



Introduction to Archaeogenetics

(by) Selina Carlhoff & James A. Fellows Yates (by)

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?



SUMMER
SCHOOL
2021



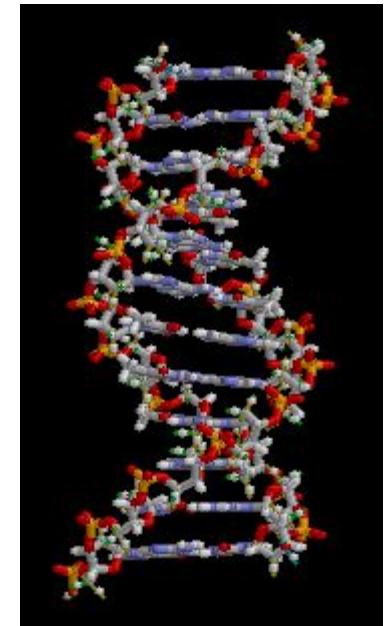
Doorway to
Human
History





1 What is archaeogenetics?

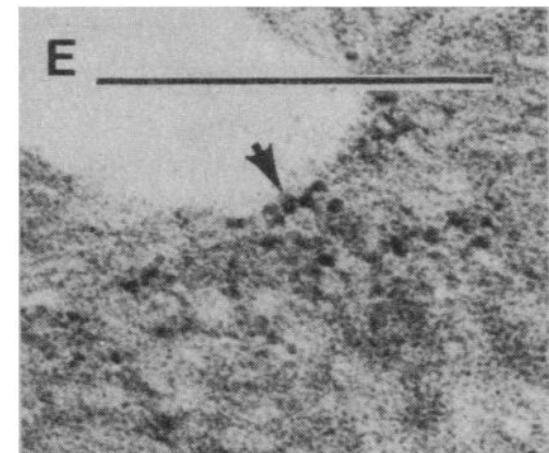
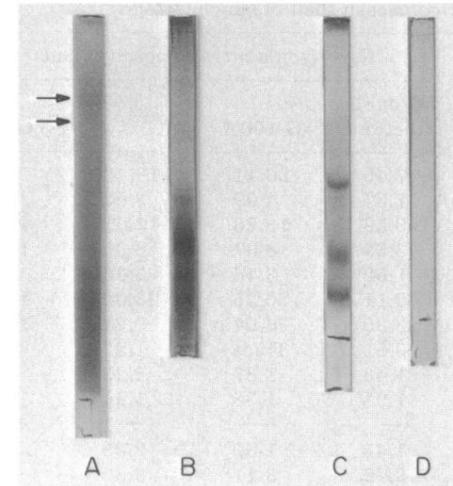
- = “arkhaios” (“ancient”) + genetics (“the study of heredity”)
- the study of ancient genetic material (aDNA)
- DNA = genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses
- combine knowledge of ancient and present-day genomics to understand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





2.1 First evidence for ancient cell organelles

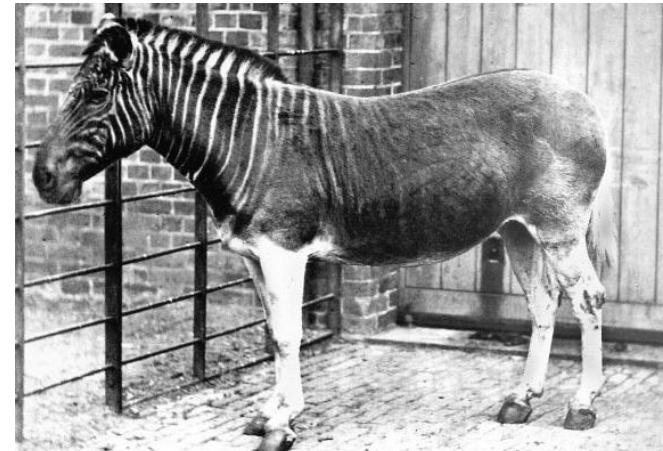
- **1972** Wyckoff: The Biochemistry of Animal Fossils
- **1976** Weiner, Lowenstam & Hood: Characterization of 80-million-year-old mollusk shell proteins *PNAS*
 - peptide bonds can last for up to 100,000,000 years in fossil shells and bones
- **1982** Poinar & Hess: Ultrastructure of 40-Million-Year-Old 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 Polymerase Chain Reaction
 - 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

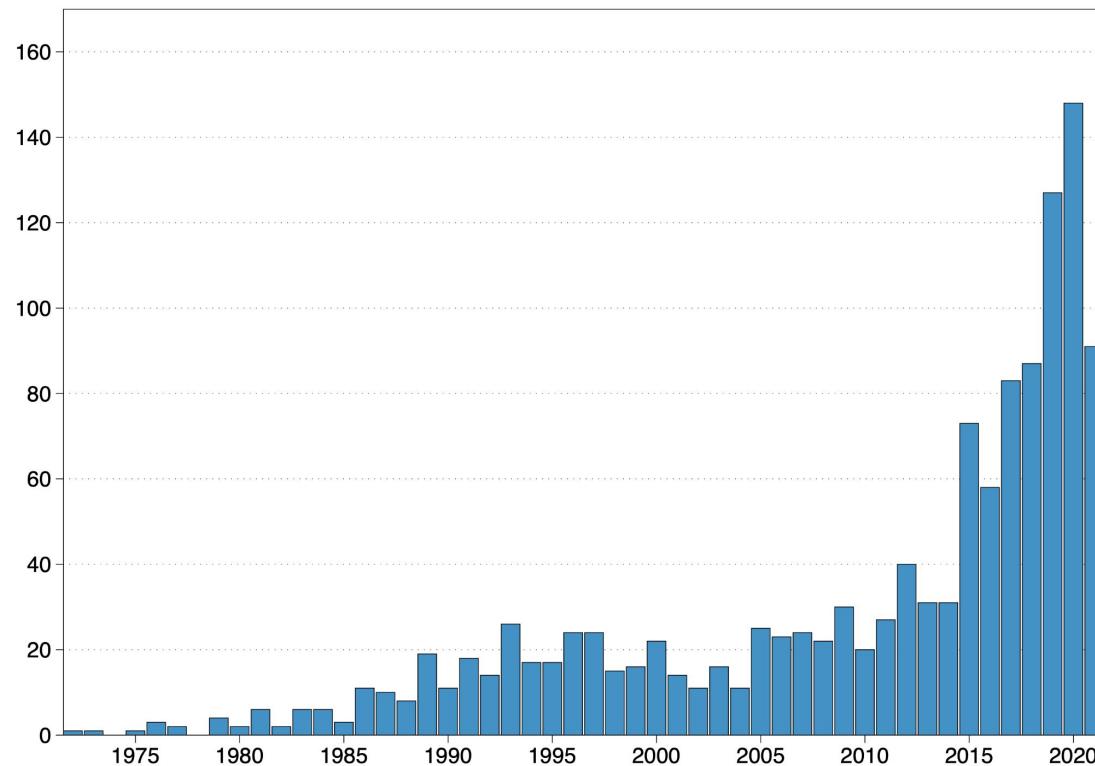
- **1993** Hagelberg & Clegg: Genetic polymorphisms in prehistoric Pacific islanders determined by analysis of ancient bone DNA *Proc. Biol. Sci.*
- **1993** Stone & Stoneking: Ancient DNA From a Pre-Columbian Amerindian Population *Am. J. Phys. Anthropol.*
- Human DNA studies became the most contentious 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



SUMMER
SCHOOL
2021

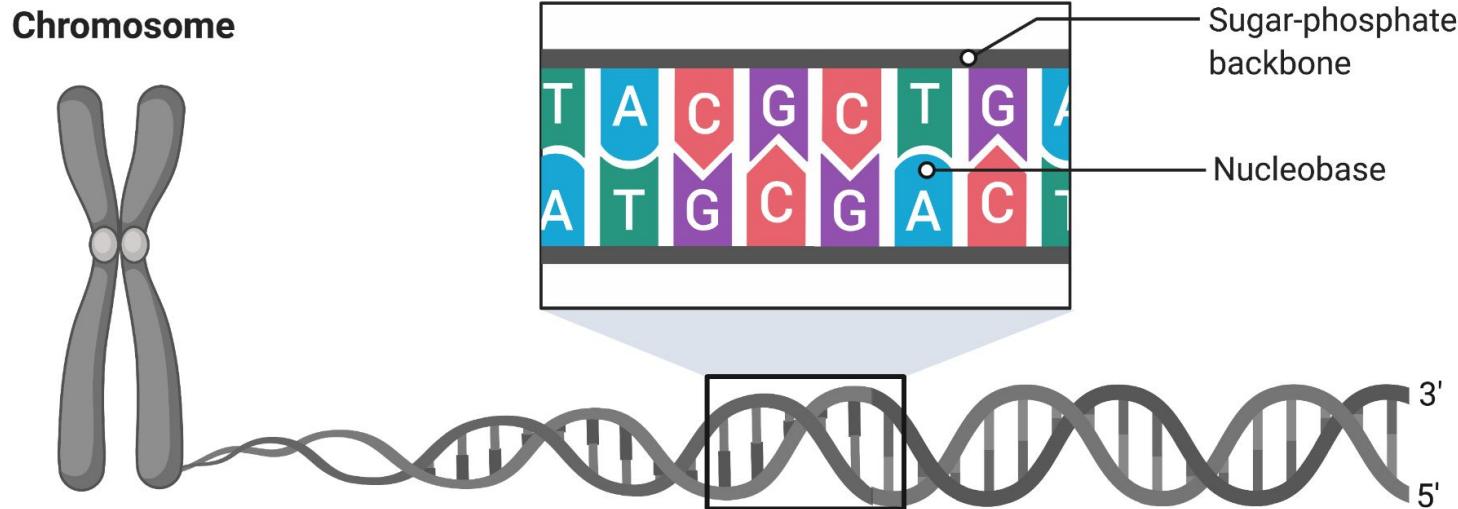


Doorway to
Human
History

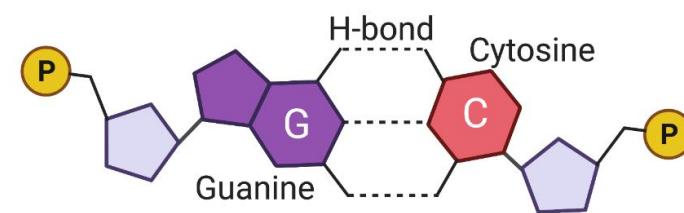
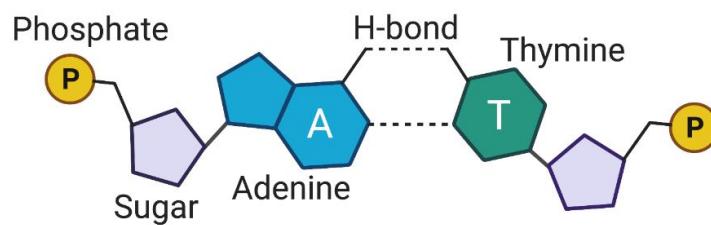




