

Ancient DNA and the New Science of the Human Past

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Take-home messages

Population history is profoundly surprising

We are all mixed – no one is “pure”

A new scientific instrument

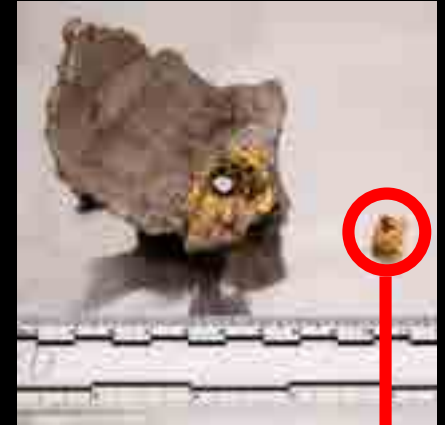
Bones



Clean room



Prepare



Sequencing

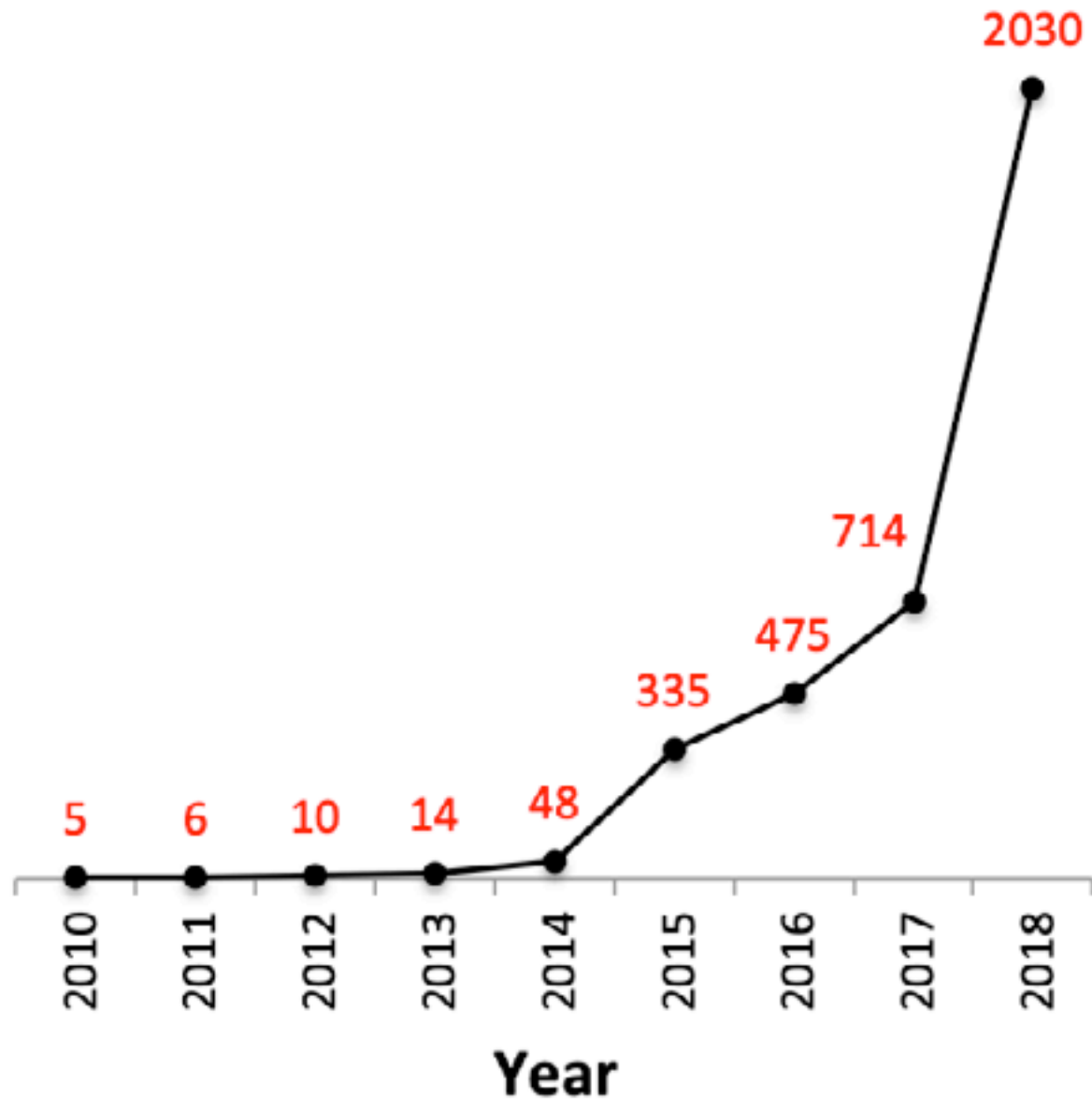


Purification

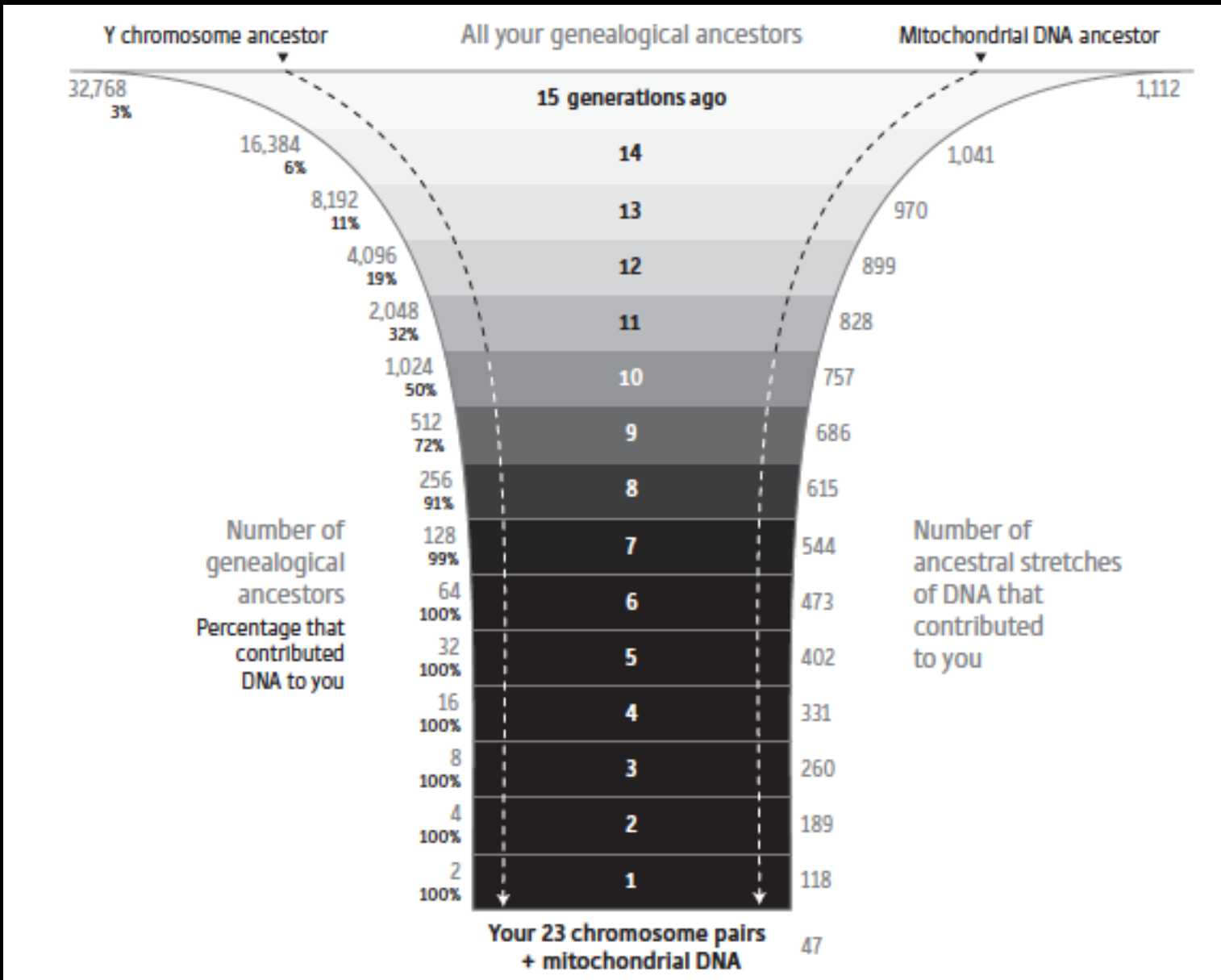


Powder

Published Ancient Genomes



How the Genome Reveals the Past



You are not one person

You contain a multitude

Four surprises

The Genome Revolution is showing us again and again that we were wrong

First surprise – Archaic Humans



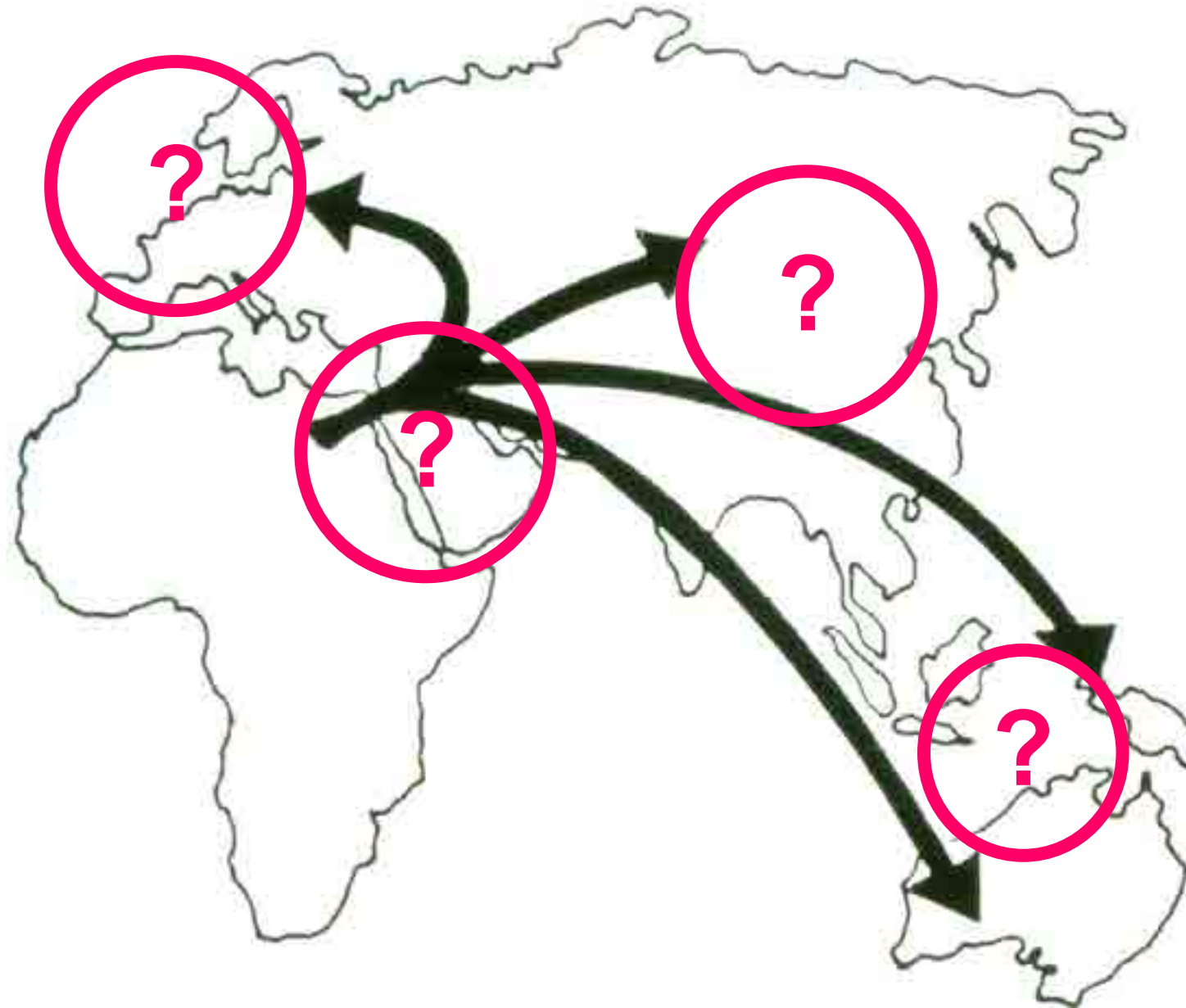
Cro-Magnon



La Ferrassie

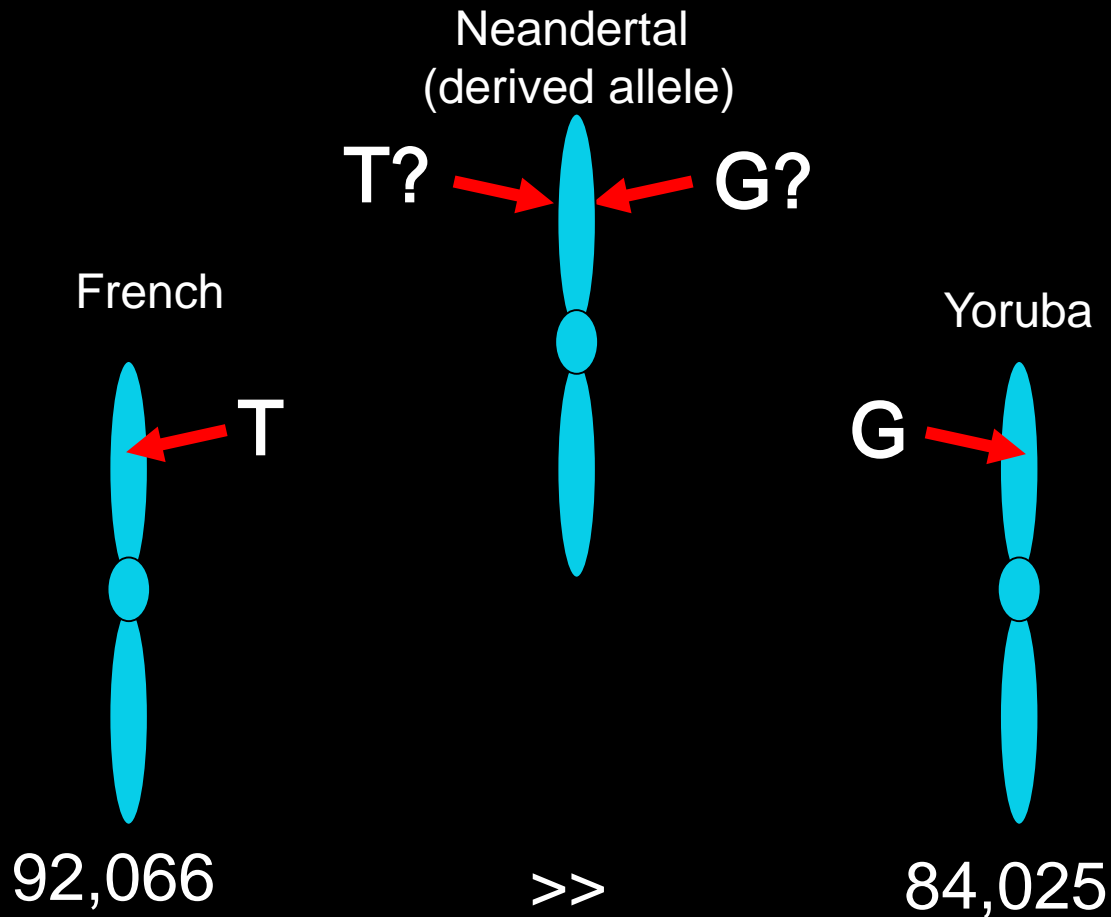


Was there interbreeding?



