



MPI-SHH SUMMER SCHOOL 2021

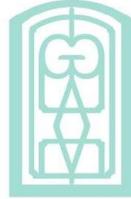
Doorway
to Human History

Microbial Archaeology

Dr. Irina Velsko and Zandra Fagernäs



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2021



Doorway to
Human
History



Who are we?

Irina



- Has a Ph. D. in microbiology
- Works with dental calculus
- Also knows about living microbes
- Genetics, proteomics, metabolomics

Zandra



- Is trying to get a Ph. D. in microbiology
- Works with dental calculus
- Does a lot of lab work
- Genetics, proteomics



Is anyone working with ancient microbes?
Planning a project with ancient microbes?
Think ancient microbes are cool?

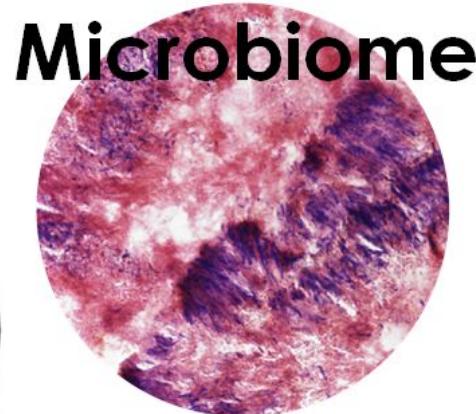
Write in the chat!



Why study microbes?



Disease



Microbiome



Cuisine



Where can you find ancient microbes?



Microbes are everywhere!!!





Disease



Past pathogens

- Changes in human lifestyle exposed us to new pathogens
 - Domesticated animals
 - Higher population densities
 - Mobility
- Epidemics and disease outbreaks have been recorded
 - Cause is often unknown
- Traditionally researched through palaeopathology of skeletal assemblages
- In the 1990s, aDNA came into the picture
- First genome published in 2011 (*Yersinia pestis*)



What pathogens?

Bacteria

- *Brucella melitensis* (brucellosis)
- *Gardnerella vaginalis* (bacterial vaginosis)
- *Helicobacter pylori* (GI ulcers)
- *Mycobacterium leprae* (leprosy)
- *Mycobacterium tuberculosis* (tuberculosis)
- *Tannerella forsythia* (periodontal disease)
- *Treponema pallidum* (syphilis/jaws/bejel)
- *Vibrio cholerae* (cholera)



What pathogens?

Viruses

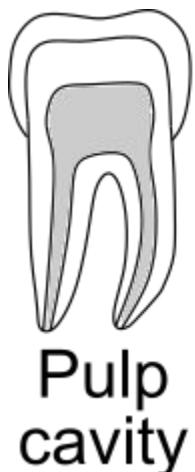
- HBV (viral hepatitis)
- HIV (AIDS)
- Influenza virus (influenza)
- VARV (smallpox)

Eukaryotes

- *Phytophthora infestans* (potato blight)
- *Plasmodium falciparum* and *Plasmodium vivax* (malaria)



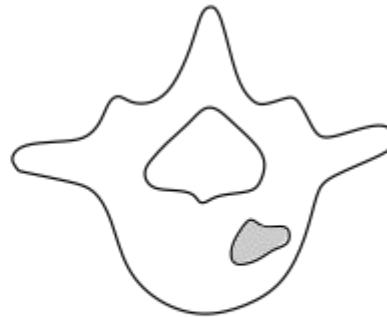
Where can we find pathogens?



