer et al. (2012)
Prüfer et al. (2014)
Qin & Stoneking (2015)
Jacobs et al. (2019)
Bergström et al. (2020)

5.3 PopGen - Steppe Expansion

a

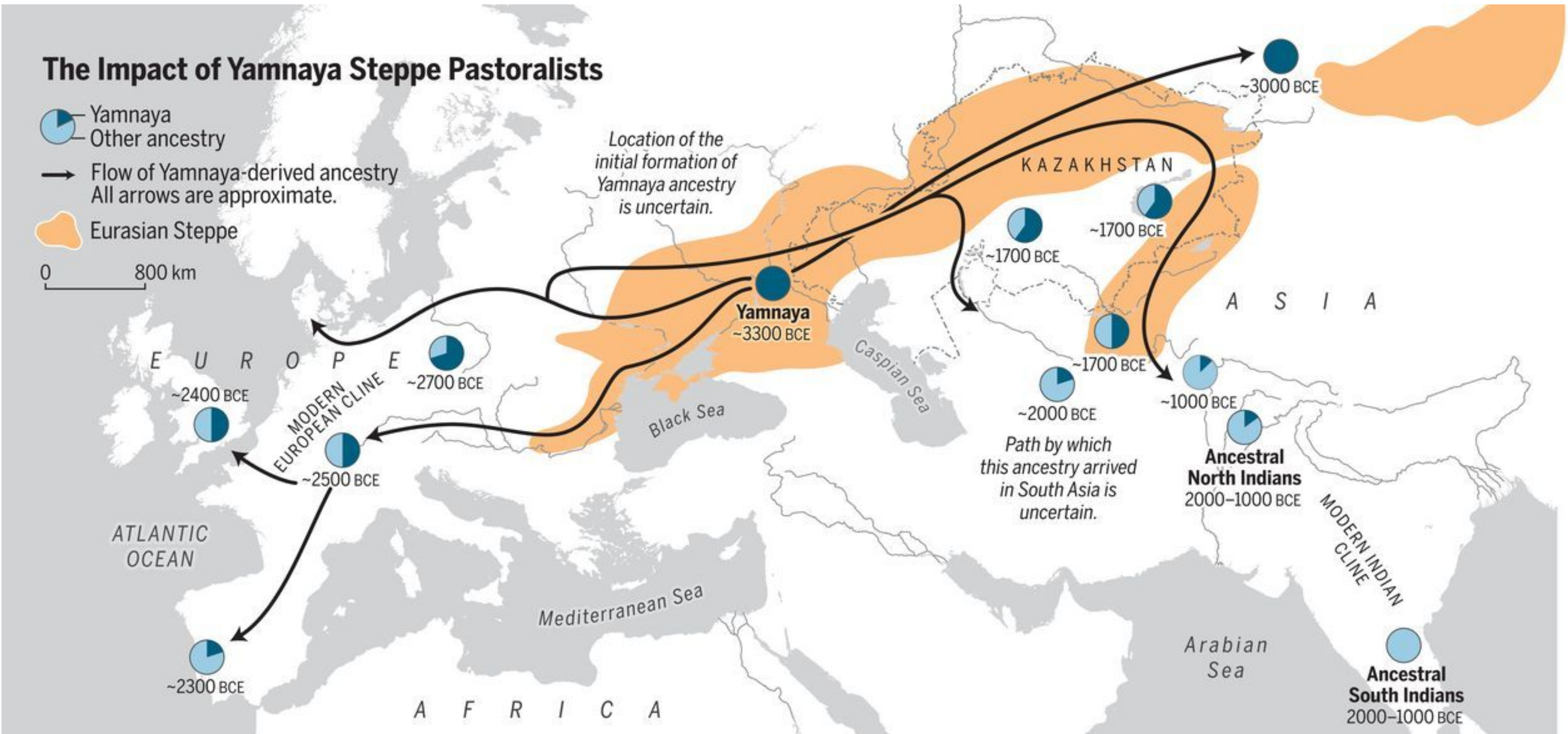


Time (ky BC)	Group	West	Central	East
0.9	Iron Age		Hungary IA (1)	
1.1	Late Bronze Age		Halberstadt (1) Hungary BA (2)	
2.2–1.6	Early Bronze Age		Unetice (8)	
2.5–2.2	Late Neolithic		Alberstedt (1) BenzigerodeHeimburg (3) Bell Beaker (6) Karsdorf (1) Corded Ware (4)	
3.3–2.7	Late Copper Age (steppe)		Hungary CA (1) Sweden NHG (3)	Yamnaya (9)
4–3	Mid Neolithic	La Mina (4)	Iceman (1) Esperstedt (1) Baalberge (3) Sweden MN (1)	
6–5.5	Early Neolithic	Els Trocs (5)	Stuttgart (1) LBK (12) LBKT (1) Hungary EN (8) Starcevo (1)	
6–4.6	Holocene hunter-gatherer	La Brana1 (1)	Loschbour (1) Hungary HG (1) Sweden MHG (1) Motala (7)	Karelia (1) Samara (1)
43–22	Pleistocene hunter-gatherer			MA1 (1) Kostenki14 (1) Ust Ishim (1)



Haak et al. (2015)

5.3 PopGen - Steppe Expansion



Allentoft et al. (2015)
Haak et al. (2015)
Jones et al. (2015)
Mathieson et al. (2015)
Lazaridis et al. (2016)
Olalde et al. (2018) & (2019)
Narasimhan et al. (2019)