3.1 The structure of DNA



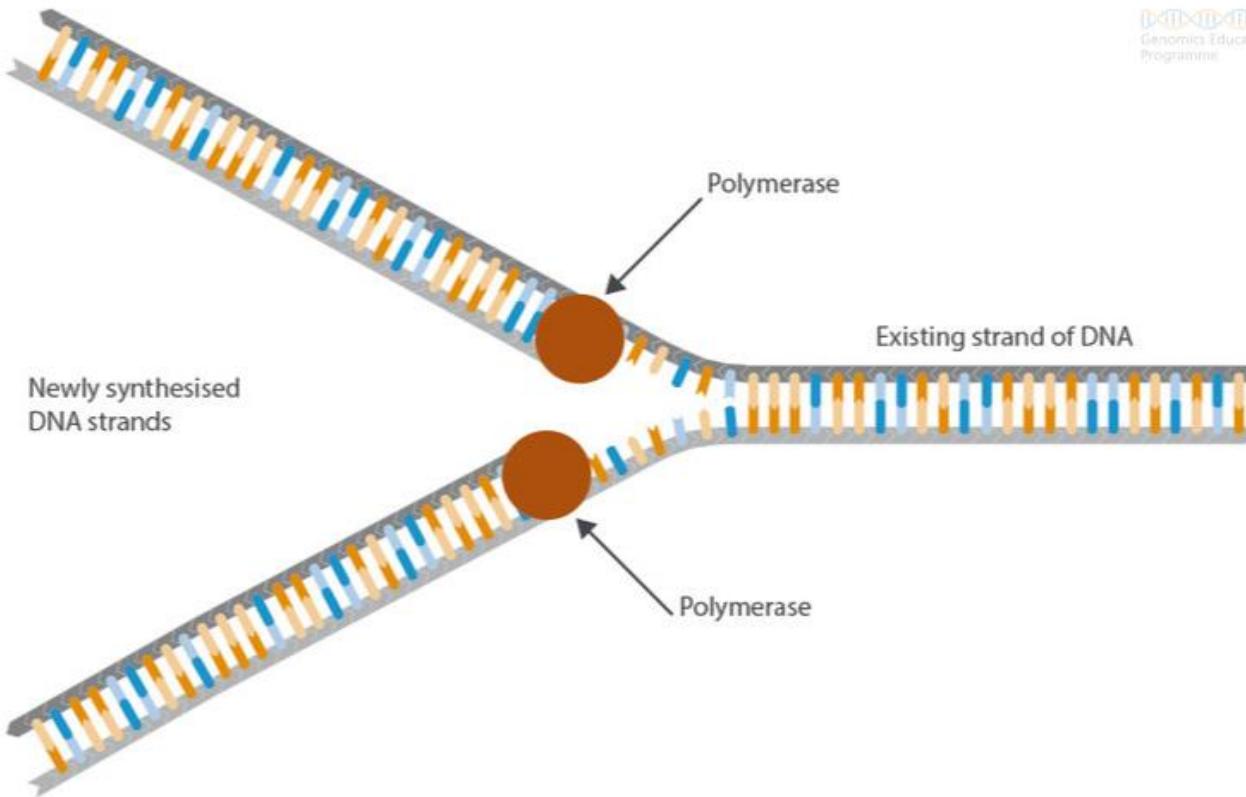
Complementary nucleobase pairing



created with BioRender



3.2 DNA replication



Genomics Education
Programme

@genomicsedu

www.genomicseducation.hee.nhs.uk

/genomicsedu



[CC-BY 2.0](#)

SUMMER
SCHOOL
2021
Doorway to
Human
History



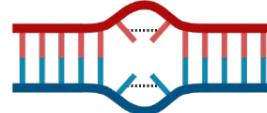


3.2 ancient DNA

- 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



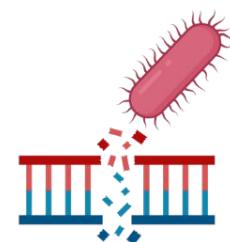
no enzymatic repair



crosslinks



nuclease fragmentation



microbe digestion

- fragmentation and damage

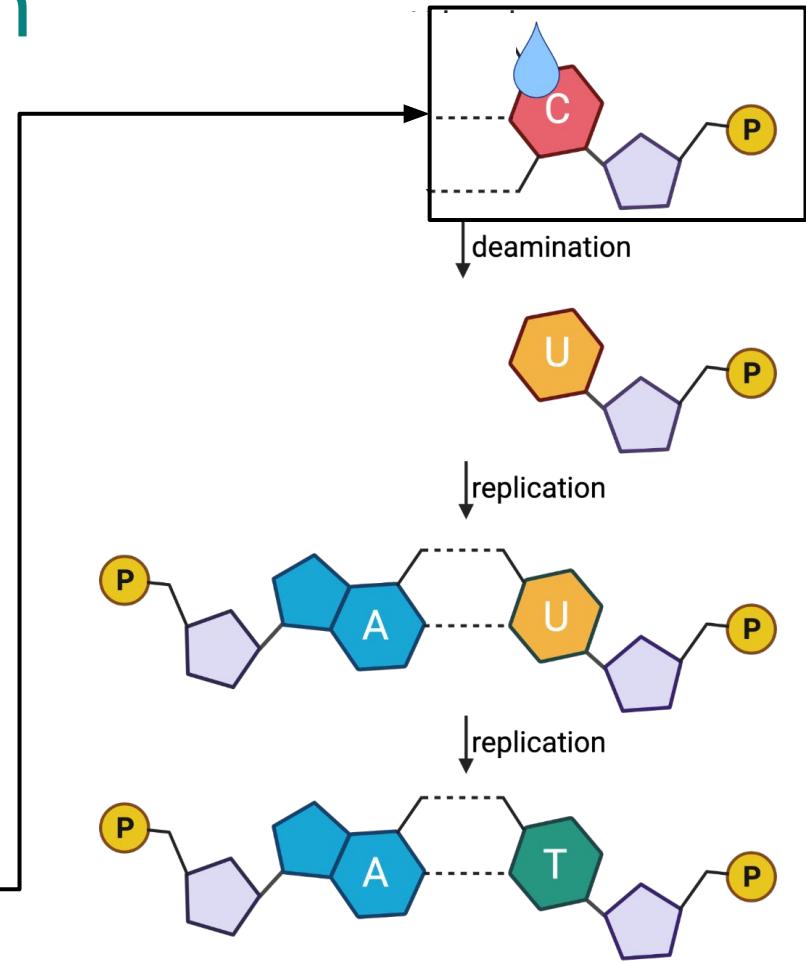
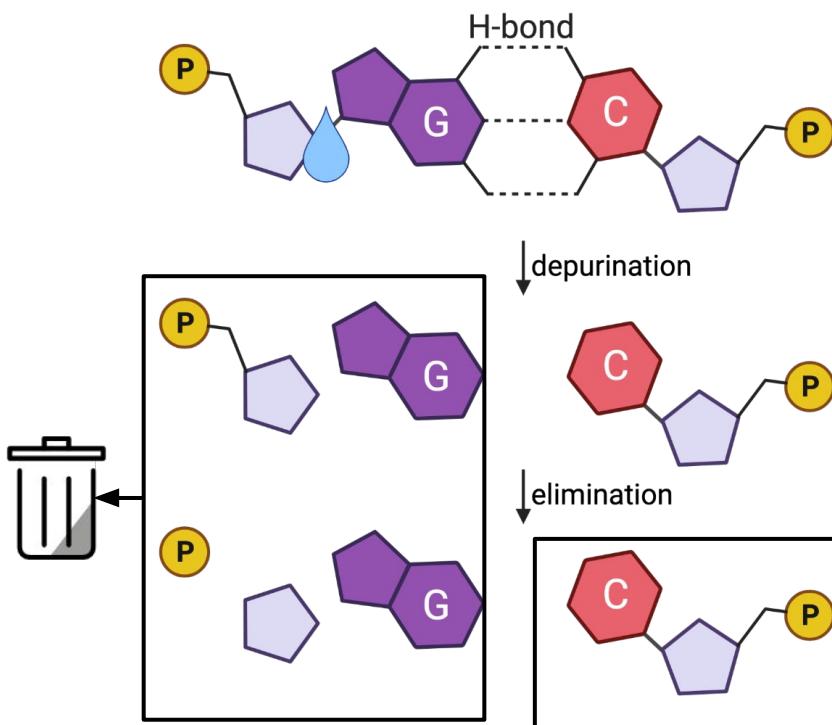


created with BioRender





3.3 aDNA degradation



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

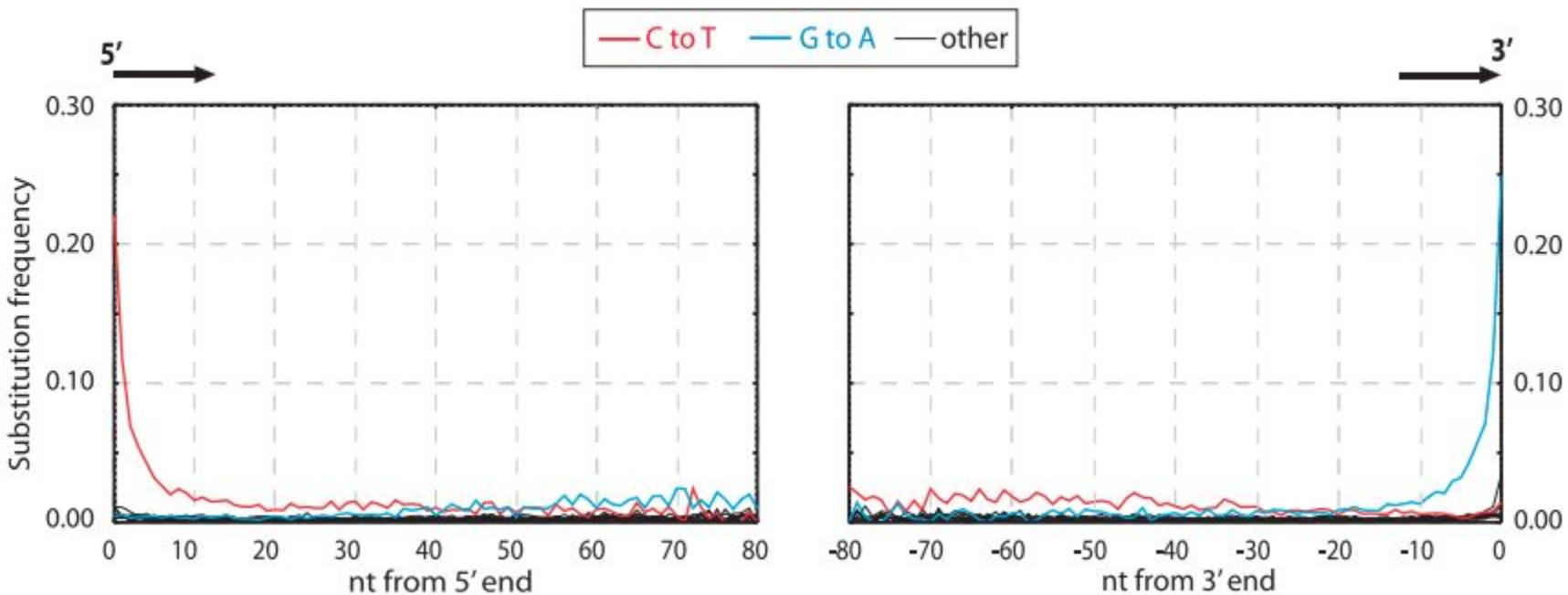


created with BioRender





3.4 aDNA “damage pattern”

