The Origins of The Modern Horse,

The Noblest Conquest Of Mankind

UNIVERSITY OF COPENHAGEN

Centre for GeoGenetics

Lorlando@snm.ku.dk
+4521849646

Horses As Keys To Past Societies

A Windows Into The History of Civilisation

Horses Had A Far-Reaching Impact On Human Societies

Transportation, Communication, Warfare, Agriculture

Domesticated Horses, A Mine For Geneticists

An Extra-ordinary Phenotypic Diversity

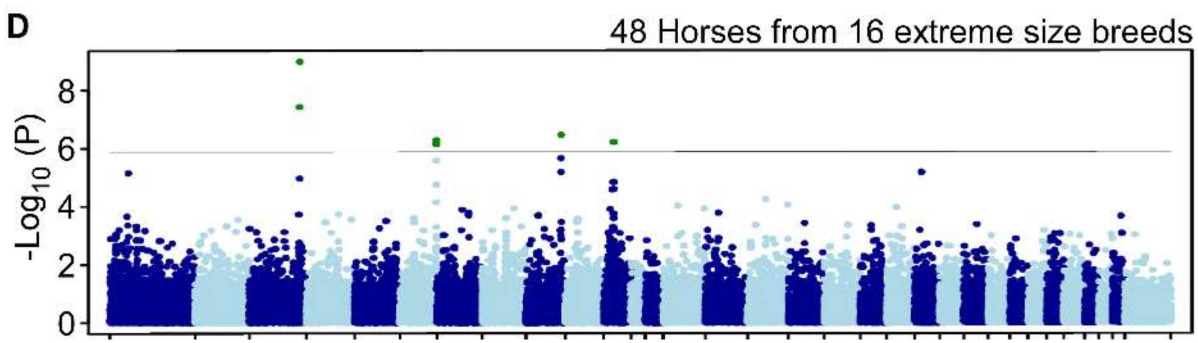




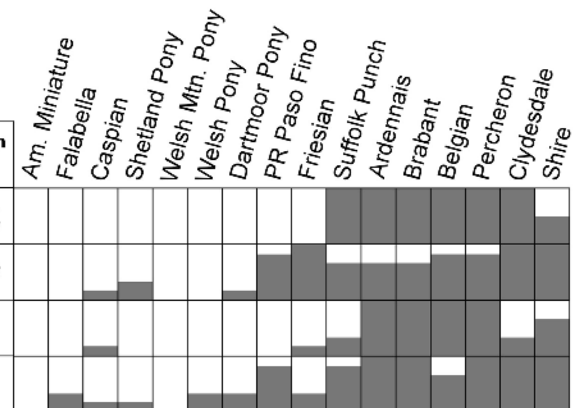
Deciphering The Genetic Makeup of (Complex) Traits

Domesticated Horses, A Mine For Geneticists

An Extra-ordinary Phenotypic Diversity



Chr.	Position	Alleles: Little	Alleles: Big	P-value	Fraction of Variance Explained	Genes in Locus
3	105,547,002	T	C	1.05×10^{-9}	0.685	*LCORL, NCAPG*
6	81,481,064	C	T	5.21×10^{-7}	0.556	*HMGA2*
9	75,550,059	C	T	3.48×10^{-7}	0.567	*ZFAT*
11	23,259,732	G	A	6.19×10^{-7}	0.589	*LASP1*
4 Loci Together					0.835	



Makvandi-Nejad et al. PLoS One (2012)

Four Loci Explain 83% of Size Variation in the Horse

The Process of Horse Domestication

ANIMALS AND PLANTS

UNDER

DOMESTICATION.

BY CHARLES DARWIN, M.A., F.R.S., &c.

SECOND EDITION, REVISED. FOURTH THOUSAND.

IN TWO VOLUMES.—VOL. I.

WITH ILLUSTRATIONS.

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1875.

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DOMESTIC DOGS AND CATS.

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CHAPTER II.

HORSES AND ASSES.

