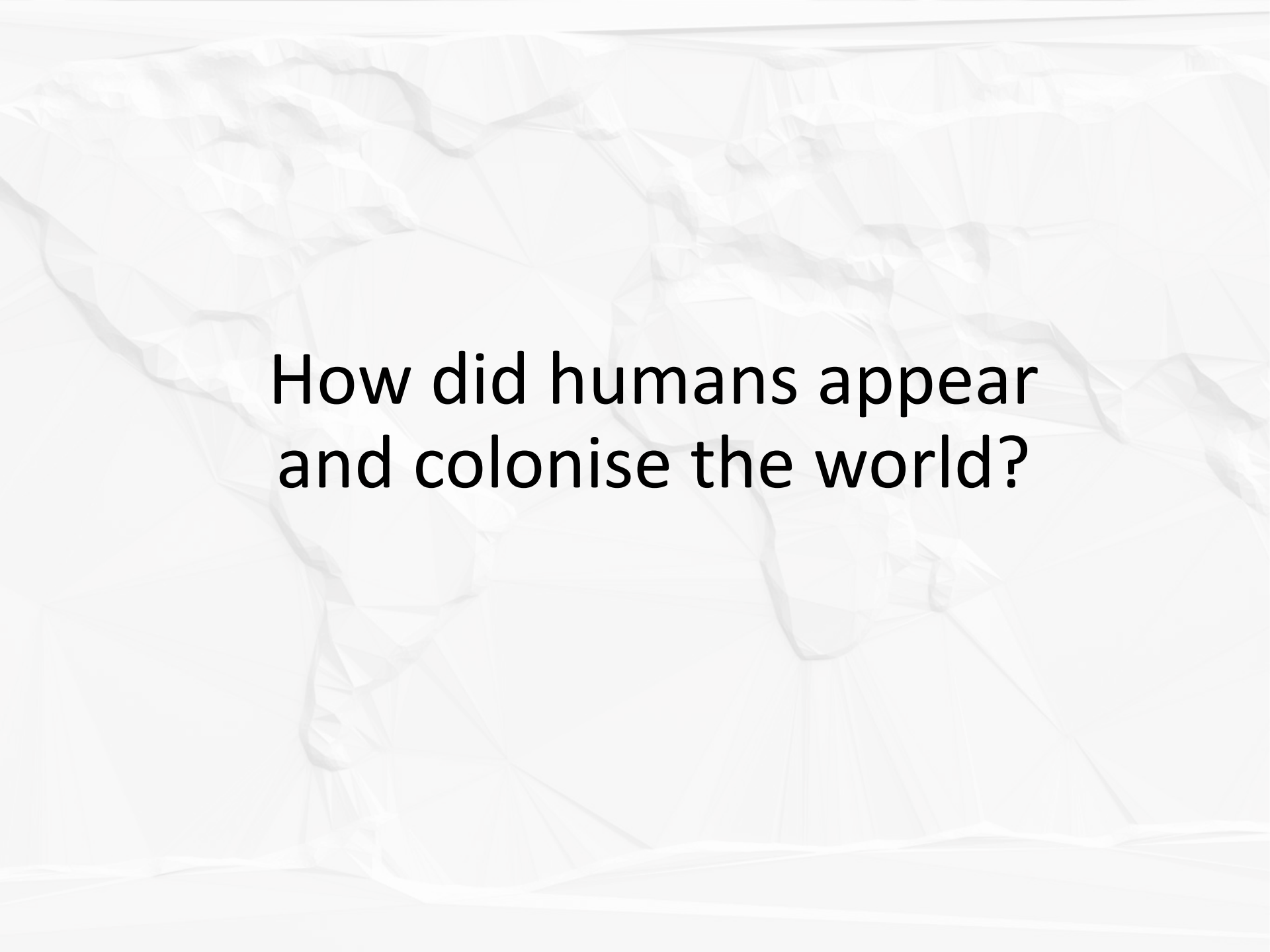


How Genetic Adaptation Helped Humans Colonise the Globe

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University College London

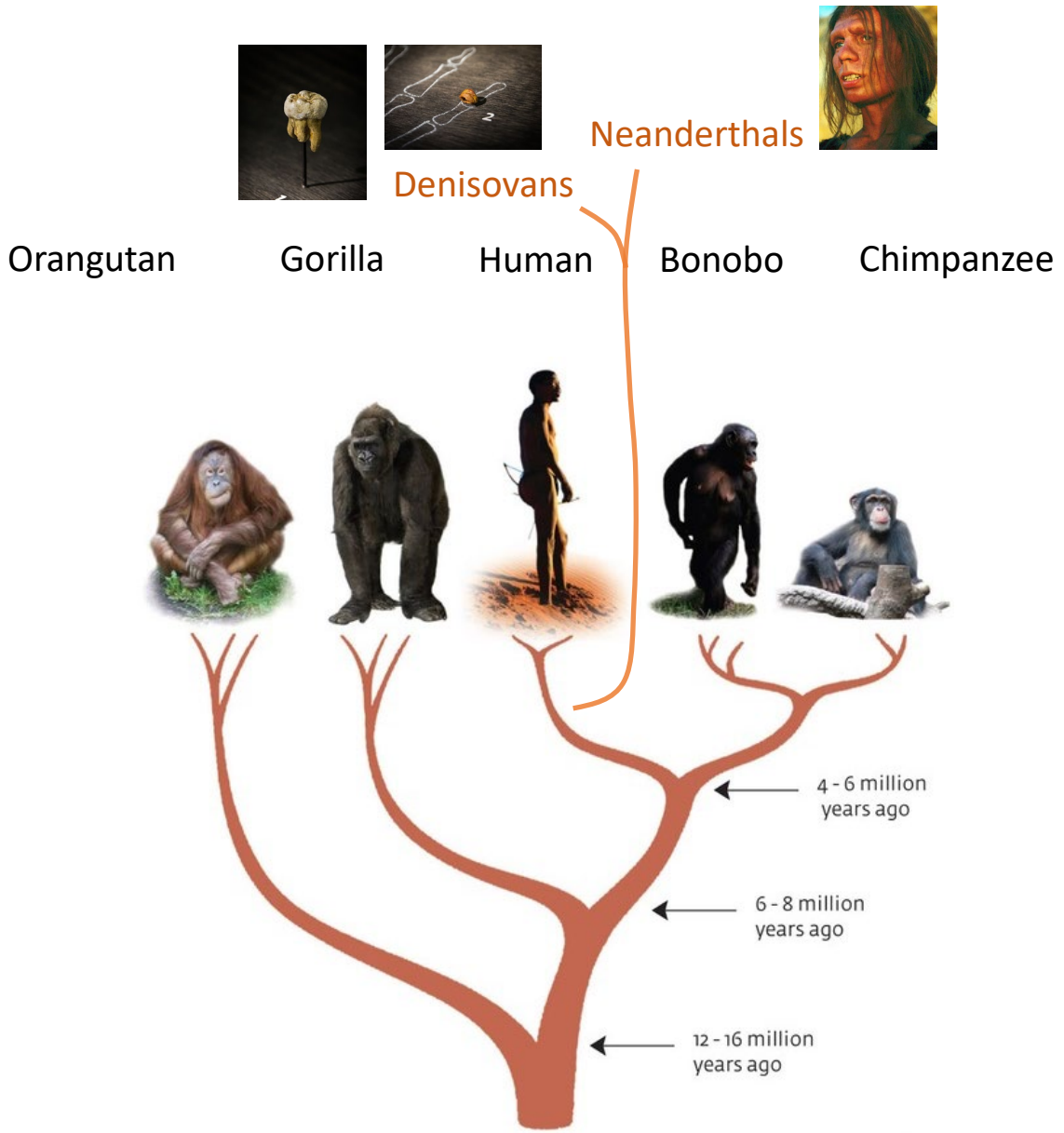


How did humans appear
and colonise the world?