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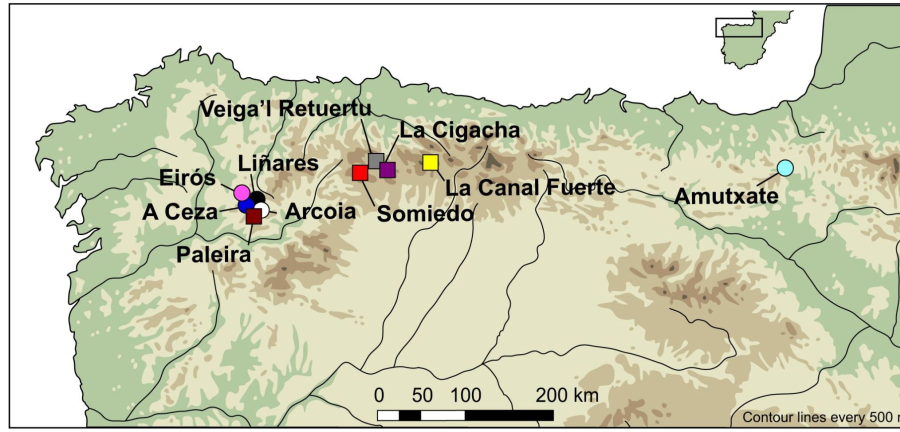
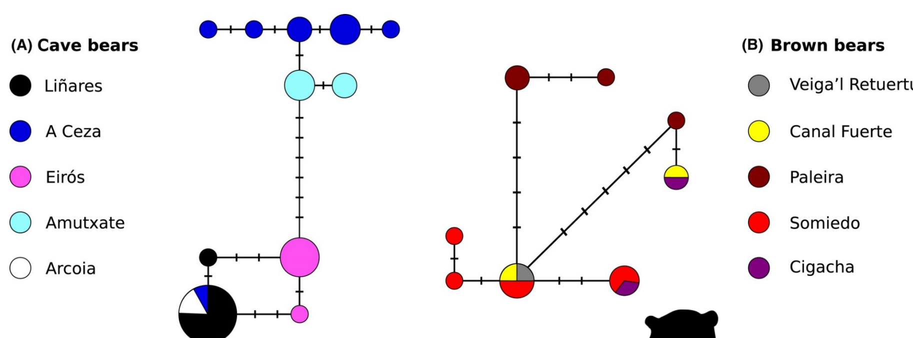
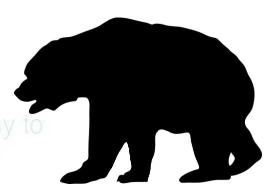
5.5 PopGen - Animals

Fortes et al. (2016) Mol. Ecol.

- Behaviour and social differences between cave bear vs brown bears
    - Reconstruct family relationships via mitochondrial haplotypes
- Results:
    - Cave bear lineages: same in same cave
    - Brown bear lineages not consistent
    - Predictable hibernating behaviour = humans can hunt
    - Harder to hunt = less likely to be hunted

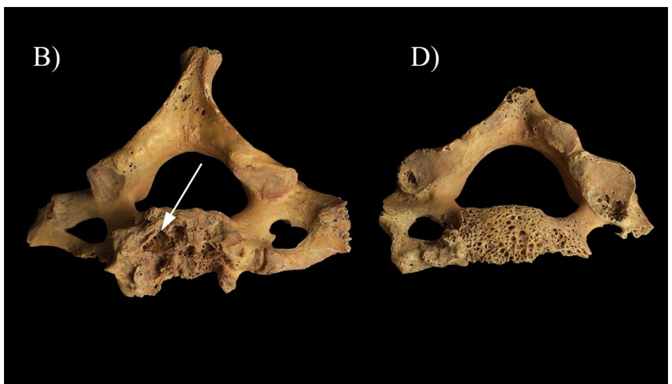






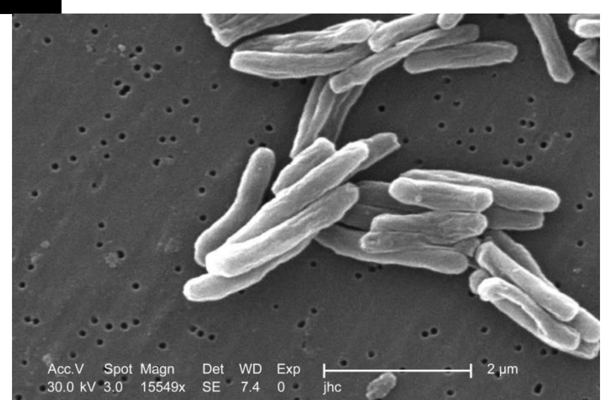
5.4 Palaeopathology and infectious disease

- What was the cause of death?
  - Cause of bone lesions?
  - What if no skeletal pathologies?
  - Chronic disease vs lethal disease?
  - What caused unusual attritional profiles?