Pulp
cavity



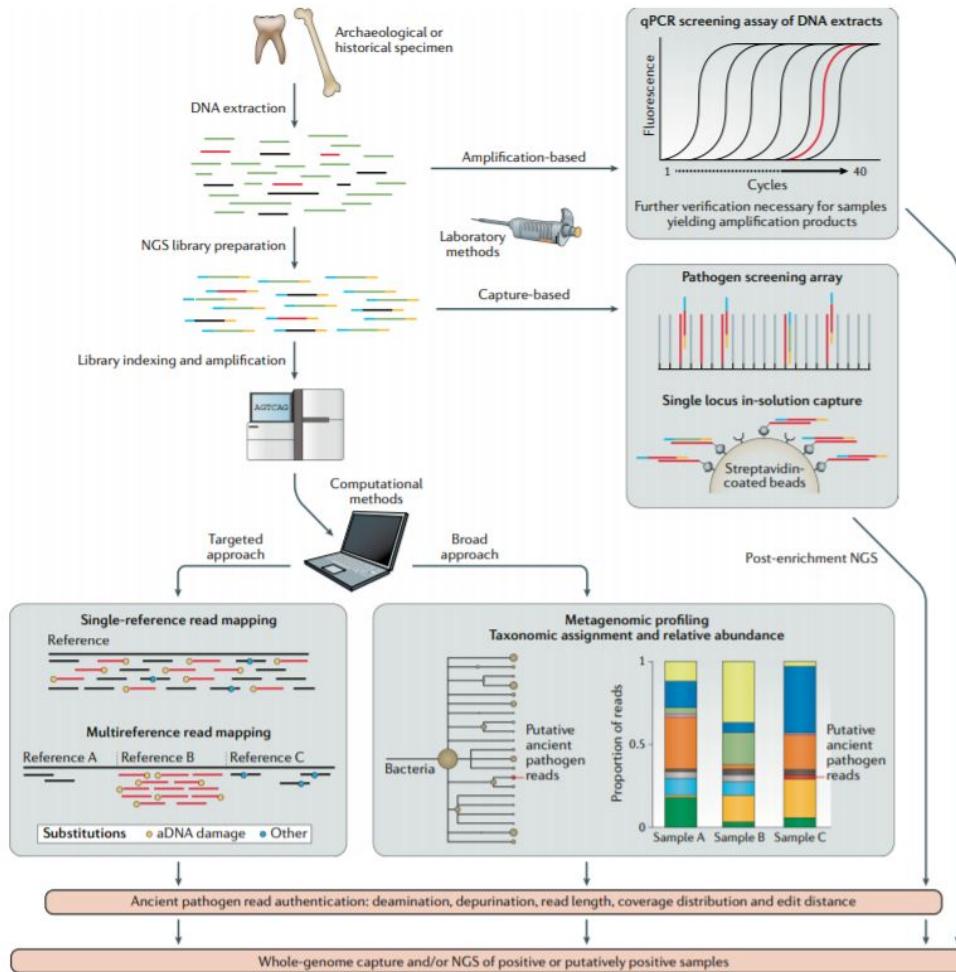
Bones



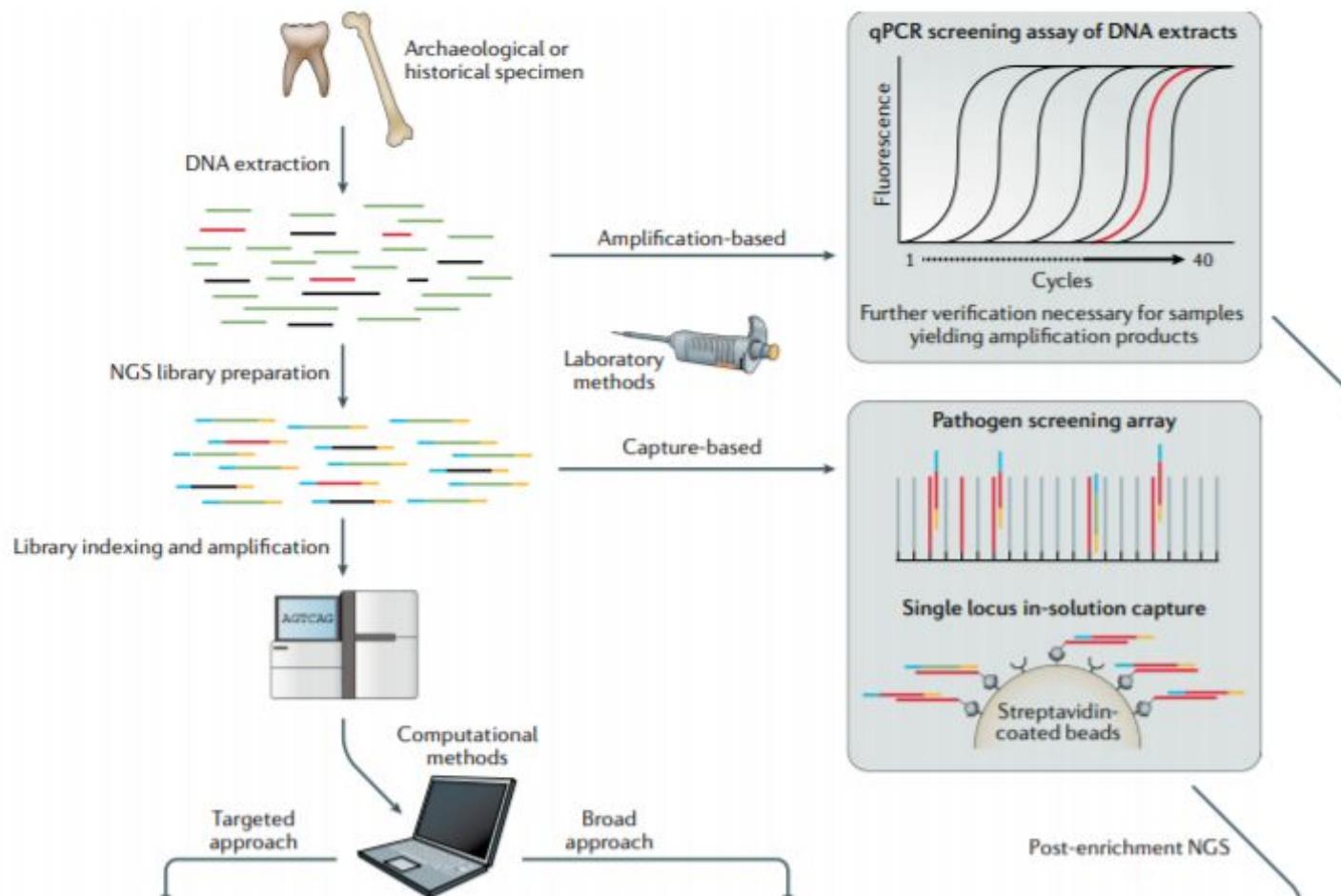
Skeletal
lesions



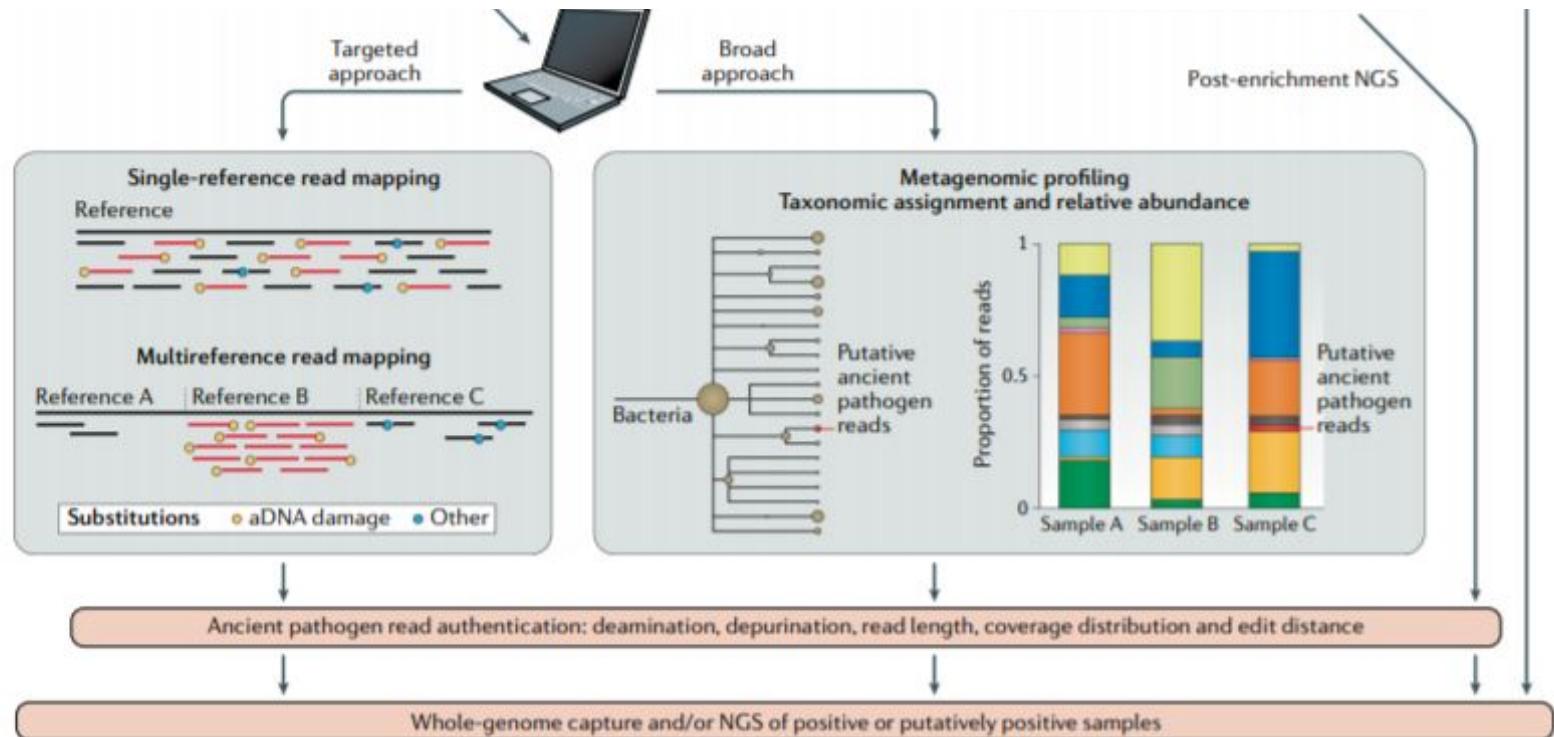
Ancient pathogens



Ancient pathogens

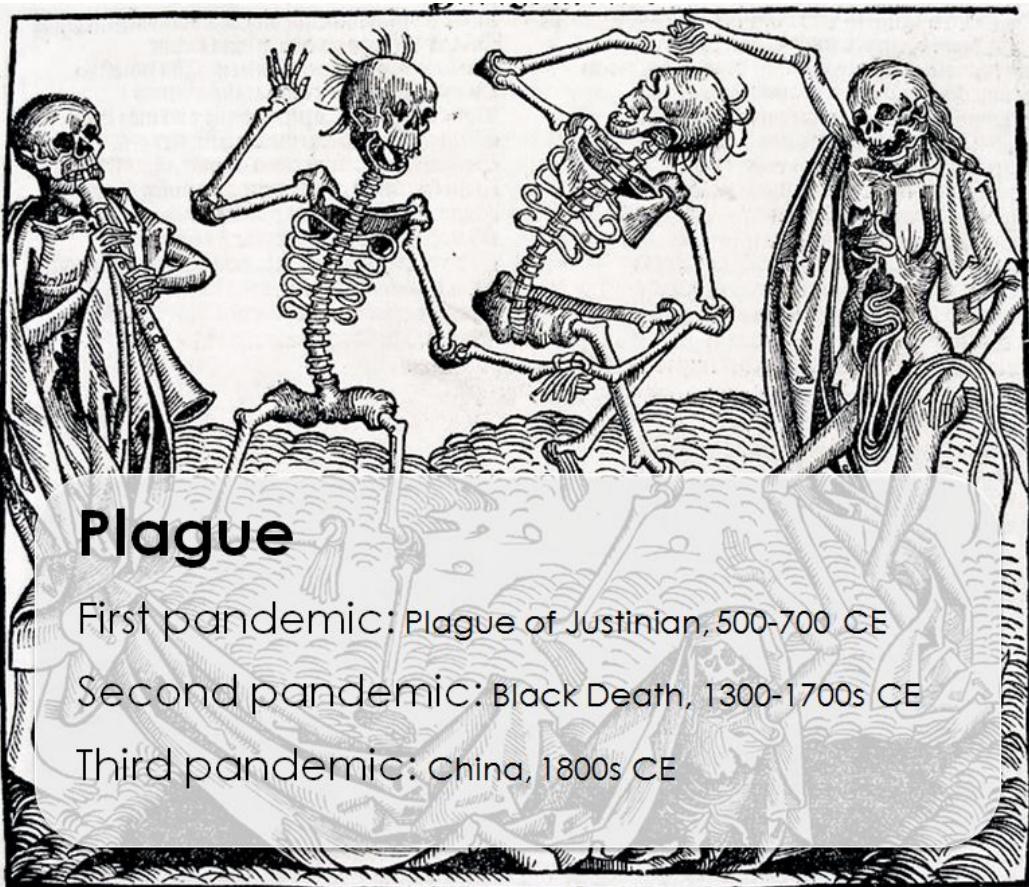


Ancient pathogens



1. Plague
2. Cocolitzli





The Dance of Death (1493) from the Nuremberg Chronicle





Plague
First pande
Second p...
Third p...
The

Emerging Microbes & Infections
2020, VOL. 9
<https://doi.org/10.1080/22221751.2020.1807412>

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Two fatal cases of plague after consumption of raw marmot organs

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ABSTRACT
Marmots are an important reservoir of *Yersinia pestis* and a source of human plague in Mongolia. We present two fatal cases of plague after consumption of raw marmot organs and discuss the distribution of natural foci of *Y. pestis* in Mongolia.

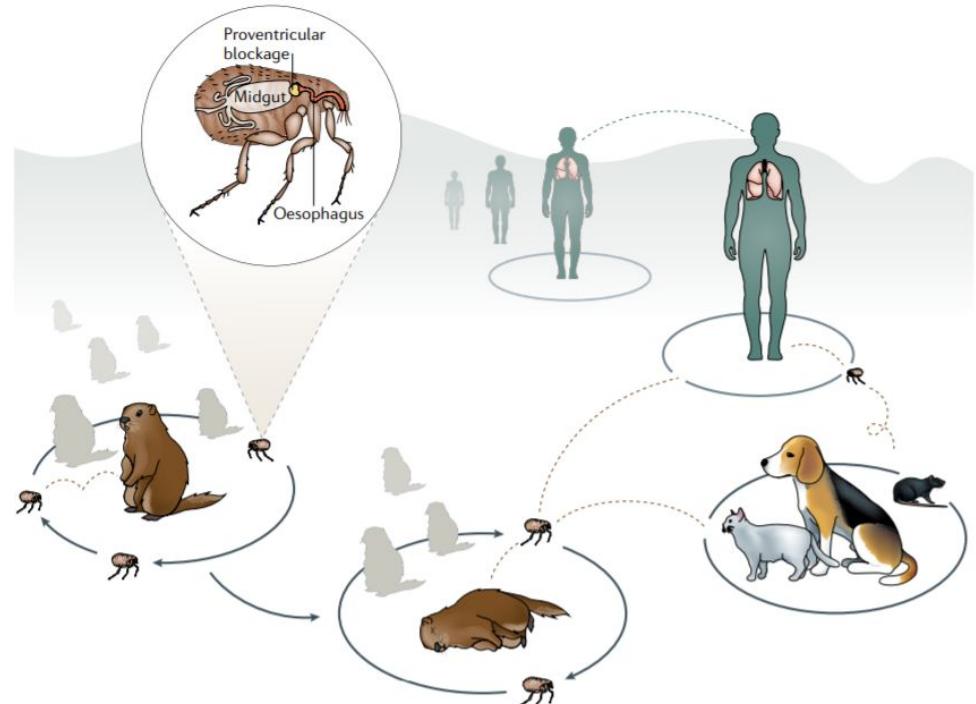
ARTICLE HISTORY Received 12 May 2020; Revised 25 July 2020; Accepted 5 August 2020

KEYWORDS Plague; Mongolia; marmot; epidemiology; sepsis



Yersinia pestis

- Not human-adapted
- Maintained in wild rodents
 - Still has active foci
- Transmitted by fleas
 - Blocks gut
 - Flea feeds more



Spyrou *et al.* 2019 Nat Rev Genet.



Plague in humans

1. Bubonic

- Most common
- Bacteria travel to lymph nodes, cause ‘buboës’
- Up to 60% mortality if untreated

2. Pneumonic

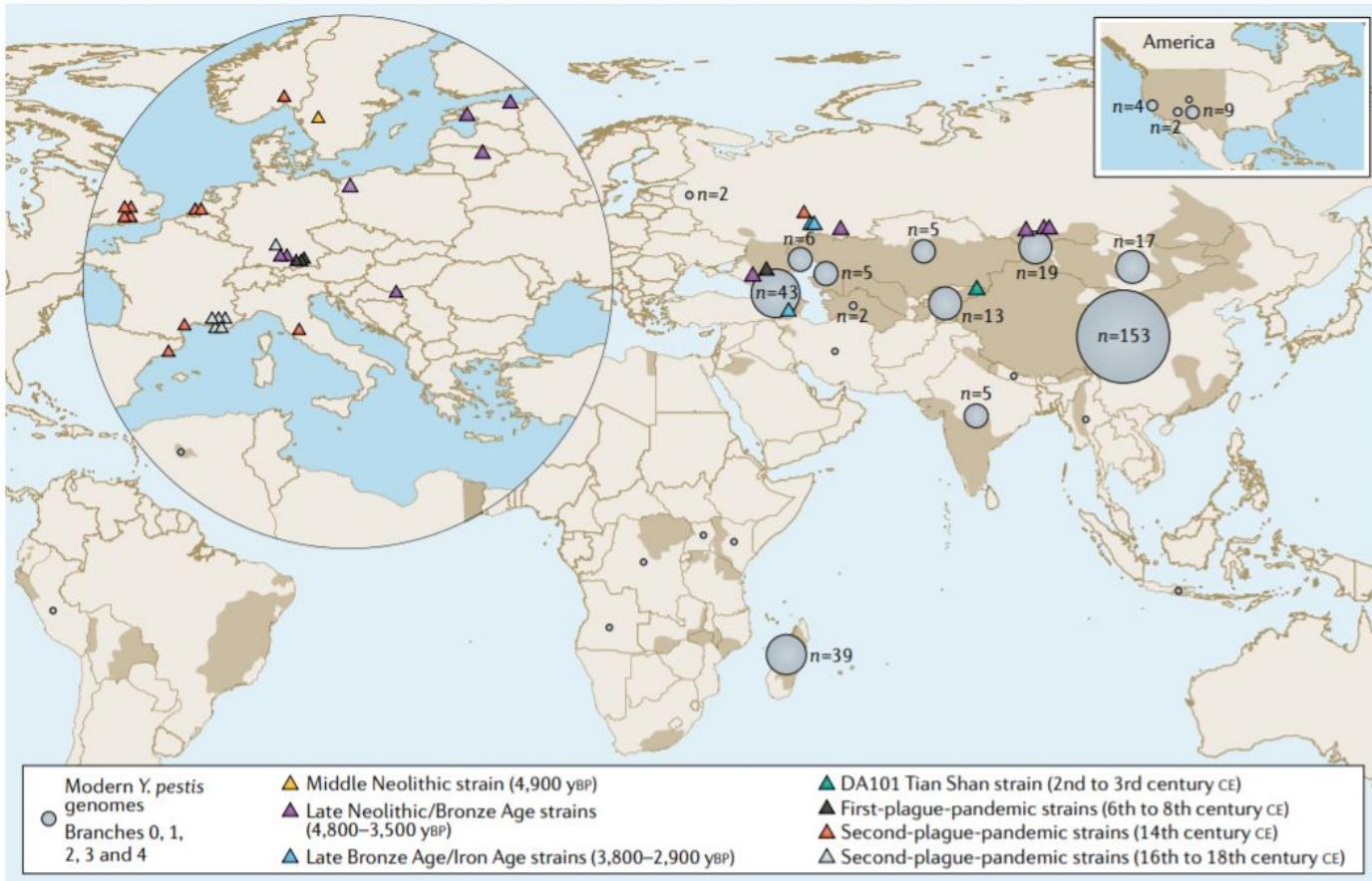
- Bacteria have travelled to the lungs
- Human-to-human transmission
- Nearly to 100% mortality if untreated

3. Septicaemic

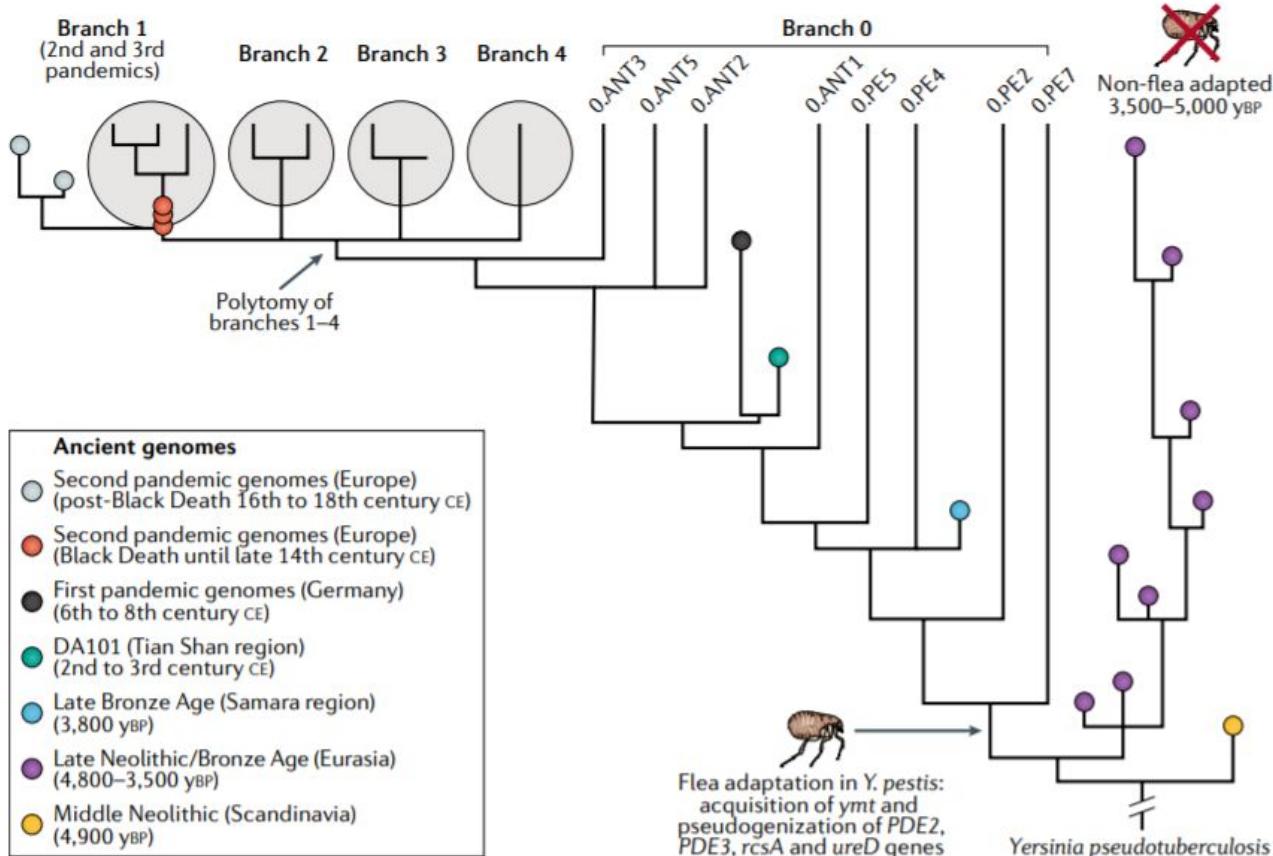
- Spreading in the bloodstream
- Nearly to 100% mortality if untreated



Yersinia pestis genomes



Yersinia pestis aDNA



Spyrou *et al.* 2019 Nat Rev Genet.