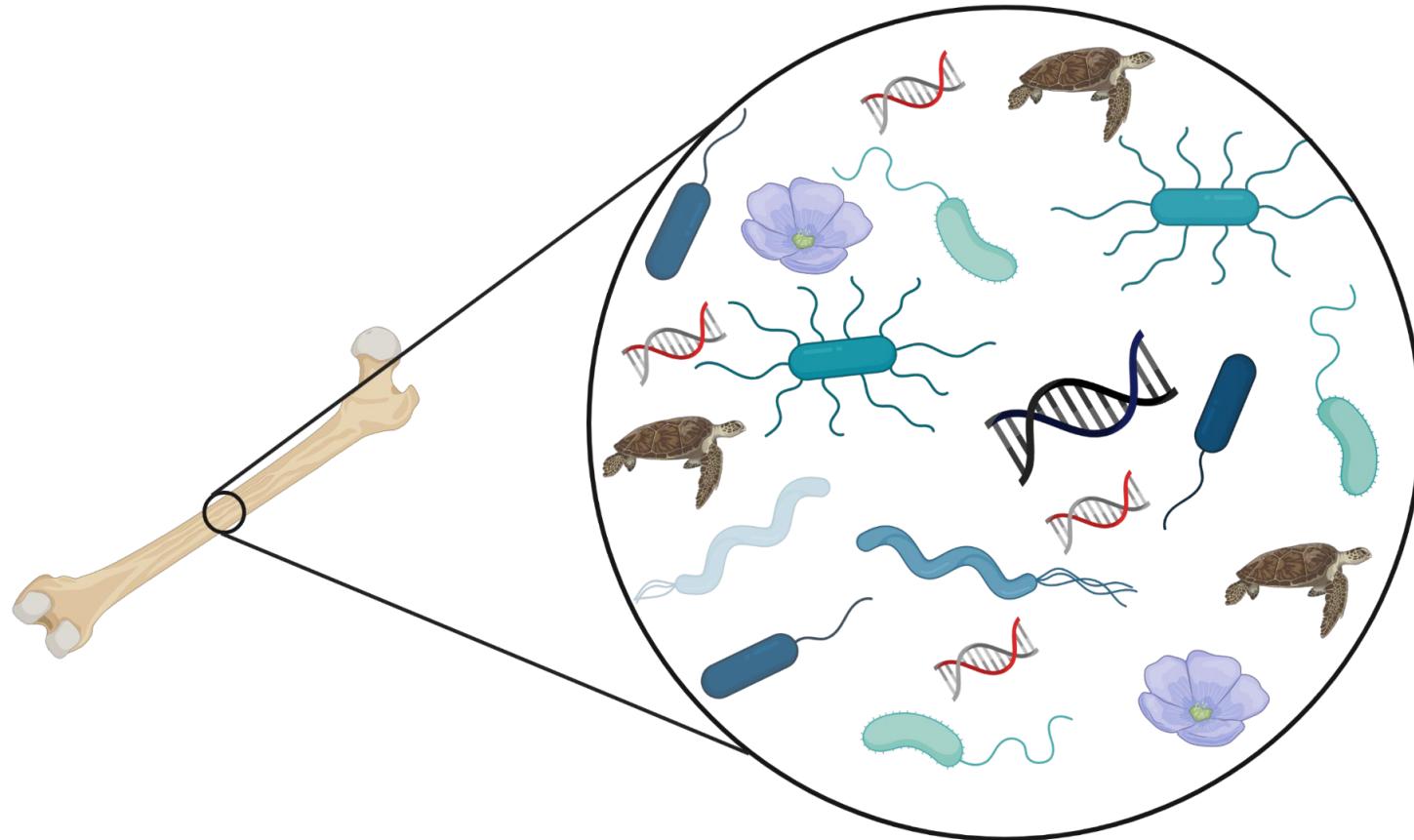


Briggs et al. (2007)





3.5 Contamination



created with BioRender





Laboratory methodology



SUMMER
SCHOOL
2021

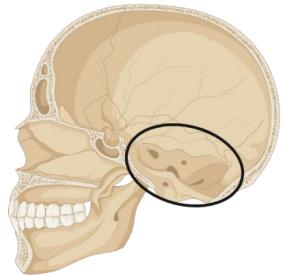


Doorway to
Human
History

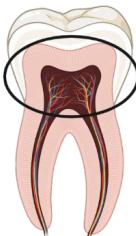




4.1 Sources of aDNA



petrous part of the temporal bone



teeth



dental calculus



skin & hair



coprolites



sediment



bones



parchment



archaeobotanical remains



ceramics



specimen archives



shells



created with BioRender

SUMMER
SCHOOL
2021



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)