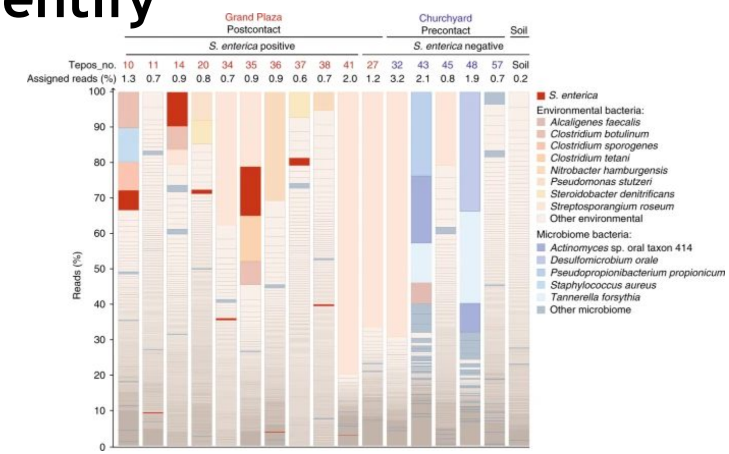
Dabernat et al. (2014) PLOS ONE

openmoji.org



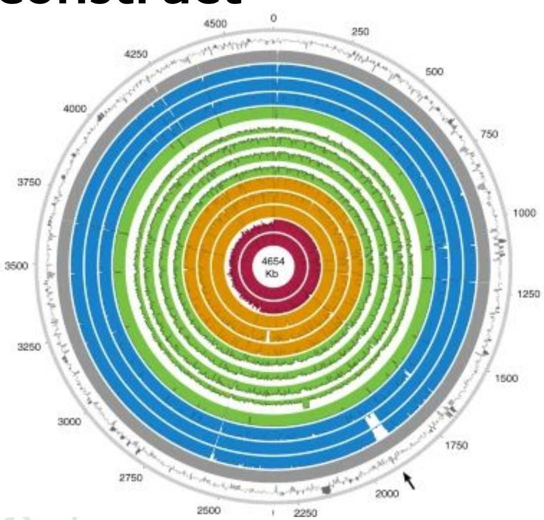
5.4: How to detect Ancient Pathogens

Identify



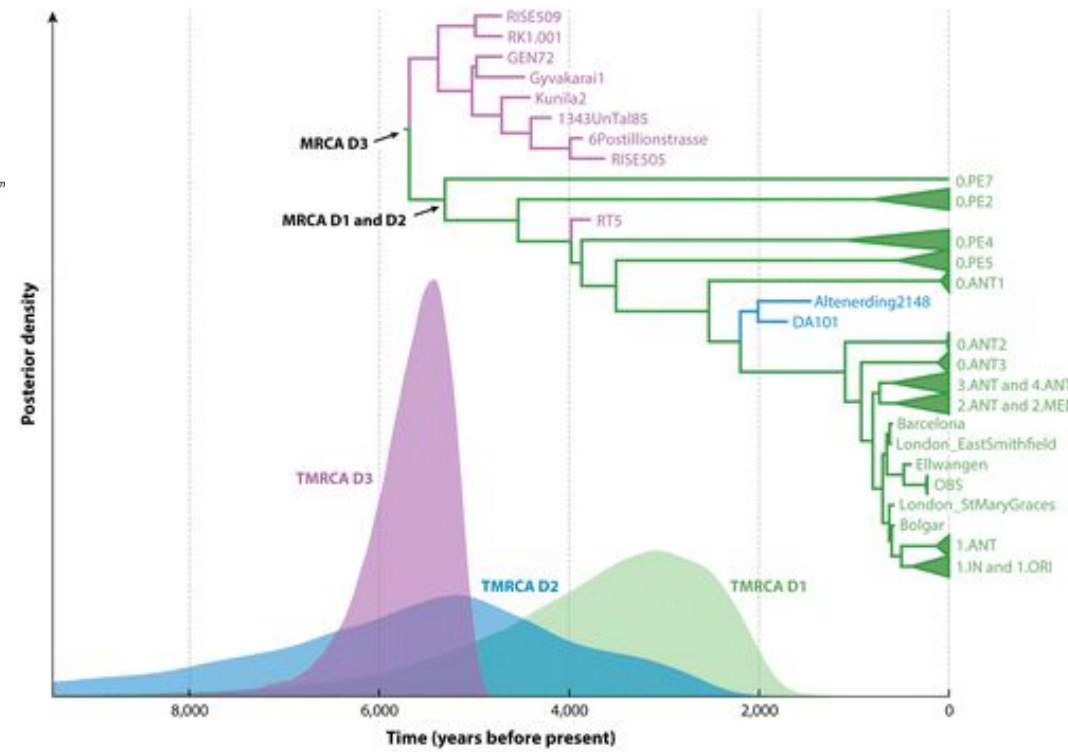
Vågene et al (2018) Nat. Eco. Evo

Reconstruct



Spyrou et al. (2019) Nat. Coms

Relationship



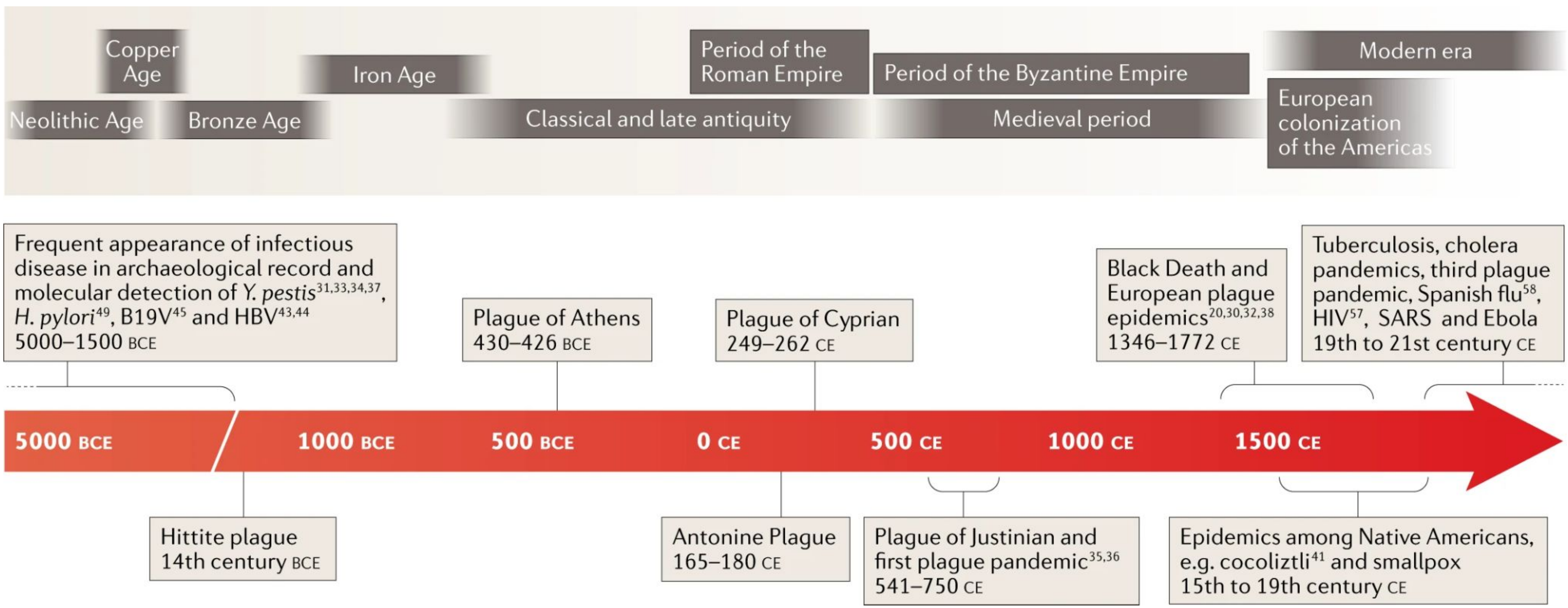
Bos KI, et al. 2019.
Annu. Rev. Microbiol. 73:639–66

Date

→ G4L
Microbial archaeology
Weds 18th @ 11.00

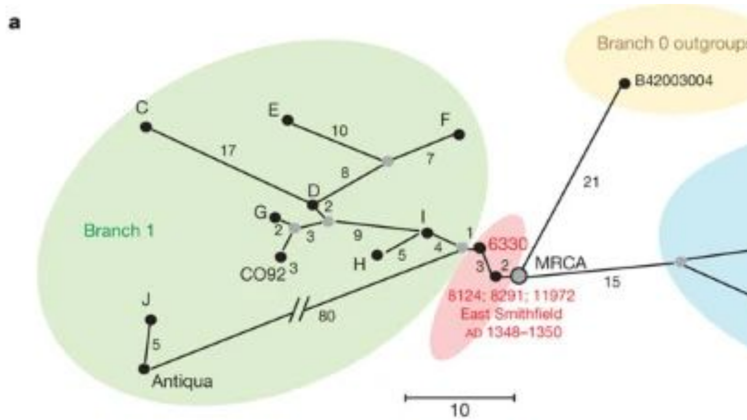
→ G8W
Phylogenetics Workshop
Weds 25th @ 13.30