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Doorway to
Human History

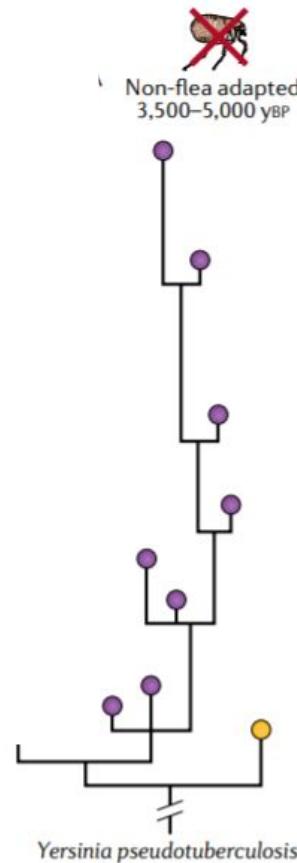


Yersinia pestis aDNA

- Not flea-adapted
 - Not bubonic
- How was plague transmitted?
- What was the host population?
- Spread mirrors human migrations

● Late Neolithic/Bronze Age (Eurasia)
(4,800–3,500 yBP)

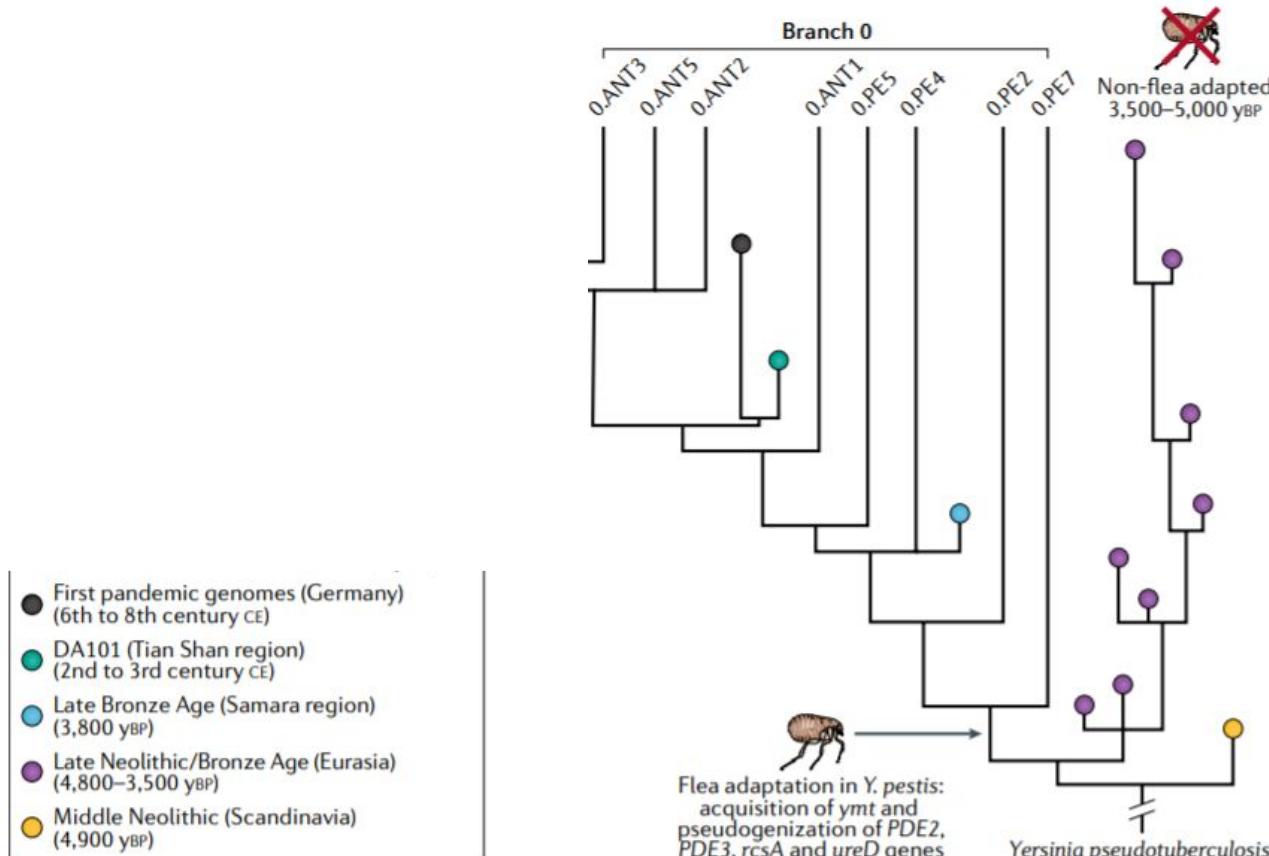
● Middle Neolithic (Scandinavia)
(4,900 yBP)



Spyrou et al. 2019 Nat Rev Genet.



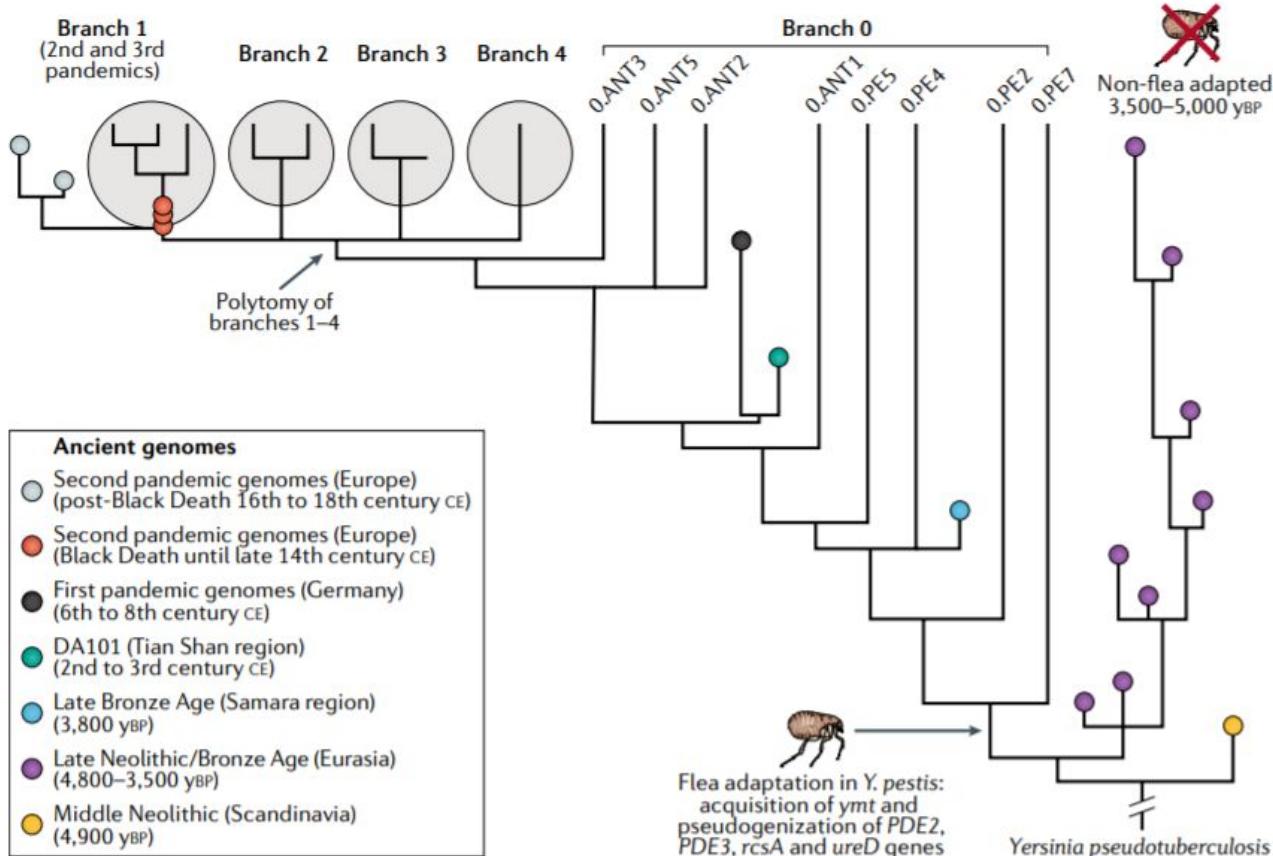
Yersinia pestis aDNA



Spyrou *et al.* 2019 Nat Rev Genet.



Yersinia pestis aDNA



Spyrou et al. 2019 Nat Rev Genet.



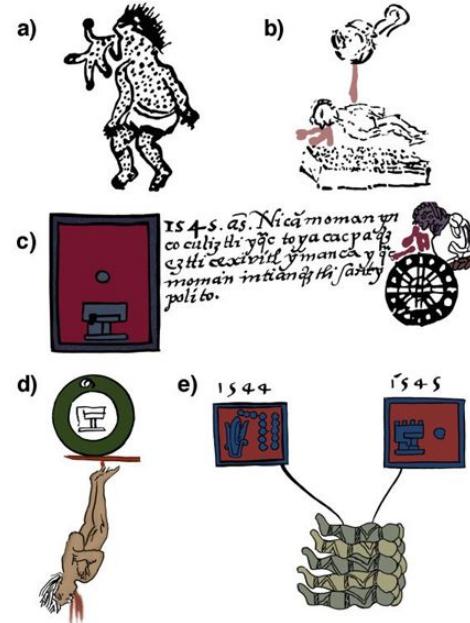
Yersinia pestis summary

- By studying ancient genomes we have learned about
 - Transmission
 - Virulence
 - Evolution

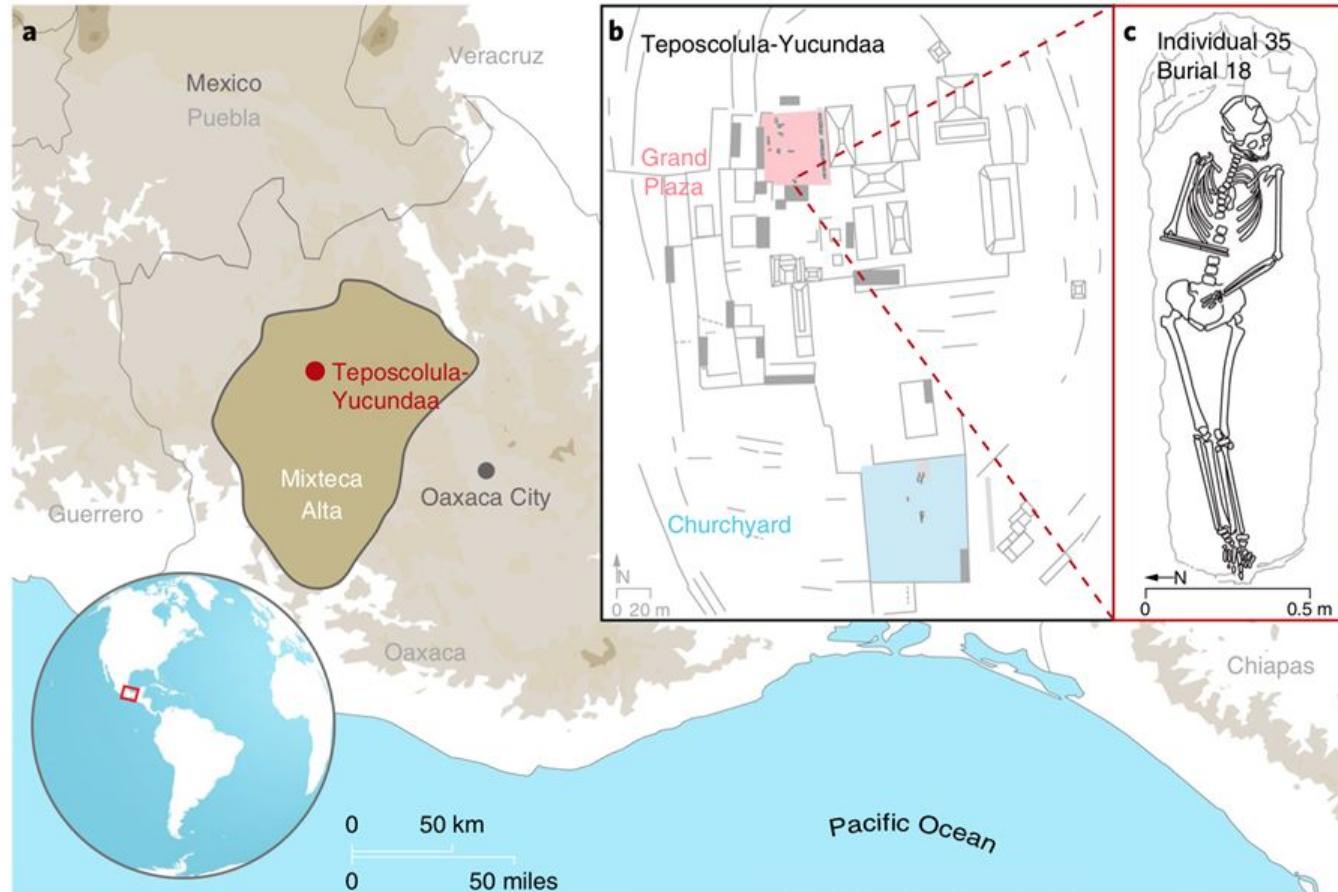


Cocolitzli

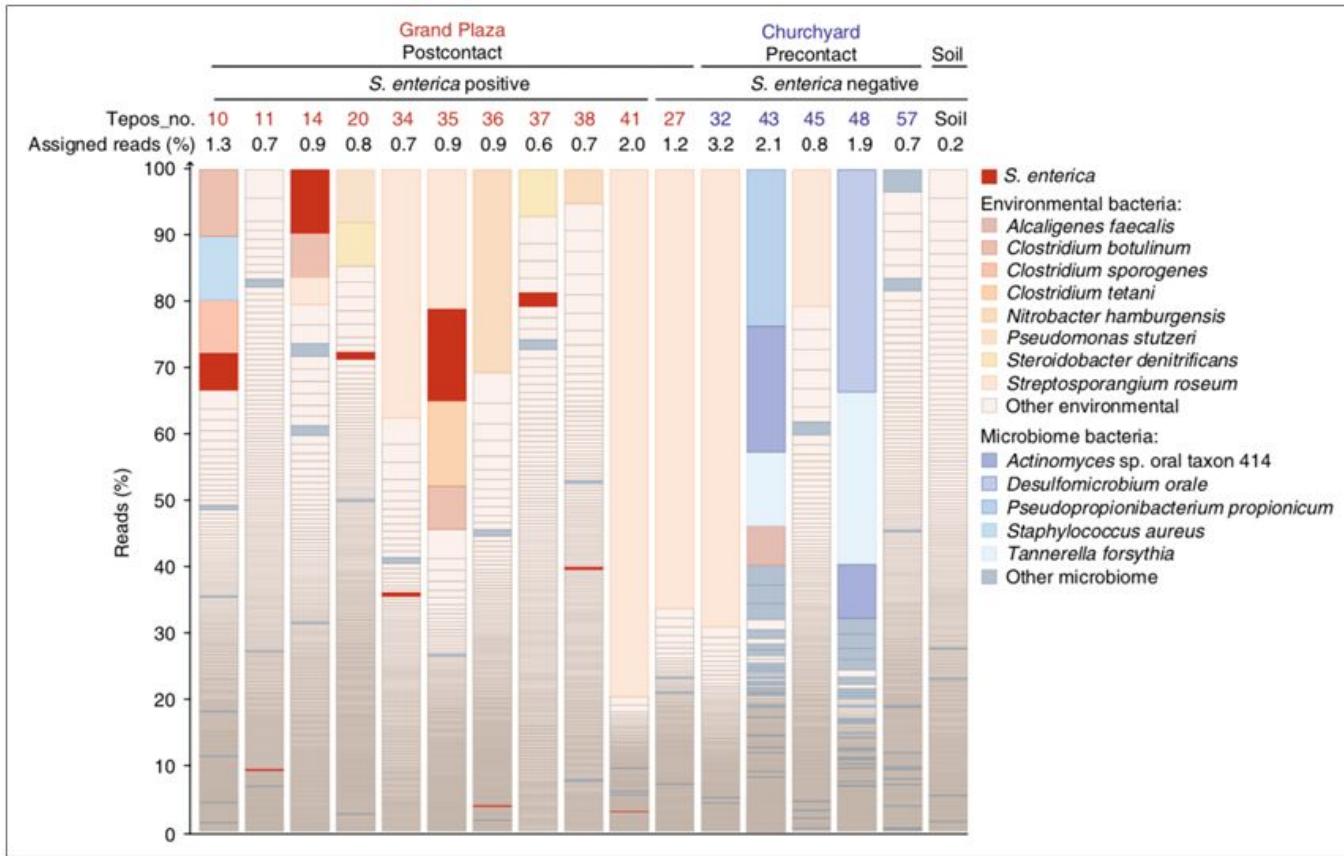
- Poorly understood epidemic, mortality 60-90%
- During 16th century, started in Central Mexico
- Many indigenous sources depicting the epidemic
- No certainty on what the cause was
 - Typhoid fever
 - Epidemic typhus
 - Plague
 - Influenza
 - Hemorrhagic fever



Cocolitzli-associated burial



Metagenomic screening



Cocolitzli-causing bacterium?