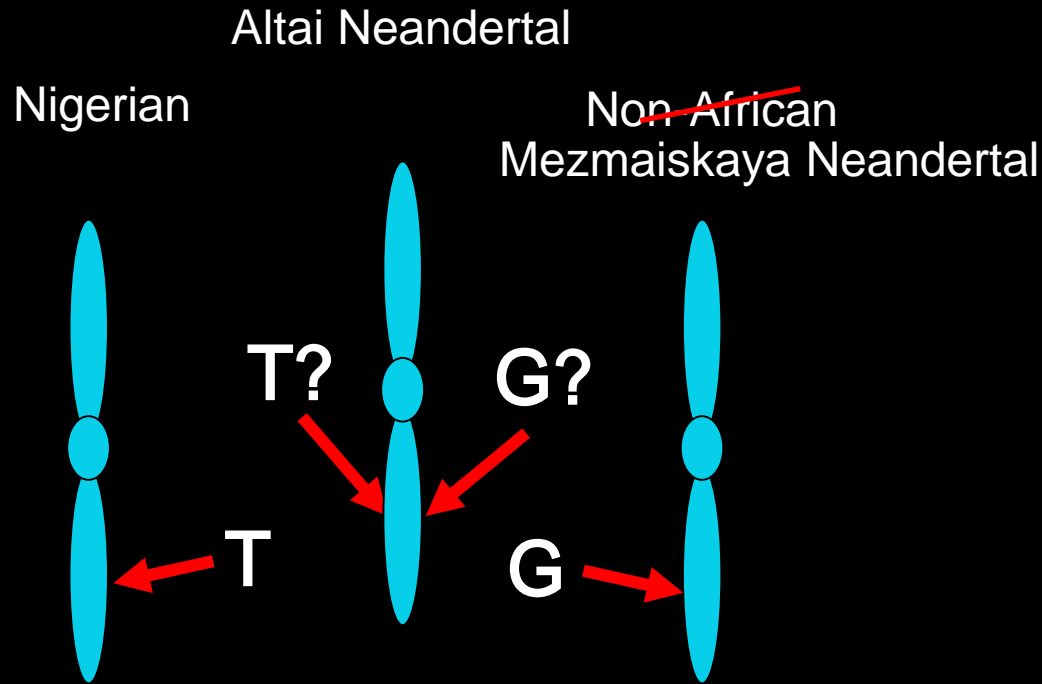
Test for gene flow

Does Neandertal match some humans than others?



Very significant:
10.5 stand. dev.

Estimated Neandertal gene flow is ~2%



“How much of the way is a non-African to a Neandertal?”

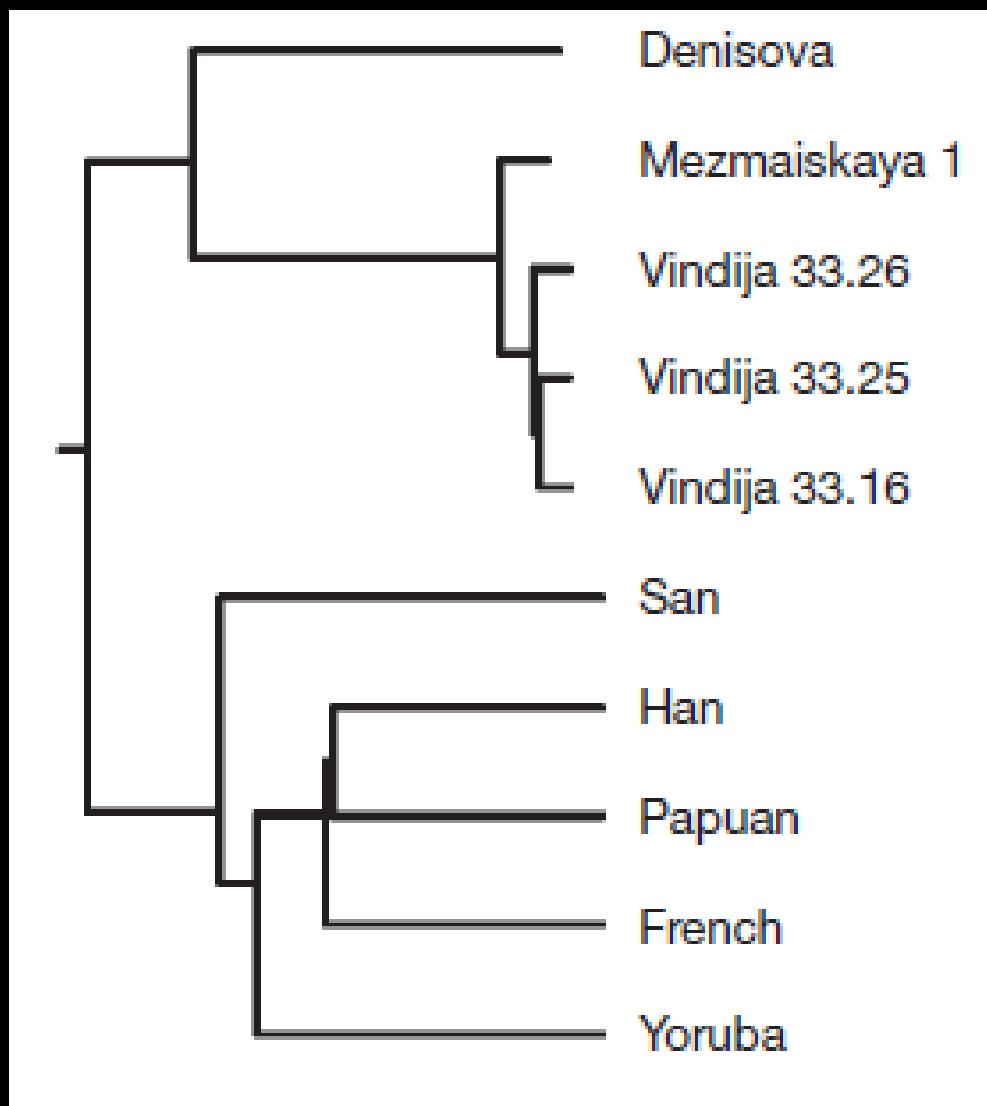
1.72 ± 0.12% Europeans

1.89 ± 0.13% East Asians

Denisova – A Genome in Search of a Fossil Record

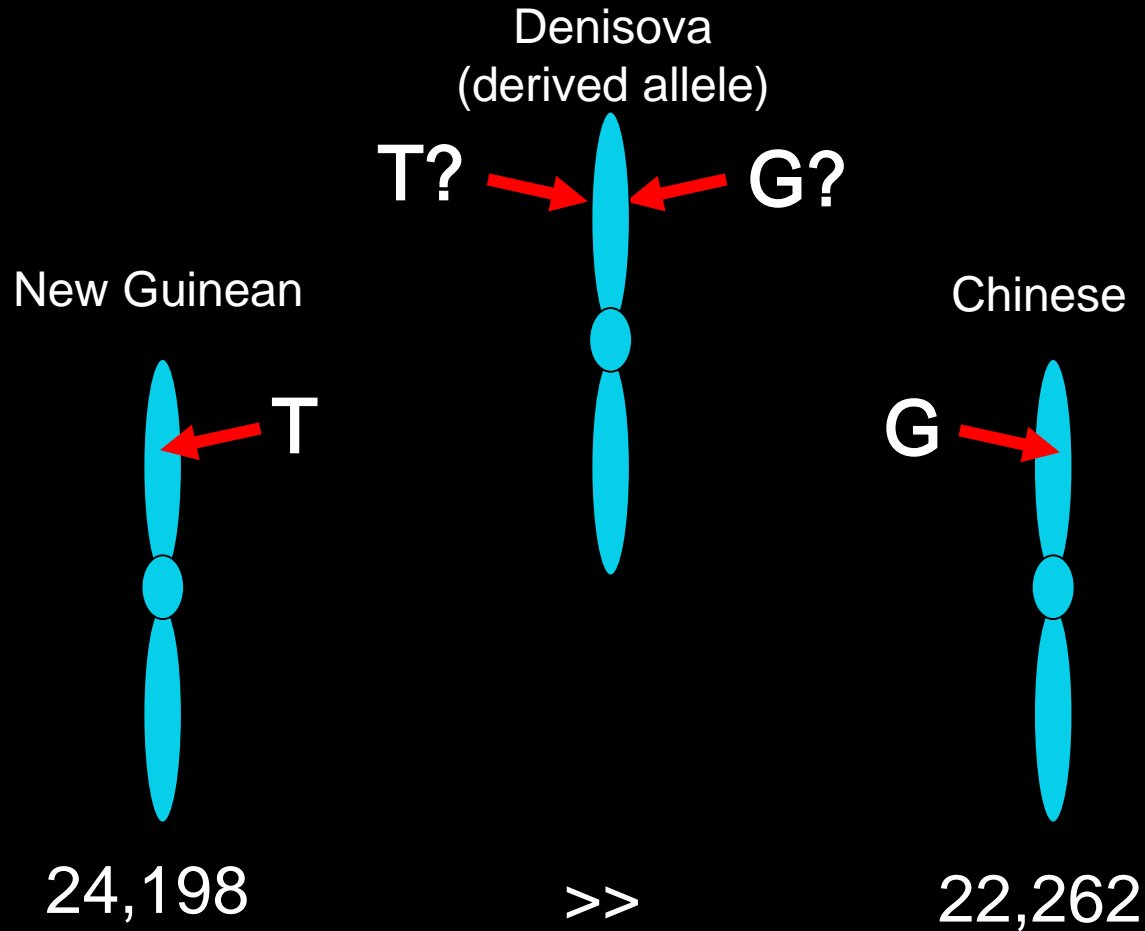


“Denisovans” are a distinct group separated by ~400,000 years from Neanderthals



Does Denisova match some humans than others?

Reich, Green et al. 2010

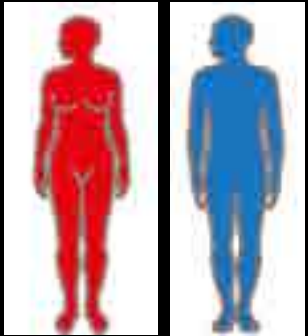
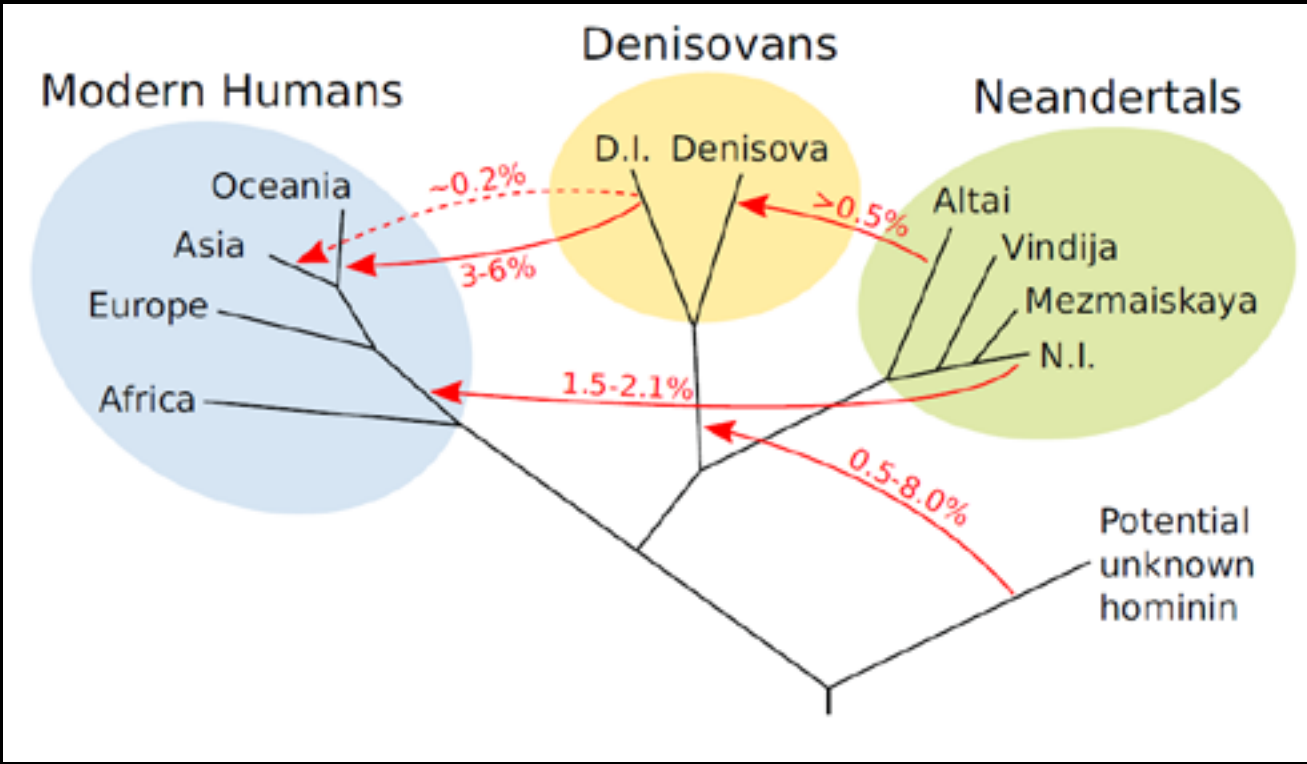


Very significant: 5.8 stand. dev.