Human evolution



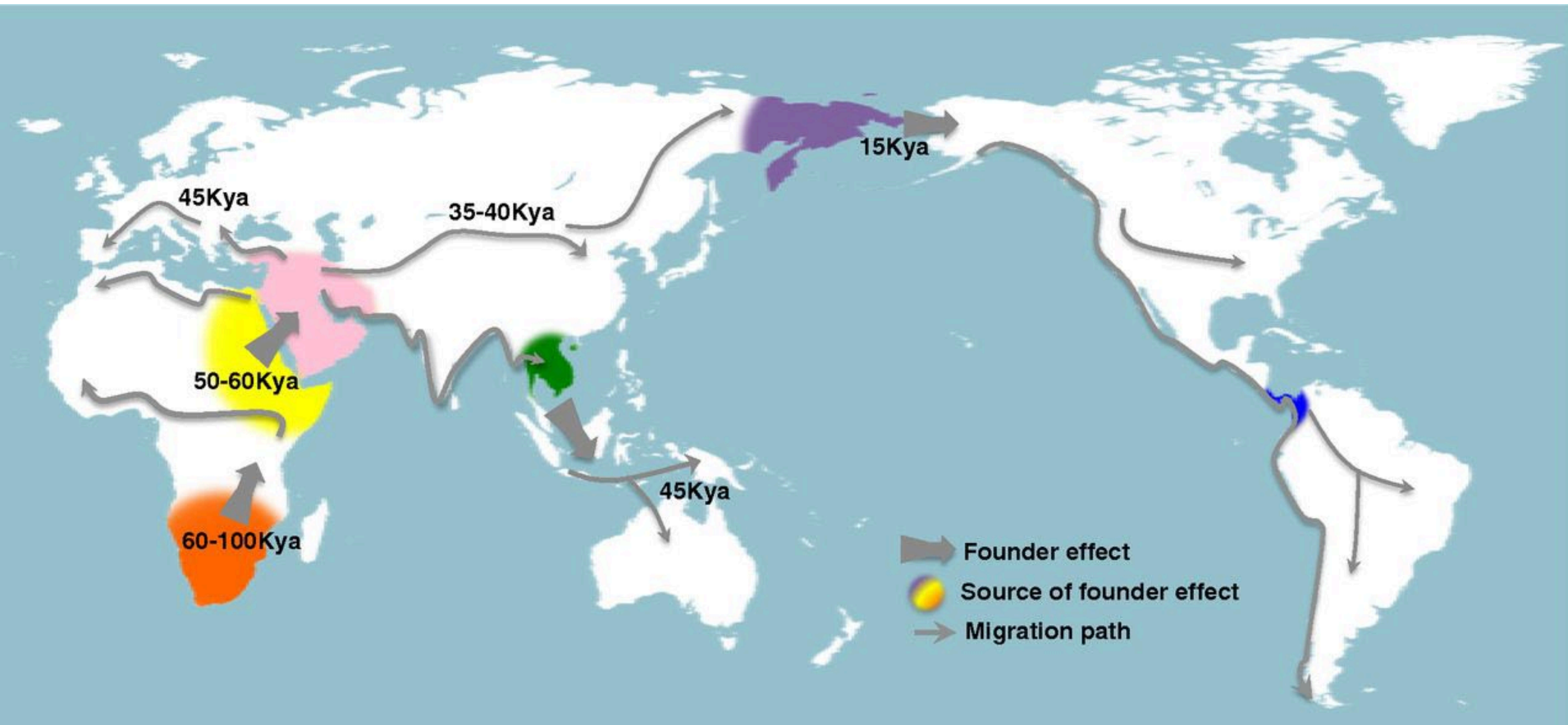
Human evolution



Human evolution



Human demographic history



We are highly homogeneous

Humans are genetically and phenotypically extremely similar, both within and across populations.

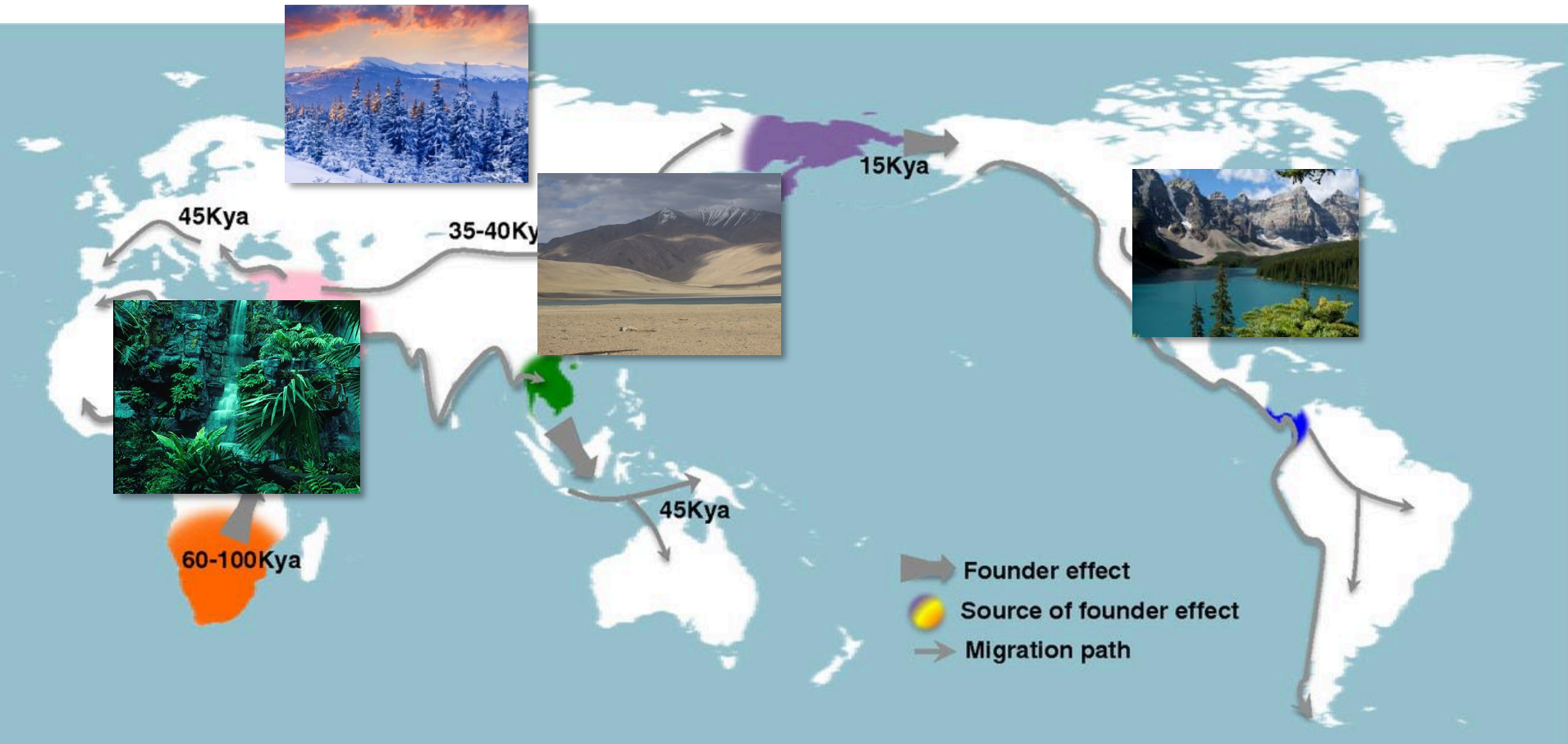
On average, 1/1000 of bases (letters) in the genome differ between any pair of individuals.

Of those, 90% vary within populations and only 10% differ among populations.



Even the 10% do not represent biological differences among “*races*”, which are society constructs and not biological entities.

Human environments



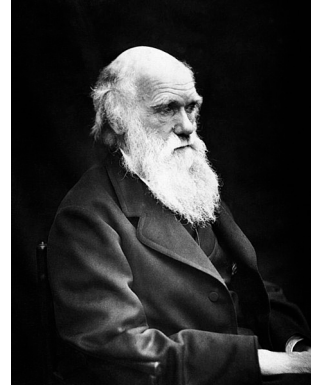
Humans were under strong pressure to adapt locally



How do humans adapt to their
local environment?

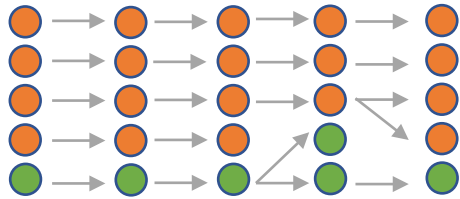
How do we learn about those
adaptations?