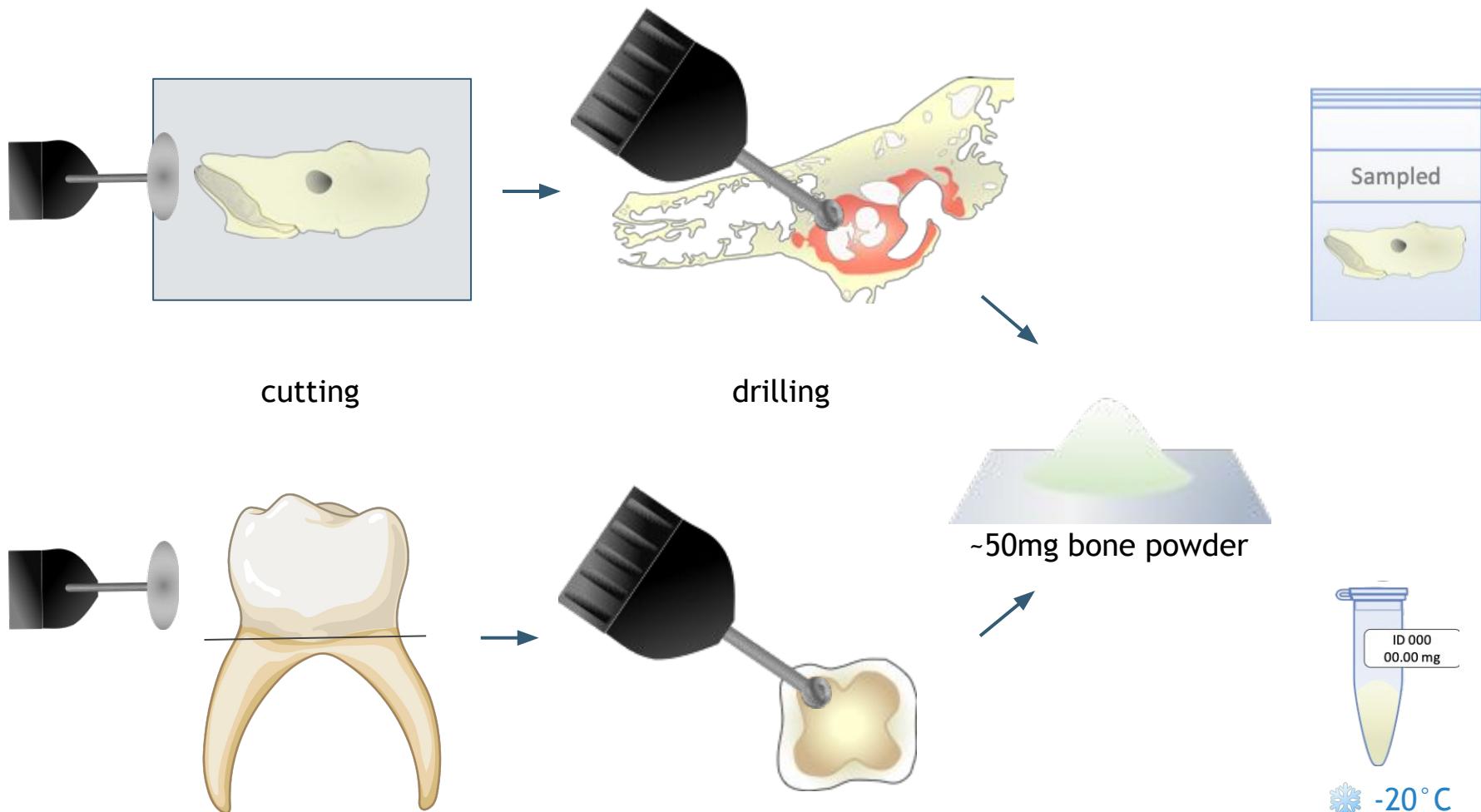
4.2 Clean room protocol

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





4.3 Sample preparation

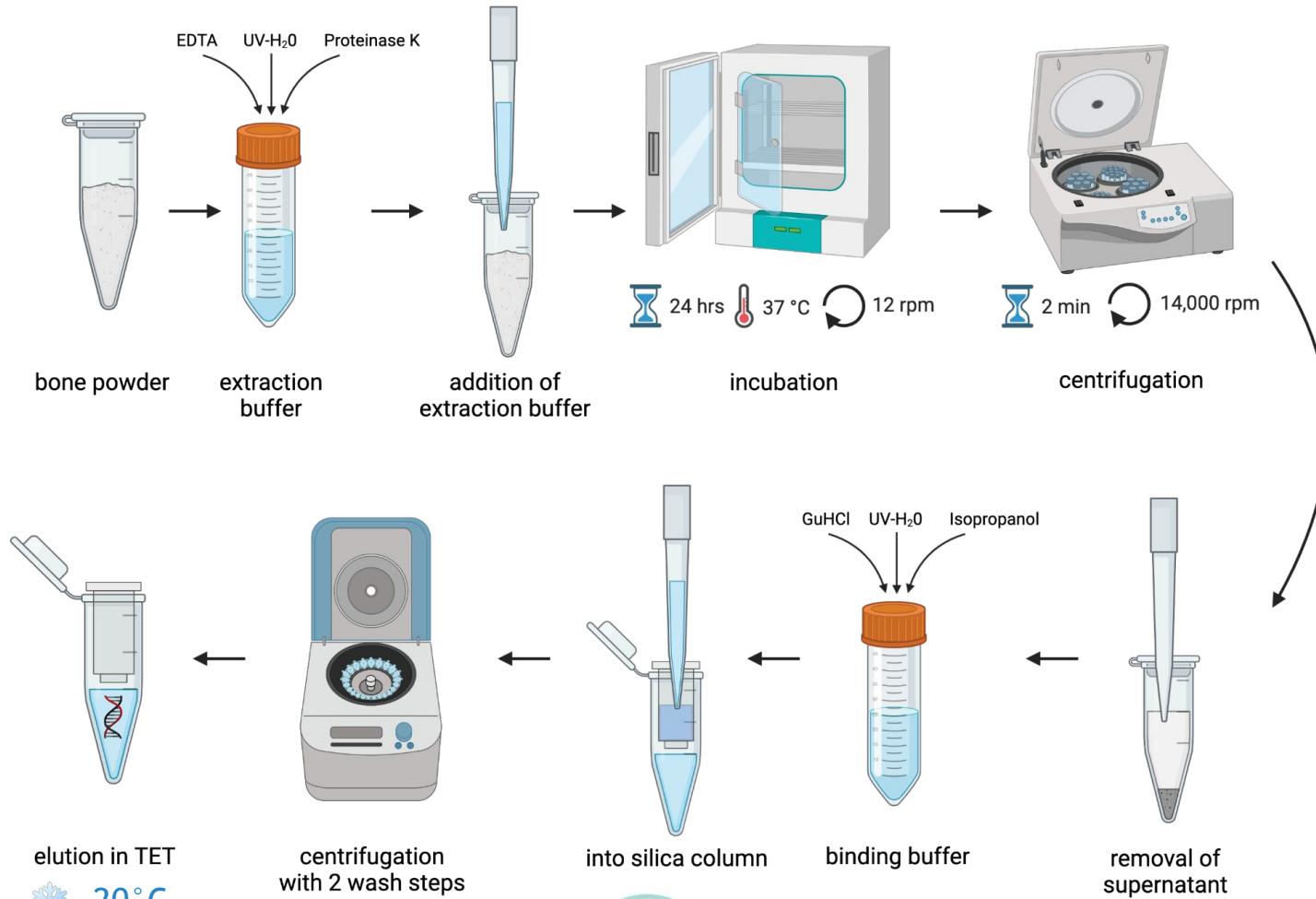


created with BioRender





4.4 DNA extraction

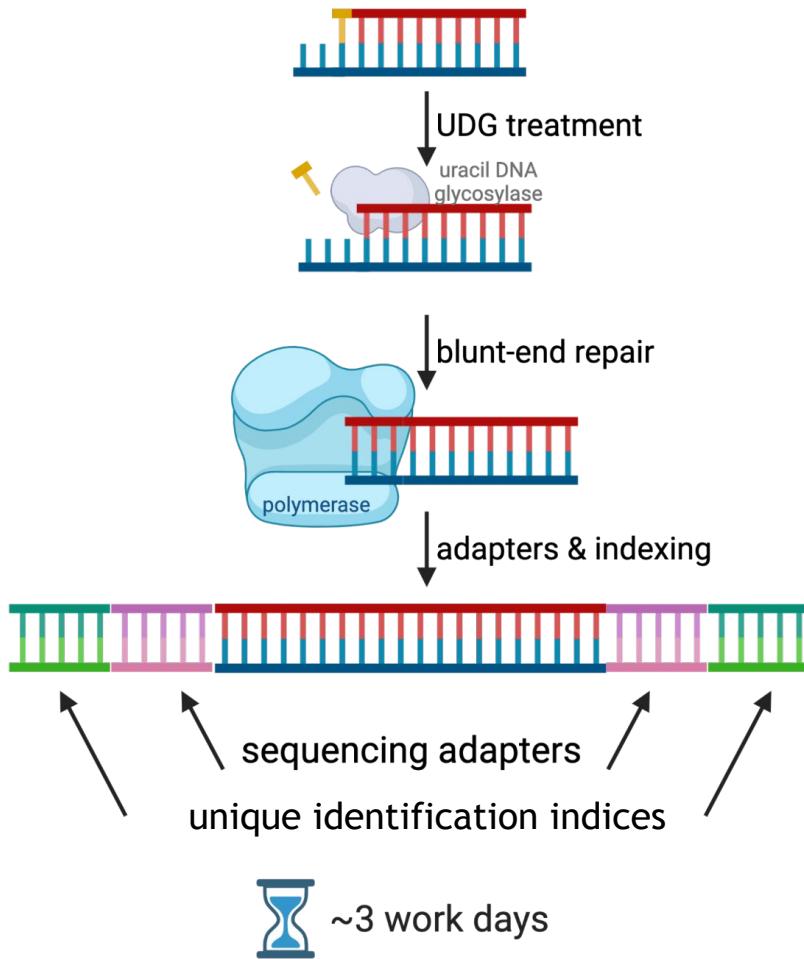


created with BioRender

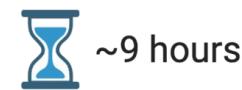




4.5 Library preparation



automated liquid-handling workstation



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

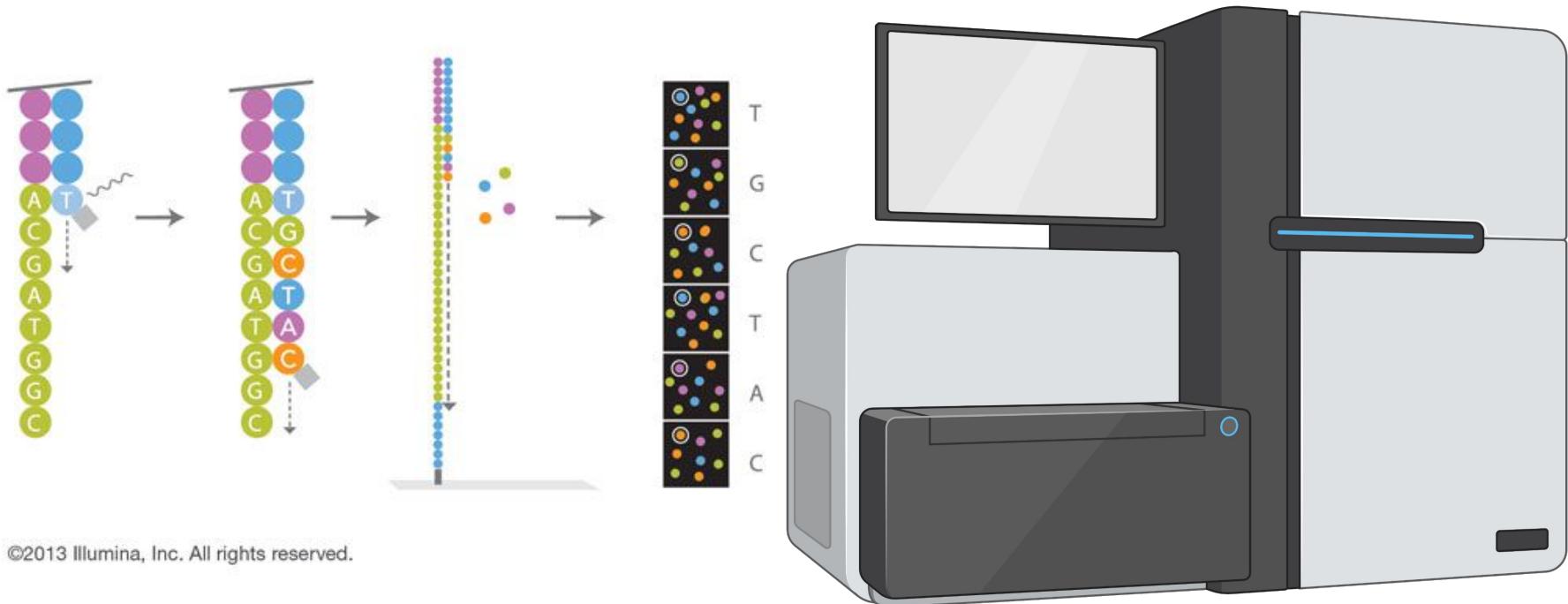


created with BioRender





4.6 Sequencing



©2013 Illumina, Inc. All rights reserved.

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



created with BioRender





What do we study with aDNA?



SUMMER
SCHOOL
2021



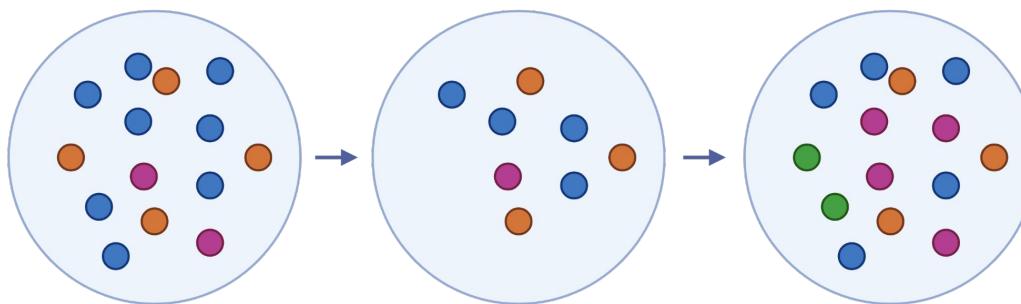
Doorway to
Human
History





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



created with BioRender

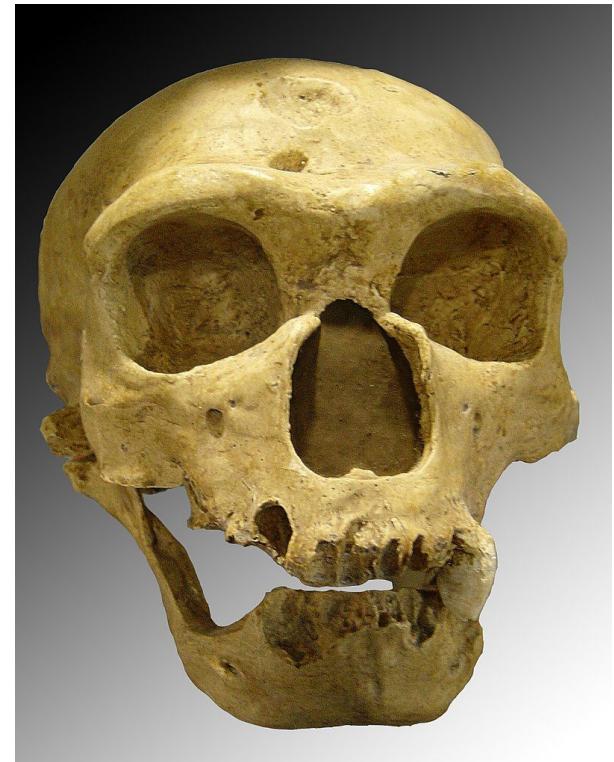




5.2 PopGen - Extinct Hominins

**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





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)

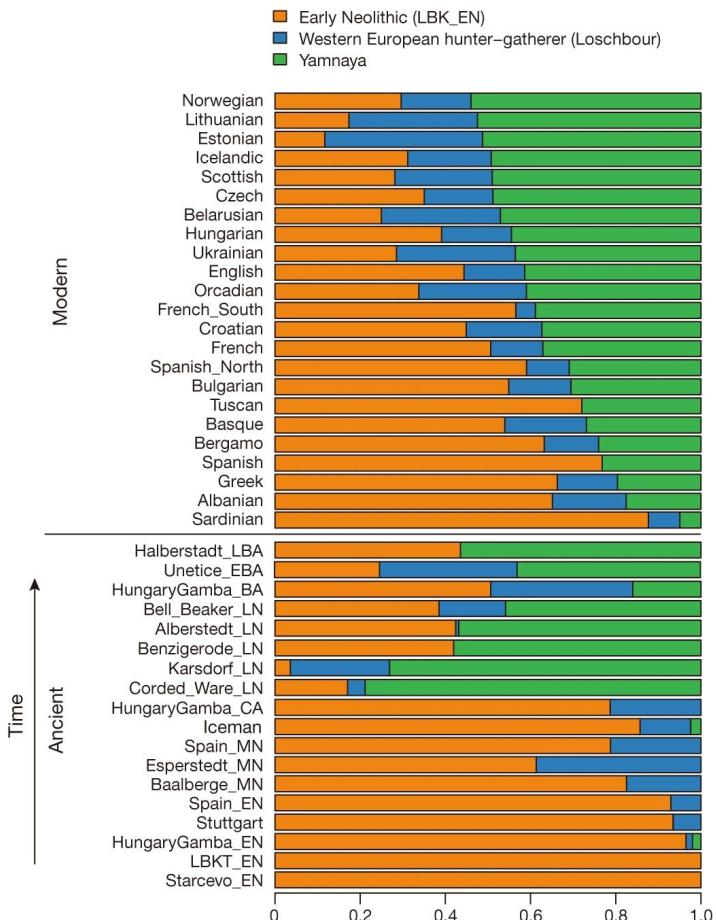
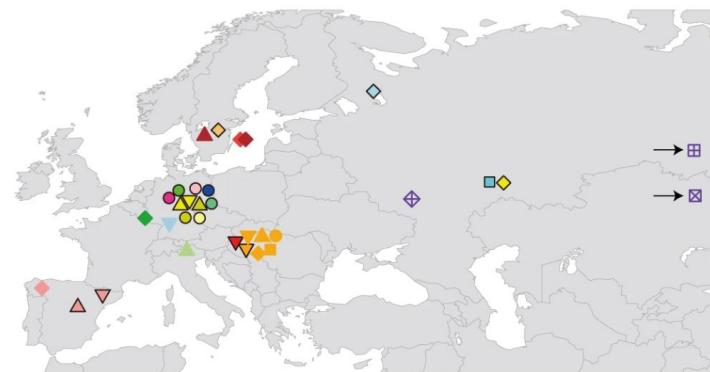
Reich et al. (2010) & (2011)
Meyer et al. (2012)
Prüfer et al. (2014)
Qin & Stoneking (2015)
Jacobs et al. (2019)
Bergström et al. (2020)