Estimated to contribute 4-6% of New Guinean ancestry

Pandora's Box of Archaic Mixtures

Prufer et al. 2014



Slon 2018:
girl with
Neanderthal mother
and Denisovan father

Second surprise – There is no “Genetic Switch”

>400,000 years ago

Tripling of brain size compared to other apes

100,000 – 50,000 years ago

Appearance of “modern human” behavior

What Makes Modern Humans Distinctive?

Human revolution ~50,000 year ago

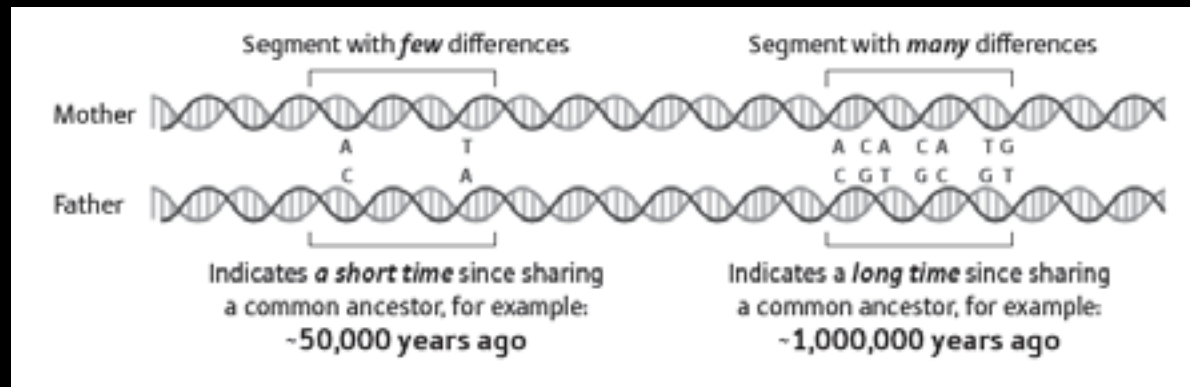
- ÿ Complex tools
- ÿ Deliberate burials
- ÿ Art and figurines

Richard Klein suggested a “Genetic Switch”

Mutation that rose in frequency allowing complex behavior



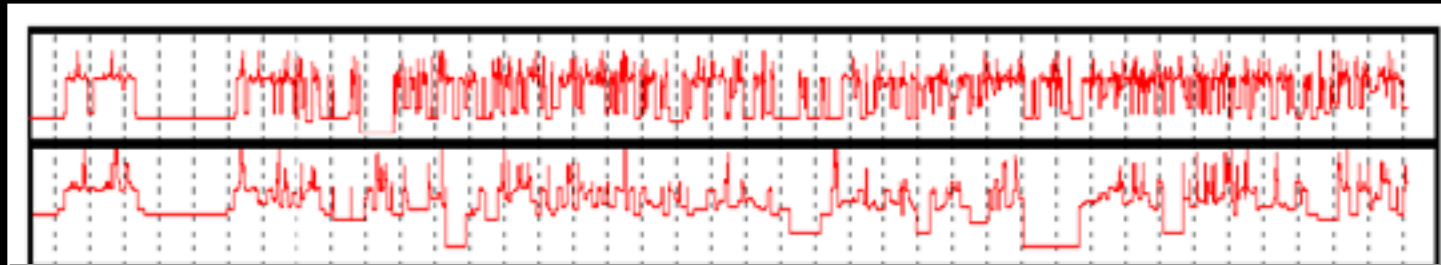
There is little room for Klein's "Genetic Switch"



Can estimate the date of the shared ancestor of the two copies of the genome each person carries at each position (Li and Durbin Nature 2010)

Person 1

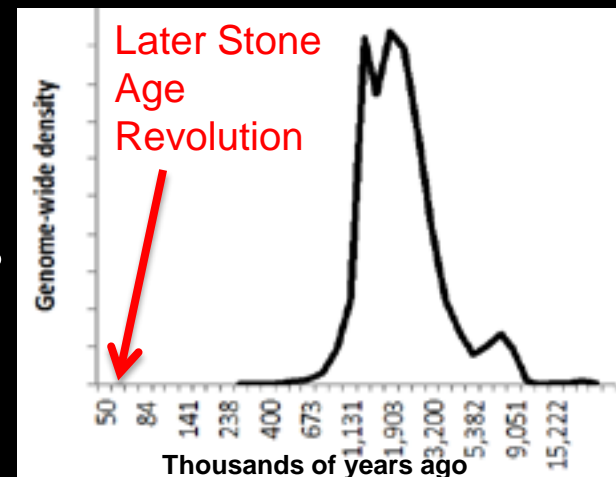
Person 2



↑ time
↑ time

Maximum over 40 diverse genomes shows no common ancestors within ~300,000 years

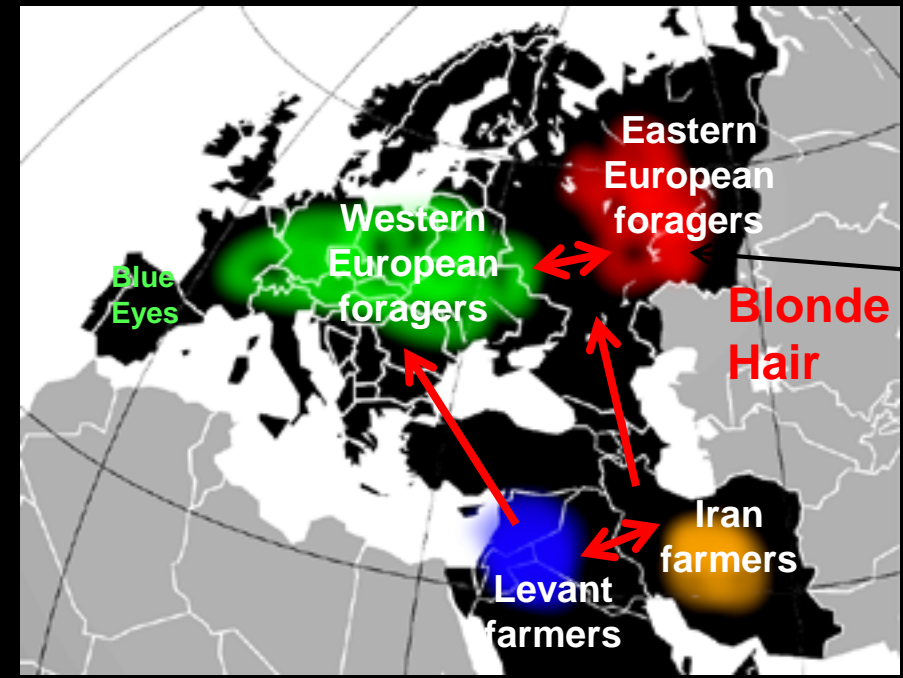
(Mallick et al. Nature 2016)



Third surprise – “White People” are a recent phenomenon

Derived from 4 sources as different from each other as Europeans / East Asians

Lazaridis et al. Nature 2016



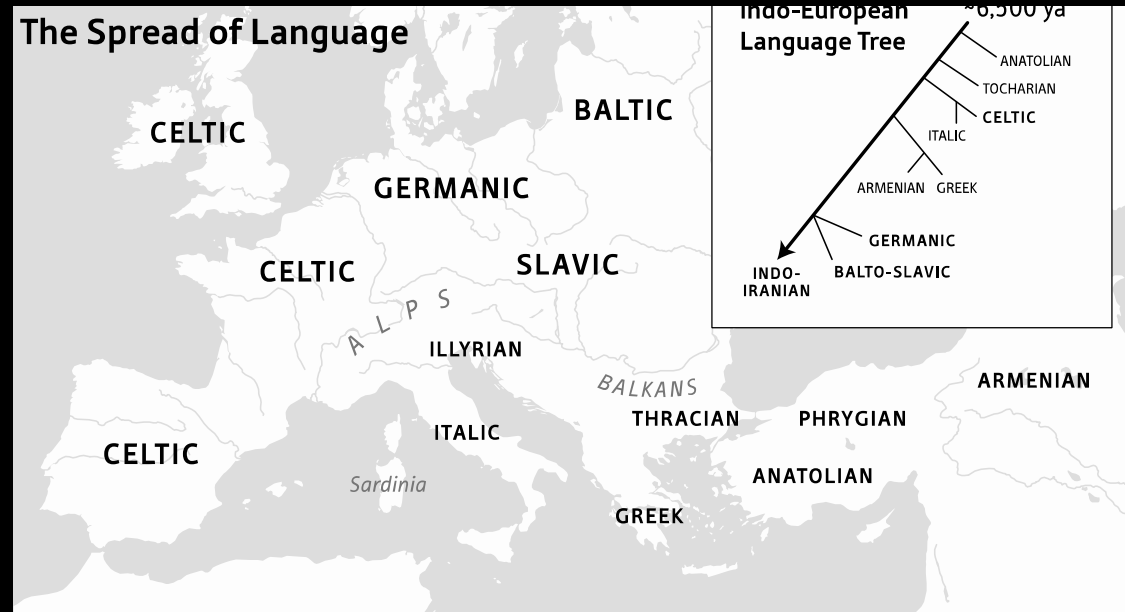
By 4,000 years ago we observe present-day low population differentiation

Are cultural changes propelled by movement of people?

The 230 Year-Old Problem of Indo-European Origins

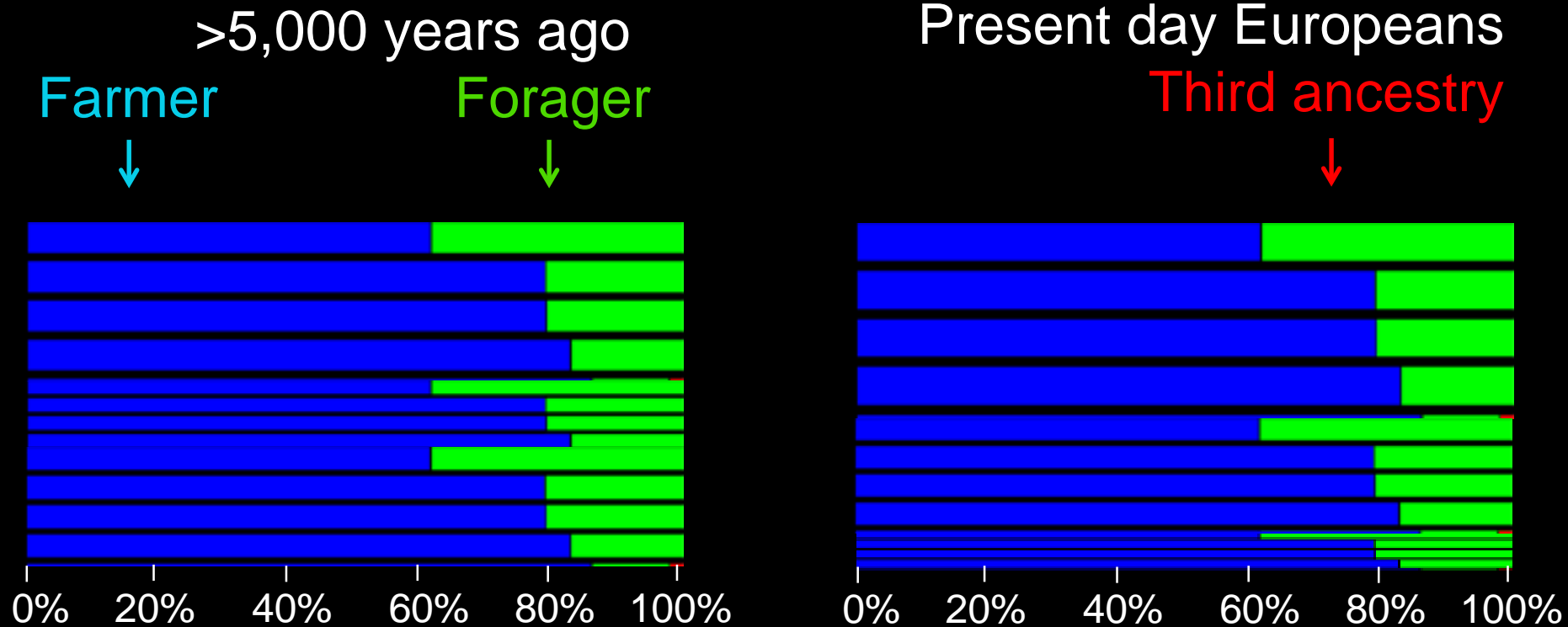
"The **Sanskrit** language, whatever may be its antiquity, is of a wonderful structure; more perfect than the **Greek**, more copious than the **Latin**, and more exquisitely refined than either, yet bearing to both of them a stronger affinity, both in the roots of verbs and in the forms of grammar, than could possibly have been produced by accident; so strong indeed that no philologer could examine them all three, without believing them to have sprung from some **common source**, which, perhaps, no longer exists."