Adaptation by natural selection

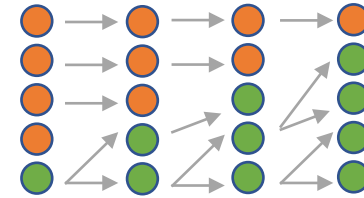


Natural selection that mediates adaptation to a new environment is *positive selection*:

Neutral evolution



Positive selection



Species adapt by natural selection

Natural selection that mediates adaptation to a new environment is *positive selection*:

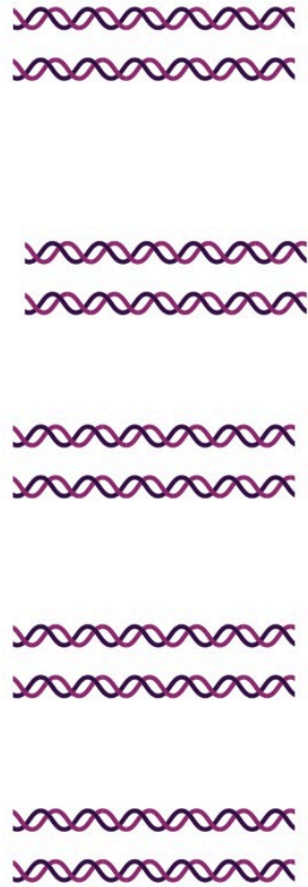
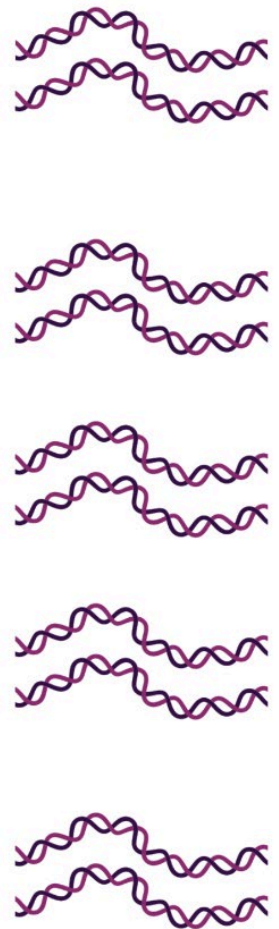
Neutral evolution



Positive selection



Genomes



AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

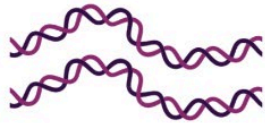
AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

AGTGGTGTACGTGC...
AGTGGTGTACGTGC...

Genomes



AGTGGTGCACGTGC...
AGTGGTGCACGTGC...



AGTGGTGCACGTGC...
AGTGGTGCACGTGC...



AGTGGTGCACGTGC...
AGTGGTGCACGTGC...



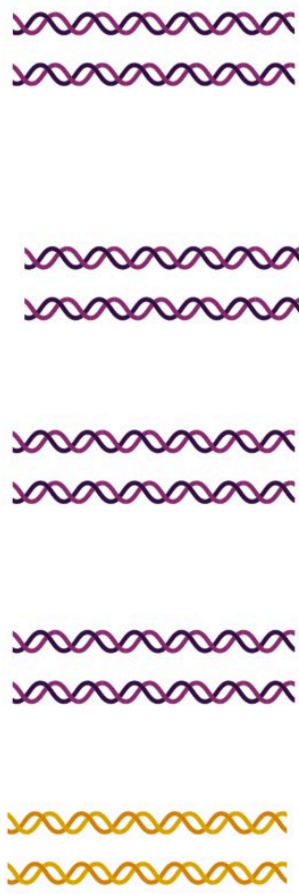
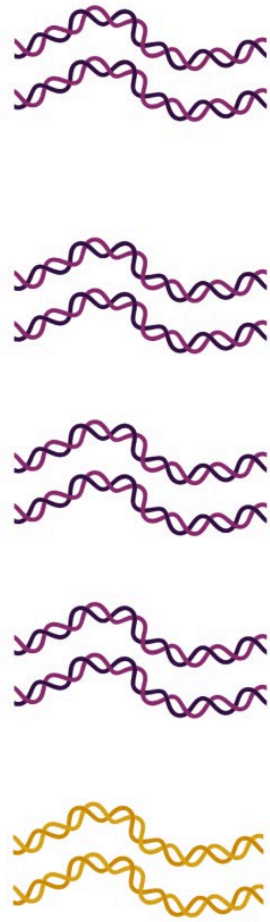
AGTGGTGCACGTGC...
AGTGGTGCACGTGC...



AGTGGTGTACGTGC...
AGTGGTGTACGTGC...

Genomes

Variant (polymorphism)



2 alleles (C, T)

AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

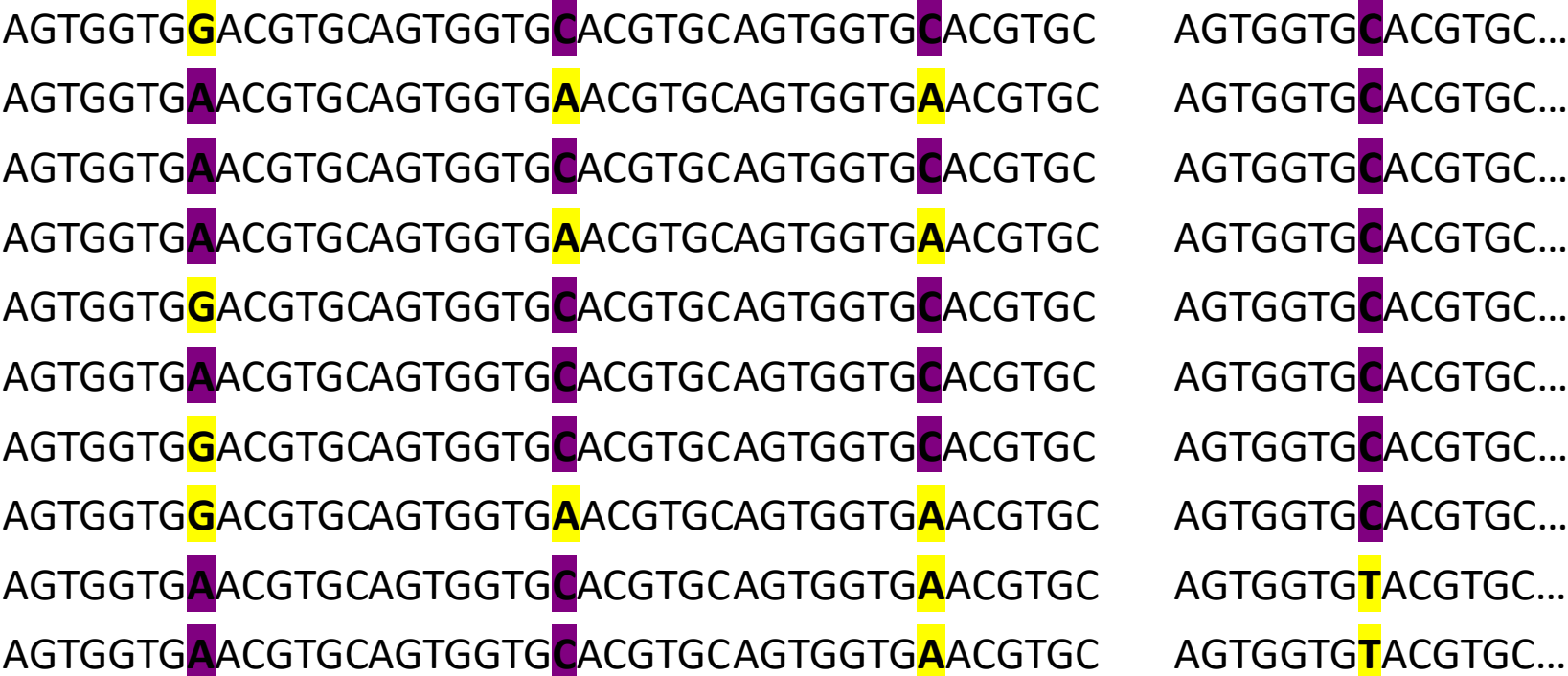
AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

AGTGGTGCACGTGC...
AGTGGTGCACGTGC...

AGTGGTGTACGTGC...
AGTGGTGTACGTGC...

Frequency of T = 20%

Genomes



40%

30%

50%

20%

Genomes

AGTGGTGGACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGC...
AGTGGTGAACGTGCAGTGGTGAACGTGCAGTGGTGAACGTGCAGTGGTGCACGTGC...
AGTGGTGAACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGC...
AGTGGTGAACGTGCAGTGGTGAACGTGCAGTGGTGAACGTGCAGTGGTGCACGTGC...
AGTGGTGGACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGC...
AGTGGTGAACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGC...
AGTGGTGGACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGC...
AGTGGTGGACGTGCAGTGGTGAACGTGCAGTGGTGAACGTGCAGTGGTGCACGTGC...
AGTGGTGAACGTGCAGTGGTGCACGTGCAGTGGTGAACGTGCAGTGGTGTACGTGC...
AGTGGTGAACGTGCAGTGGTGCACGTGCAGTGGTGAACGTGCAGTGGTGTACGTGC...

Thousands of genomes of modern humans around the world.