- *Salmonella enterica* subsp. *enterica* serovar Paratyphi C
 - Enteric fever
 - Infected individuals shed bacteria after symptoms have ended
 - Asymptomatic carriers
- Little is known about the past of this disease

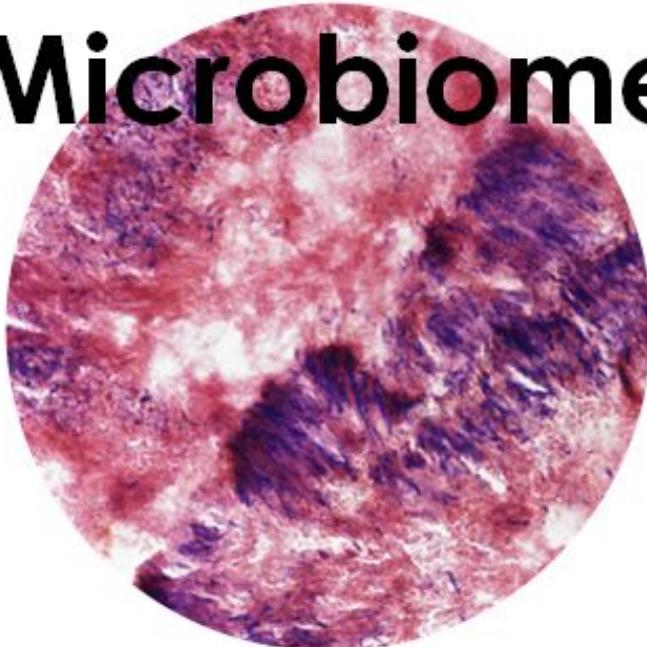


Cocolitzli summary

- First molecular evidence of what may have caused the epidemic
- More research needed
- We can start to solve ancient mysteries using aDNA
 - Connected with other lines of evidence



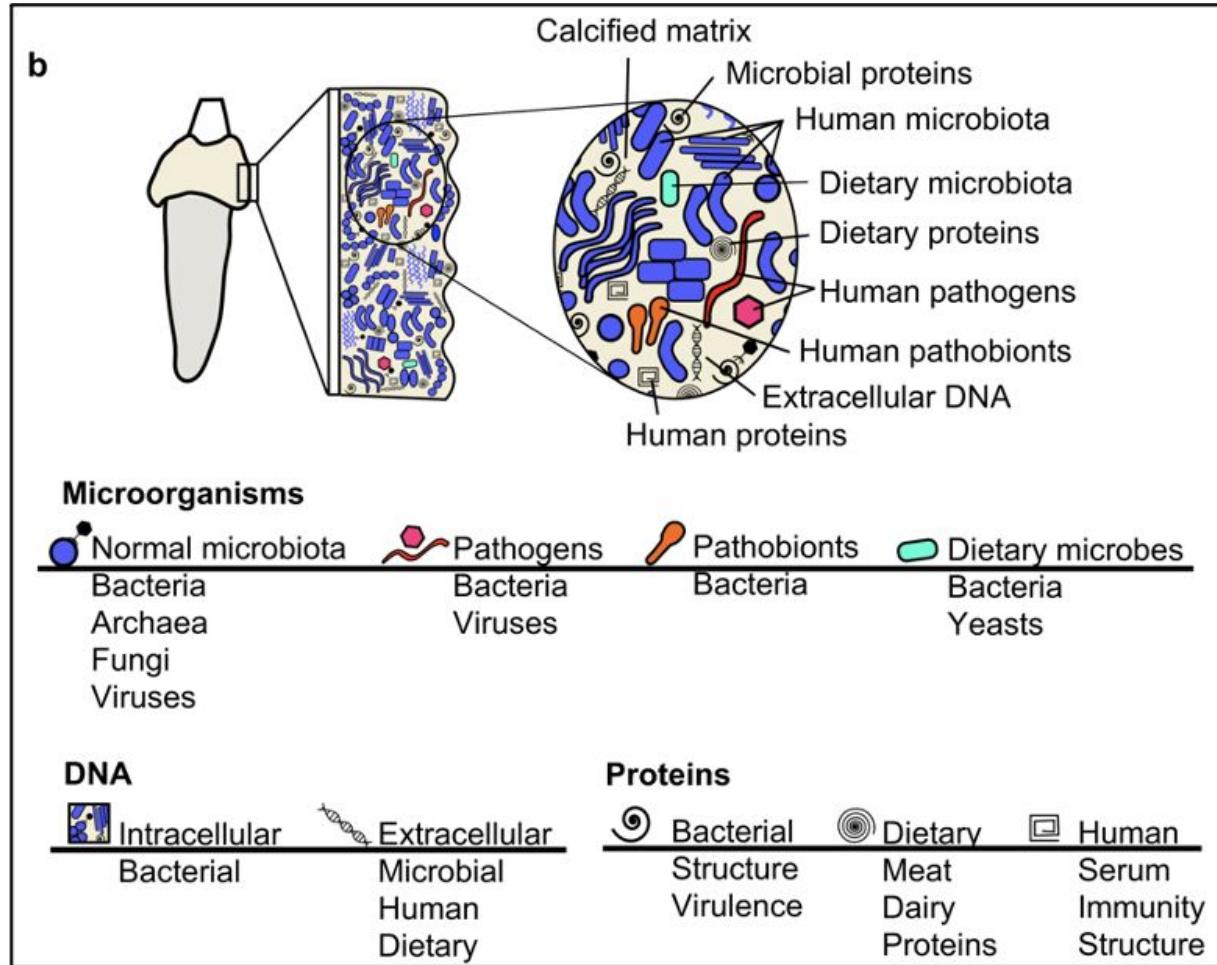
Microbiome



What is a microbiome?



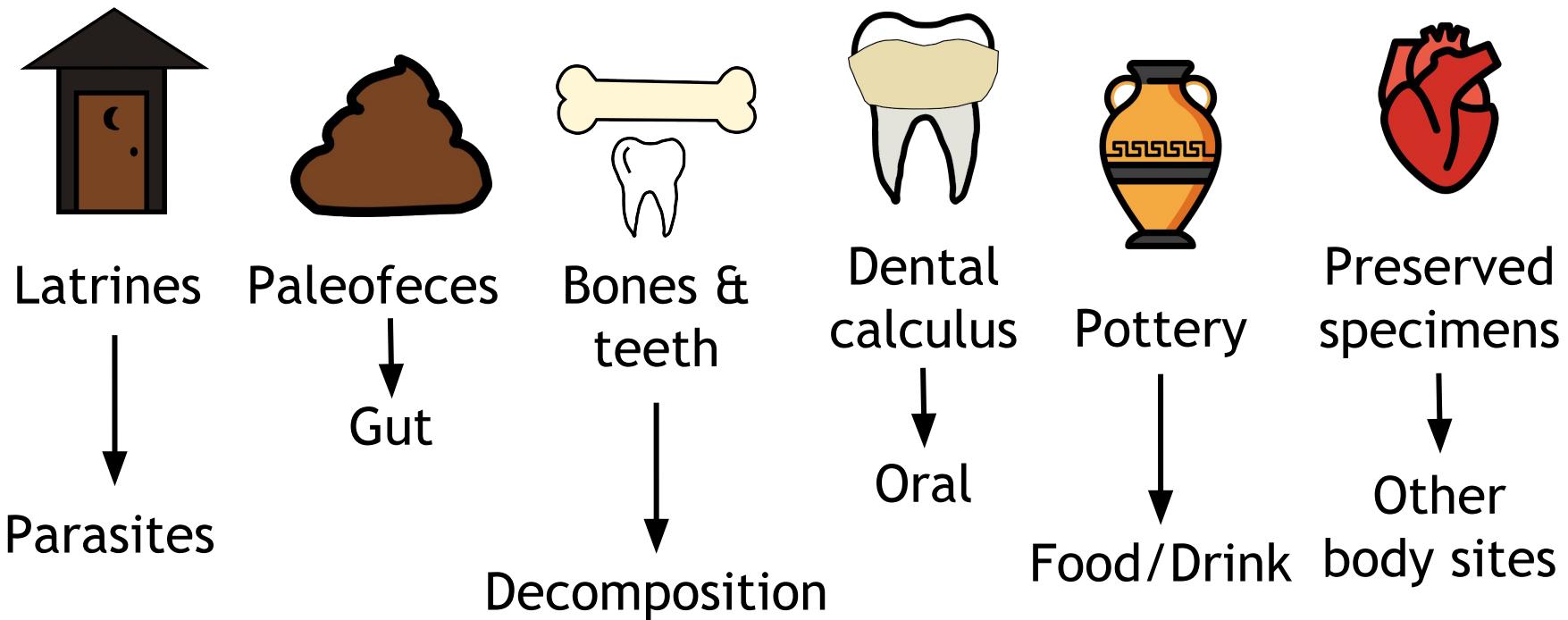
Historic dental calculus
(~200 years old)



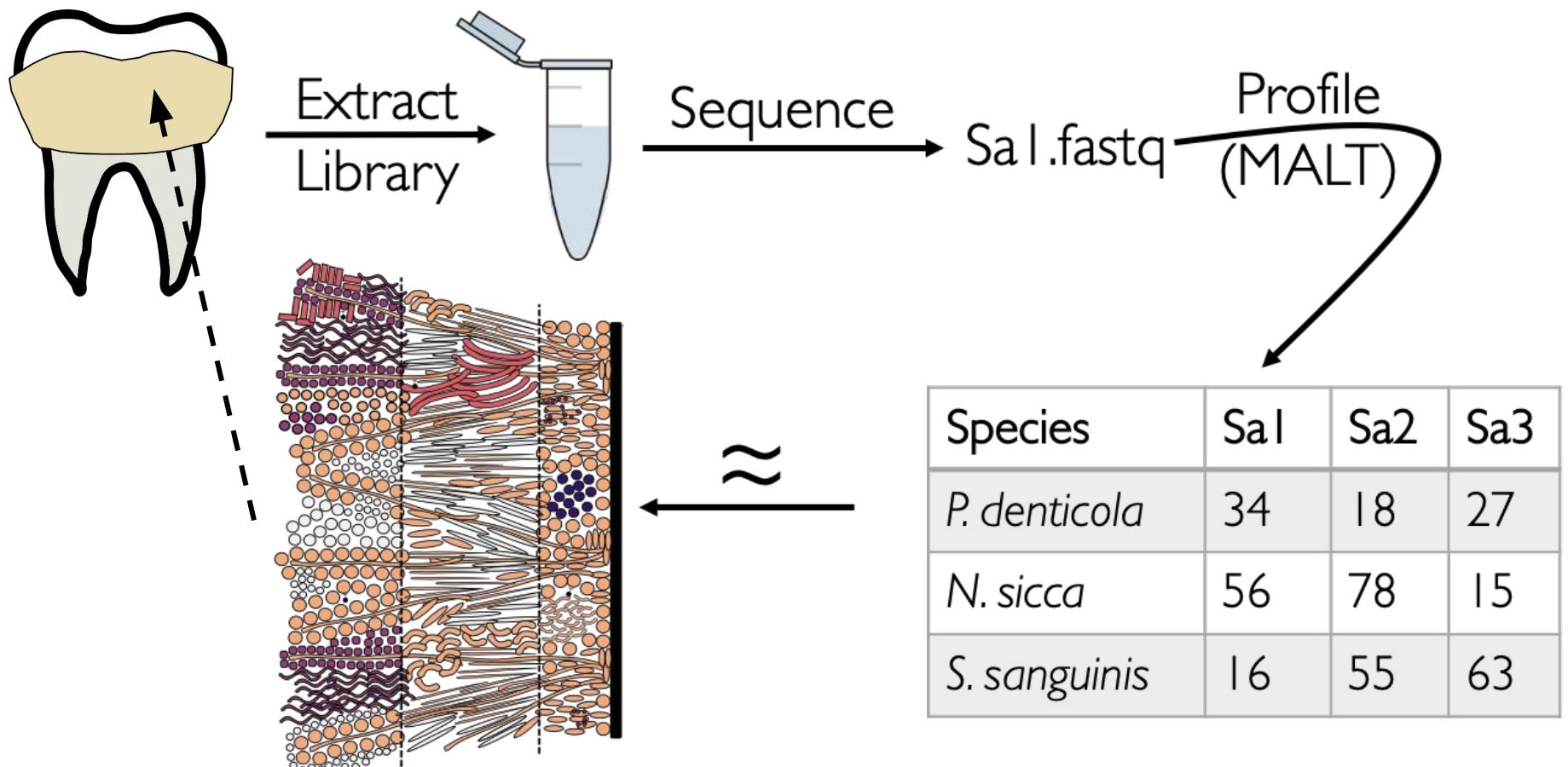
Modified from Velsko and Warinner 2017 *Bioarchaeology International*



Where are archaeological microbiomes?