HORSE.—DIFFERENCES IN THE BREEDS—INDIVIDUAL VARIABILITY OF—DIRECT EFFECTS OF THE CONDITIONS OF LIFE—CAN WITHSTAND MUCH COLD—BREEDS MUCH MODIFIED BY SELECTION—COLOURS OF

Horse Comparative Genomics

Przewalski's Horses

- IUCN: EW (1996), CE (2008), EN (2011)
- Major Demographic Bottleneck (12 Founders)
- Possibly Admixed

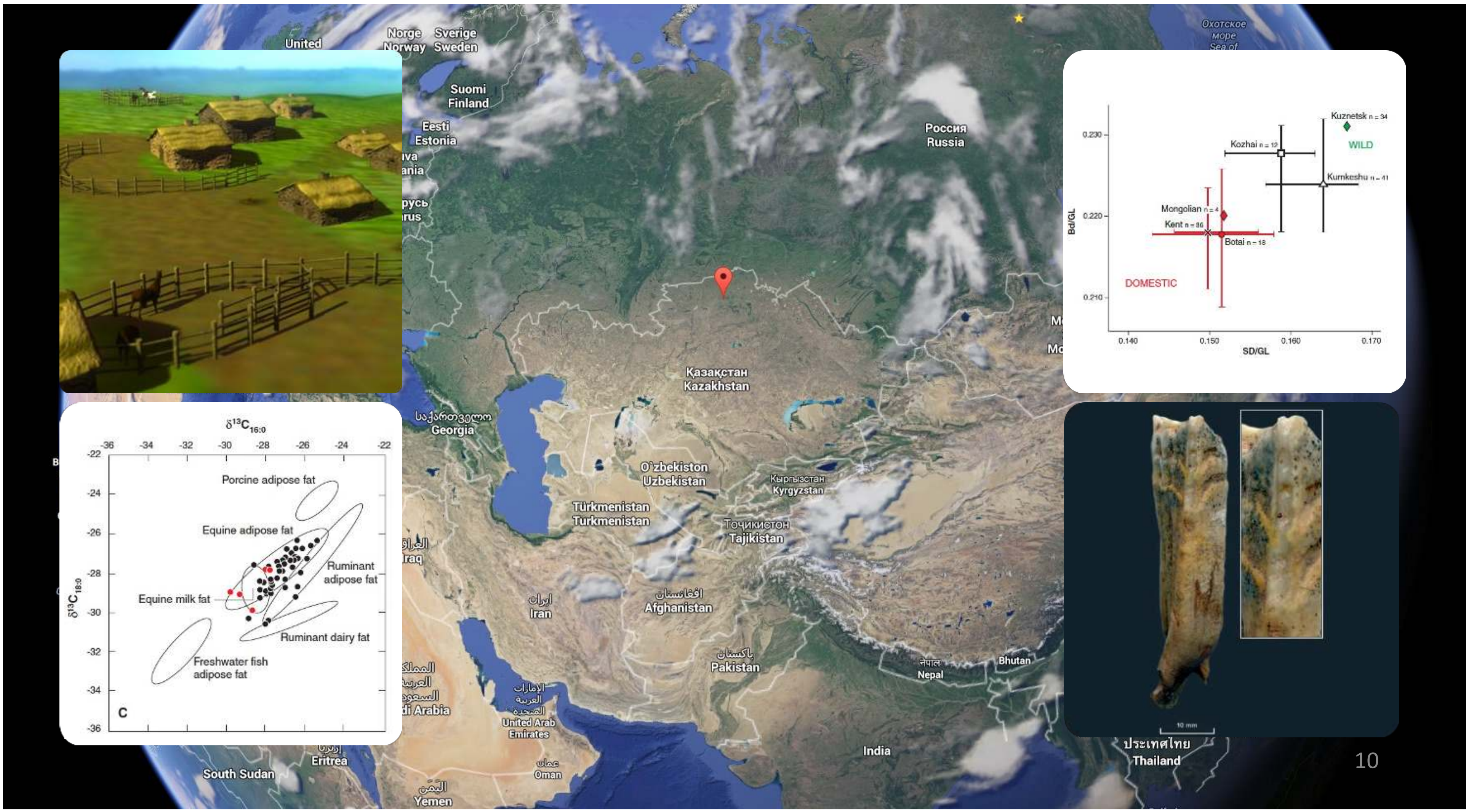
Engaging Into Conservation Priorities

When Did We First Domesticate Horses?