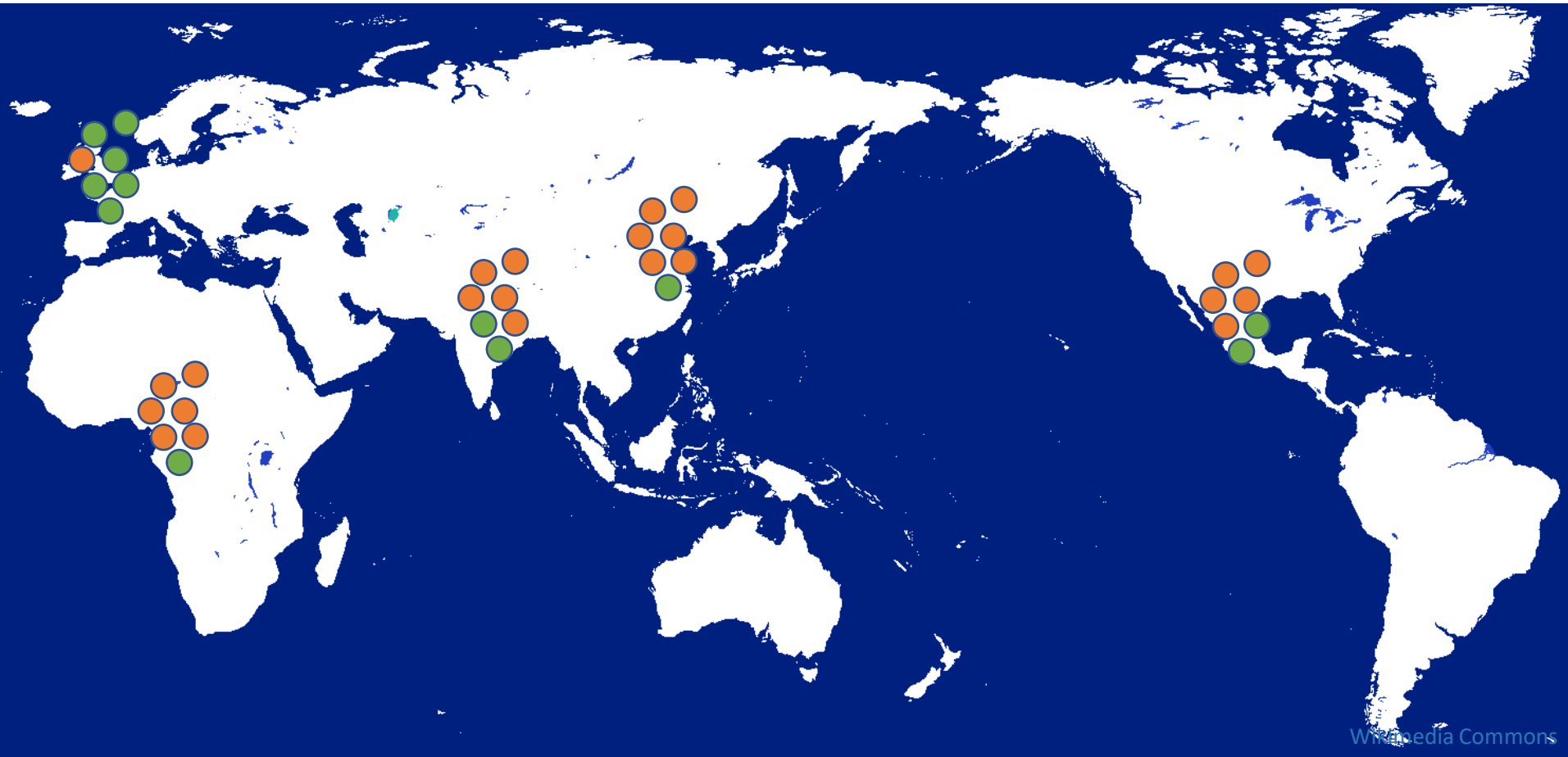
AG..GTGGAC.TGC AGTG.TGACG..C AGT.GTGCAC..GC AGTGGT...GTGC...

Hundreds of genomes from old human remains

AGTGGTGGACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGCAGTGGTGCACGTGC...

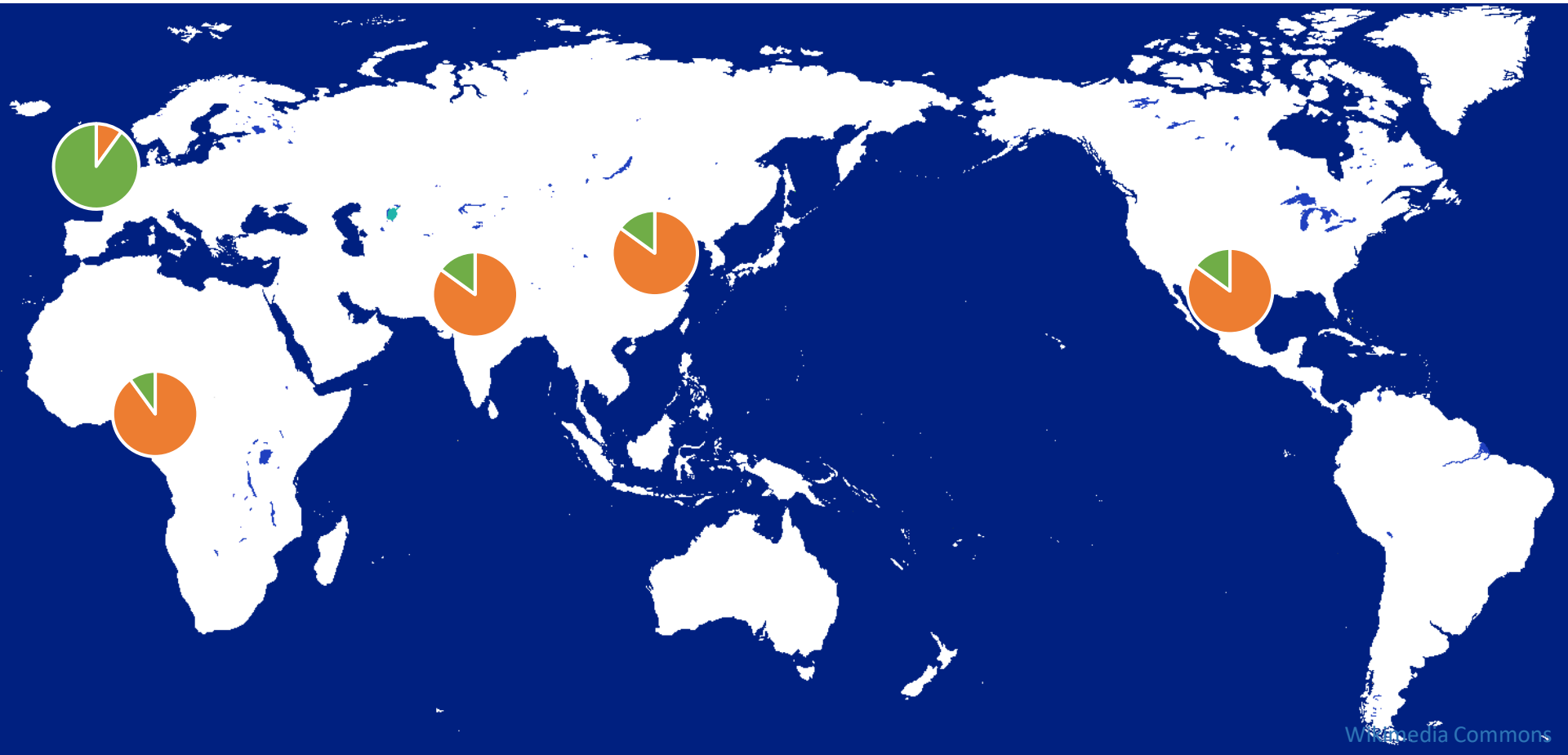
A few genomes from archaic humans (Neanderthals and Denisovans)