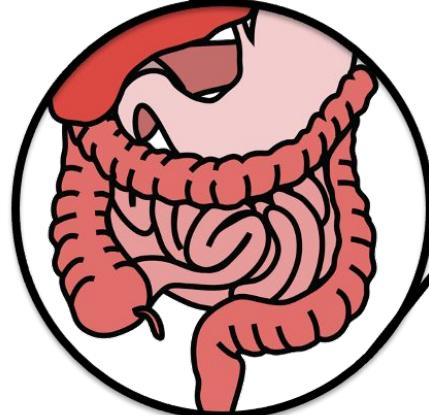
How do we study microbiomes?



Dental calculus and paleofeces are common ancient human microbiomes

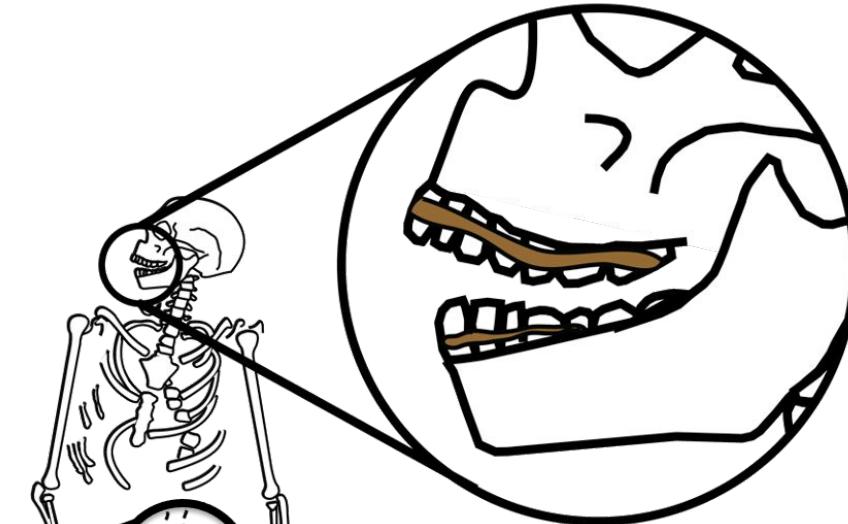


Hübner et al. in prep



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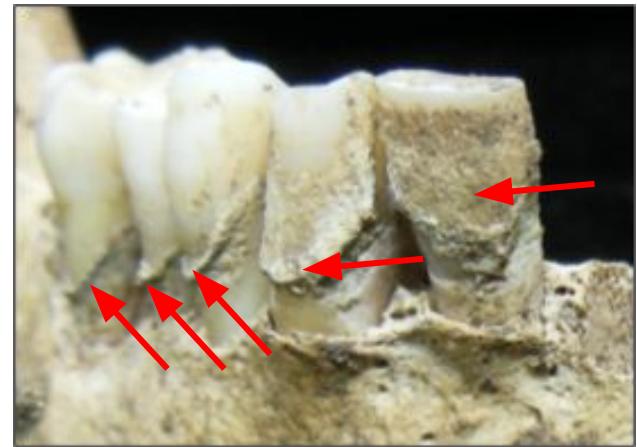


Warinner et al. 2014



Ancient dental calculus...

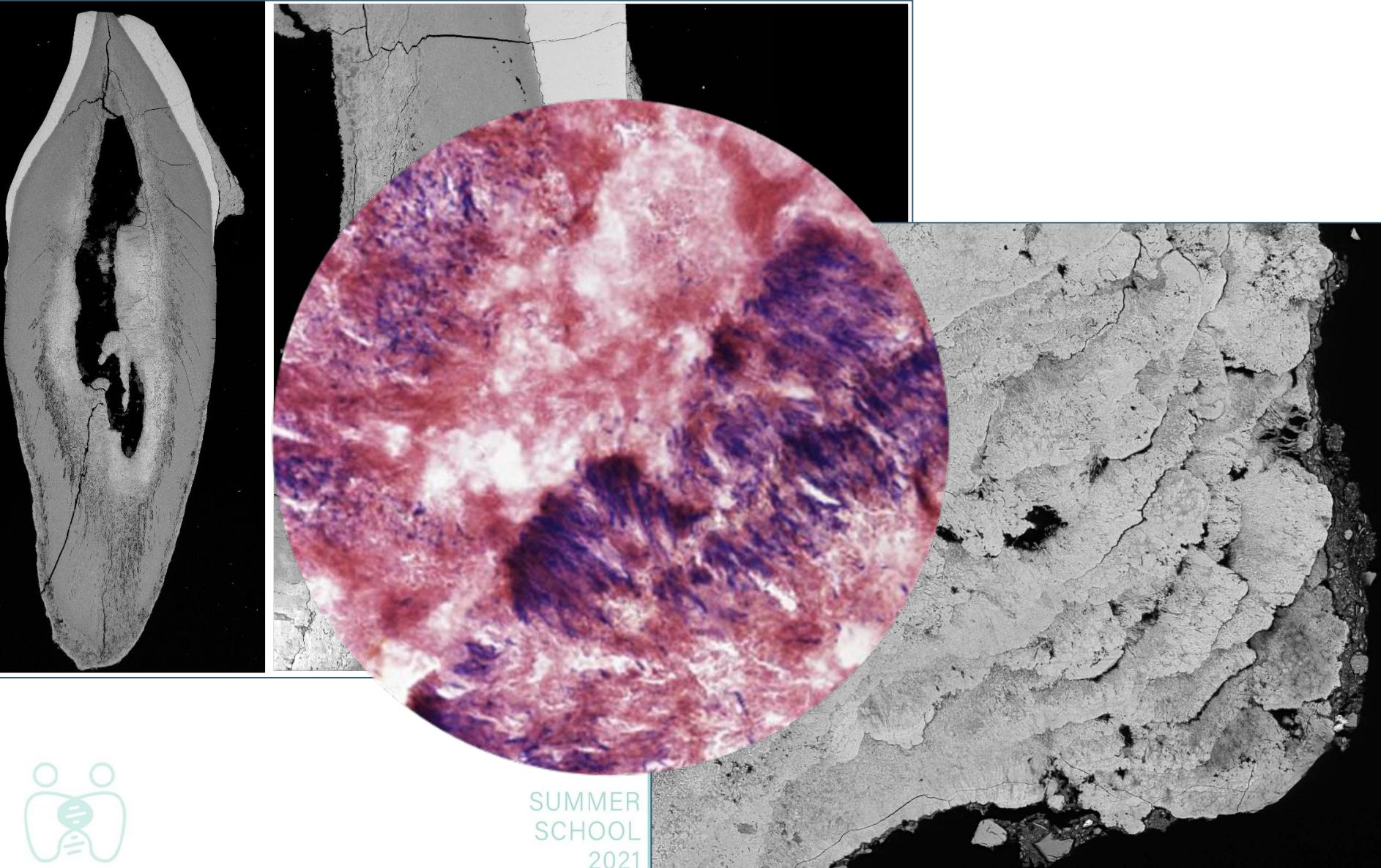
- Mineralized dental plaque
 - associated diseases: dental cavities, periodontitis
- Ubiquitous in archaeological record
- Highly stable human microbiome
 - across time
 - across geography



Historic dental calculus
(~200 years old)

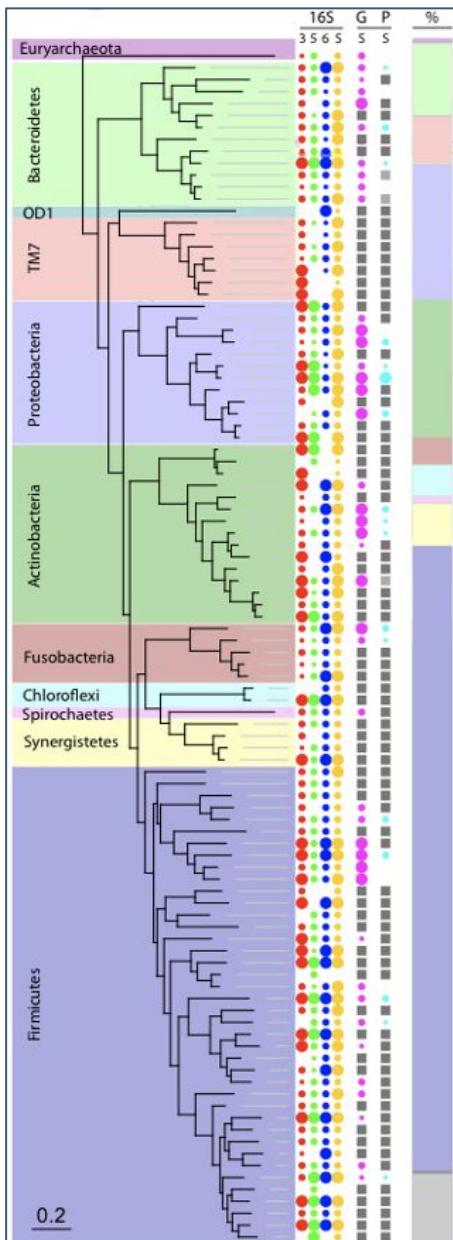


Ancient dental calculus looks like modern dental plaque

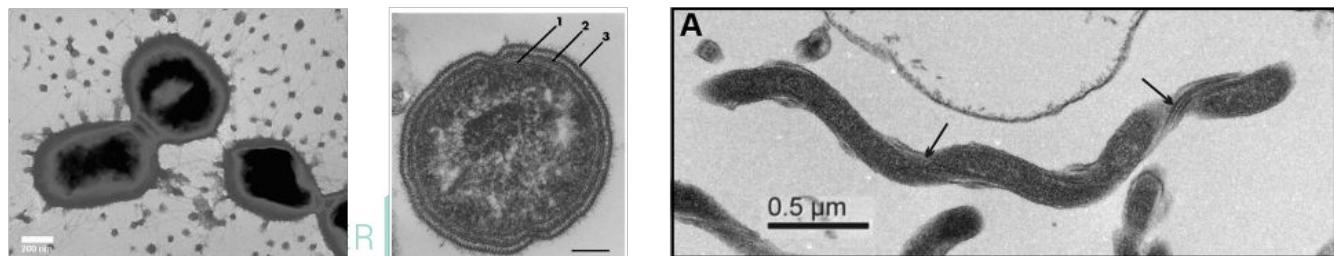


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Ancient dental calculus resembles modern dental plaque



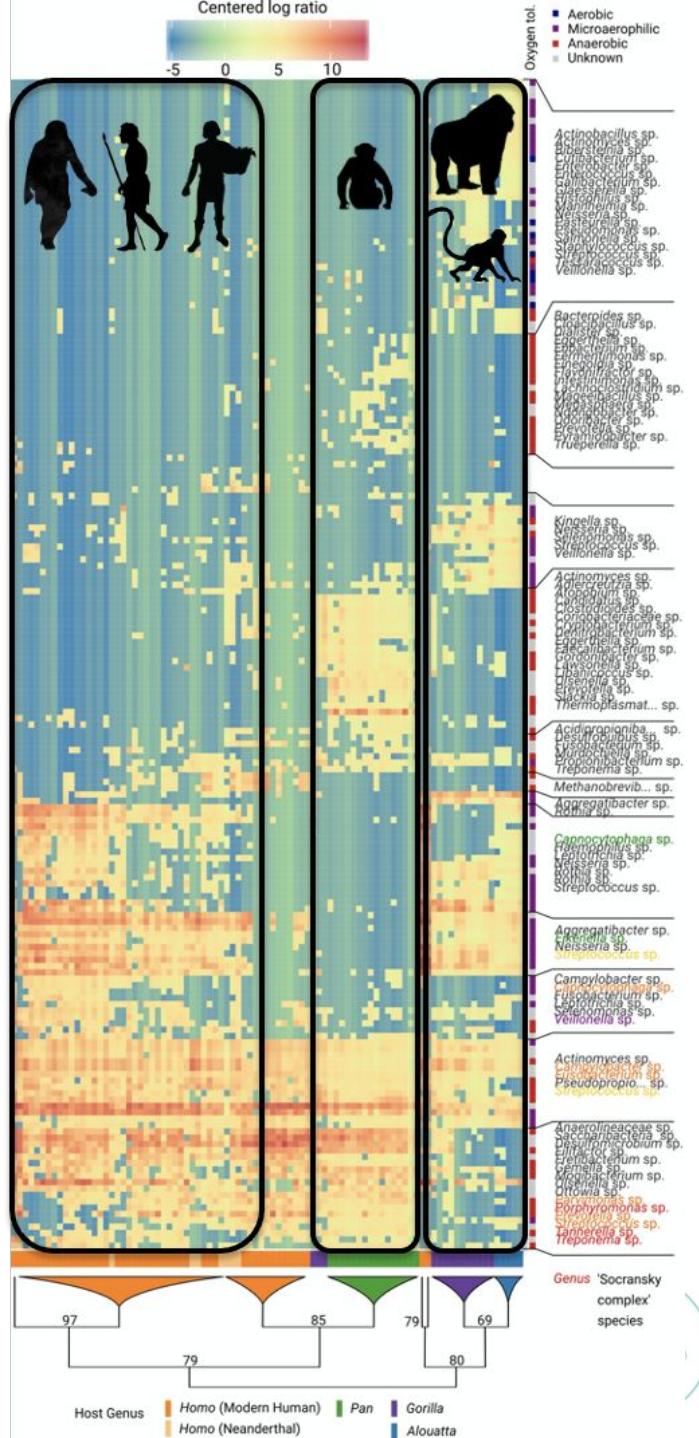
Pathogen ^{a,b}	Genes (contigs)	Proteins (peptides)	Virulence	Resistance	Plasmid	CTn/Phage
<i>Porphyromonas gingivalis</i>	802 (2588)	7 (72)	++	+		+
<i>Tannerella forsythia</i>	1099 (11279)	10 (137)	++	+		+
<i>Treponema denticola</i>	917 (6106)	3 (15)	++	+	+	+