William Jones – Kolkata, 1786



Before 5,000 years ago Europeans were a mixture of two ancestries but today there is a third

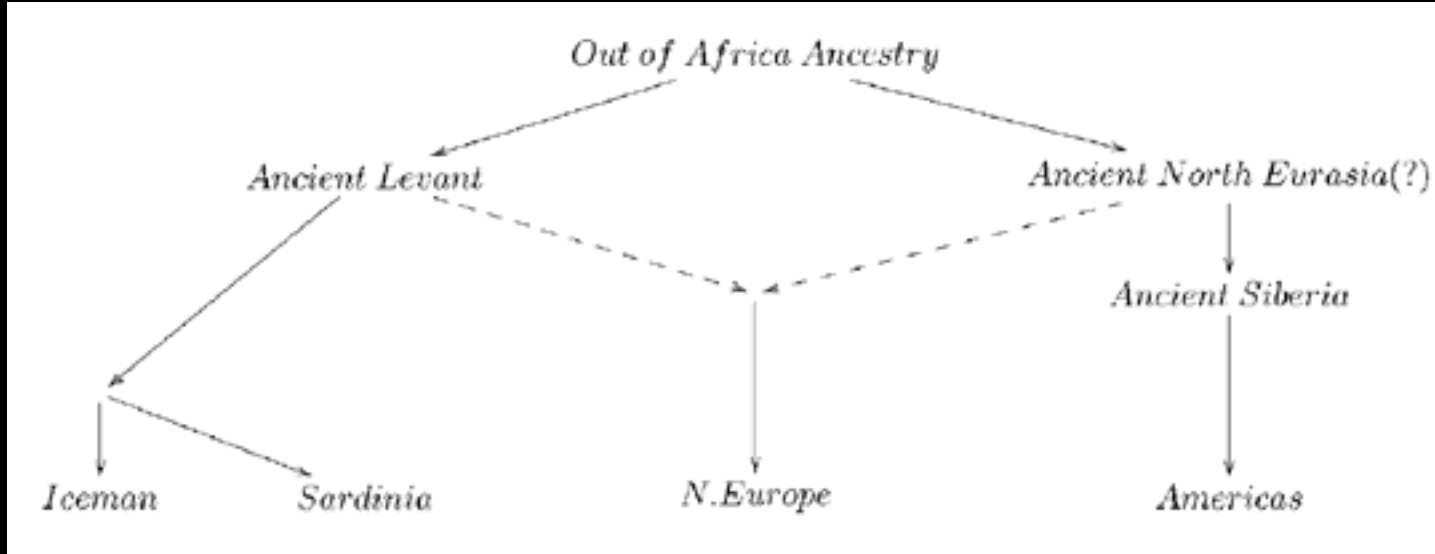
Lazaridis et al. *Nature* 2014; Haak et al. *Nature* 2015



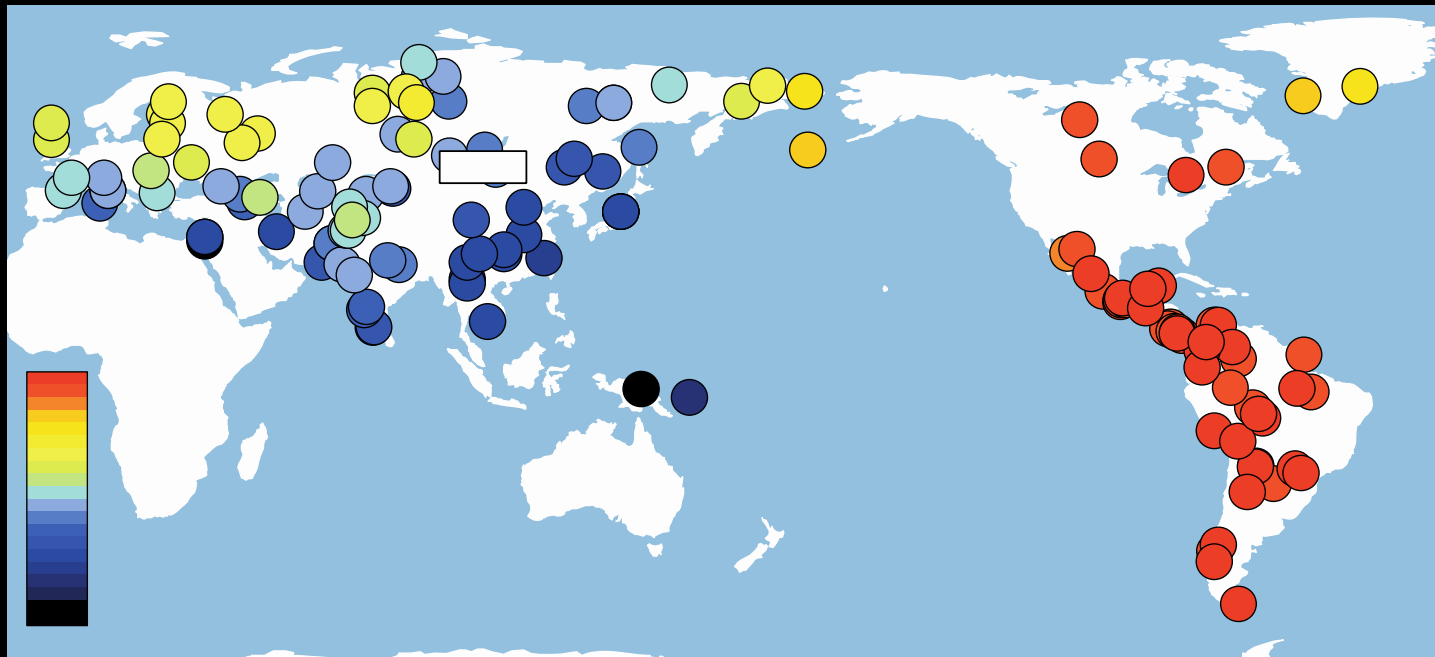
When did third ancestry arrive?

Discovery of Europe's 3rd Ancestral Population

Patterson et al. *Genetics* 2012



“The ghost of North Eurasia”



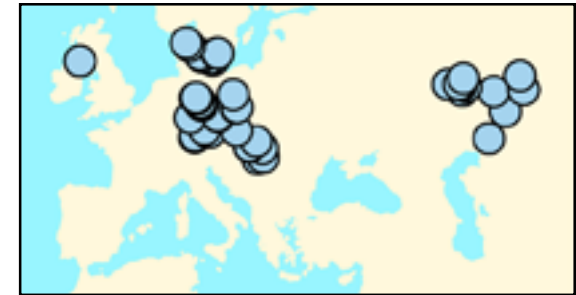
“The ghost is found”

(Raghavan et al. *Nature* 2015 validated our lab's prediction)

The third population arrives after 5,000 years ago

Haak et al. *Nature* 2015; Lazaridis et al. *Nature* 2017

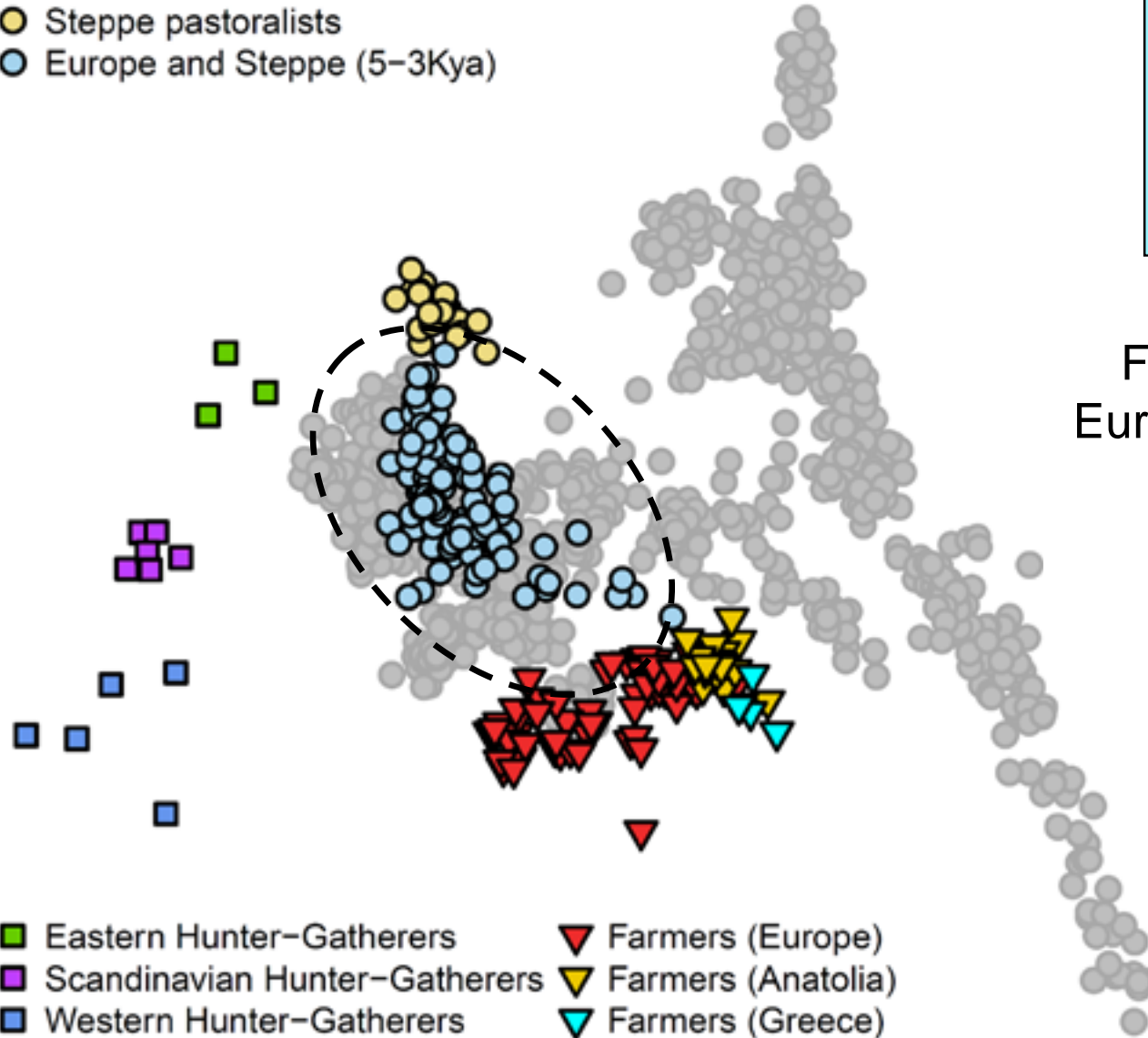
- Steppe pastoralists
- Europe and Steppe (5–3Kya)



Formation of modern
Europe <5,000 years ago

years ago

- Eastern Hunter-Gatherers
- Scandinavian Hunter-Gatherers
- Western Hunter-Gatherers
- ▼ Farmers (Europe)
- ▼ Farmers (Anatolia)
- ▼ Farmers (Greece)

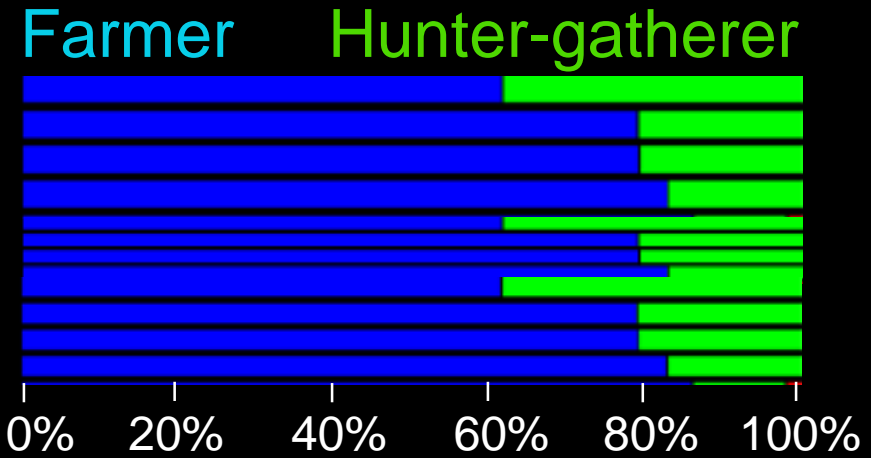


Summary: Europe massively transformed by two migrations

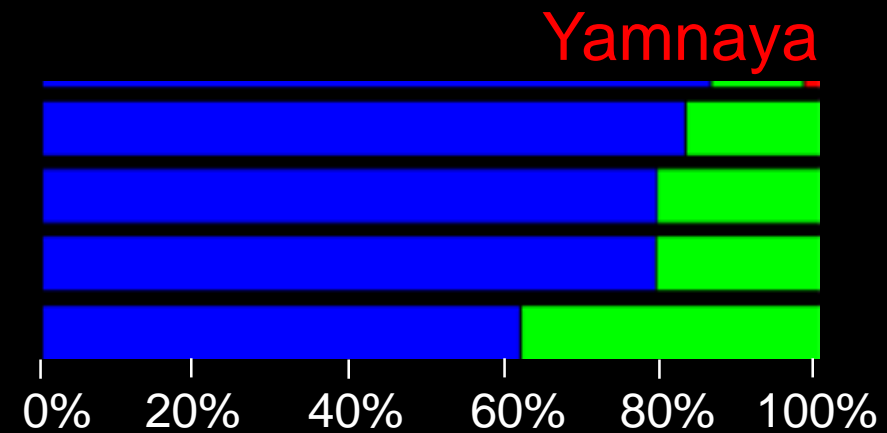
Haak et al. *Nature* 2015



Who were the Yamnaya?