5.4 Why study Ancient Pathogens

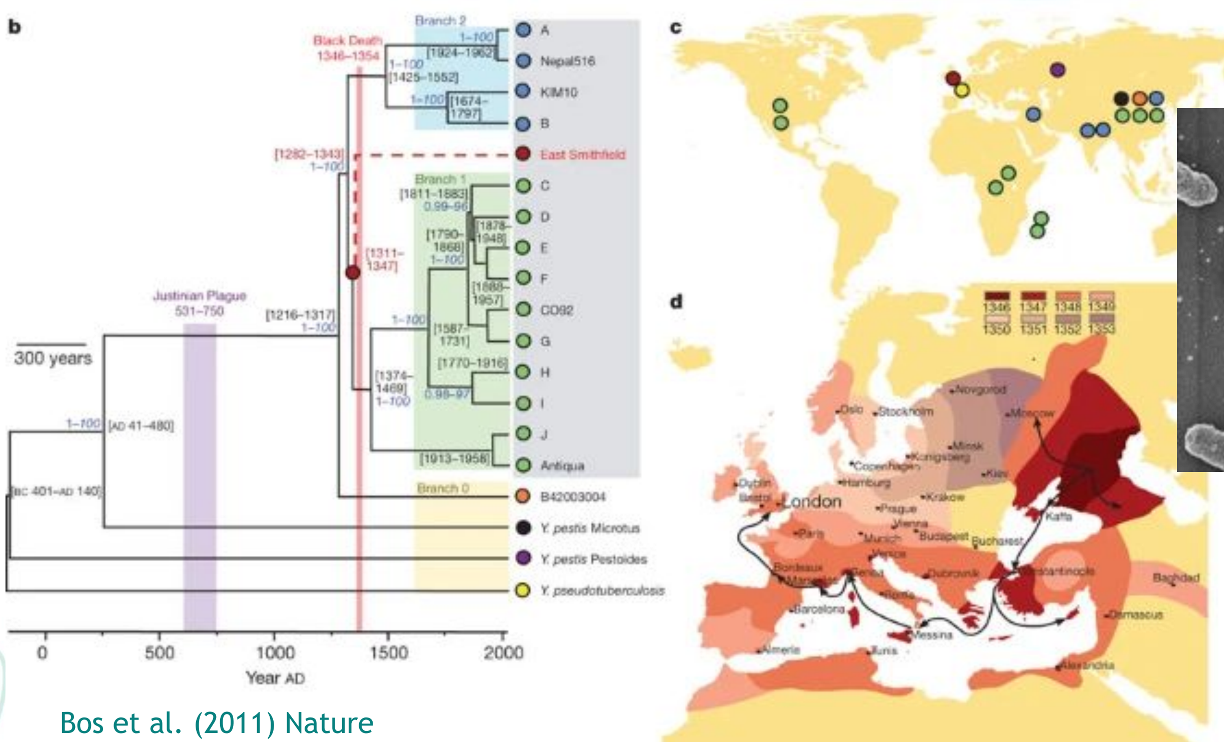


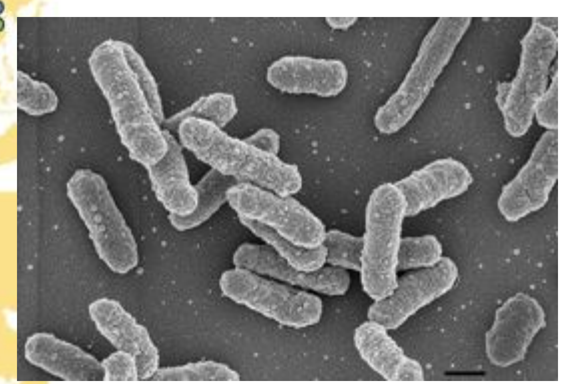
Spyrou et al. (2019) Nature Reviews Genetics

5.4 Example: Cause of Black Death



The Black Death of 1347–1351, caused by the bacterium *Yersinia pestis*[2,3], provides one of the best historical examples of an emerging infection with rapid dissemination and high mortality, claiming an estimated 30–50% of the European population in only a five-year period[4]. Discrepancies in epidemiological trends between the medieval disease and modern *Y. pestis* infections have ignited controversy over the pandemic's aetiologic agent[5,6]. Although ancient DNA investi-