Calculus microbiomes are conserved through time

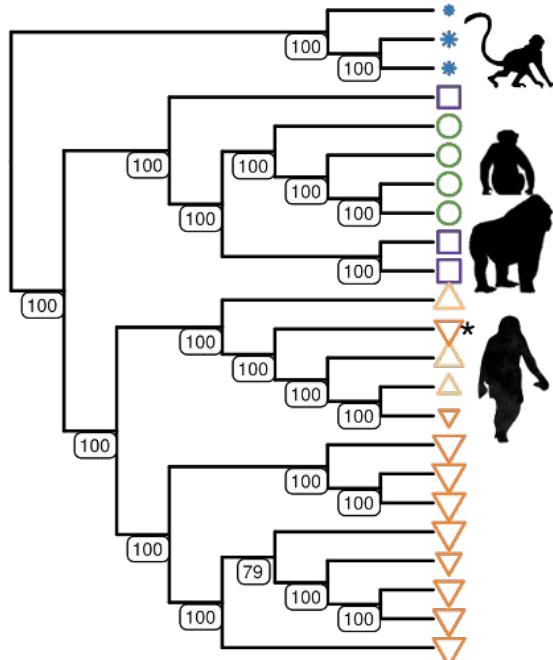


Modified from Fellows Yates, et al. 2021 PNAS

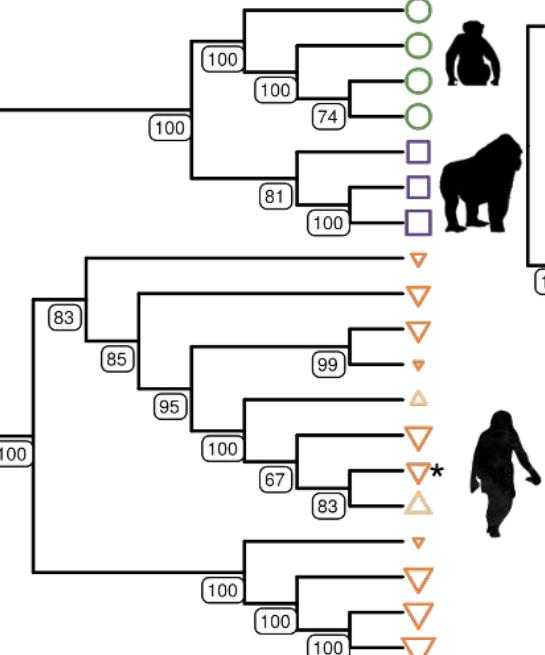


Microbial species evolution traces host evolution

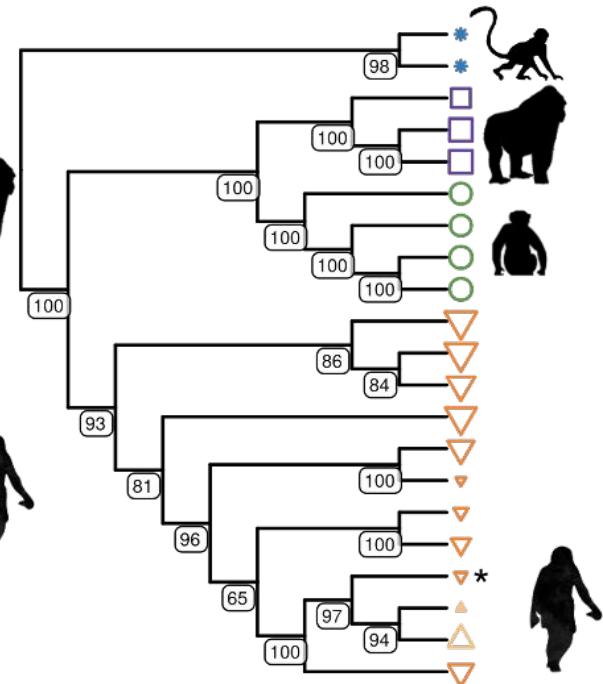
Actinomyces (dentalis DSM 19115)



Fretibacterium (fastidiosum)



Tannerella (forsythia 92A2)



Host genus

* Alouatta

□ Gorilla

○ Pan

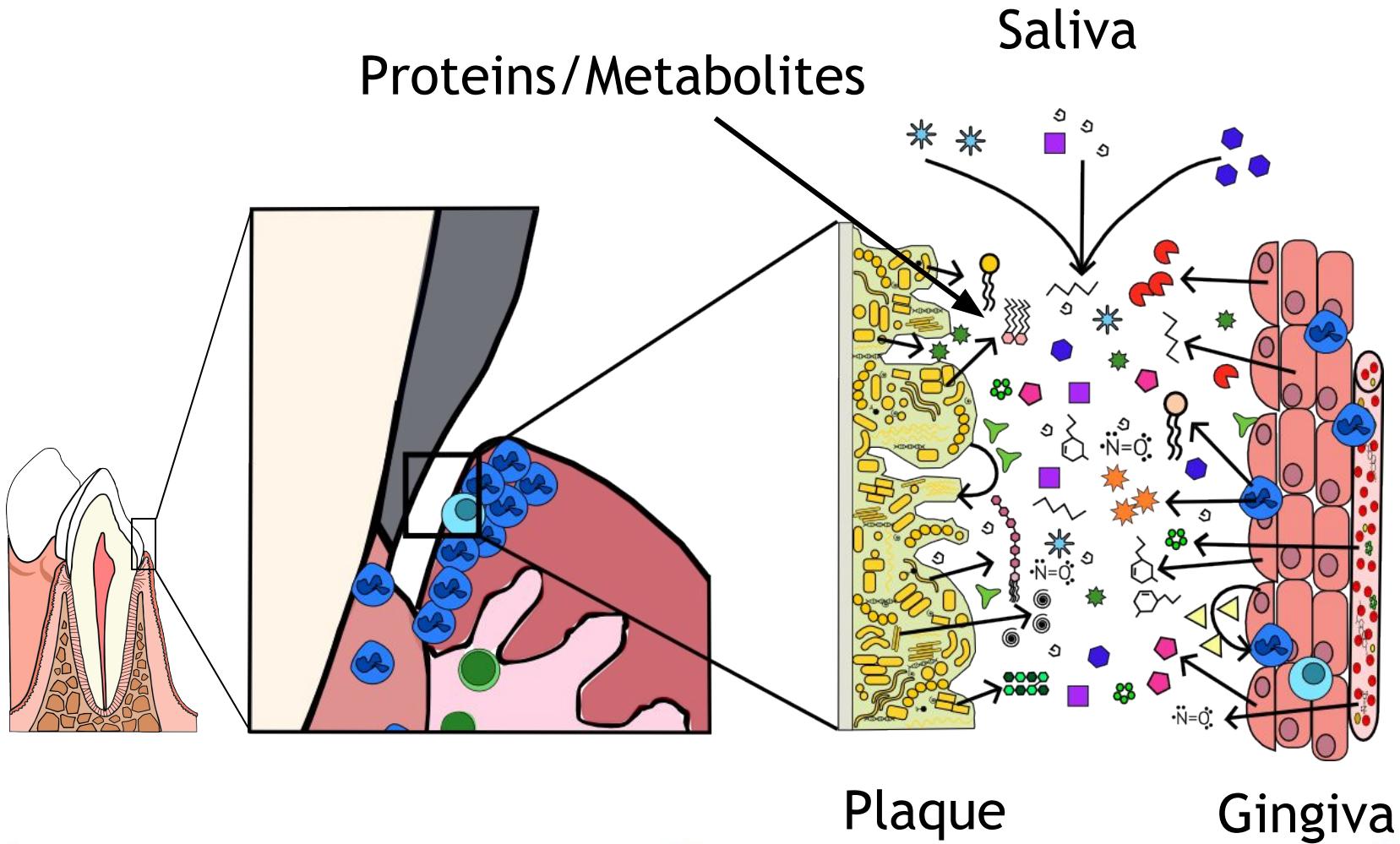
△ Homo (Neanderthal)

▽ Homo (Modern Human)

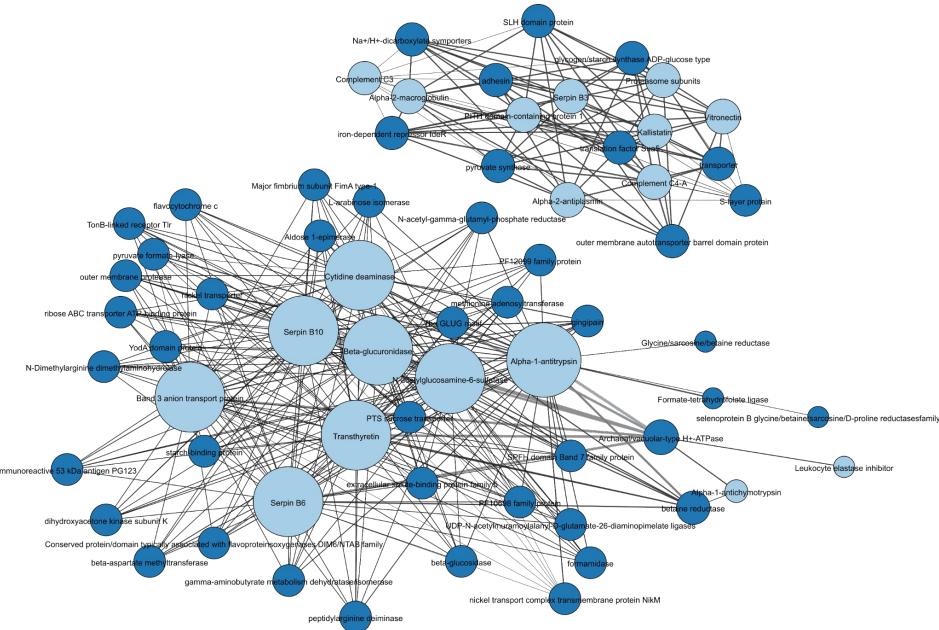
Modified from Fellows Yates, et al. 2021 PNAS