Genetic local adaptation



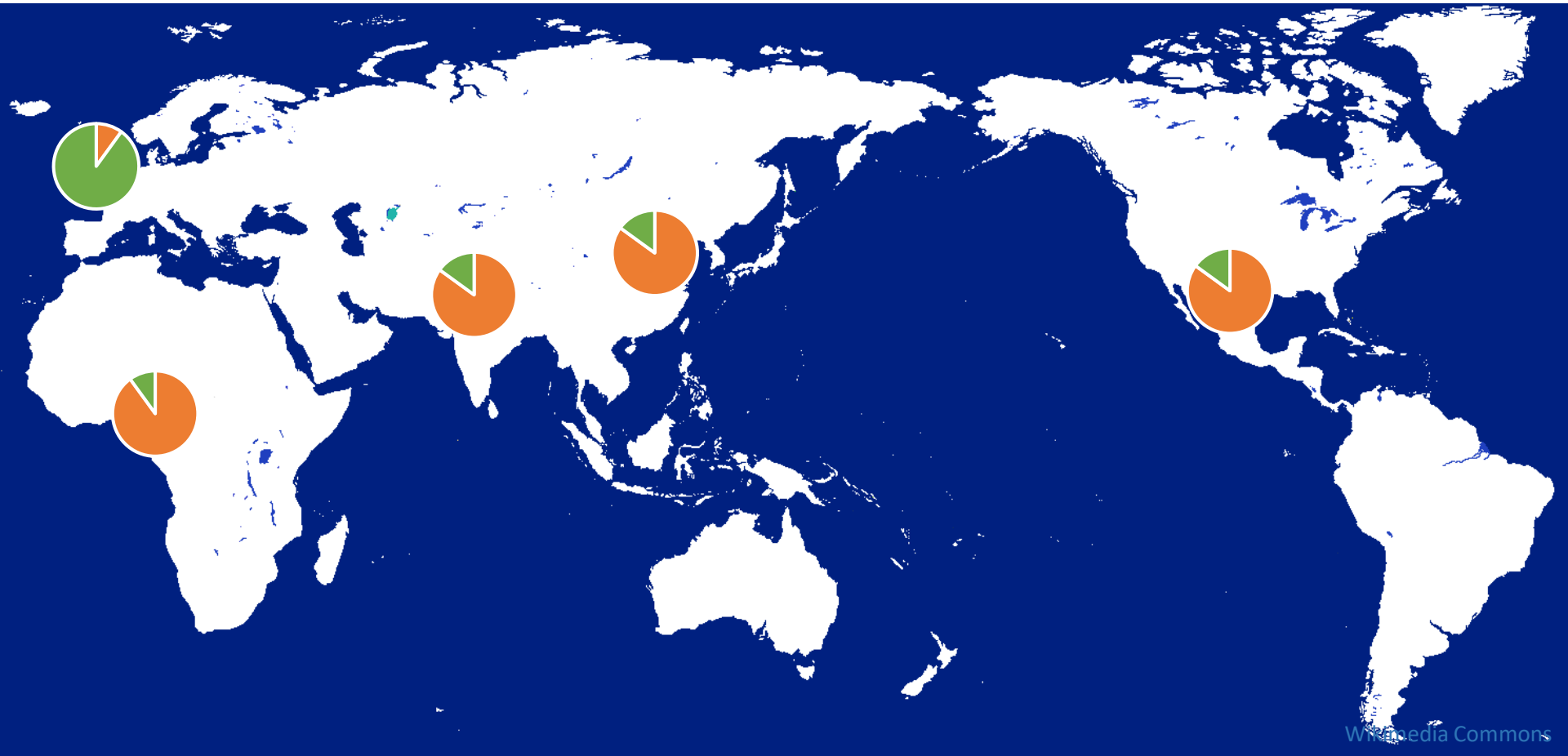
A particular population is genetically adapted to its local environment (locally adapted).

Genetic adaptation



A particular population is genetically adapted to its local environment (locally adapted).

Genetic signatures of local adaptation



A genetic variant shows striking differences in allele frequency across populations.

Genetic signatures of local adaptation

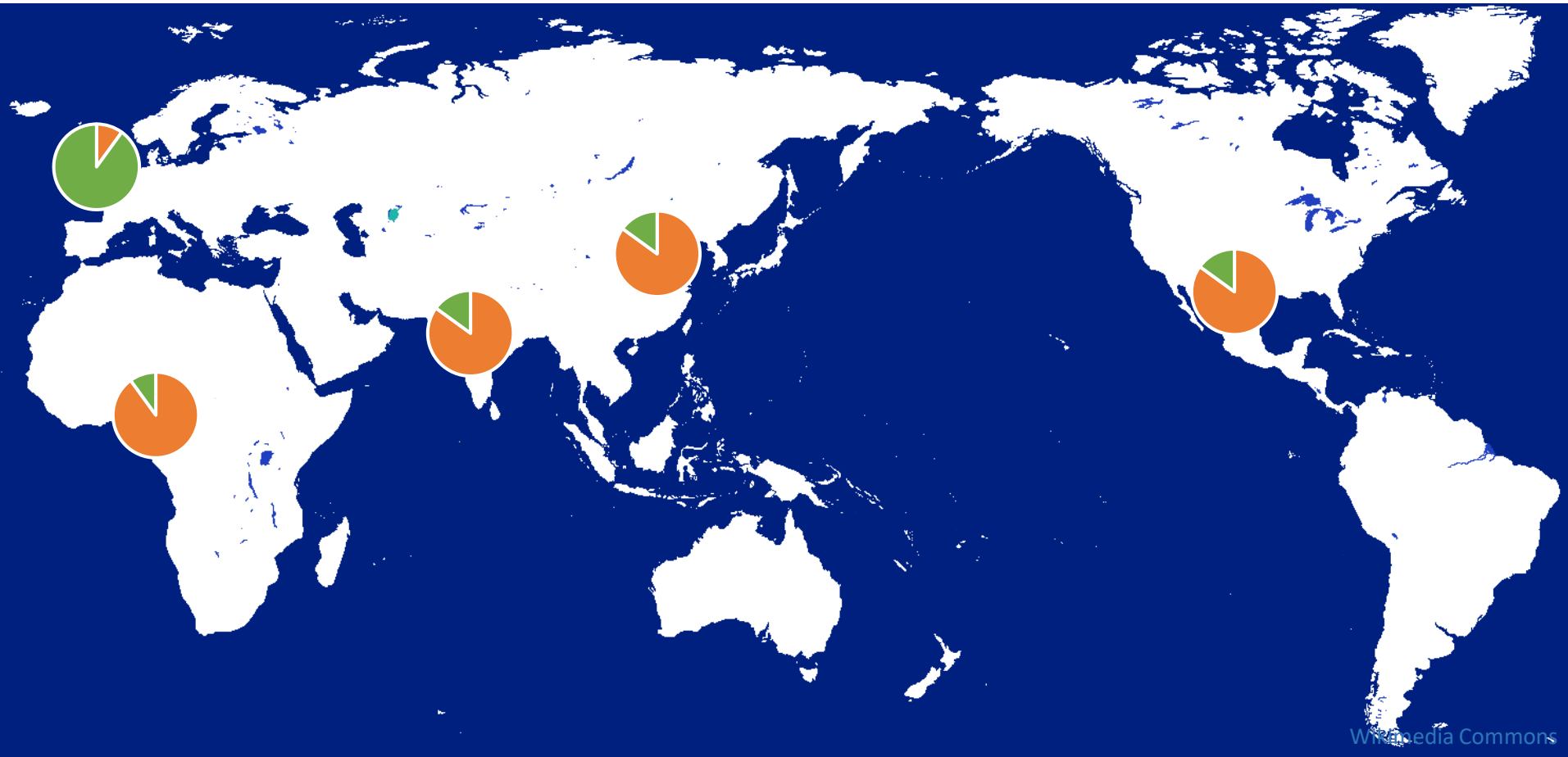
We cannot observe the past.

We cannot experiment in humans.

We have to rely on the *signatures* that positive selection leaves in genomes.