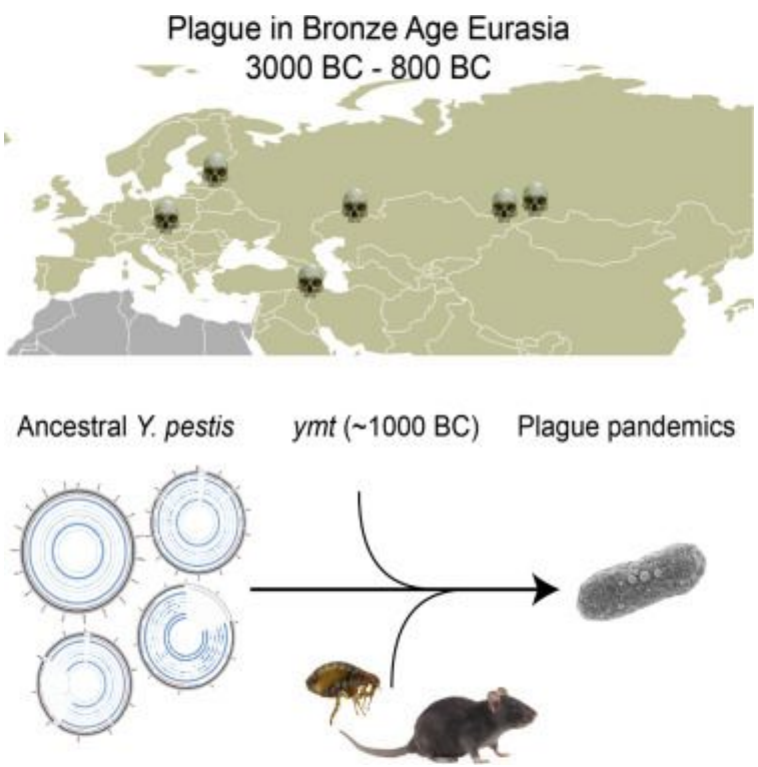




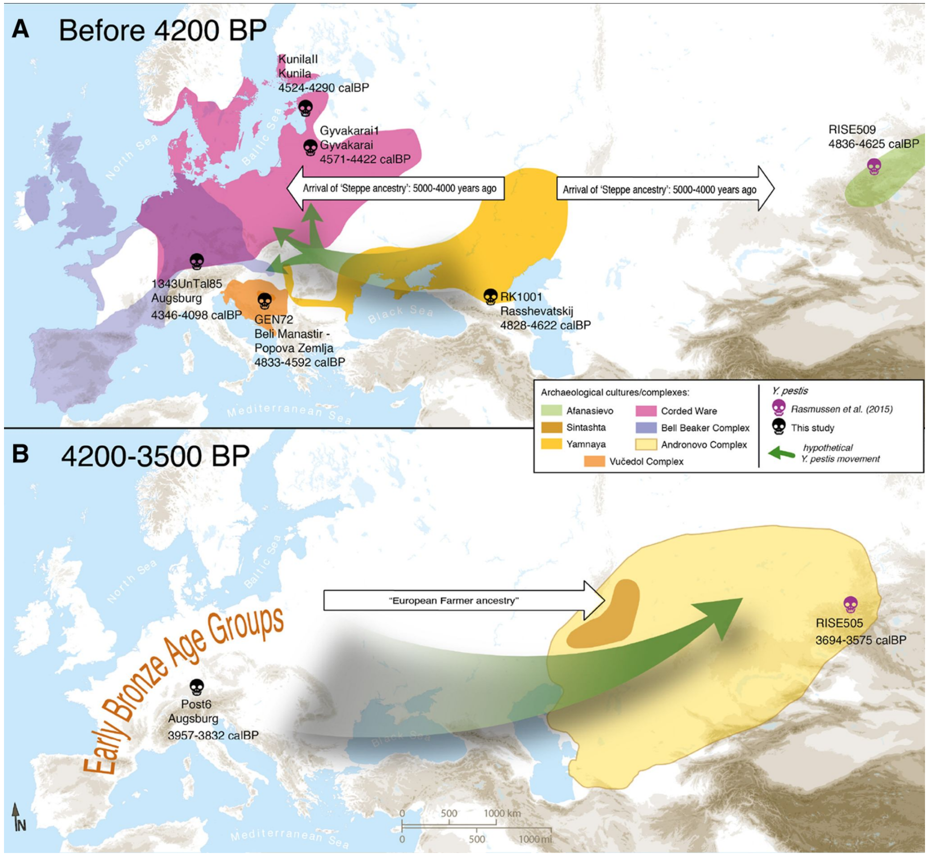
Quelle: Muhsin Özel, Gudrun Holland, Rolf Reissbrodt/RKI

Bos et al. (2011) Nature

5.4 Example: Mystery Epidemic?

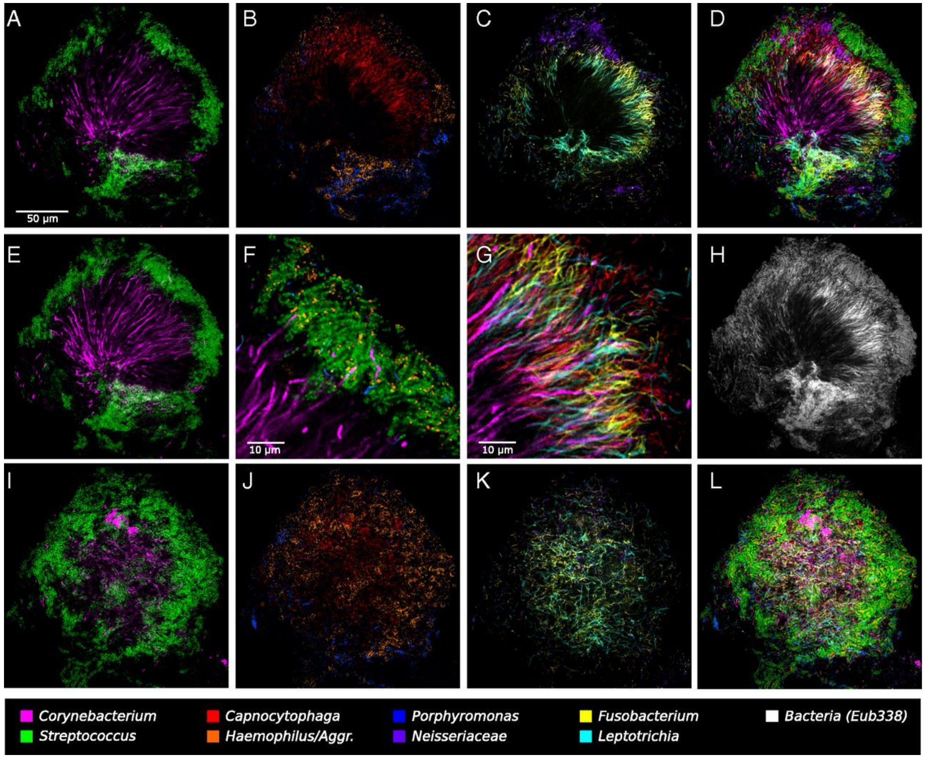


Rasmussen et al. (2015) Cell

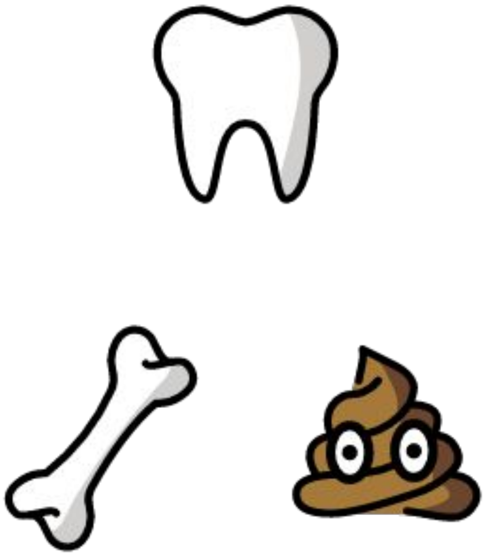


Andrades Valtueña (2017) Curr. Bio.

5.5 What: Ancient (Human) Microbiomes



Mark Welch, J. L. et al. (2016) doi: 10.1073/pnas.1522149113.