Farmers arrive, mix with local hunter-gatherers 8,500-5,000 years ago

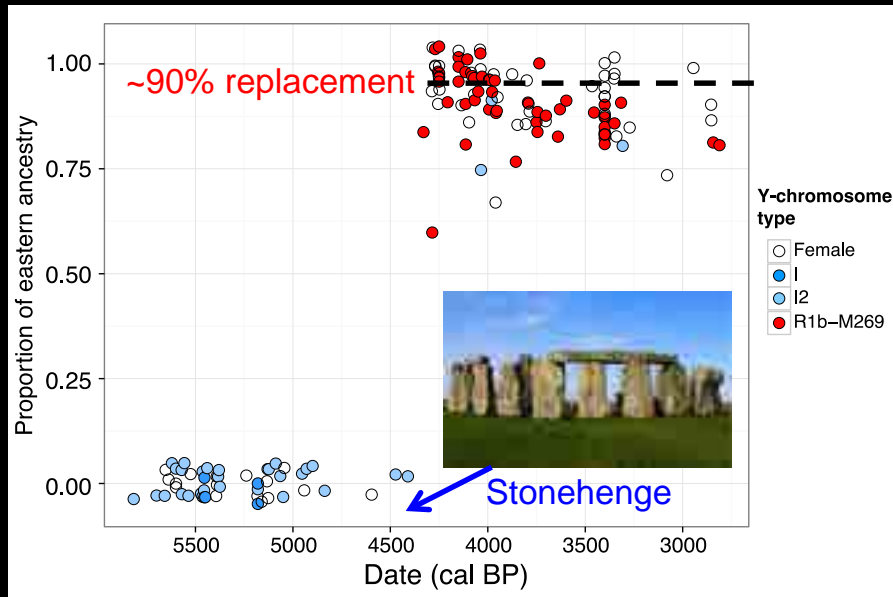


Yamnaya-farmer mix <5,000 years ago

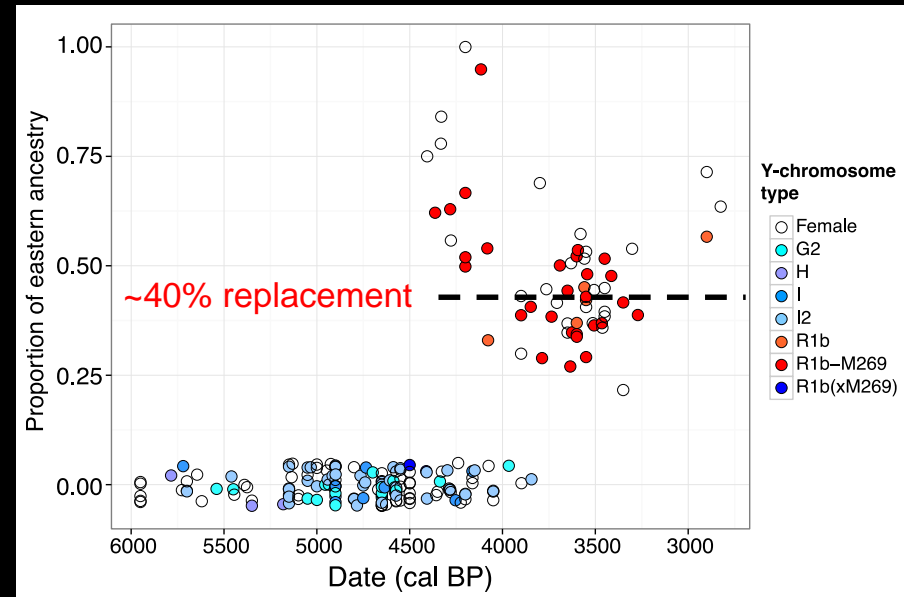
Yamnaya ancestry spreads West

Olalde et al. *Nature* 2018; Olalde et al. *Science* 2019

Britain



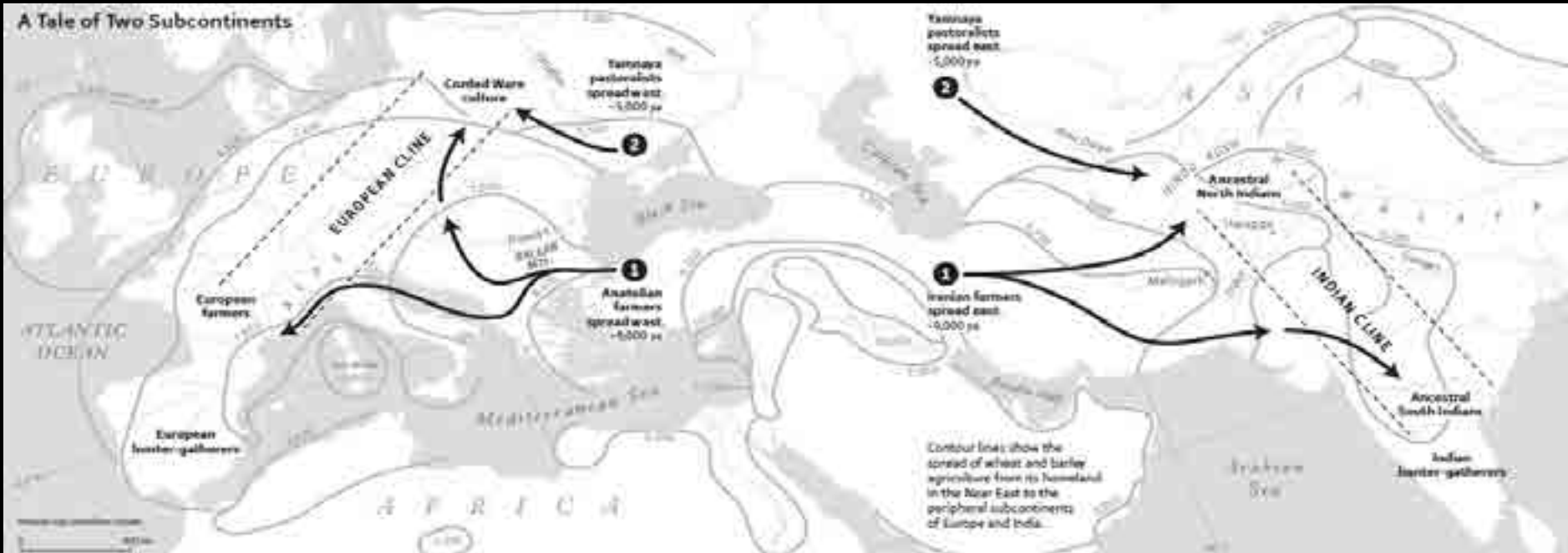
Iberia



Iberia: **100% Y chromosome** despite only 40% whole genome replacement

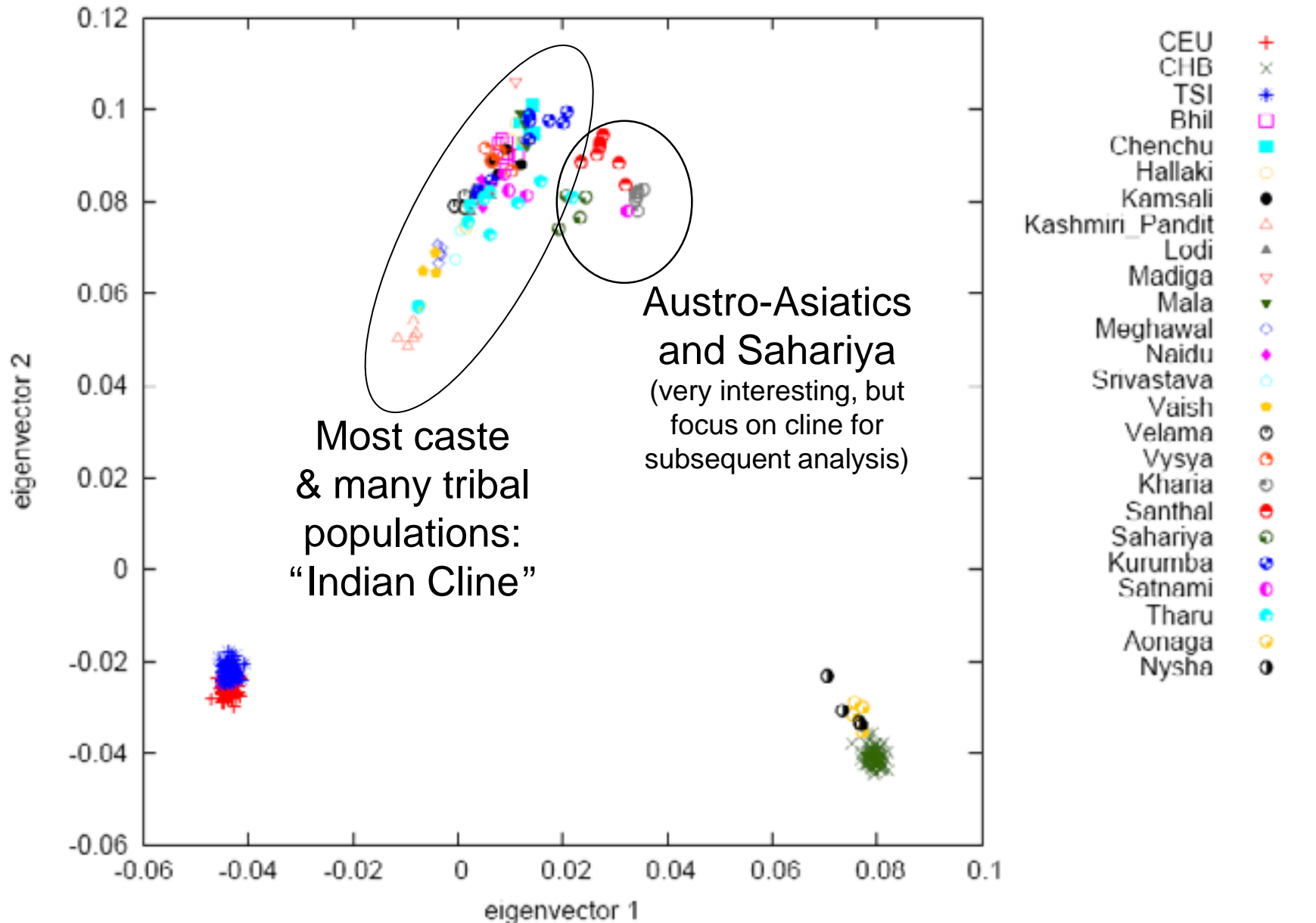
Fourth surprise

The parallel prehistories of South Asia and Europe



What We Learned About South Asian Population History Before Ancient DNA

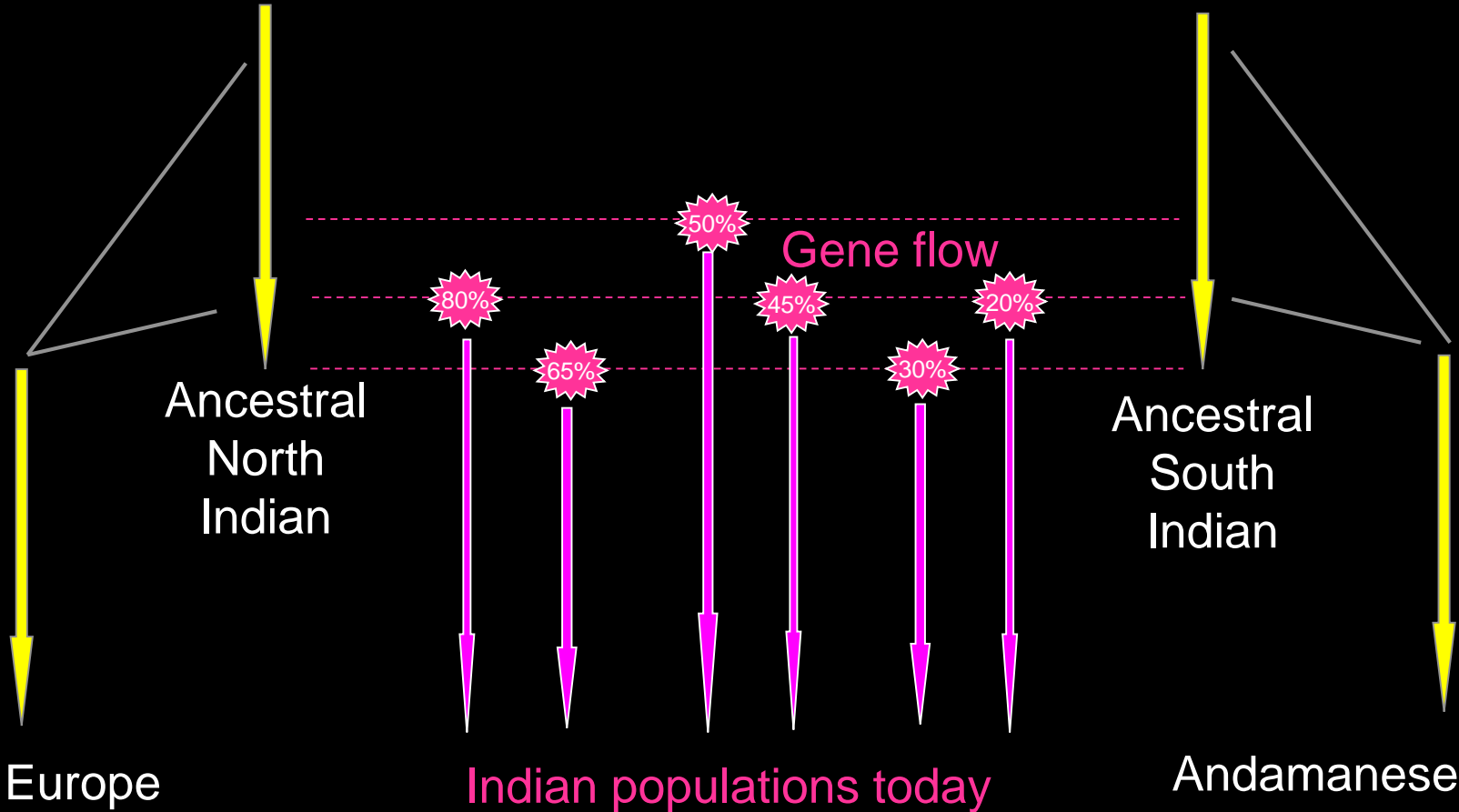
Reich, Thangaraj et al. *Nature* 2009



Our Model of Population History in 2009

Simple Mixture of Two Ancestral Populations

>10,000
years
ago



present

Europe

Indian populations today

Andamanese

Ancestral
North
Indian

Ancestral
South
Indian

Gene flow

Everybody is mixed – no one is “pure”

West Eurasian-related ancestry is 20-80% and is significantly correlated to caste and language

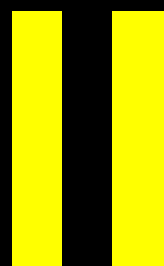
Populations	West Eurasian (ANI%)	Language-family	Traditional Caste / Social group
Madiga	32.0 ± 1.7	Dravidian	Lower caste
Mala	34.3 ± 1.7	Dravidian	Lower caste
Kallar*	37.7 ± 1.8	Dravidian	Tribal
Vysya	37.9 ± 1.8	Dravidian	Middle caste
Chamar*	38.7 ± 1.7	Indo-European	Tribal
Bhil	38.9 ± 1.6	Indo-European	Tribal
Scheduled caste/ tribe*	40.5 ± 1.9	Dravidian	Lower caste
Dushadh*	41.0 ± 1.8	Indo-European	Lower caste
Velama*	43.4 ± 1.7	Dravidian	Upper caste
Dharkar*	47.8 ± 1.5	Indo-European	Nomadic group
Kanjar*	48.2 ± 1.7	Indo-European	Nomadic group
Kshatriya*	54.6 ± 1.6	Indo-European	Upper caste
Kshatriya	60.9 ± 1.3	Indo-European	Upper caste
Brahmin*	61.2 ± 1.4	Indo-European	Upper caste
Brahmin	62.8 ± 1.4	Indo-European	Upper caste
Sindhi+	64.3 ± 1.3	Indo-European	Urban
Kashmiri Pandit	65.2 ± 1.3	Indo-European	Upper caste
Pathan+	70.4 ± 1.2	Indo-European	Urban

What is history behind ANI-ASI admixture?