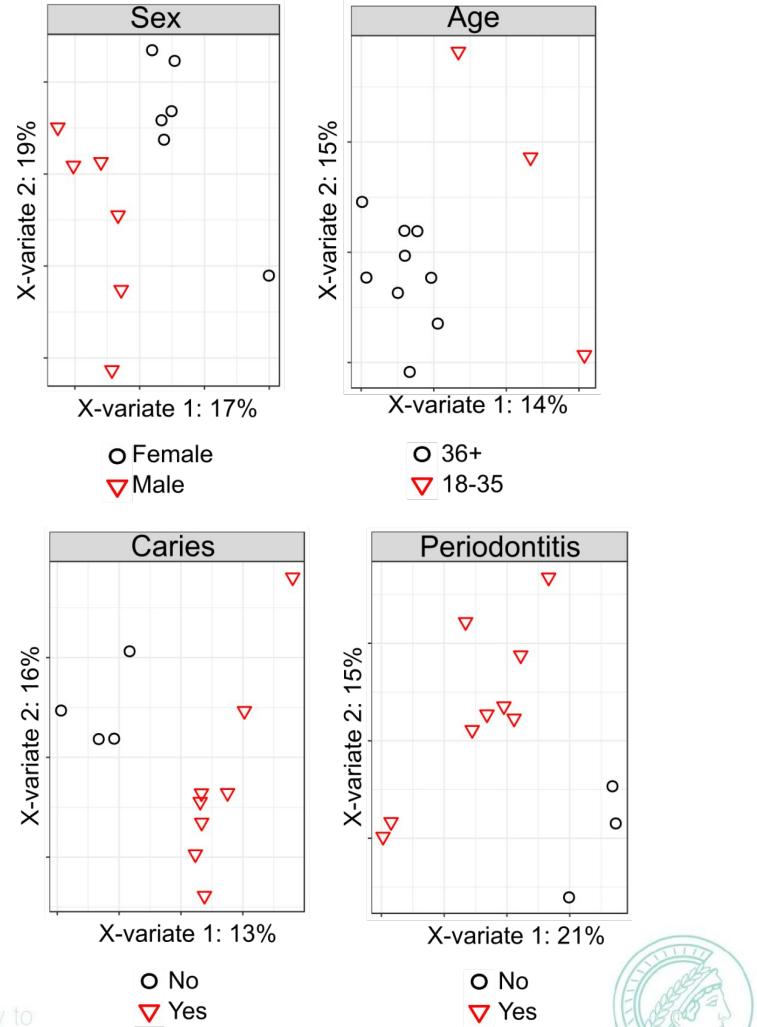
Biofilms are metabolically active



Proteins and metabolites preserve in ancient dental calculus



Modified from Velsko, et al. 2019 *Microbiome*

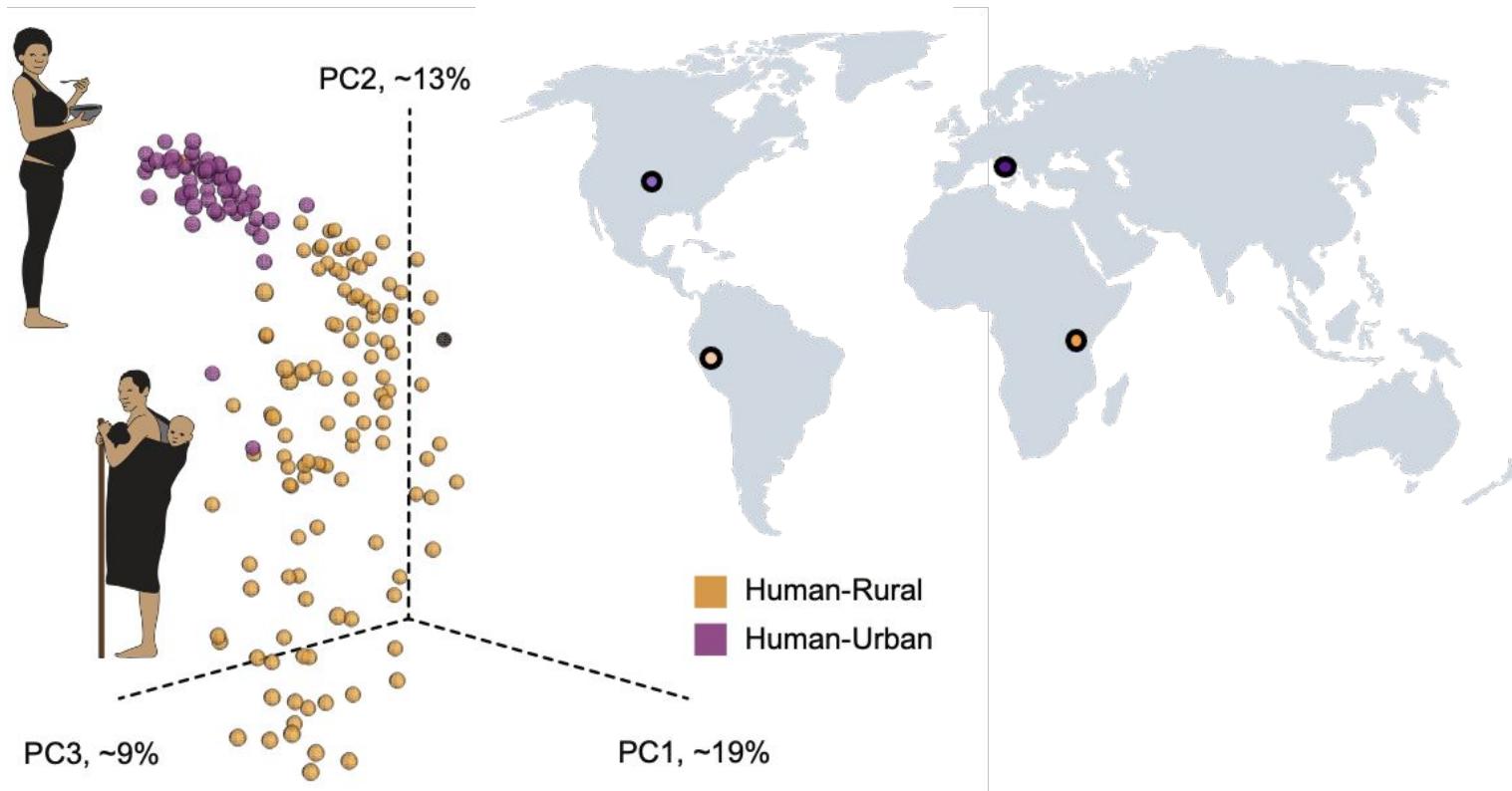


Paleofeces

- Feces preserved under exceptional conditions
 - very dry (arid, salty)
- Associated with many inflammatory disorders
 - diseases of civilization/industrialization
- Uncommon in archaeological record
- Highly variable human microbiome



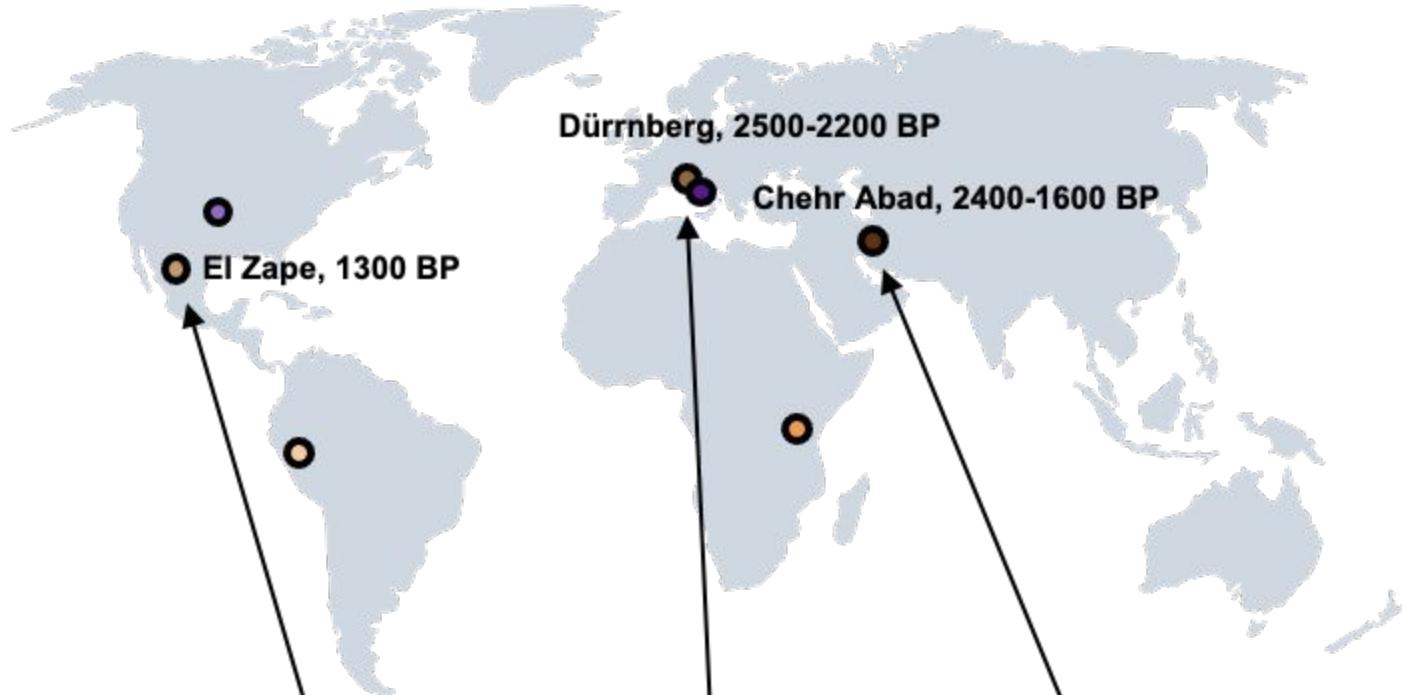
Rural and urban gut microbiomes differ



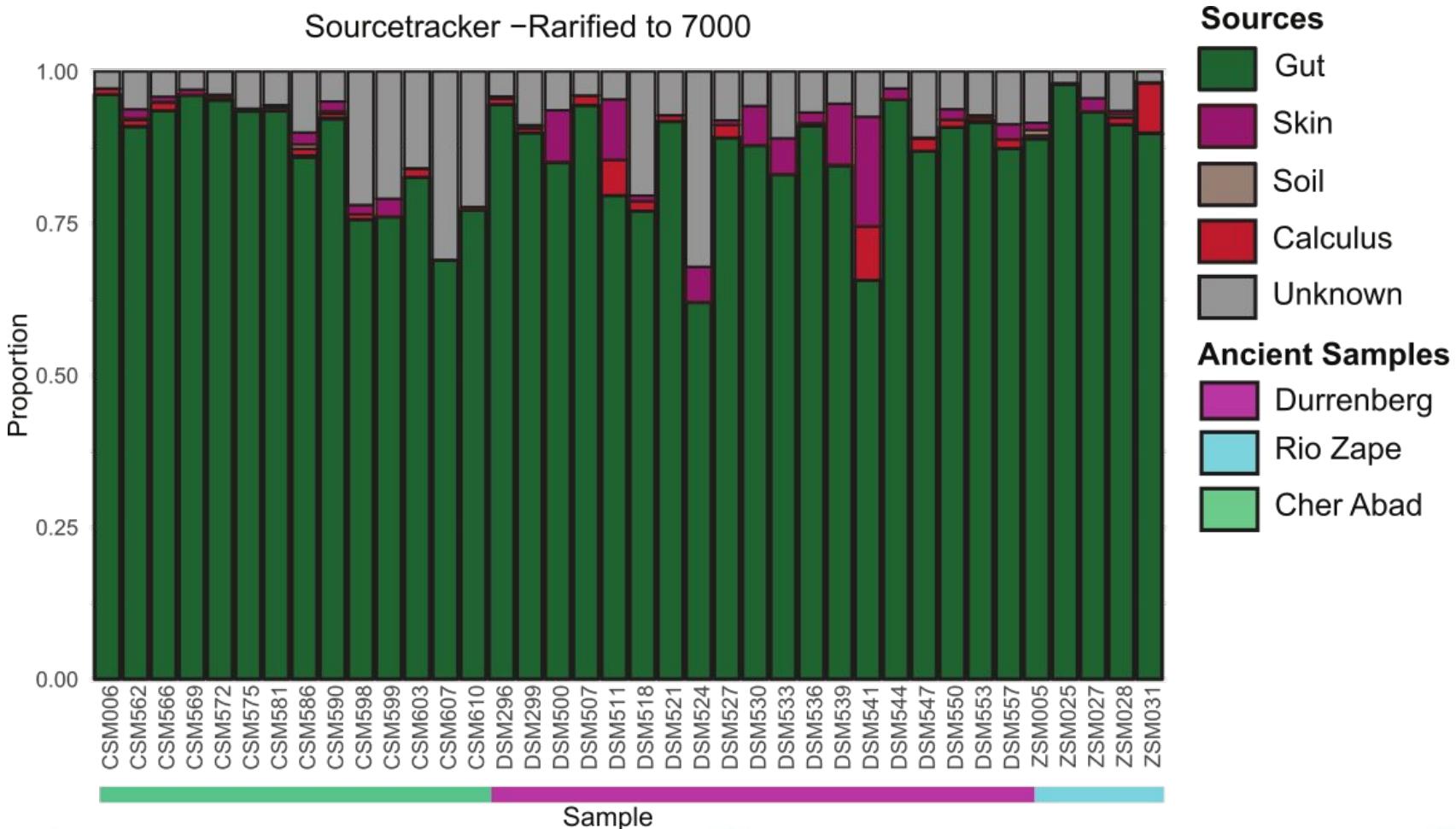
Paleofeces species composition

- When do changes happen?
- What drives changes?