5.3 PopGen - Steppe Expansion

a

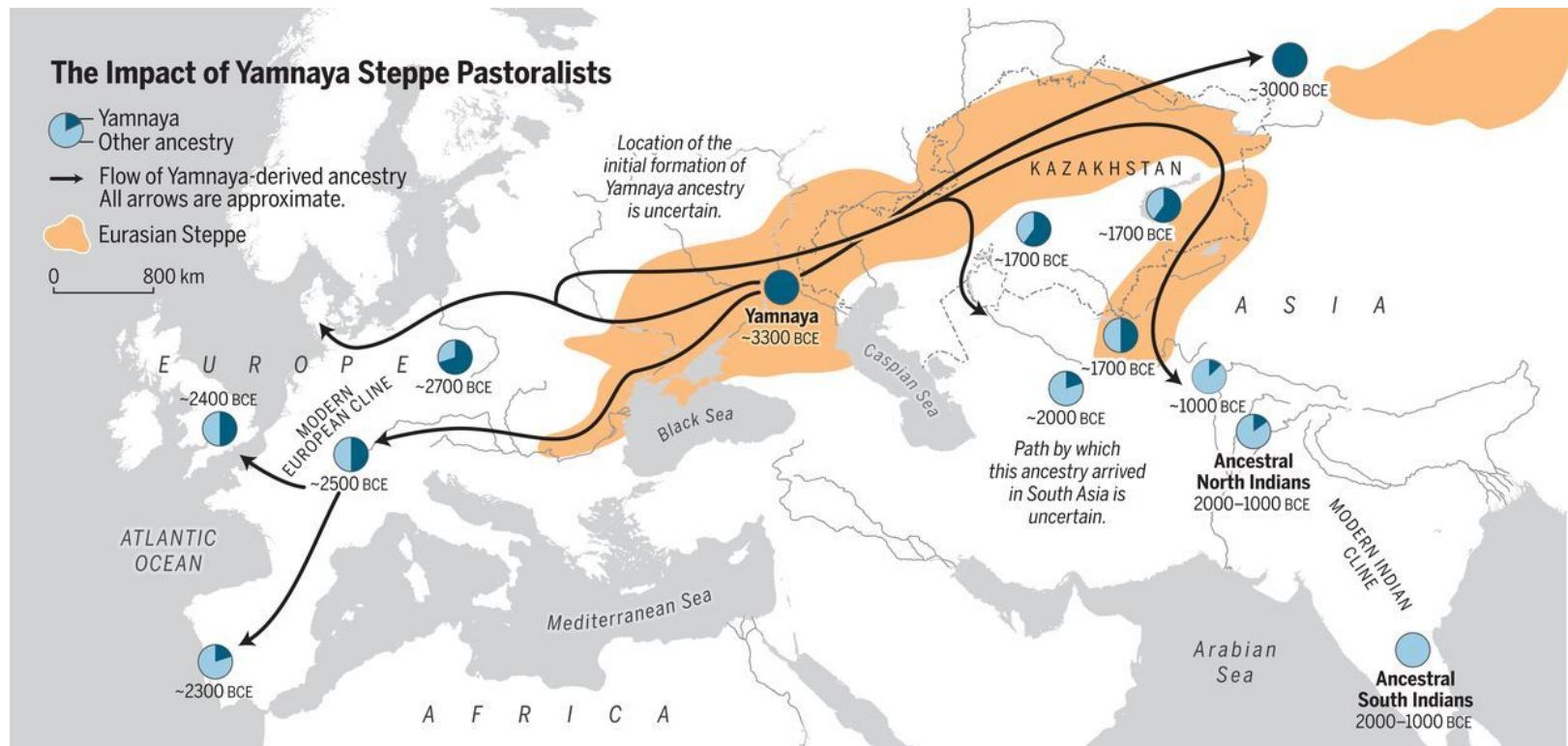


Haak et al. (2015)





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)

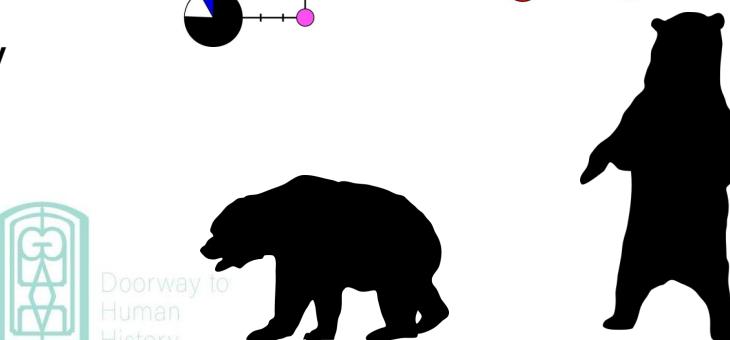
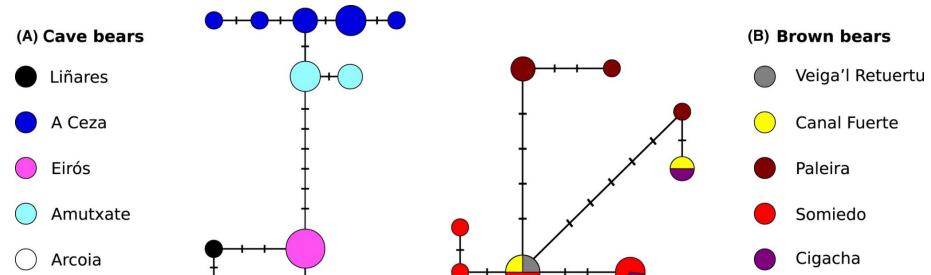
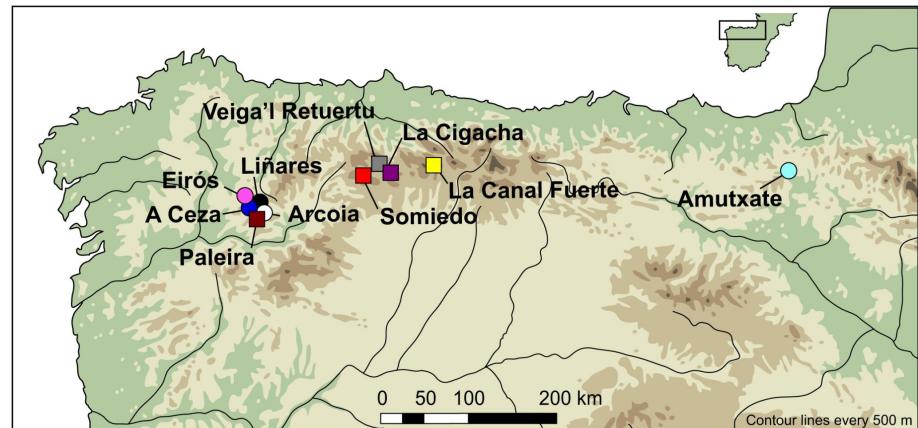




5.5 PopGen - Animals

Fortes et al. (2016) Mol. Ecol.

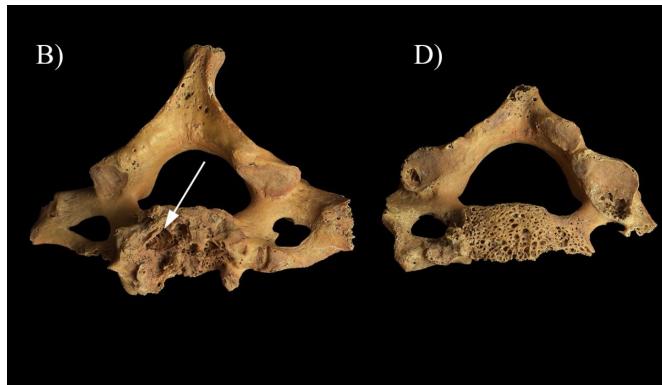
- Behaviour and social differences between cave bear vs brown bears
 - Reconstruct family relationships via mitochondrial haplotypes
- Results:
 - Cave bear lineages: same in same cave
 - Brown bear lineages not consistent
 - Predictable hibernating behaviour = humans can hunt
 - Harder to hunt = less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





5.4 Palaeopathology and infectious disease

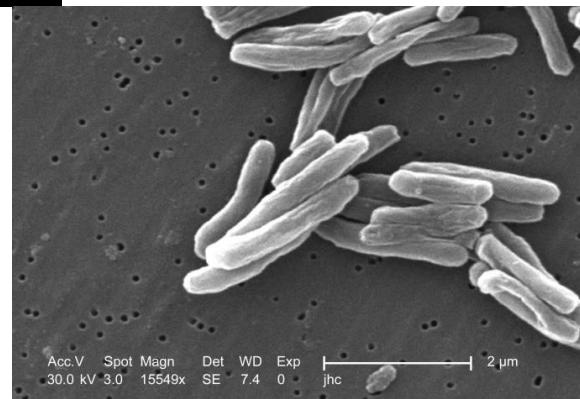
- What was the cause of death?
 - Cause of bone lesions?
 - What if no skeletal pathologies?
 - Chronic disease vs lethal disease?
 - What caused unusual attritional profiles?