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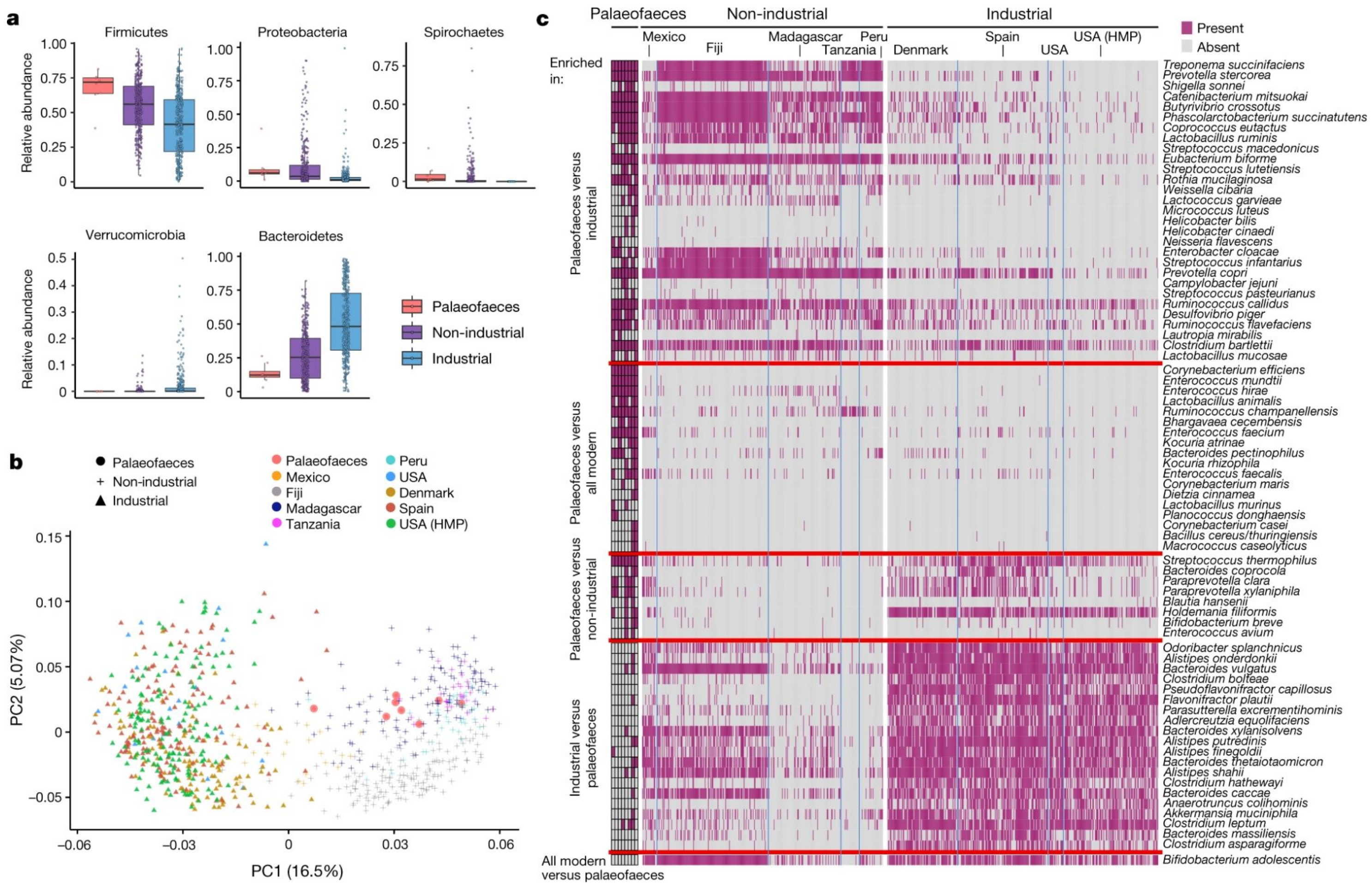
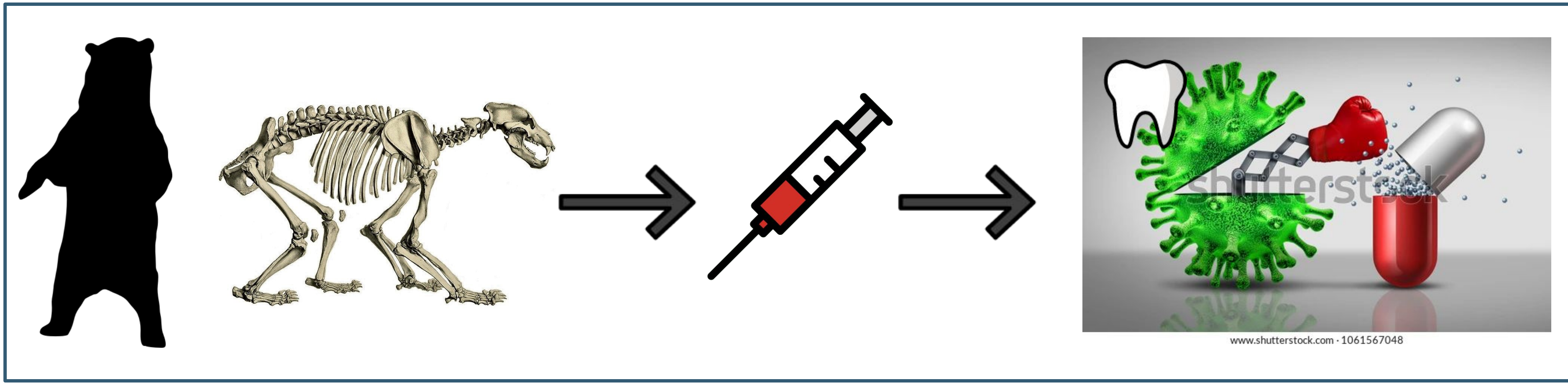
5.5 Why: Ancient Microbiomes