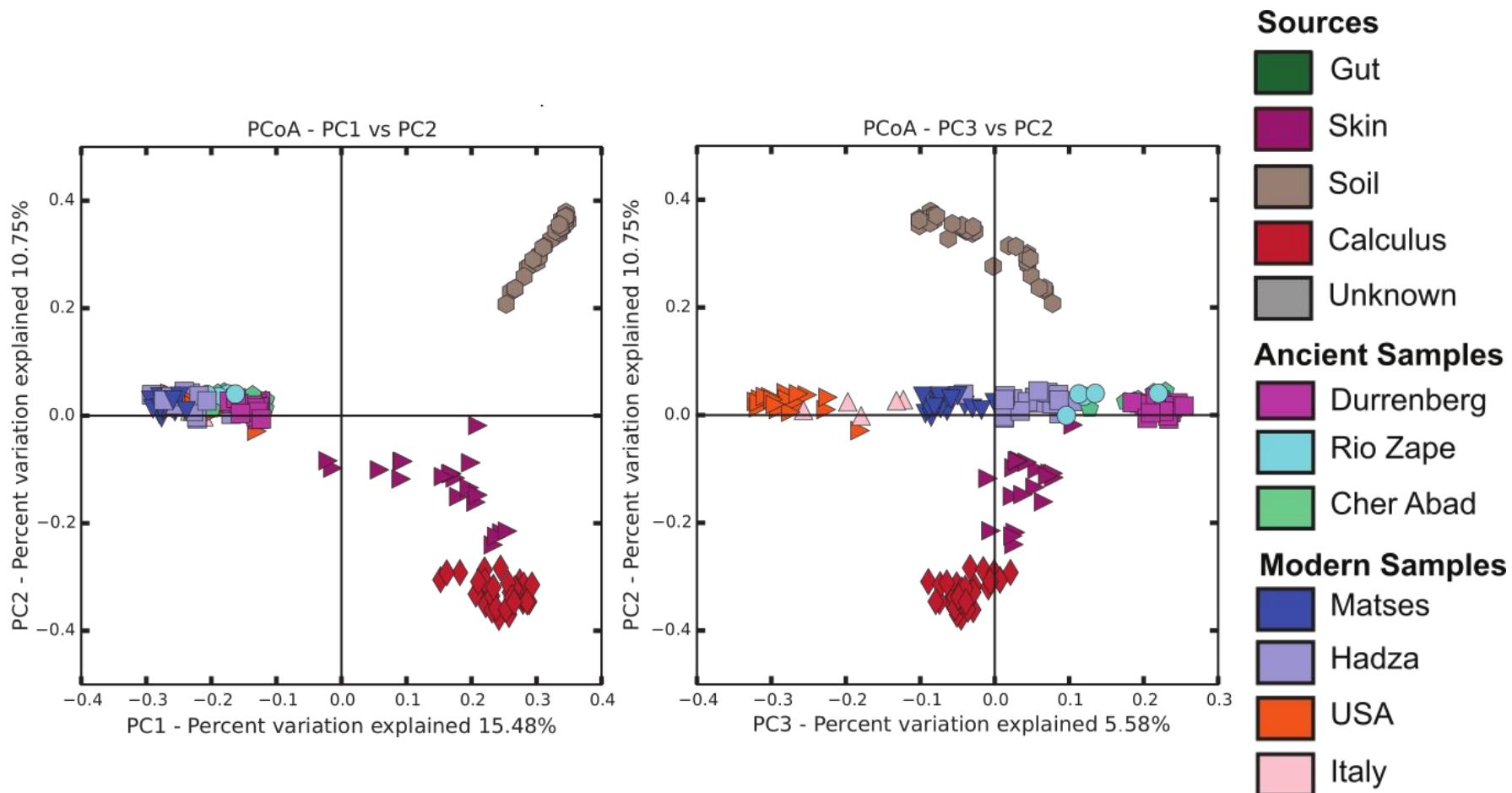




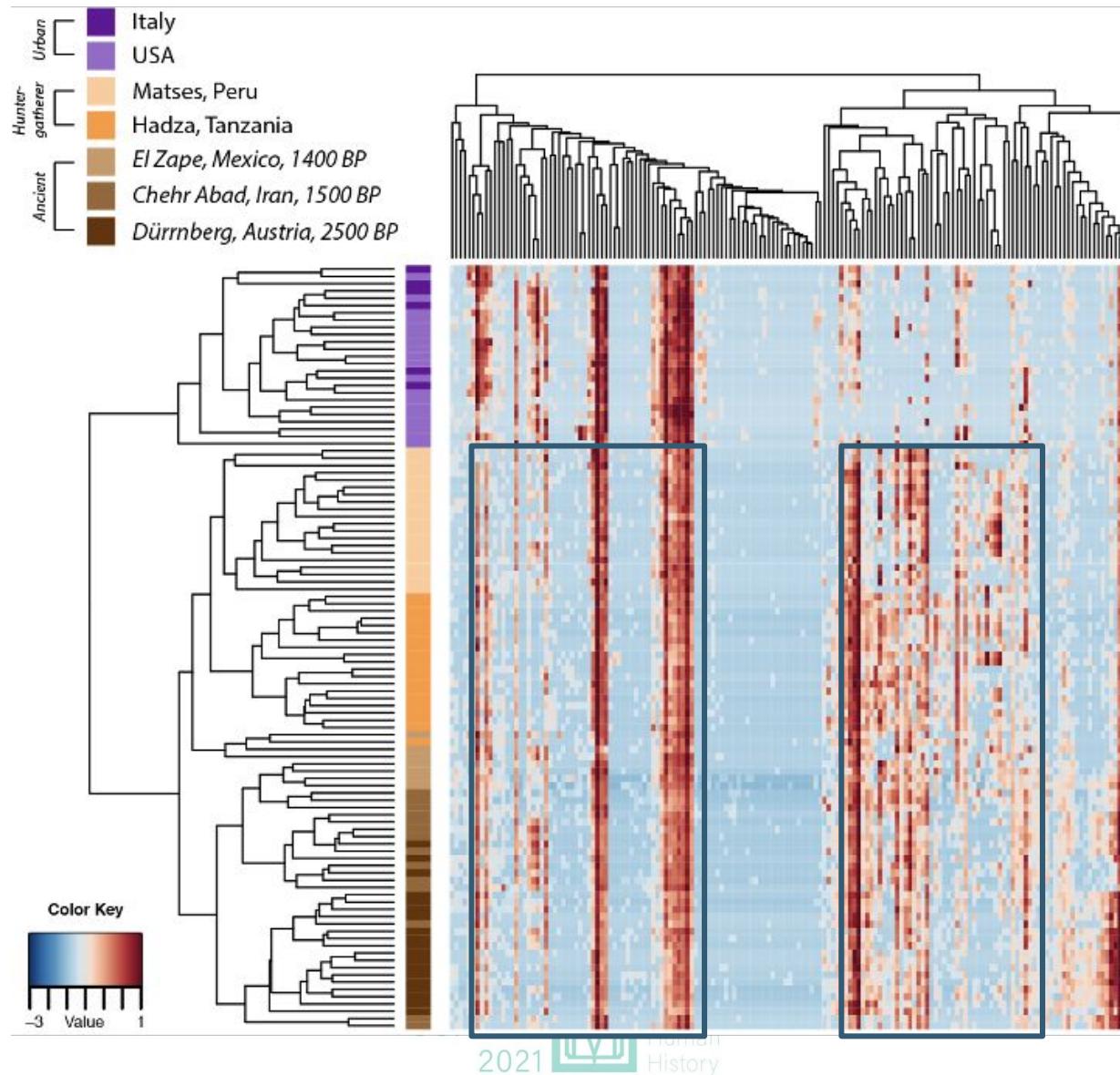
Well-preserved paleofeces resemble modern gut microbiomes



Well-preserved paleofeces resemble traditional food producer gut microbiomes



Modern guts lack species found in rural gut and paleofeces microbiomes



Microbiome take-home points

Microbiomes

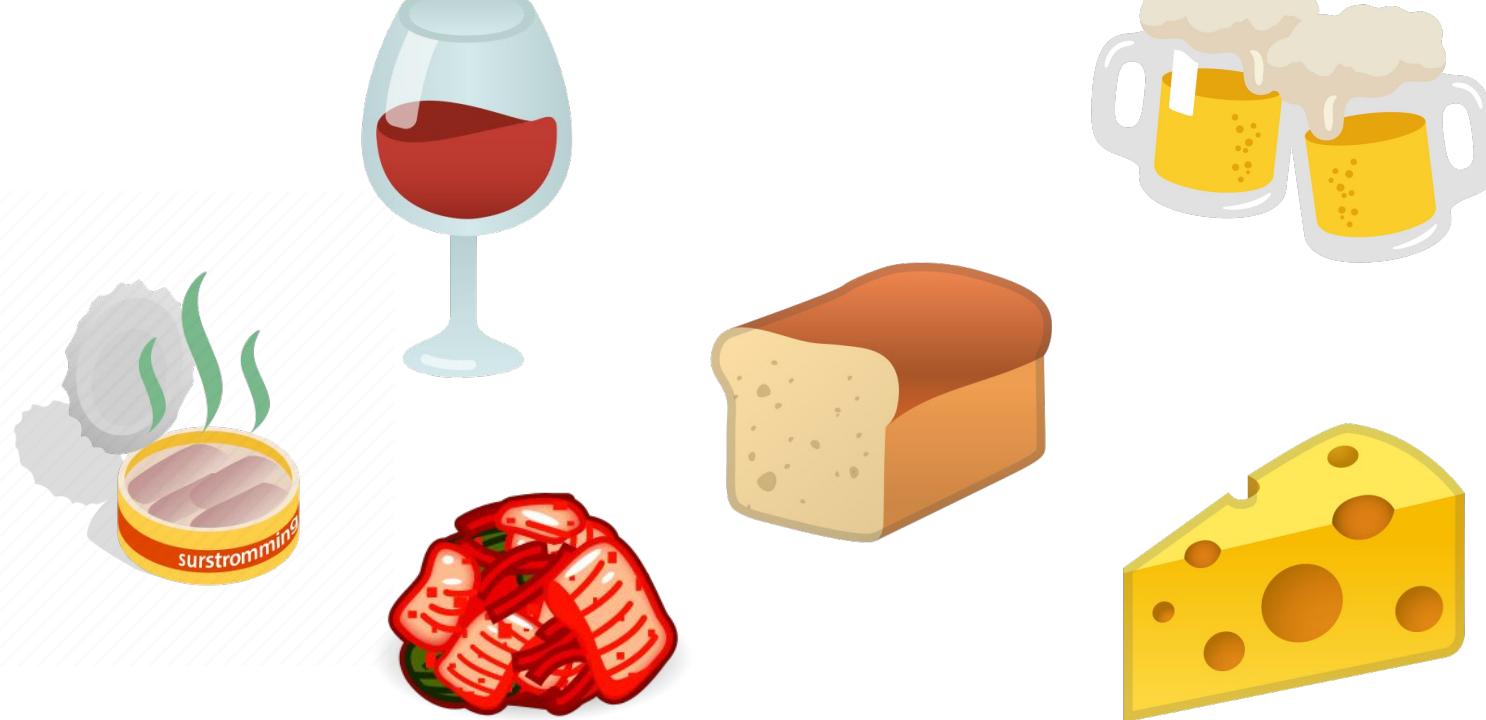
- Preserve in the archaeological record
- Contain information about
 - Microbial taxonomy
 - Microbial activity (proteins/metabolites)
- Reflect host changes
- Help us understand historic health and disease
 - Long-term changes to human condition



Cuisine



Dietary microbes



The dairy mystery



The dairy mystery

Journal of Archaeological Science 43 (2014) 178–186

Contents lists available at ScienceDirect

Journal of Archaeological Science

journal homepage: <http://www.elsevier.com/locate/jas>

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ARTICLE INFO

Article history:
Received 29 July 2013
Received in revised form
27 January 2014
Accepted 7 February 2014
Available online 18 February 2014

Keywords:
Archaeology
Ancient diet
Ancient dairy
Bronze Age
Eastern Eurasia
Proteomics

ABSTRACT

Cheese making has been inferred at several sites in northern Europe as early as the 6th millennium and was common in Egypt and Mesopotamia in 3rd millennium BC. However, the remains of cheeses have never been found and recipes of ancient dairy, its production scale, social and economic impact remain poorly understood. Here we present direct proteomics evidence for the production earliest known cheese that was found as an organic mass associated with the mummies of Early Bronze Age cemetery of Xiaohe (1980–1450 BC) in Xinjiang, China. Kefir fermentation of ruminant milk tyramitic culture of Lactobacillus kefiriophilus and other lactic acid bacteria and yeasts was the most robust, scalable, probiotic, lactose-free dairy and a key technological advance that introduced economic benefits of extensive herding into a semi-pastoral household of the Eastern Eurasia population already the Early Bronze Age.

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D 




The dairy mystery

SCIENTIFIC REPORTS

OPEN Direct evidence of milk consumption from ancient human dental calculus

SUBJECT AREAS:
PROTEOMICS
BIOMARKERS
ZOOLOGY
ARCHAEOLOGY

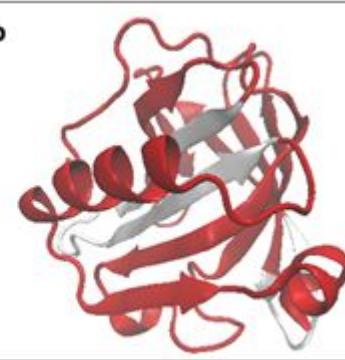
C. Warinner^{1,2*}, J. Hendy^{3*}, C. Speller³, E. Cappellini⁴, R. Fischer⁵, C. Trachsel⁶, J. Ameisborg^{7,8}, N. Lynnerup⁹, O. E. Craig¹⁰, D. M. Swallow¹⁰, A. Fotakis¹¹, R. J. Christensen¹¹, J. V. Olsen¹¹, A. Liebert¹⁰, N. Montalvo^{10,12}, S. Fiddiment¹³, S. Charlton¹³, M. Mackie¹³, A. Conci¹³, A. Bouwman⁷, F. Rohr², M. T. P. Gilbert^{1,14} & M. J. Collins³

Received 21 July 2014
Accepted 27 October 2014
Published 27 November 2014

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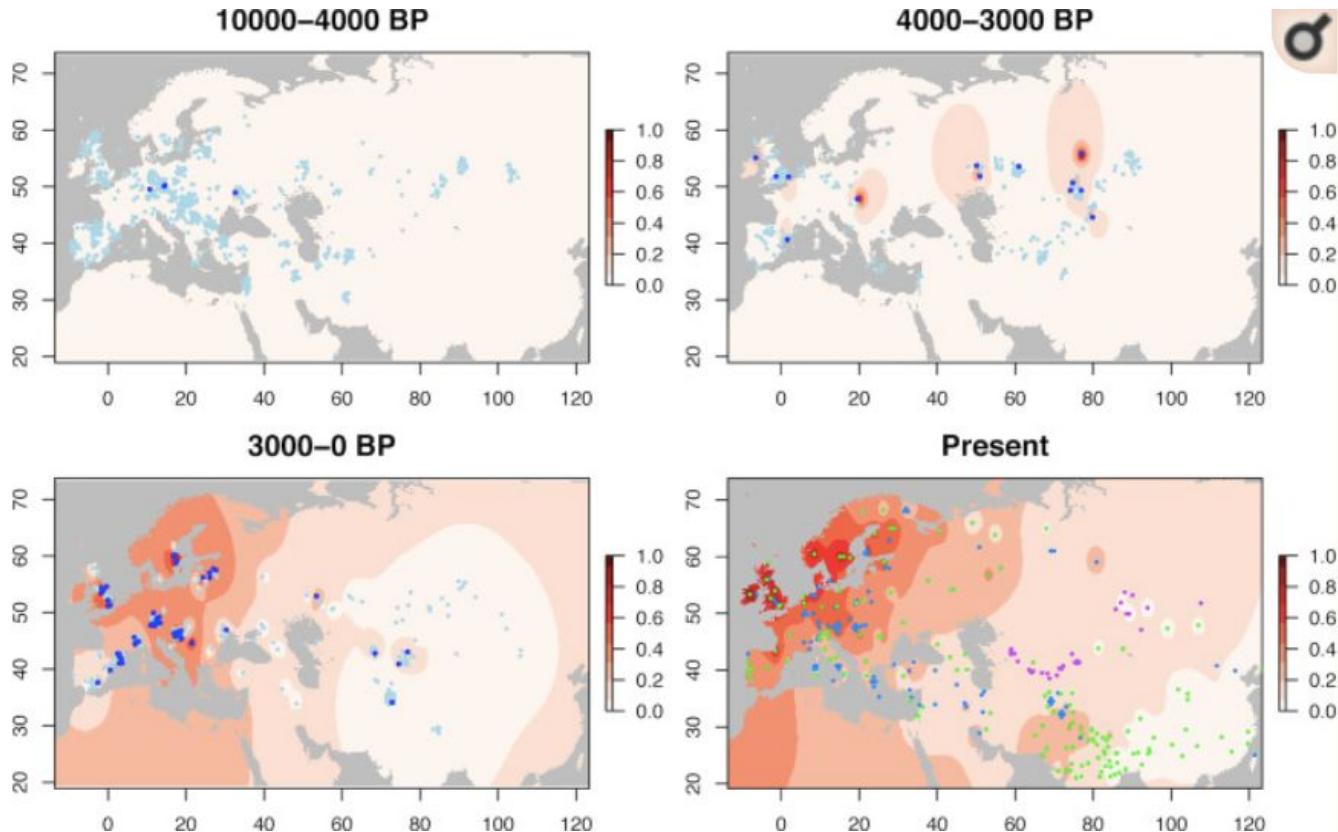
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a 

b 



Lactase persistence



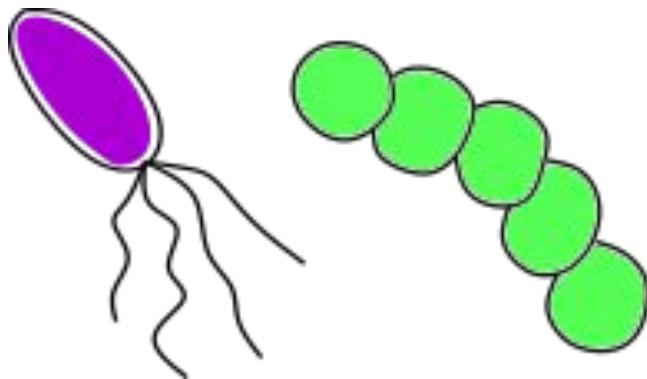
Segurel et al. 2019 PLoS Biol.



Microbes? Cooking?



The gut microbiome?



The dairy mystery

Archaeogenetics

Palaeoproteomics

Ethnography

Modern microbiology

Archaeology...

Stay tuned!



Overall conclusions slide

- Microbes are awesome.
- Microbes are abundant in the archaeological record
- They can be identified with various biomolecular techniques
- They can tell us about multiple aspects of the human past

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Discussion questions

- Are there historically recorded diseases that you might want to investigate with aDNA? What are they?
- Can you think of places to find ancient microbes other than the ones we presented?
- How can studying ancient microbes help us with modern medicine and microbiology?
- How can ancient animal samples be used to study the origin of zoonotic (animal-derived) diseases?
- How can studying microbiomes help us understand human lifestyle changes?
- How have the words used to explain/describe infectious disease evolved over time?