Dabernat et al. (2014) PLOS ONE



openmoji.org

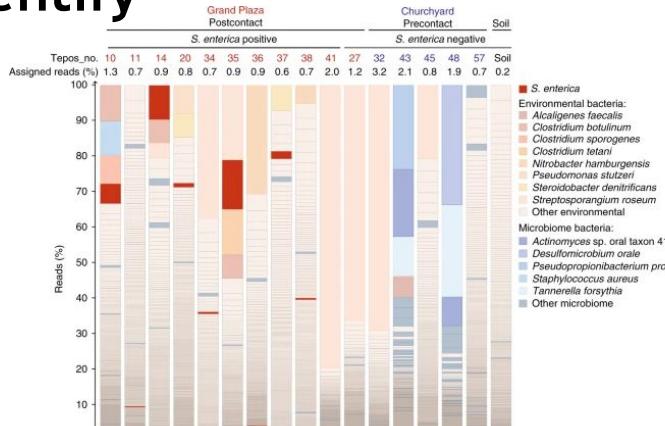


5. What can we study using aDNA?



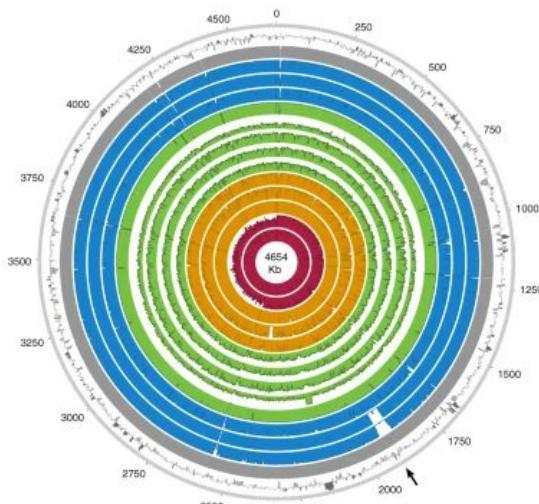
5.4: How to detect Ancient Pathogens

Identify



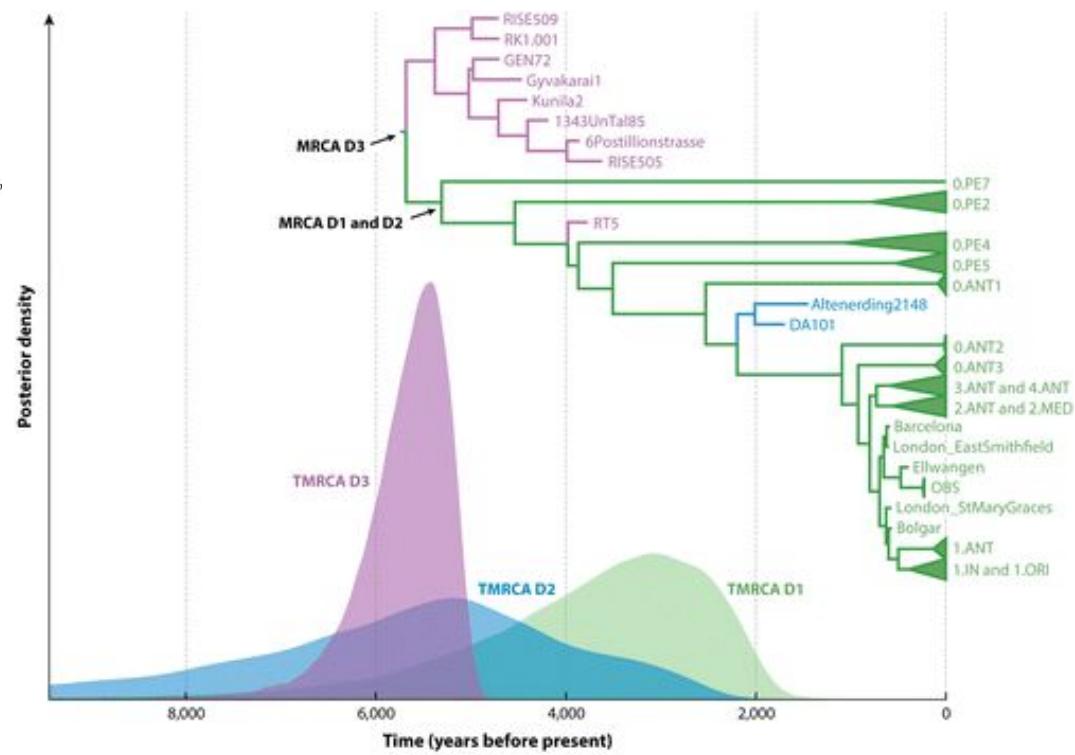
Vågene et al (2018) Nat. Eco. Evo

Reconstruct



Spyrou et al. (2019) Nat. Coms

Relationship



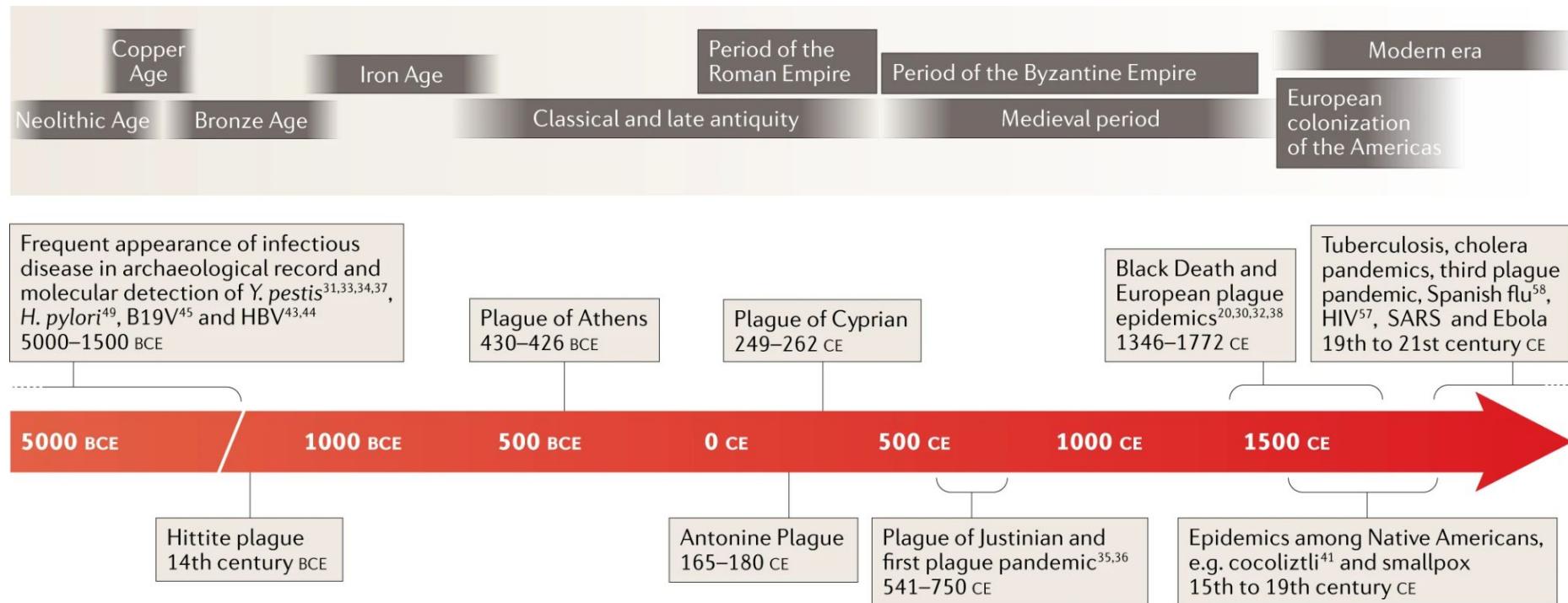
Date

→ 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

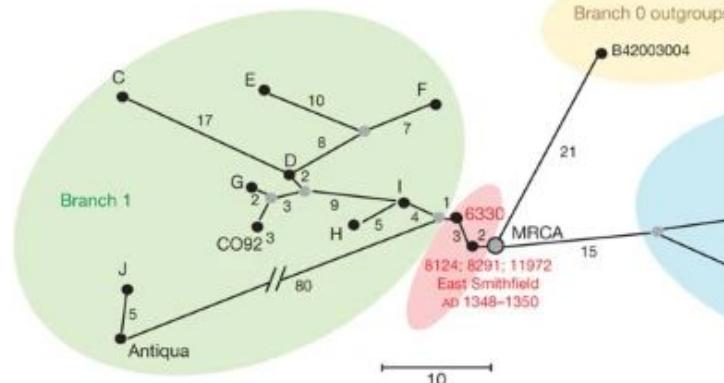


5. What can we study using aDNA?



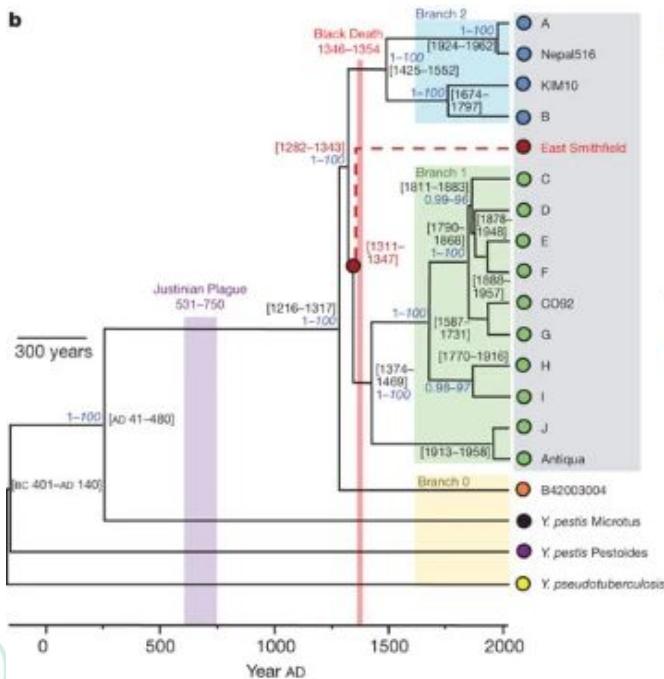
5.4 Example: Cause of Black Death

a



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 period⁴. Discrepancies in epidemiological trends between the medieval disease and modern *Y. pestis* infections have ignited controversy over the pandemic's aetiological agent^{5,6}. Although ancient DNA investi-

b

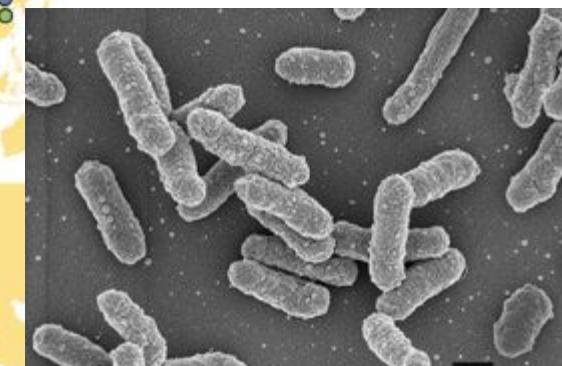


Bos et al. (2011) Nature

c



d



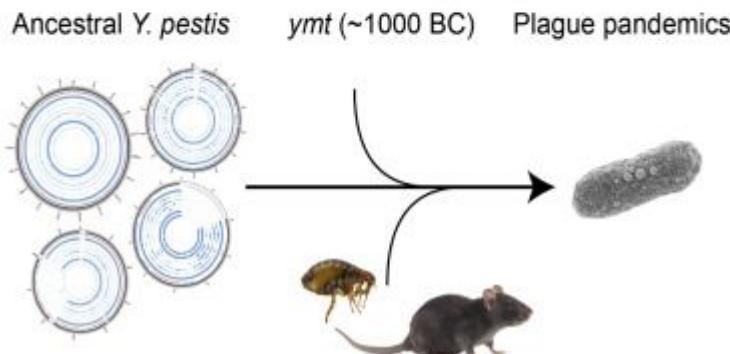
Quelle: Muhsin Özel, Gudrun Holland, Rolf Reissbrodt/RKI



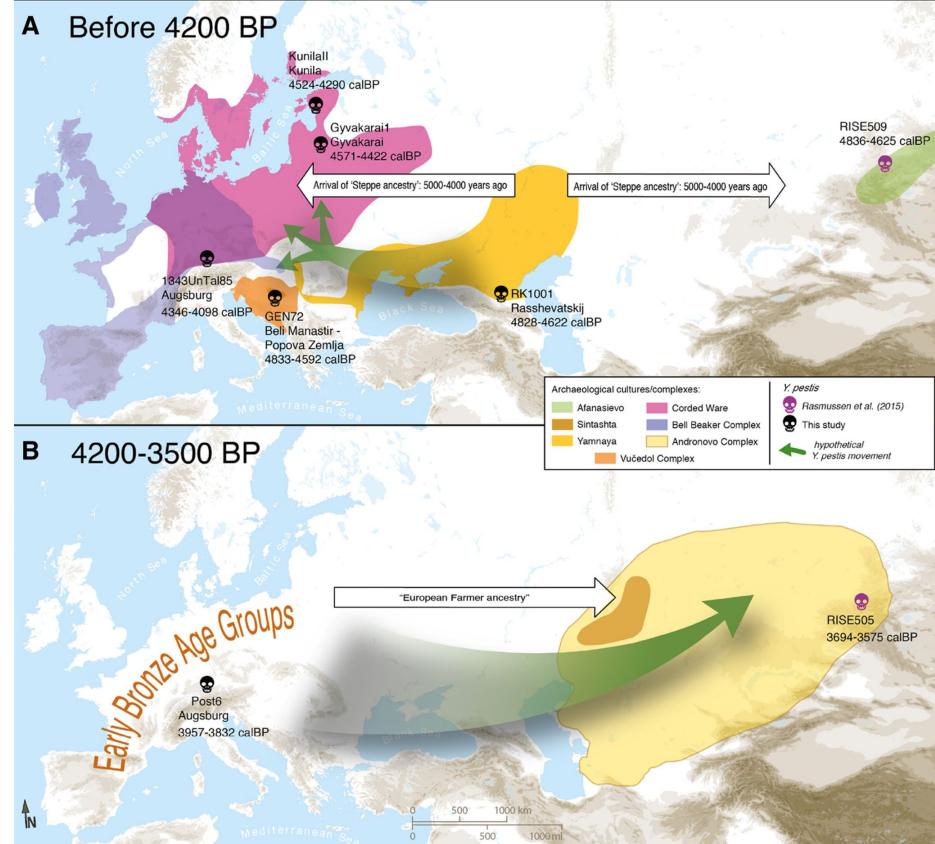
5. What can we study using aDNA?