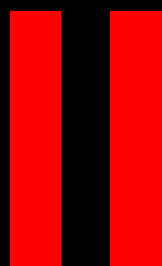
- 1) Post ice-age migrations >13,000 years ago?
- 2) Arrival of agriculture 9,000-5,000 years ago?
- 3) Collapse of Harappa and rise of archaeological cultures in Gangetic Plain <4000 years ago?

Mixture occurred 4,200-1,900 years ago

Moorjani et al. AJHG 2013



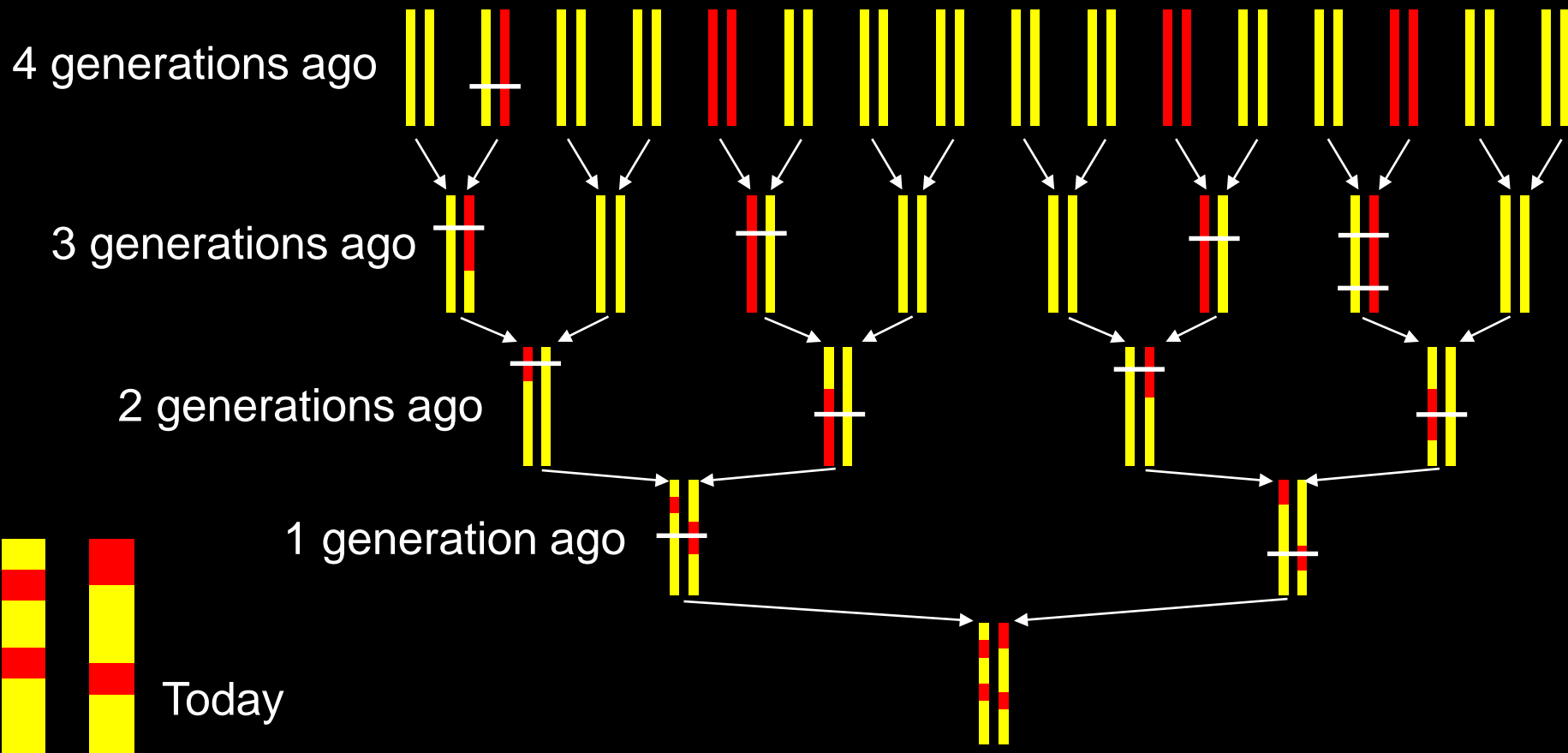
Two ANI chromosomes



Two ASI chromosomes



One ANI, one ASI chromosome



Summary of Population History Before Ancient DNA

- 1) South Asians are a mixture of two populations, ANI and ASI
- (2) They mixed convulsively 4,000-2,000 years ago in a way that is related to caste and spread of Indo-European languages
- (3) What happened next?

Yamnaya ancestry spreads East

The Genomic Formation of South and Central Asia

Narasimhan, Patterson et al. in revision



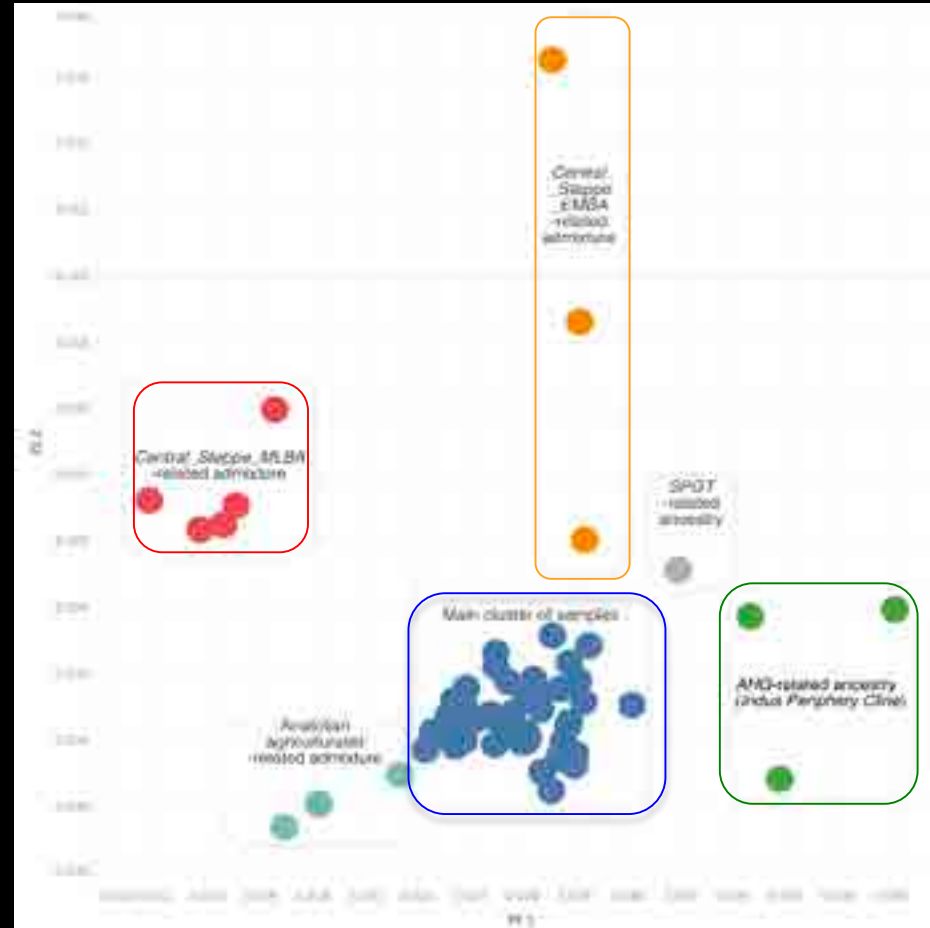
Gonur,
Turkmenistan

Genetically similar to ancient Iranians

Forager ancestry in outliers >4,000 years ago

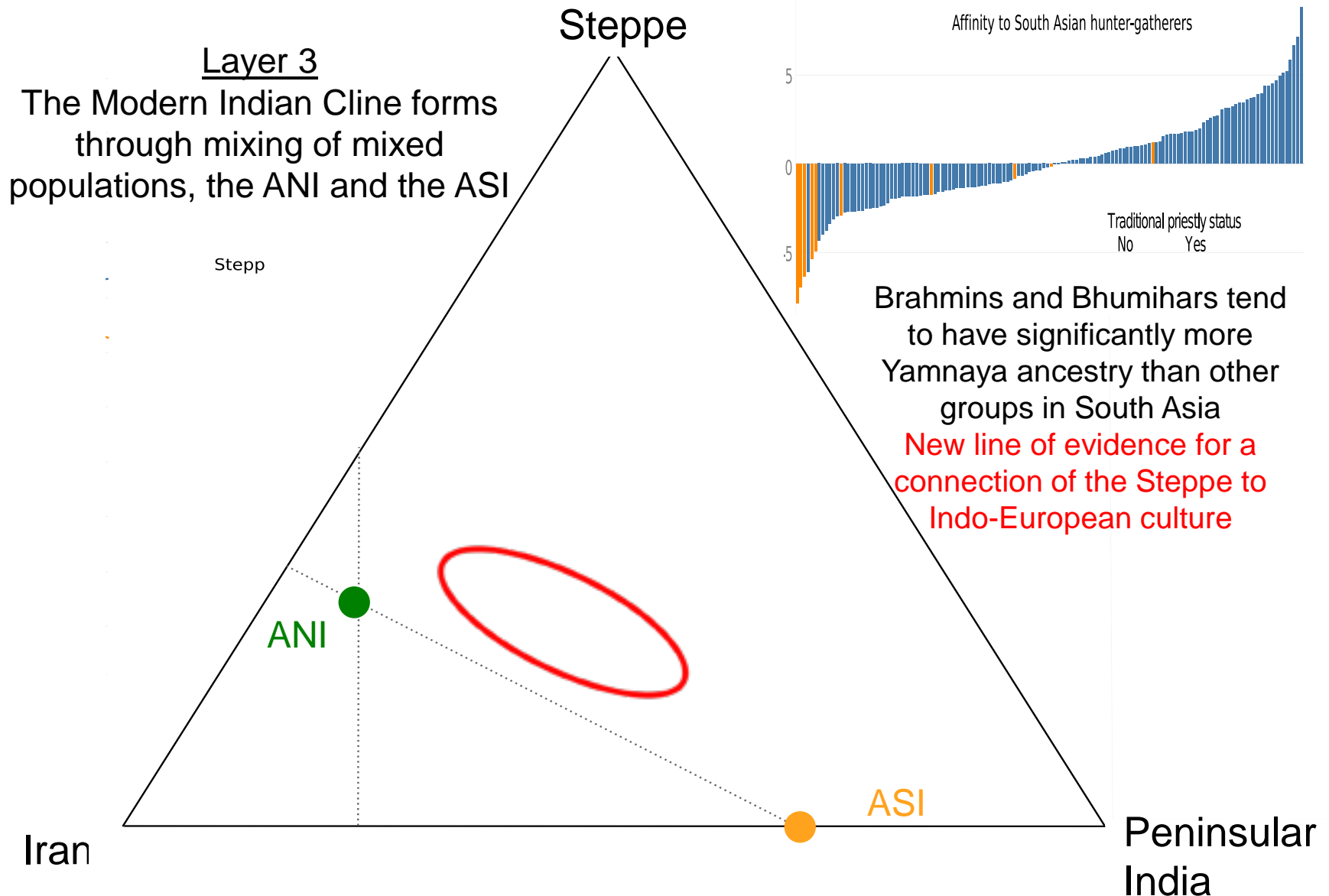
Yamnaya ancestry in outliers <4,000 years ago
(in Swat Valley South Asia >3,500 years ago)