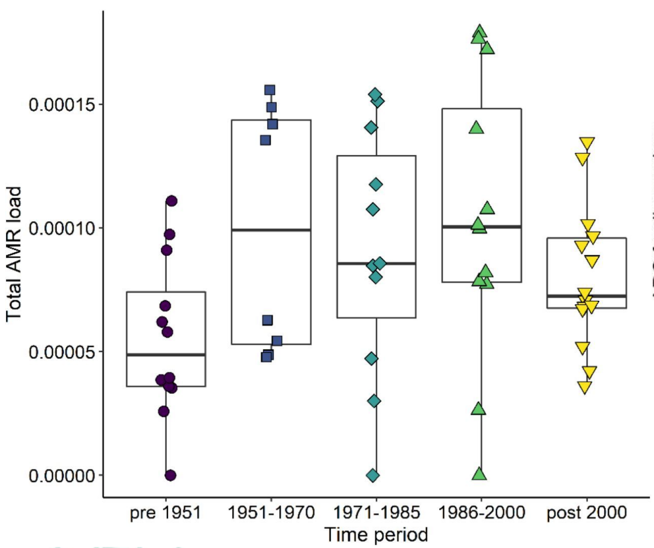


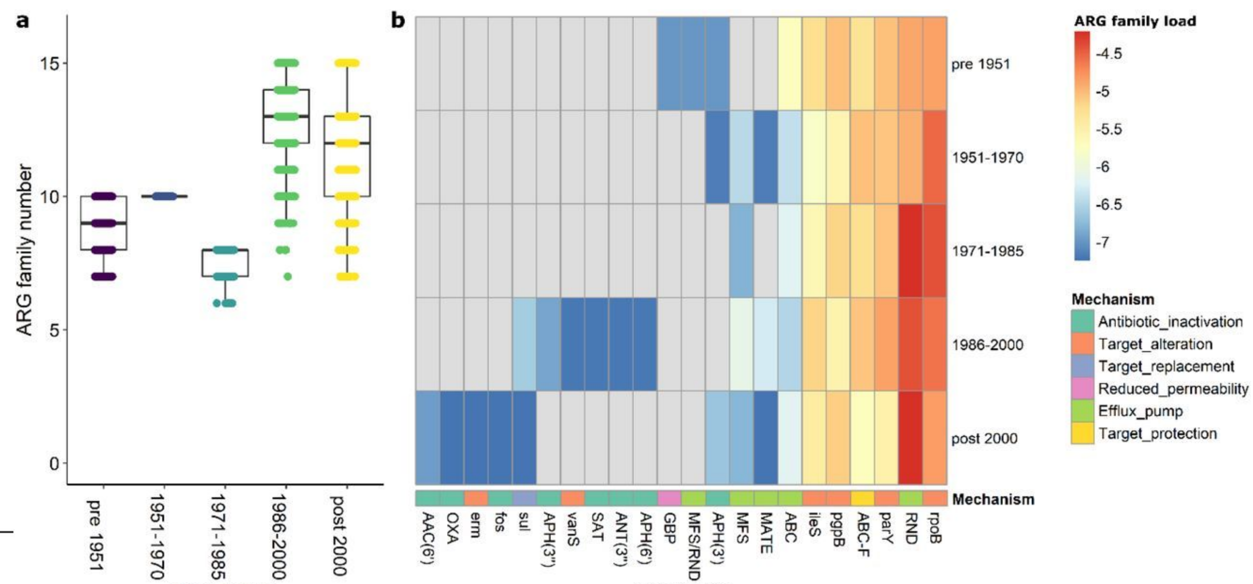
Wibowo, M. C. et al. (2021) Nature

→ G5W
Intro to ancient microbiome analysis
Thurs 19th @ 11.00

5.6 Example: oral antibiotic resistance

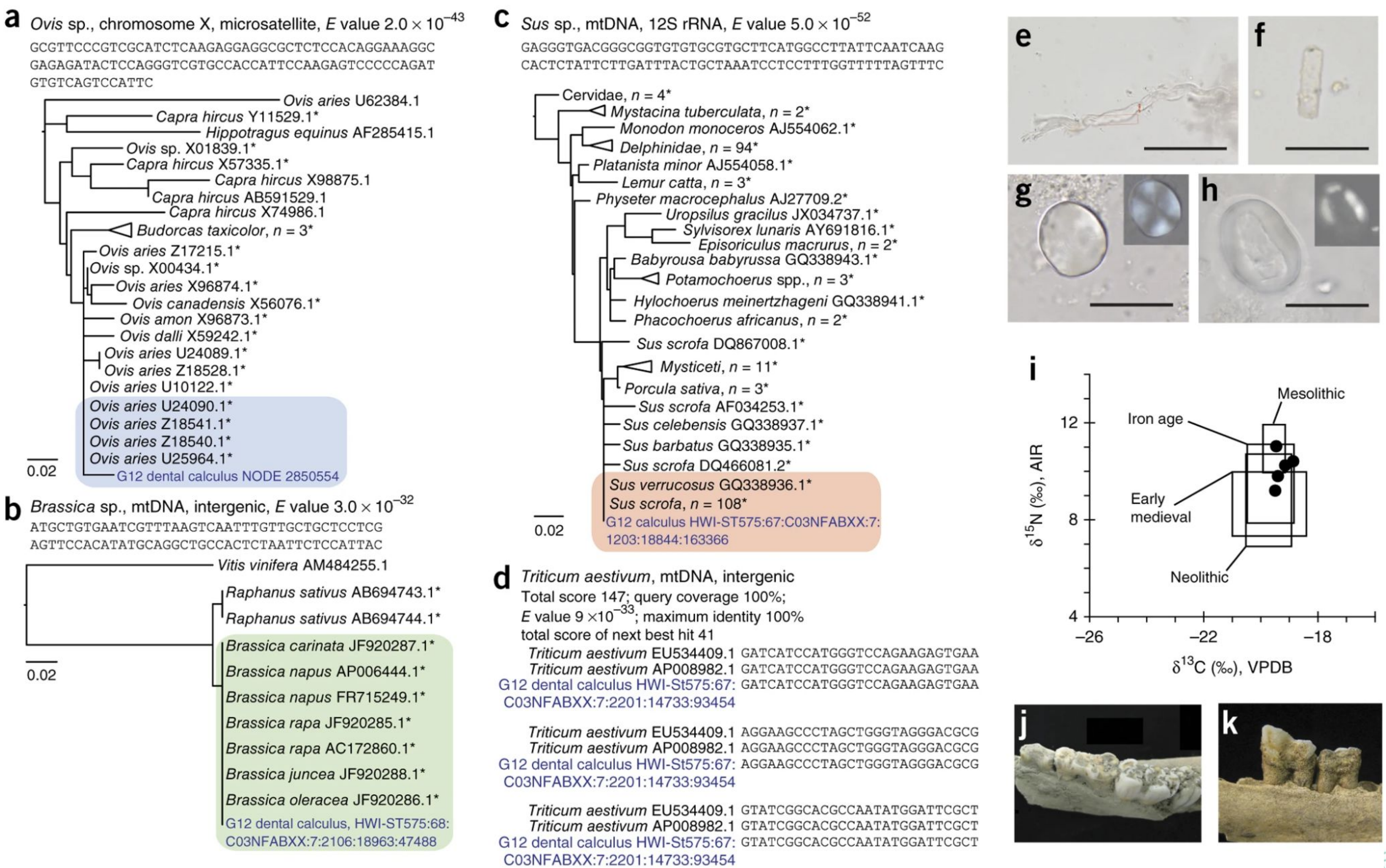






Brealey et al. (2020) bioRxiv

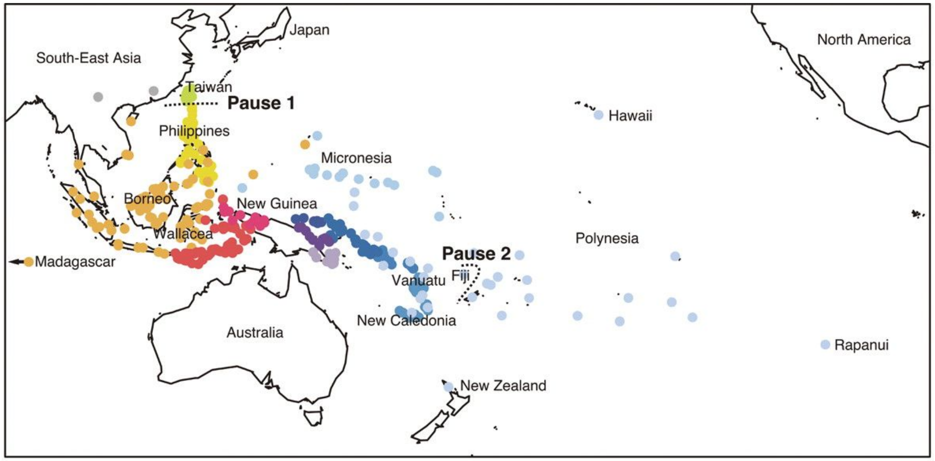
5.6 Example: diet sources



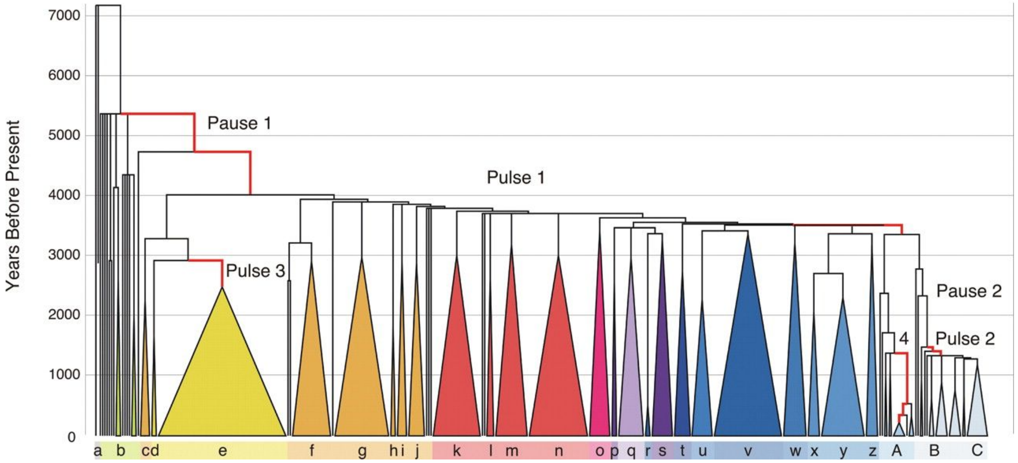
Warinner, C. et al. (2014) Nature genetics

Interface with archaeology and linguistics

6.1 Vanuatu



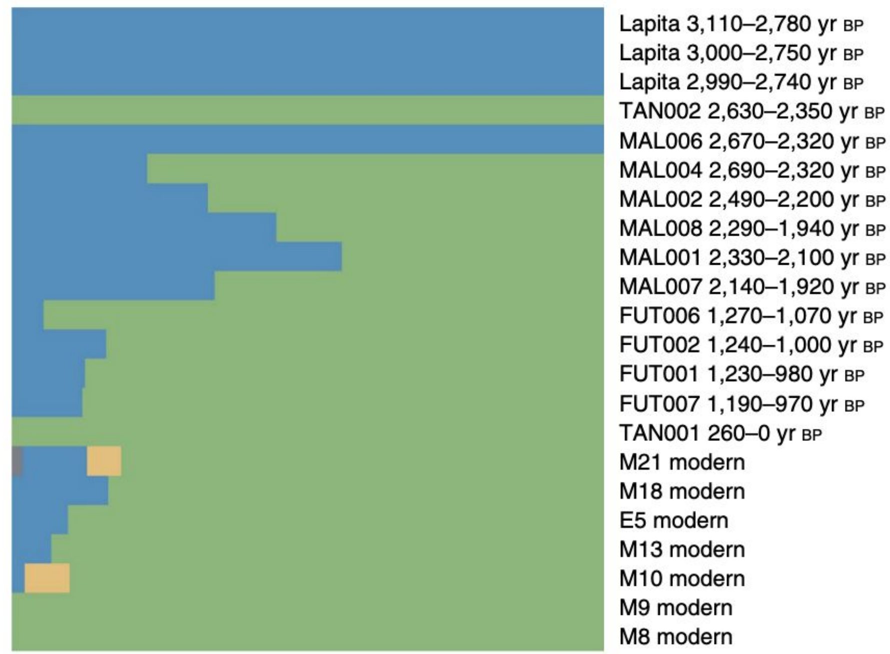
Japan
North America
South-East Asia
Taiwan
Pause 1
Hawaii
Philippines
Micronesia
Borneo
New Guinea
Wallacea
Polynesia
Pause 2
Madagascar
Vanuatu
Fiji
New Caledonia
Australia
Rapanui
New Zealand



Years Before Present
7000
6000
5000
4000
3000
2000
1000
0
Pause 1
Pulse 1
Pulse 3
Pause 2
Pulse 2
4
a b cd e f g hi j k l m n o p q r s t u v w x y z A B C

6.1 Vanuatu

- Taiwanese-related ancestry on Vanuatu & Tonga by ~2,700 BP (Lapita)
- large Papuan component in present-day ni-Vanuatu
- Papuan ancestry present by 2,500 BP
- incremental ancestry shift
- shared linguistic & cultural features with Papuans
- supports archaeological & linguistic two-wave model



Gray et al. (2009)
Skoglund et al. (2016)
Posth et al. (2018)
Lipson et al. (2018) & (2020)

Summary

How

- Early days: exploration
- aDNA exploded since 2005 and NGS sequencing
- Many sources of aDNA
    - Bone, teeth, hair, parchment, shells, calculus, palaeofaeces
- aDNA is
    - damaged
    - fragmented
    - low-abundant
    - contaminated

What

- Humans
    - Relationships with ancestors
    - Migration and interaction
- Animals
    - Impact of human activity
- Microbes
    - Cause of death
    - Evolution of Infectious disease
    - Behaviour
- (+ more!)

Archaeogenetics program:

- **Intro to NGS data processing**: James A. Fellows Yates
- **Intro to Population Gen.**: Mei-Shin Wu & Selina Carlhoff
- **Microbial Archaeology**: Irina M. Velsko & Zandra Fagernäs
- **Intro to Ancient Microbiome Analysis**: Maxime Borry
- **Keynote lecture**: Christina Warriner
- **TreeMix**: Mei-Shin Wu & Selina Carlhoff
- **Phylogenetics**: Megan Michel
- **Ethics in Archaeogenetics**: Selina Carloff

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