5.4 Example: Mystery Epidemic?



Rasmussen et al. (2015) Cell

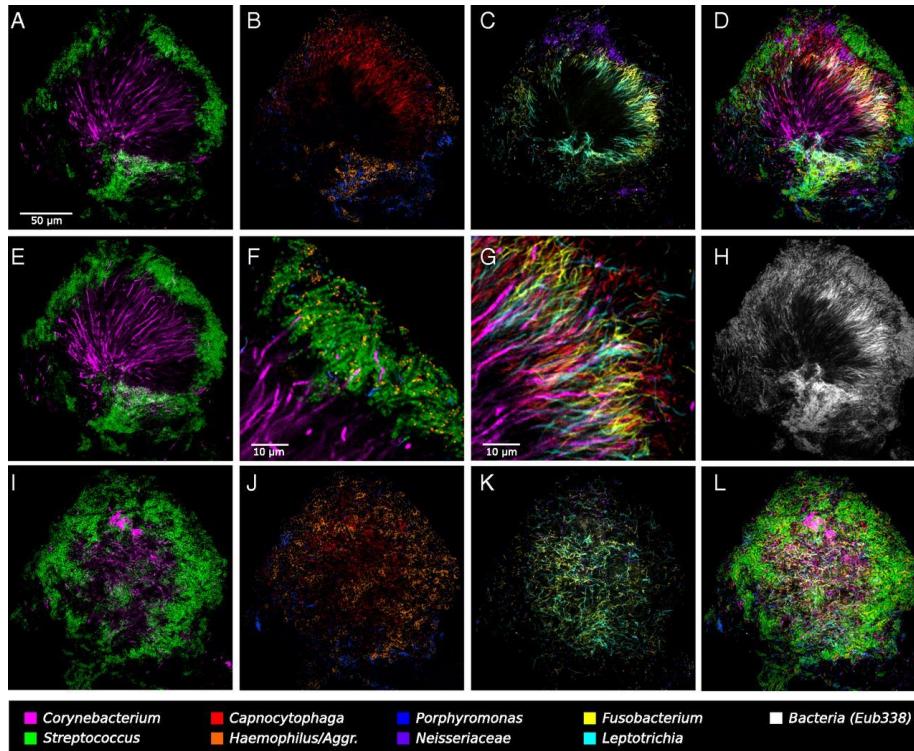


Andrades Valtueña (2017) Curr. Bio.





5.5 What: Ancient (Human) Microbiomes



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

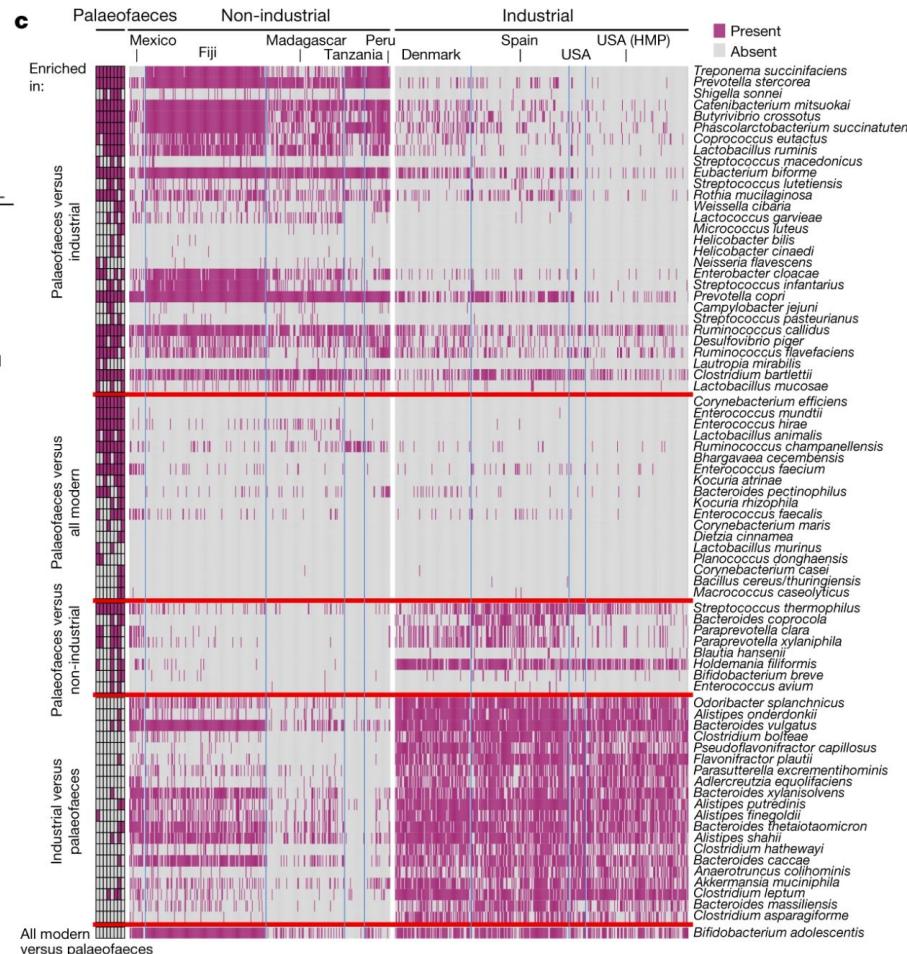
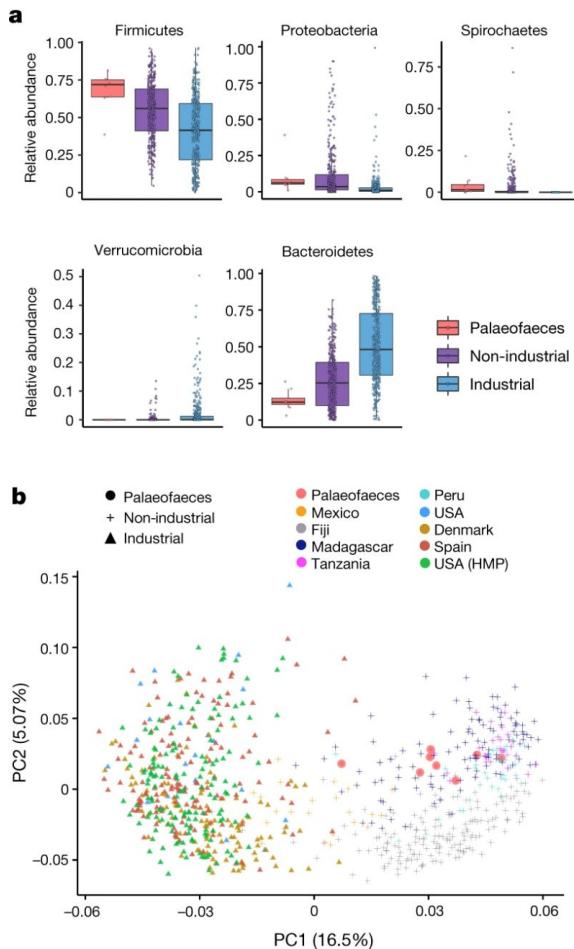
All emojis designed by OpenMoji - the open-source emoji and icon project. License: CC BY-SA 4.0



5. What can we study using aDNA?



5.5 Why: Ancient Microbiomes



→ G5W

Intro to ancient microbiome analysis
Thurs 19th @ 11.00

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

SUMMER
SCHOOL
2021



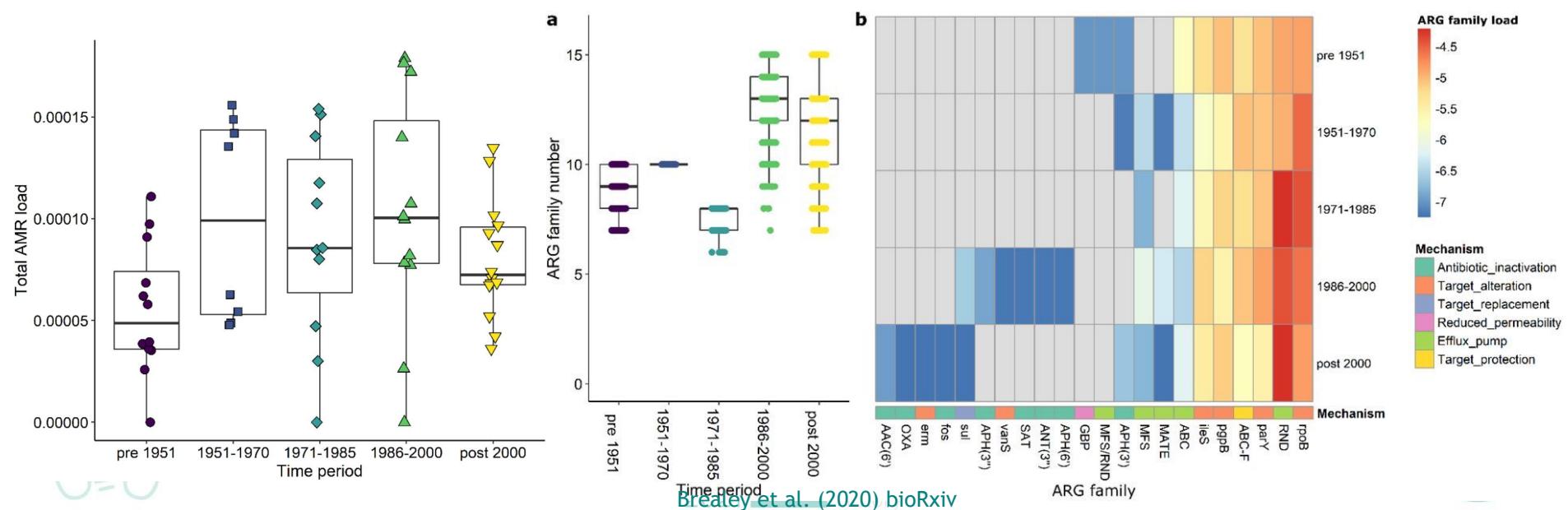
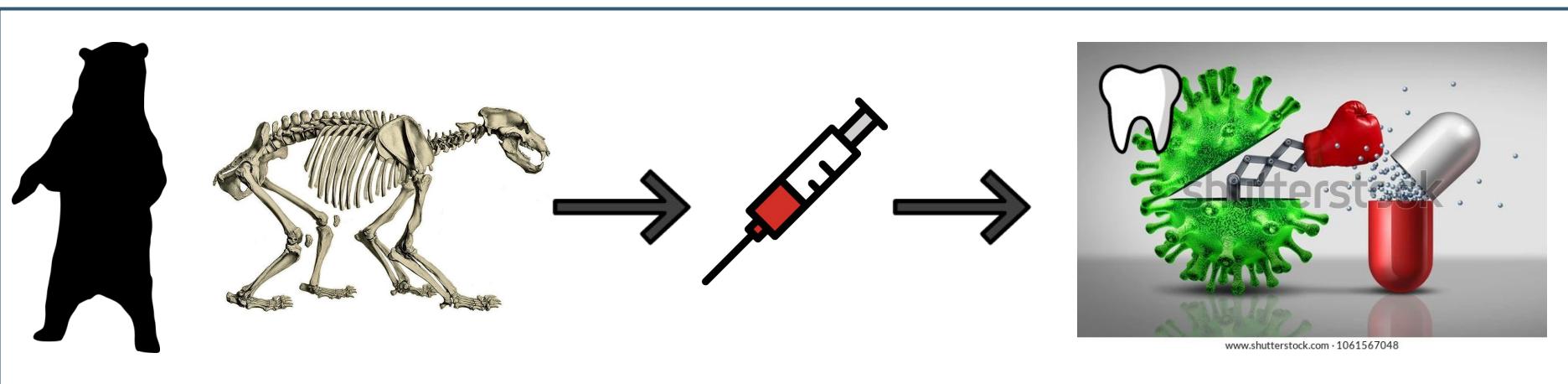
Doorway to
Human History