11 outliers admixed with South Asian ancestry



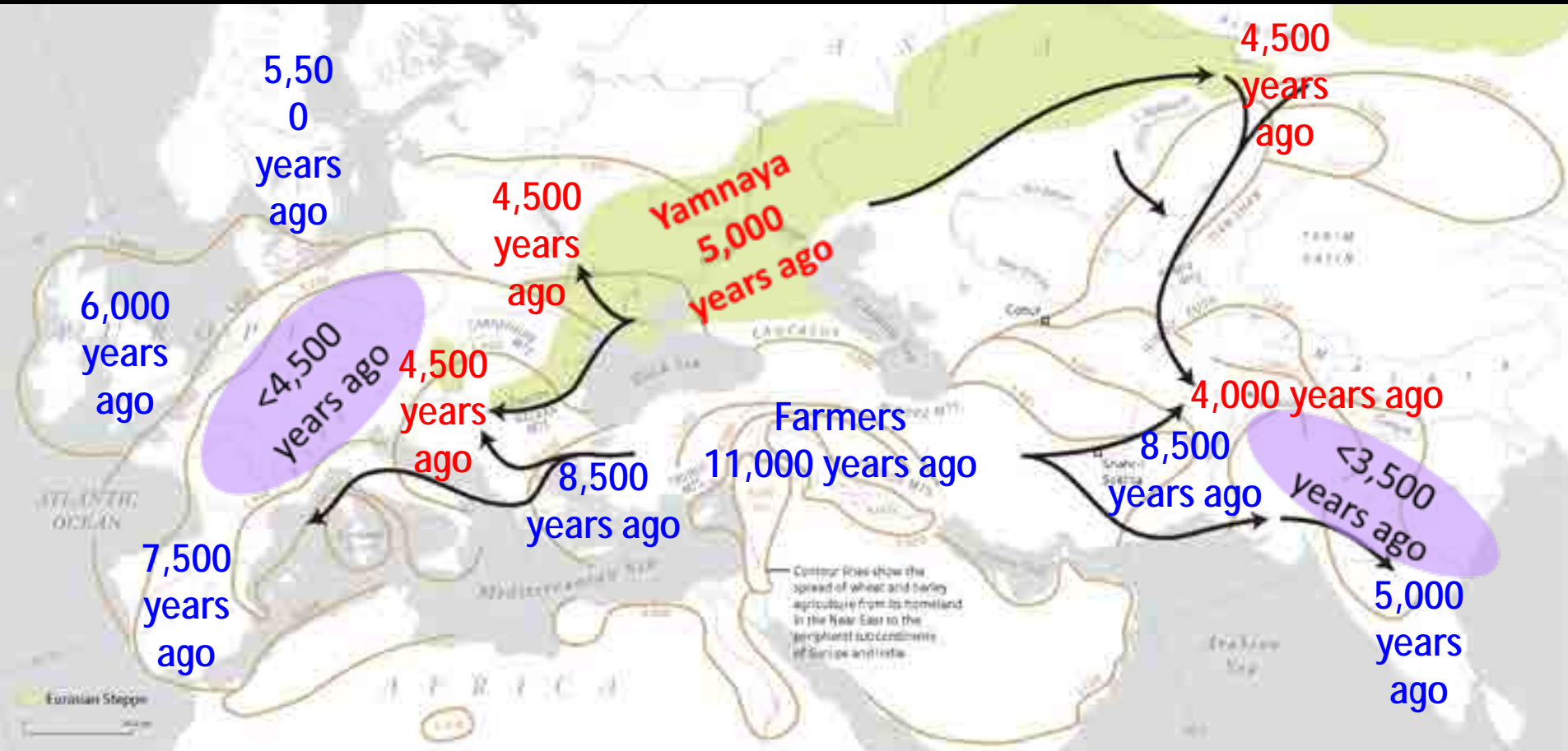
Three layers of mixture in South Asia

Narasimhan et al. in revision



Two parallel subcontinents of Eurasia – Europe and India

Haak et al. *Nature* 2015; Narasimhan et al. *bioRxiv* 2018



8,500-5,000 years ago: Mixed populations of farmers and foragers

5,000-3,500 years ago: Spread of Yamnaya ancestry

Today: Mixtures of these mixed populations

Extraordinarily High Population Structure in India Today

Indian groups are much more genetically differentiated than Europeans

	India	Europe
Average F_{ST}	0.010	0.003

By language group

Indo-European 0.008

Dravidian 0.007

By social status

Upper caste 0.006

Lower caste 0.009

By state

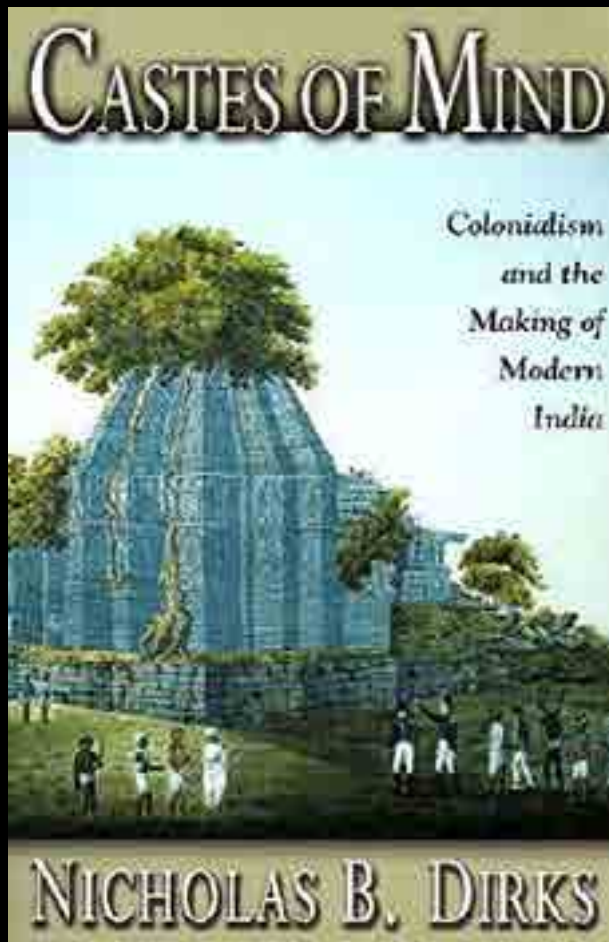
Uttar Pradesh 0.010

Andhra Pradesh 0.007

India is not a large population, but instead many small populations

The Founder Events are Old

For example in Vysya from Andhra Pradesh, 2000-3000 years old



Some have argued that 'caste' in modern India is an 'invention' of colonialism, in the sense that it became more rigid under colonial rule.

Genetics shows that many current distinctions among castes are ancient and strong endogamy must have shaped marriage patterns for thousands of years.

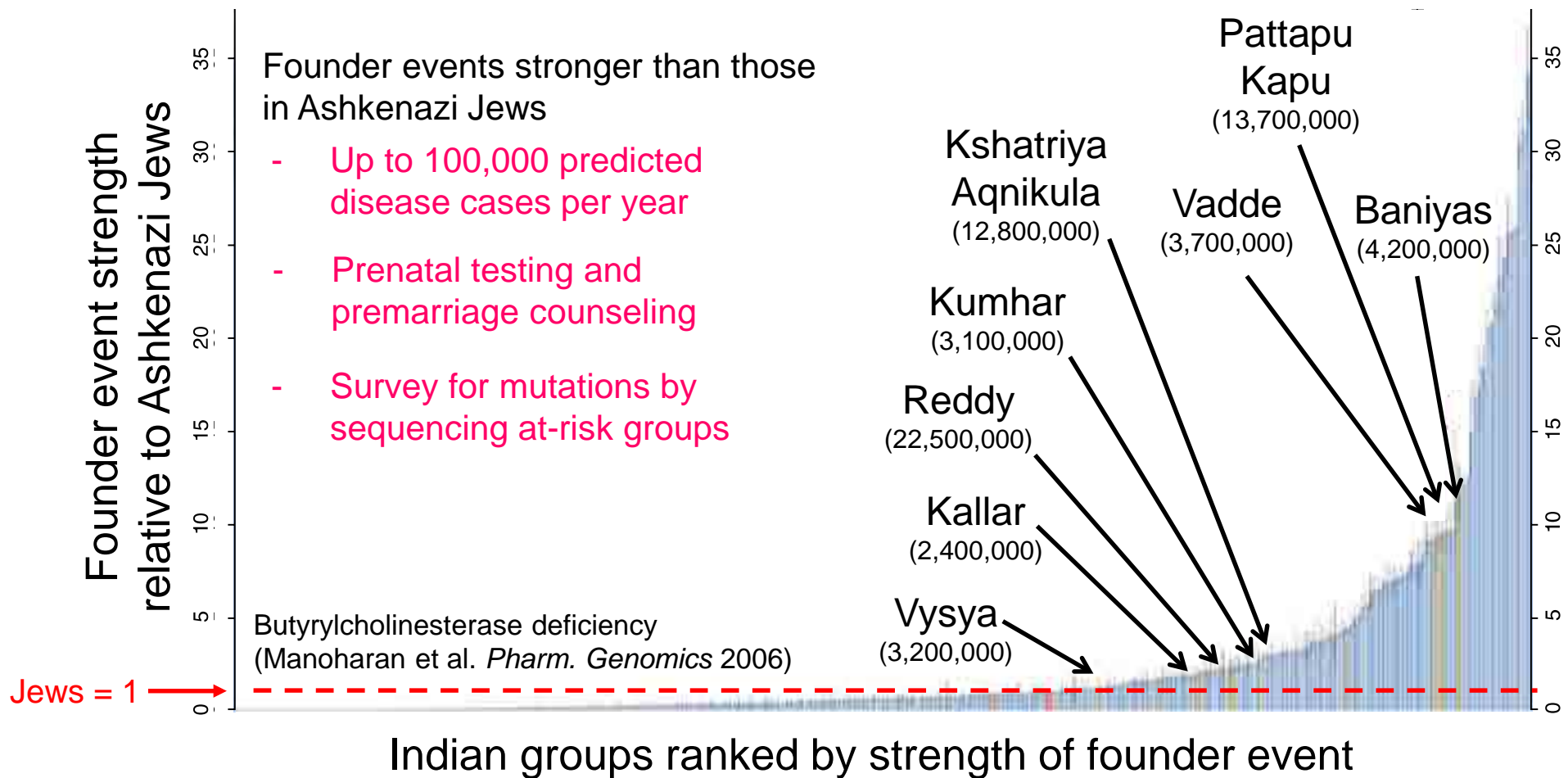
Genetics has documented a cultural change

- After 4,000 years ago, convulsive mixture to form ANI and ASI which then mixed in turn