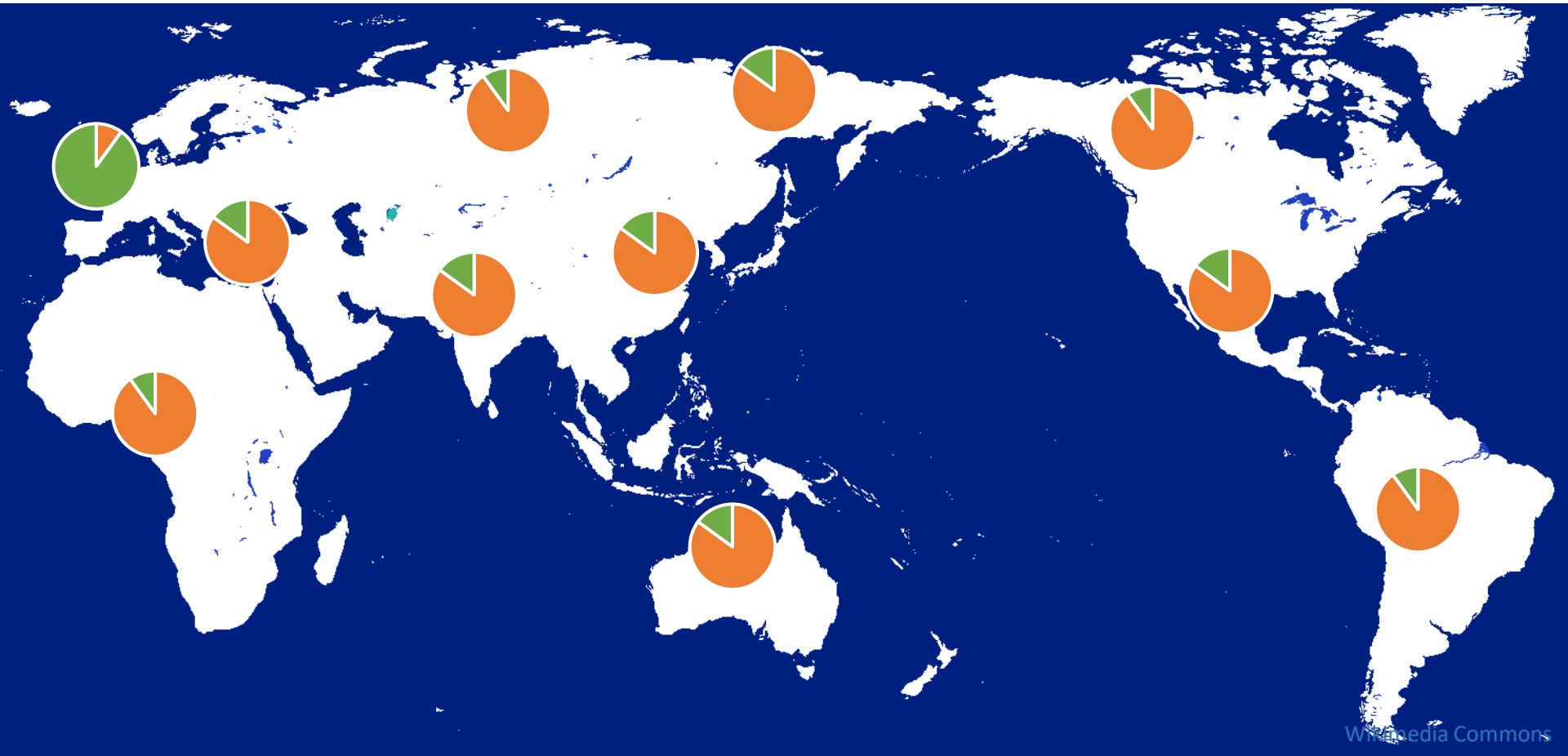


Genetic signatures of local adaptation

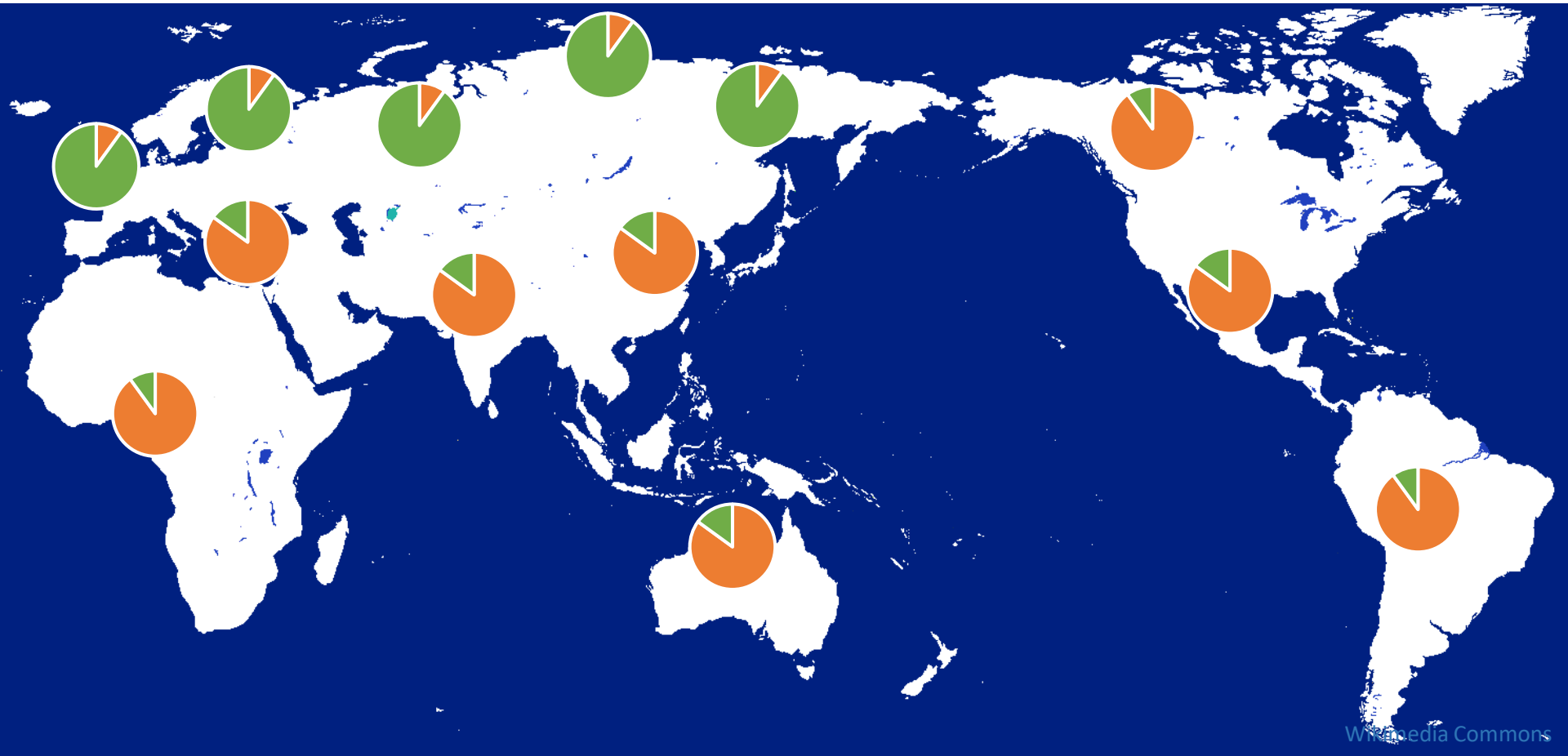


Signatures of local adaptation allow us to identify variants/genes that evolved under positive selection in specific populations and are responsible for local adaptations.

Genetic signatures of local adaptation



Genetic signatures of local adaptation



Did genetic adaptation help humans
colonise the globe?

Which adaptations?

What are their
consequences today?

Adaptation to diet



In most species, adults are unable to digest milk.

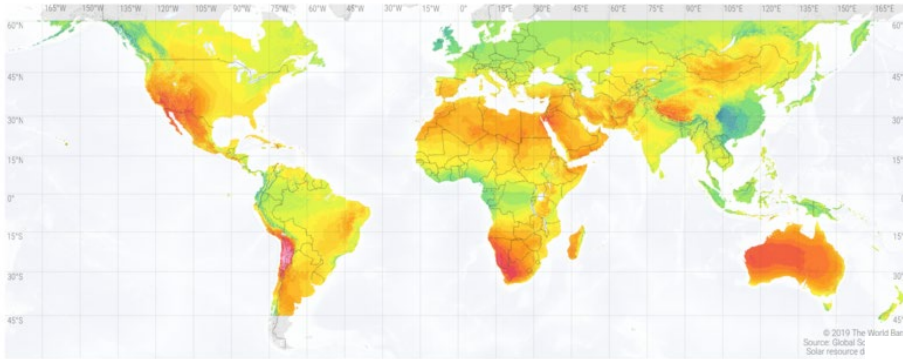
Many adult humans are able to digest milk, due to the continued expression of Lactase into adulthood.

The *Lactase* gene has some of the strongest signatures of local adaptation in the human genome.

Alleles that maintain expression of Lactase in adulthood have appeared in European and African pastoralists.

Milk provided (and provides) a source of nutrition and clean water to individuals who can consume it.

Adaptation to solar exposure



Striking differences around the world.

High levels: need protection.



Low levels: need exposure to generate Vitamin D.



Amazing diversity of skin tones world-wide.



Strong local adaptation to reduce skin pigmentation at high latitudes in multiple pigmentation-related genes (*SLC45A2*, *SLC24A5*, *TYR*, *HERC2*).