5. What can we study using aDNA?



5.6 Example: oral antibiotic resistance

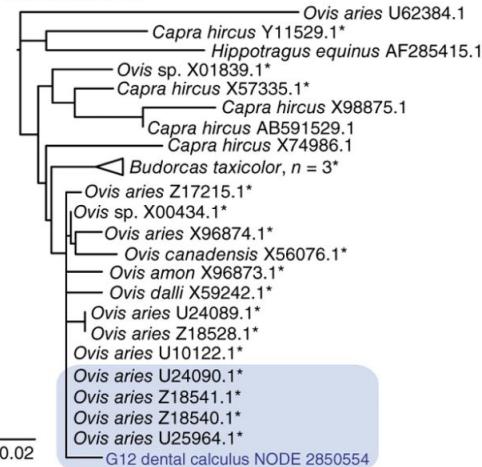




5.6 Example: diet sources

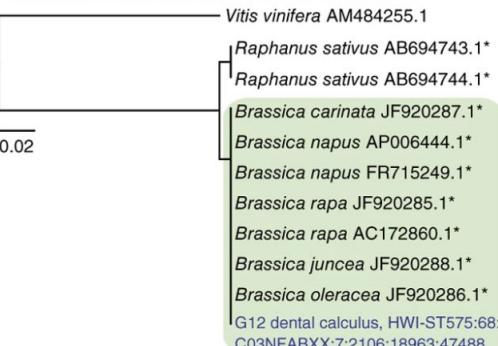
a *Ovis* sp., chromosome X, microsatellite, E value 2.0×10^{-43}

```
GGCTTCCCGTCGATCTCAAGAGGAGGGCTCTCCACAGGAAGGC  
GAGAGATACTCCAGGGTCTGCCACCATCTCAAGAGTCCCCAGAT  
GTGTCAGTCCATT
```



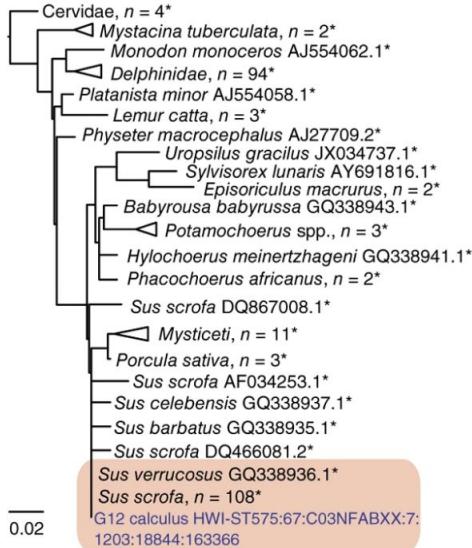
b *Brassica* sp., mtDNA, intergenic, E value 3.0×10^{-32}

```
ATGCTGTGAATCGTTAACGCAATTGTTGCTGCTCCCTCG  
AGTTCCACATATGCAGGCTGCCACTCTAATTCCTCCATTAC
```



c *Sus* sp., mtDNA, 12S rRNA, E value 5.0×10^{-52}

```
GAGGGTGACGGGGGTGTGCGTGCCTCATGCCCTTATTCAATCAAG  
CACTCTATTCTGTATTACTGCTAAATCCTCTTGGTTTTAGTTTC
```



d *Triticum aestivum*, mtDNA, intergenic

Total score 147; query coverage 100%;
 E value 9×10^{-33} ; maximum identity 100%
total score of next best hit 41

```
Triticum aestivum EU534409.1 GATCATCATGGGTCCAGAAAGACTGAA  
Triticum aestivum AP008982.1 GATCATCATGGGTCCAGAAAGACTGAA
```

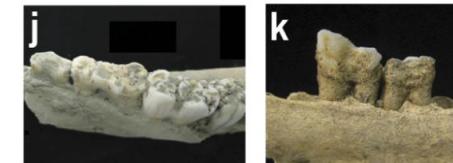
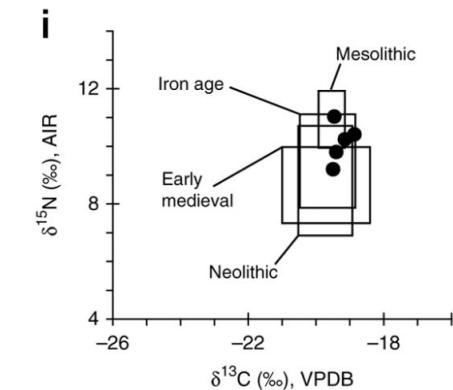
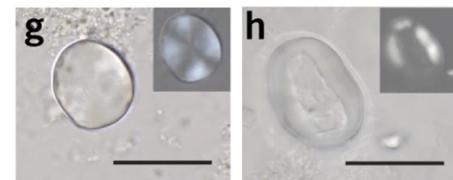
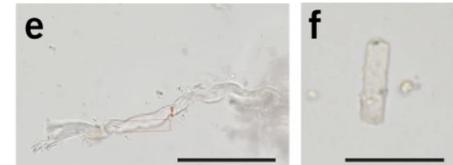
G12 dental calculus HWI-ST575:67: GATCATCATGGGTCCAGAAAGACTGAA
C03NFABXX:7:2201:14733:93454

```
Triticum aestivum EU534409.1 AGGAAGCCCTAGCTGGTAGGGACGCG  
Triticum aestivum AP008982.1 AGGAAGCCCTAGCTGGTAGGGACGCG
```

G12 dental calculus HWI-ST575:67: AGGAAGCCCTAGCTGGTAGGGACGCG
C03NFABXX:7:2201:14733:93454

```
Triticum aestivum EU534409.1 GTATCGGCACGCCAATATGGATTGCGCT  
Triticum aestivum AP008982.1 GTATCGGCACGCCAATATGGATTGCGCT
```

G12 dental calculus HWI-ST575:67: GTATCGGCACGCCAATATGGATTGCGCT
C03NFABXX:7:2201:14733:93454





Interface with archaeology and linguistics



SUMMER
SCHOOL
2021

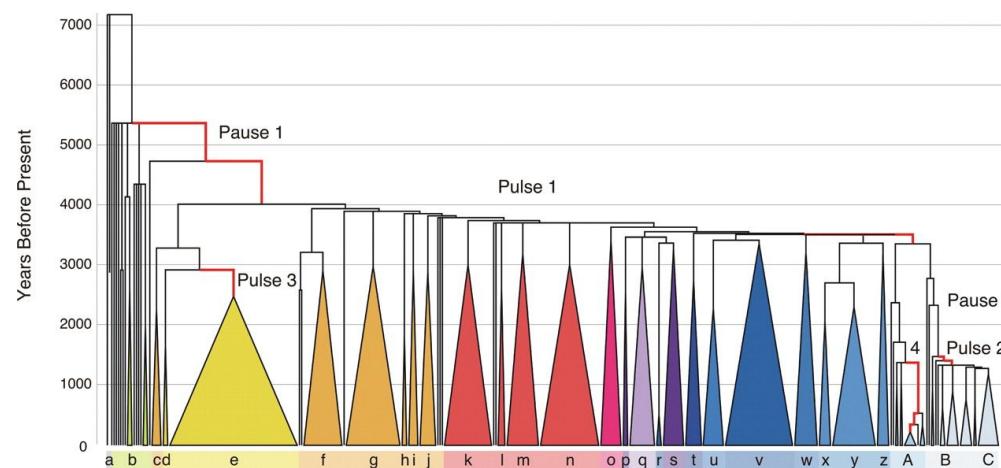
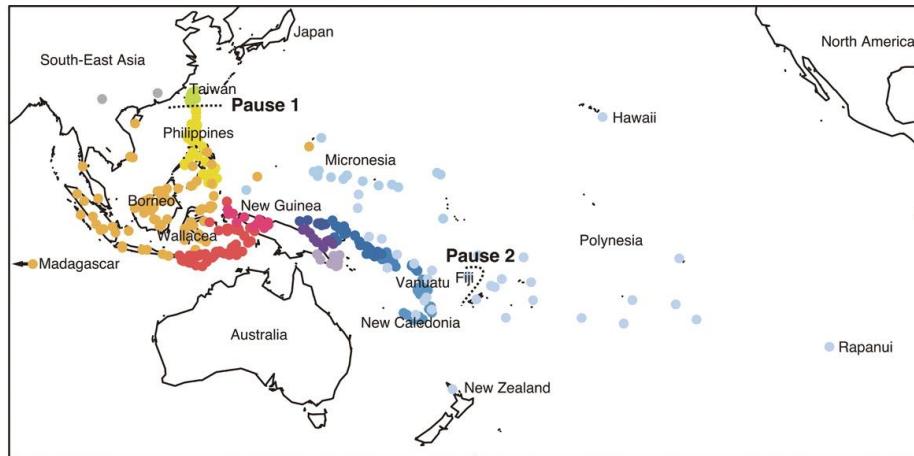


Doorway to
Human
History





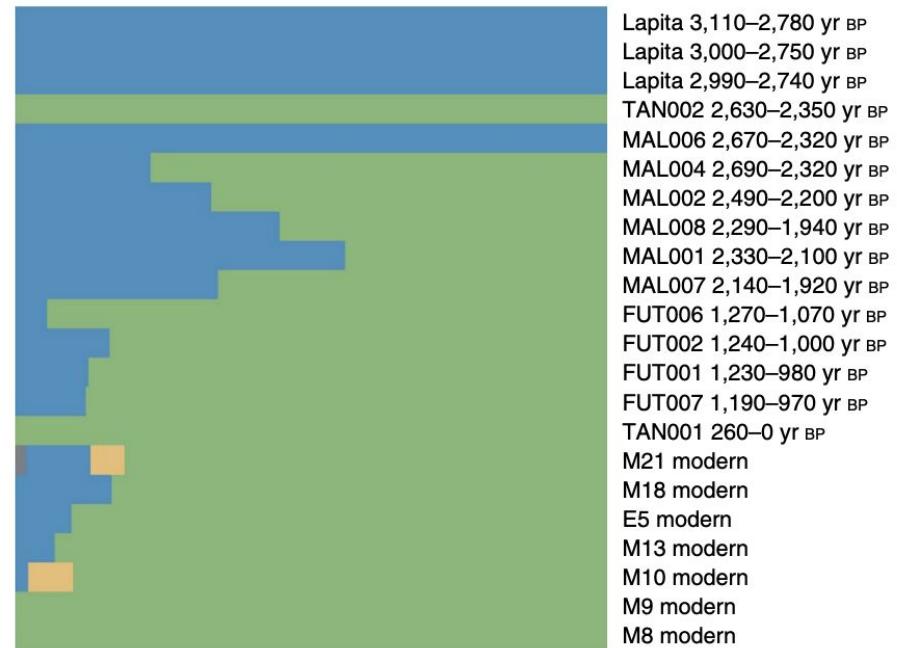
6.1 Vanuatu





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

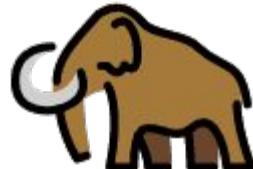




Summary

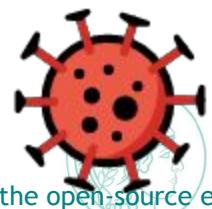
How

- 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!)



All emojis designed by OpenMoji - the open-source emoji and icon project. License: CC BY-SA 4.0

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 Carlhoff

Selina Carlhoff



selina_carlhoff@eva.mpg.de



@selina_carlhoff

James Fellows Yates



james_fellows_yates@eva.mpg.de



@james_fellows_yates



@jfy133

Currently Funded by:



Food
Transforms



SUMMER
SCHOOL
2021



Doorway to
Human
History