- A profound switch to endogamy, partly intact today

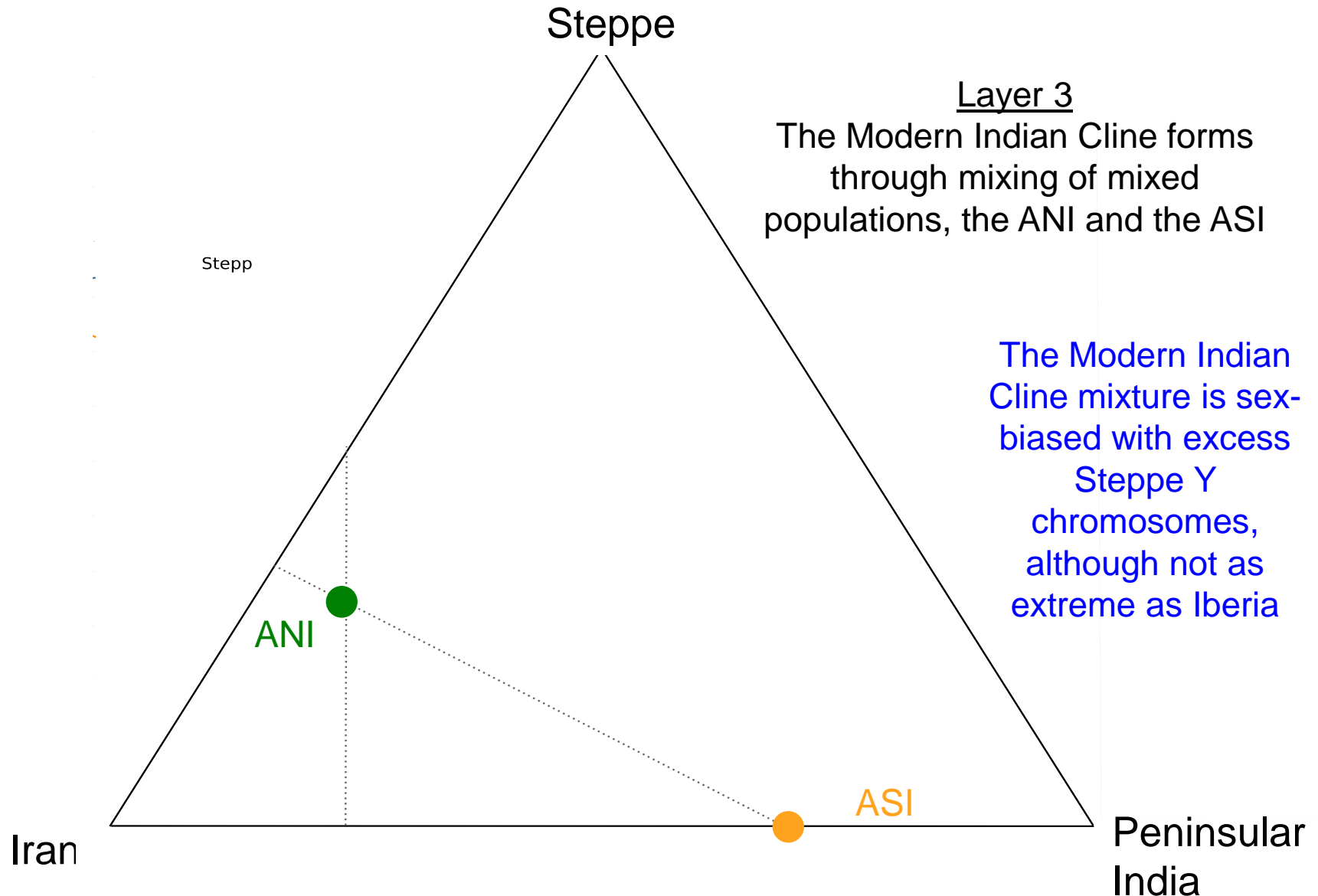
A huge medical opportunity in India

Reich et al. *Nature* 2009; Nakatsuka et al. *Nature Genetics* 2017



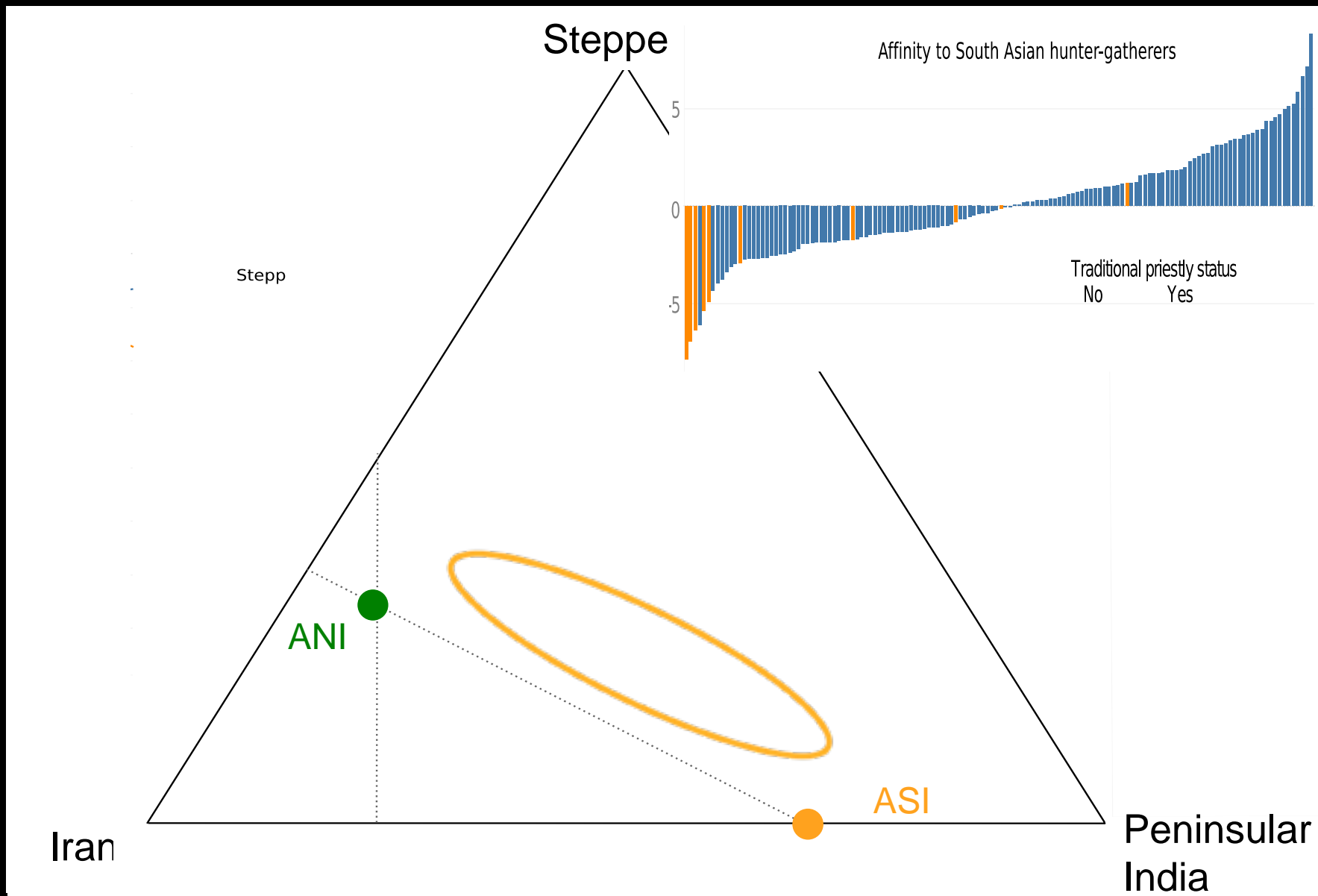
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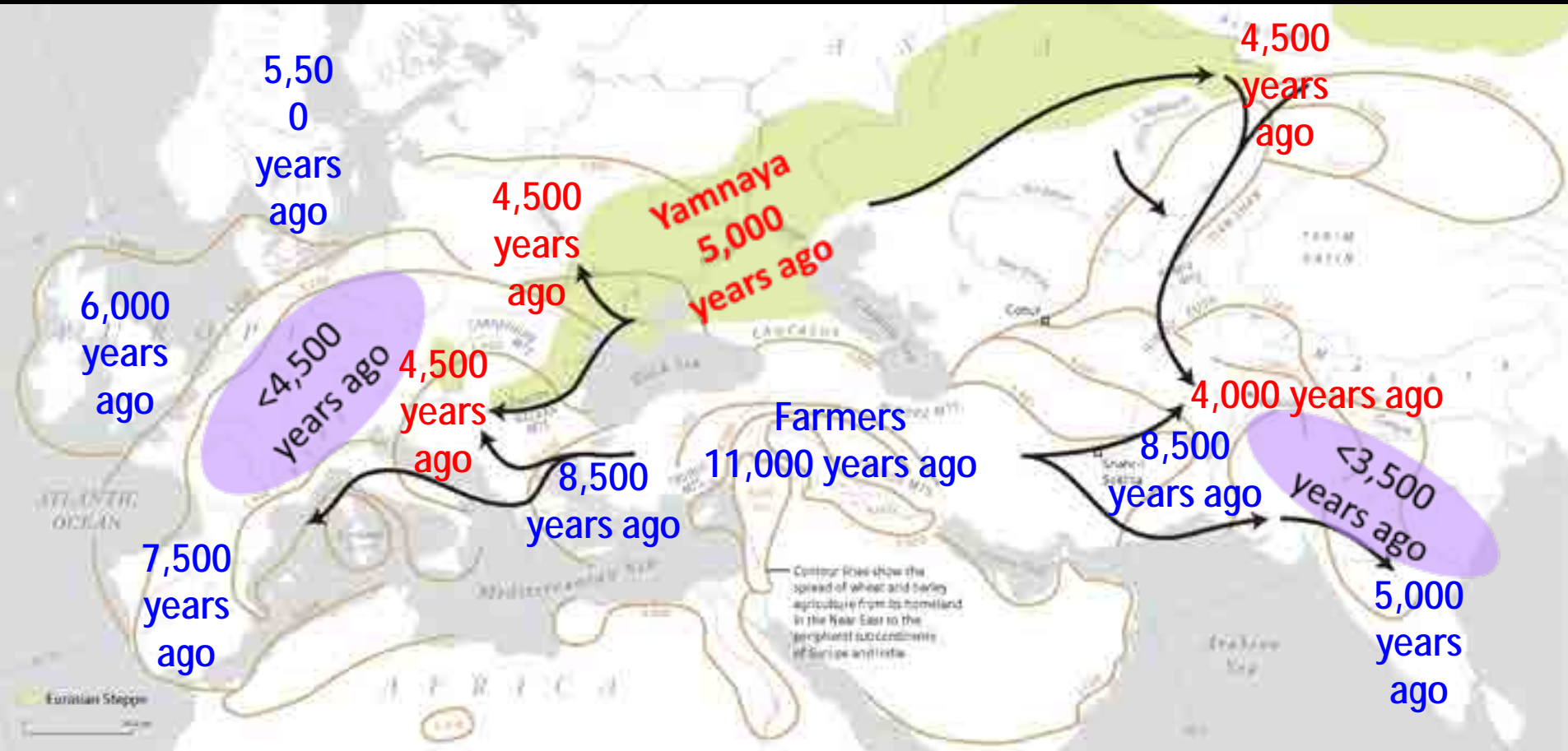
Brahmins and Bhumihars tend to have significantly more Yamnaya ancestry than other groups in India

Narasimhan et al. in revision



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Haak et al. *Nature* 2015; Narasimhan et al. *bioRxiv* 2018



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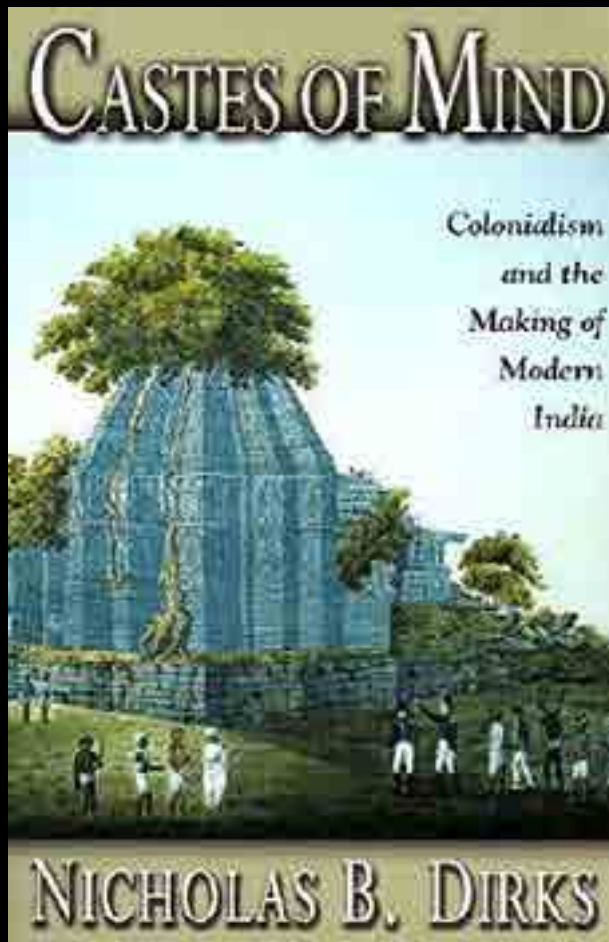
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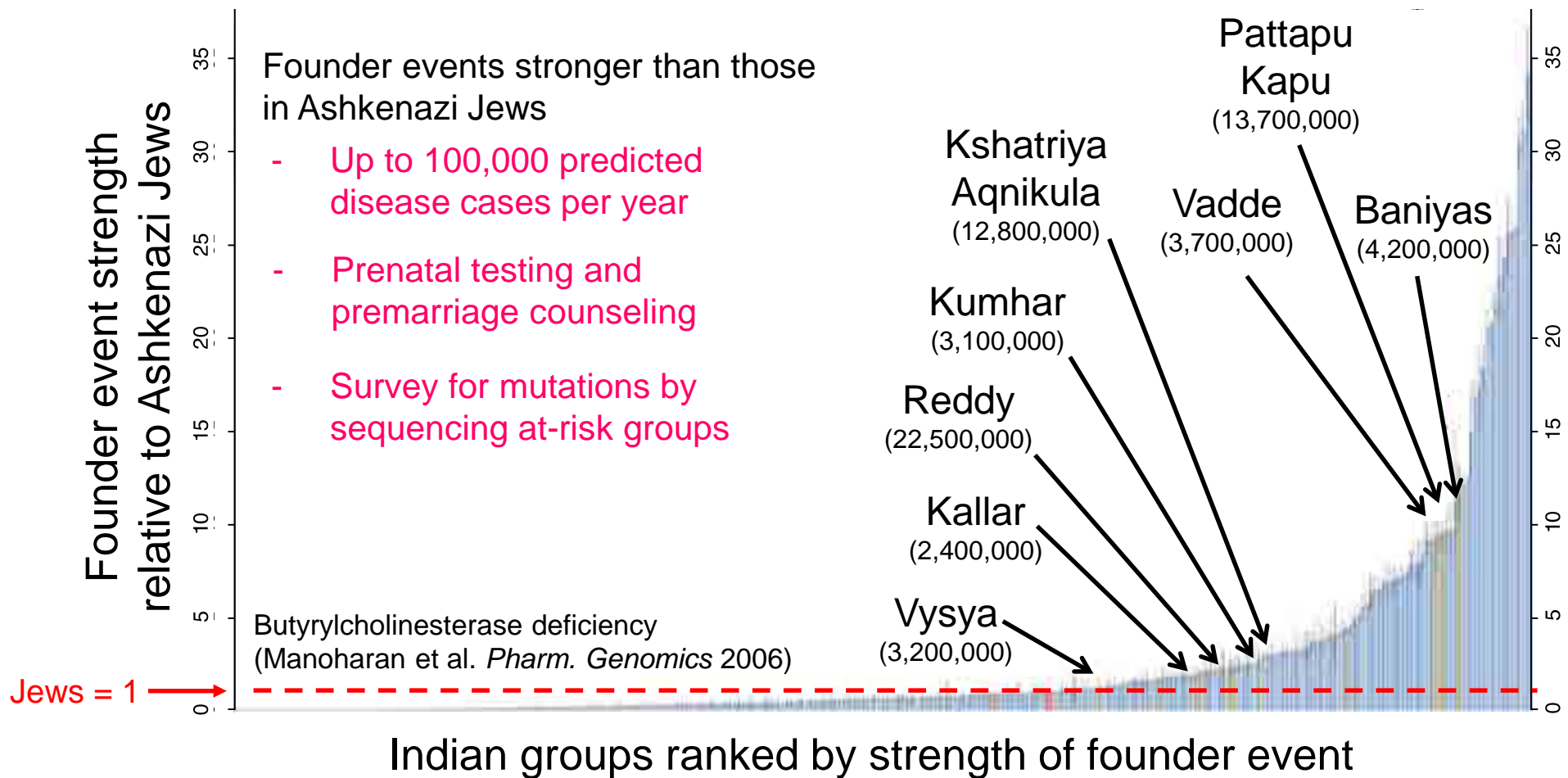
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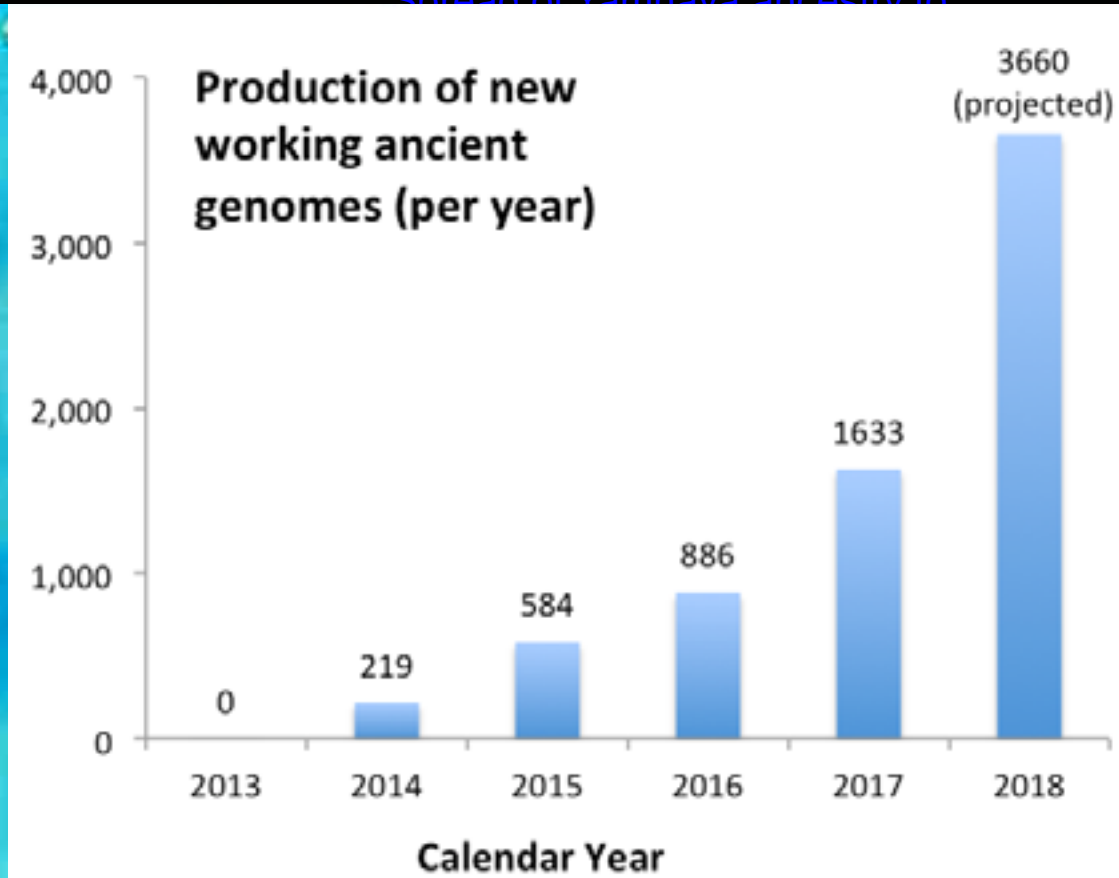
Reich et al. *Nature* 2009; Nakatsuka et al. *Nature Genetics* 2017



Toward an Ancient DNA Atlas of Humanity

Expanding Ancient DNA Toward All Times and Places

Spread of Yamnaya ancestry to



In the coming years we will see a dialogue between geneticists and archaeologists about how to integrate this disruptive technology.

This is already beginning.

Summary

Ancient DNA is teaching us that much of what we thought we knew is wrong

We are all mixed, no one is “pure”

An unusual field where scratching the surface is guaranteed to surprise