Adaptations

Solar exposure



Diet

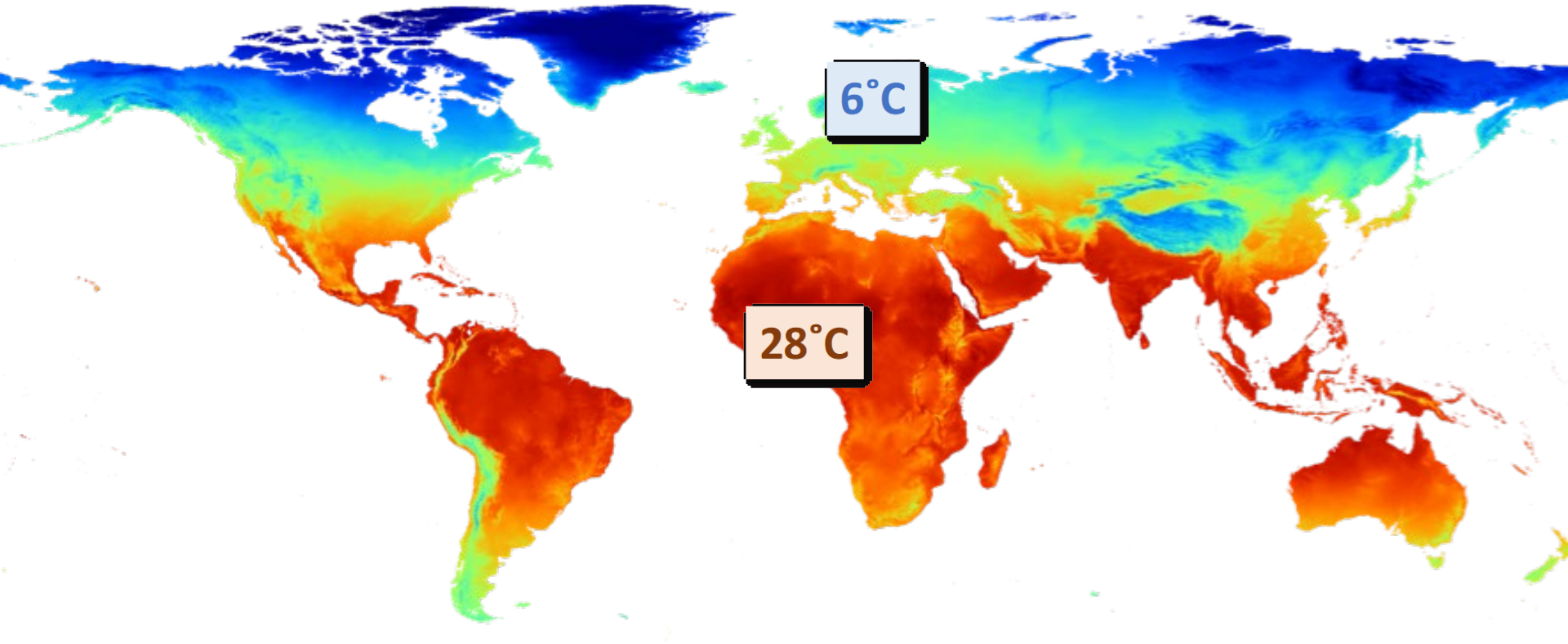


Pathogens

Height

...

Adaptation to ambient temperature



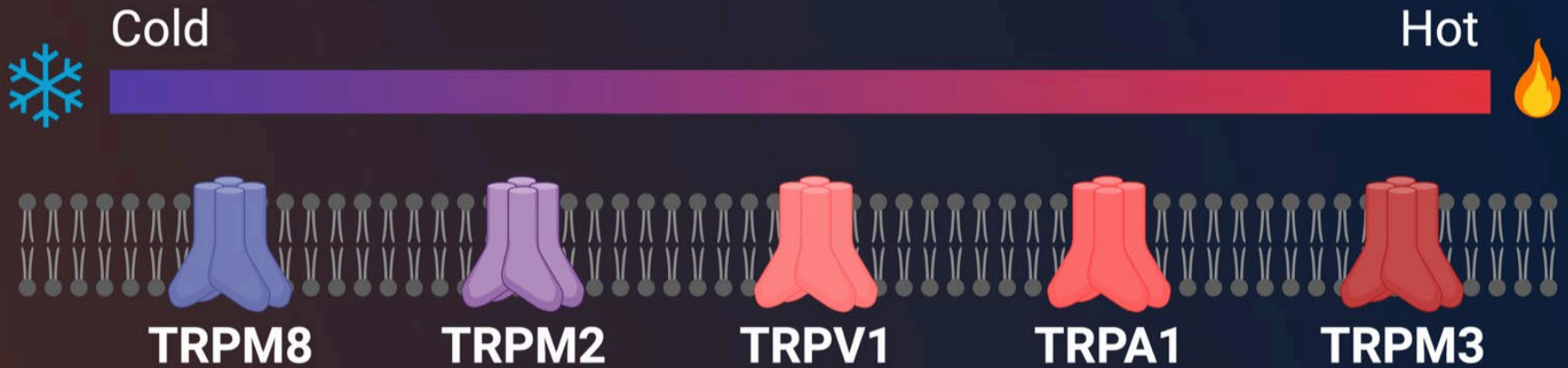
Sensing temperature



mint



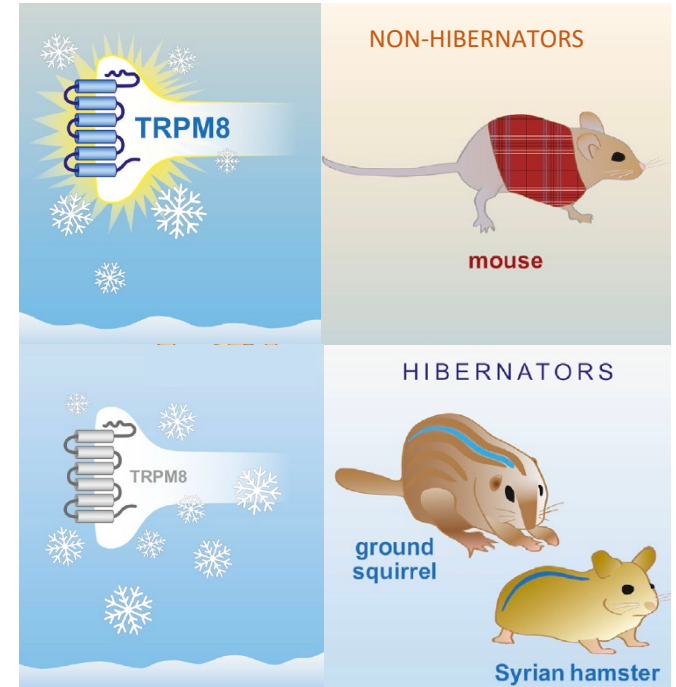
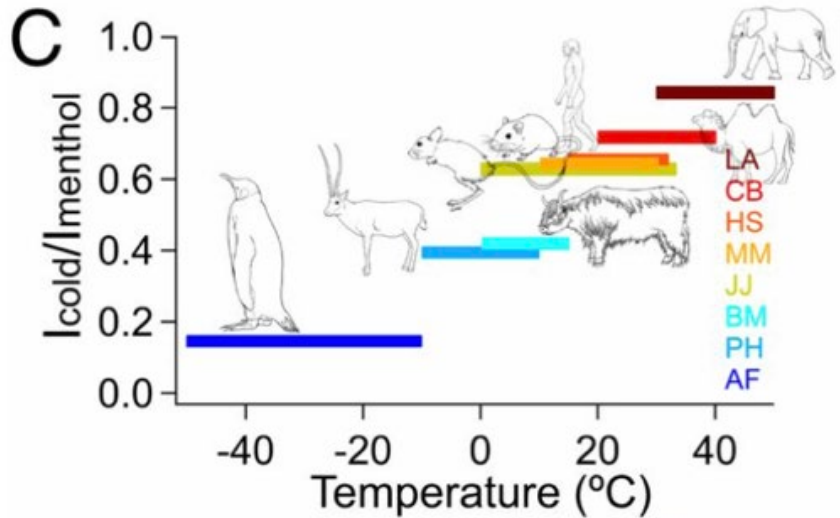
chili



TRPM8 and ambient cold



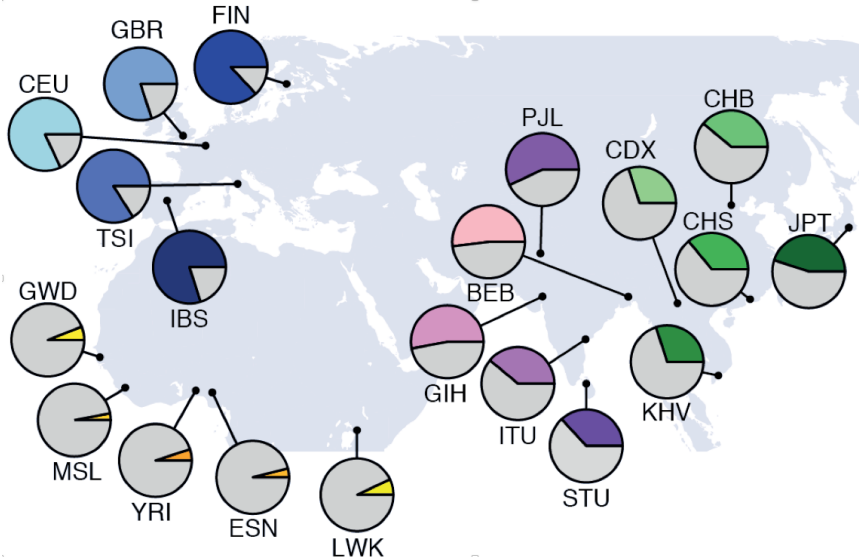
TRPM8 and adaptation to cold



TRPM8 adaptation in humans?

TRPM8 population differentiation

A likely functional genetic variant (rs10166942, C/T)



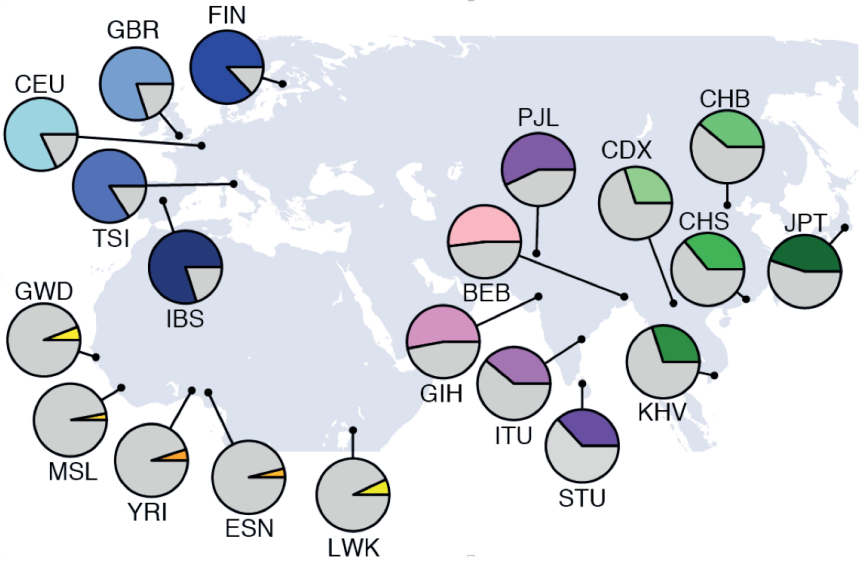
Significant correlation of allele frequency with latitude (and with temperature).

Large allele frequency differences among populations.

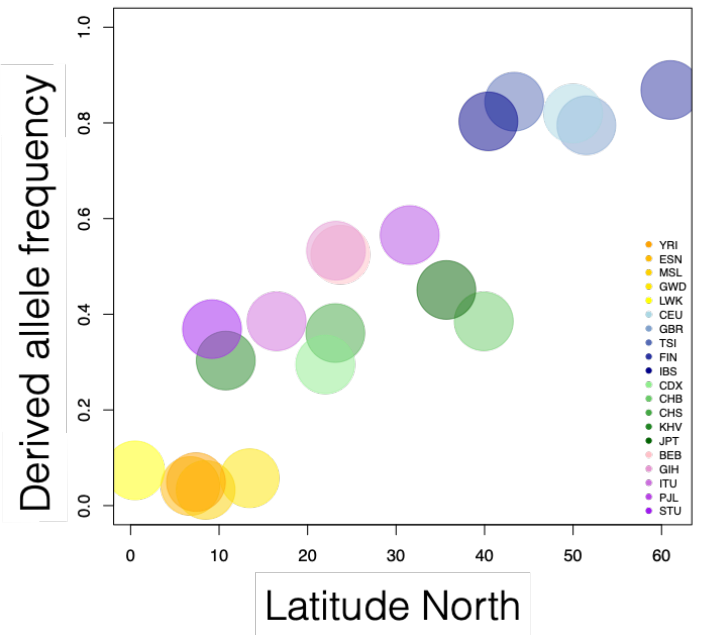
Only 0.02% of SNPs in the genome have larger allele frequency differences between Finnish and Yoruba.

Multiple additional signatures of local positive selection.

TRPM8 population differentiation



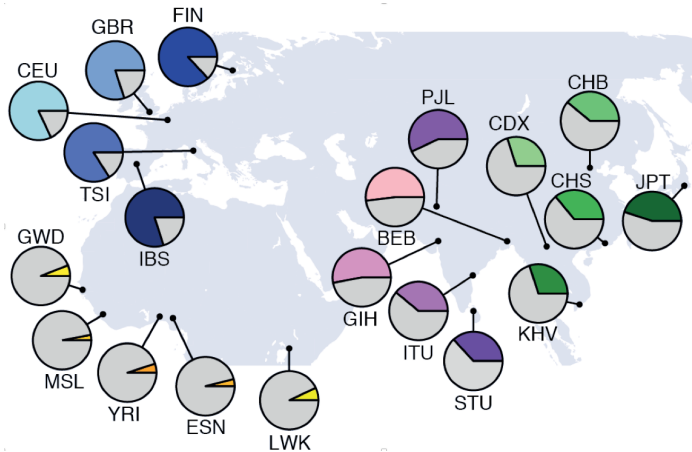
Significant correlation of allele frequency with latitude (and with temperature).



TRPM8 and local adaptation

TRPM8 has likely contributed to adaptation to increasingly cold environments as humans migrated to higher latitudes.

Generating the frequency gradient we observe today.



The derived allele increases cold sensitivity.



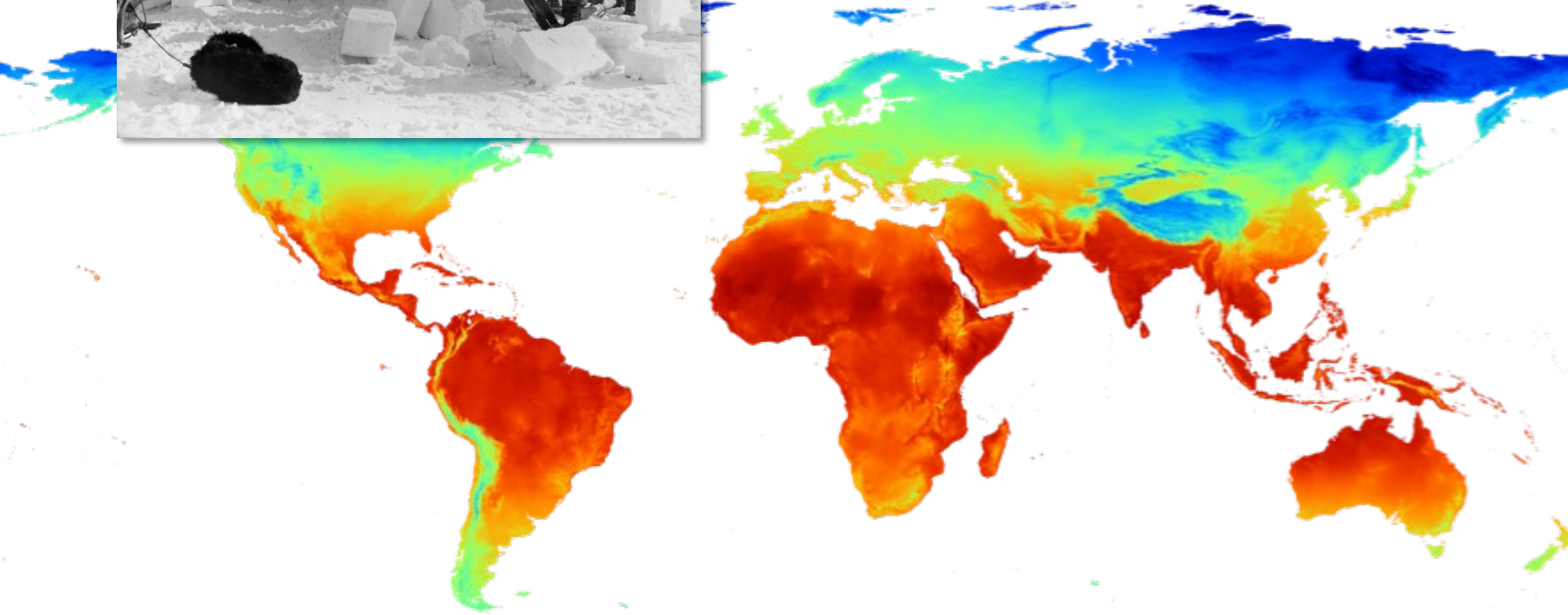
The derived allele is associated with increased risk of migraine.

This adaptation likely increased cold sensitivity and, as a side effect, also the risk of migraine in some human groups.



**What about extreme cold
habitats?**

Adaptations to the arctic



Adaptations to the arctic



In Greenlandic Inuit the strongest signatures of local adaptation are in *FADS* genes (fatty acid desaturases).

Adaptations to the arctic diet



In Greenlandic Inuit the strongest signatures of local adaptation are in *FADS* genes (fatty acid desaturases).

The mutations are associated with a number of traits and may be protective from cardiometabolic disease.



Adaptation to extreme environments



So how did genetic adaptation help humans colonise the globe?

Human populations are highly homogeneous, both genetically and phenotypically (both in our genes and in our traits).

Yet, as humans migrated around the world, local positive selection allowed them to adapt to their local environments.

This resulted in key adaptations to different climates, diets or pathogens, among other environmental factors.

In addition, specialized genetic adaptations have allowed humans to colonise extreme environments.

So how did genetic adaptation help humans colonise the globe?

These evolutionary events live now as differences among individuals and populations in important traits, including disease.

The study of genomes using evolutionary population genetics is a critical tool to better understand human evolution and the important effects of our evolutionary history to people living today.