Horse Domestication

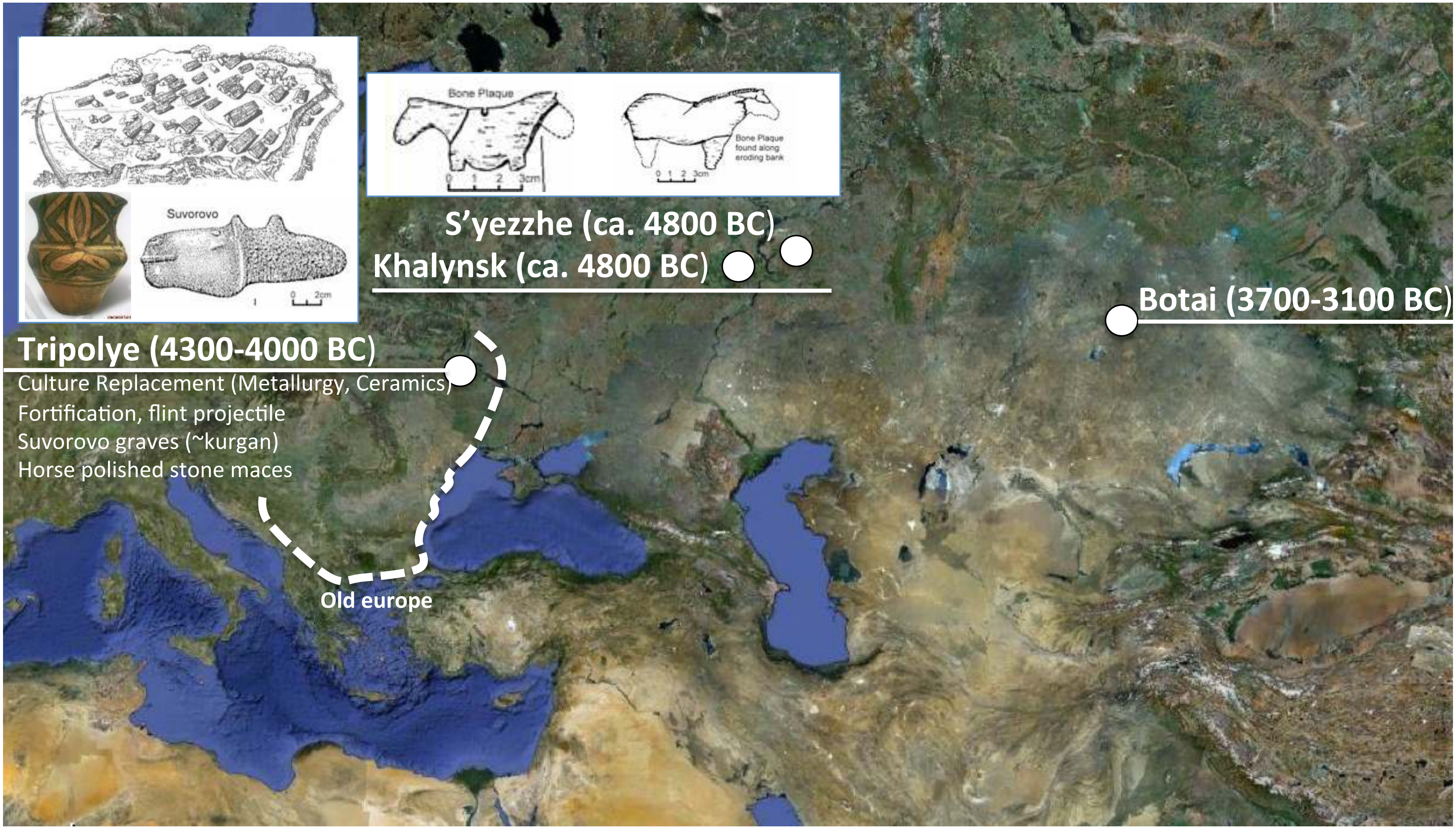
The Earliest Evidence of Horse Milking and Harnessing

Botai – 5,500 years ago



Horse Domestication

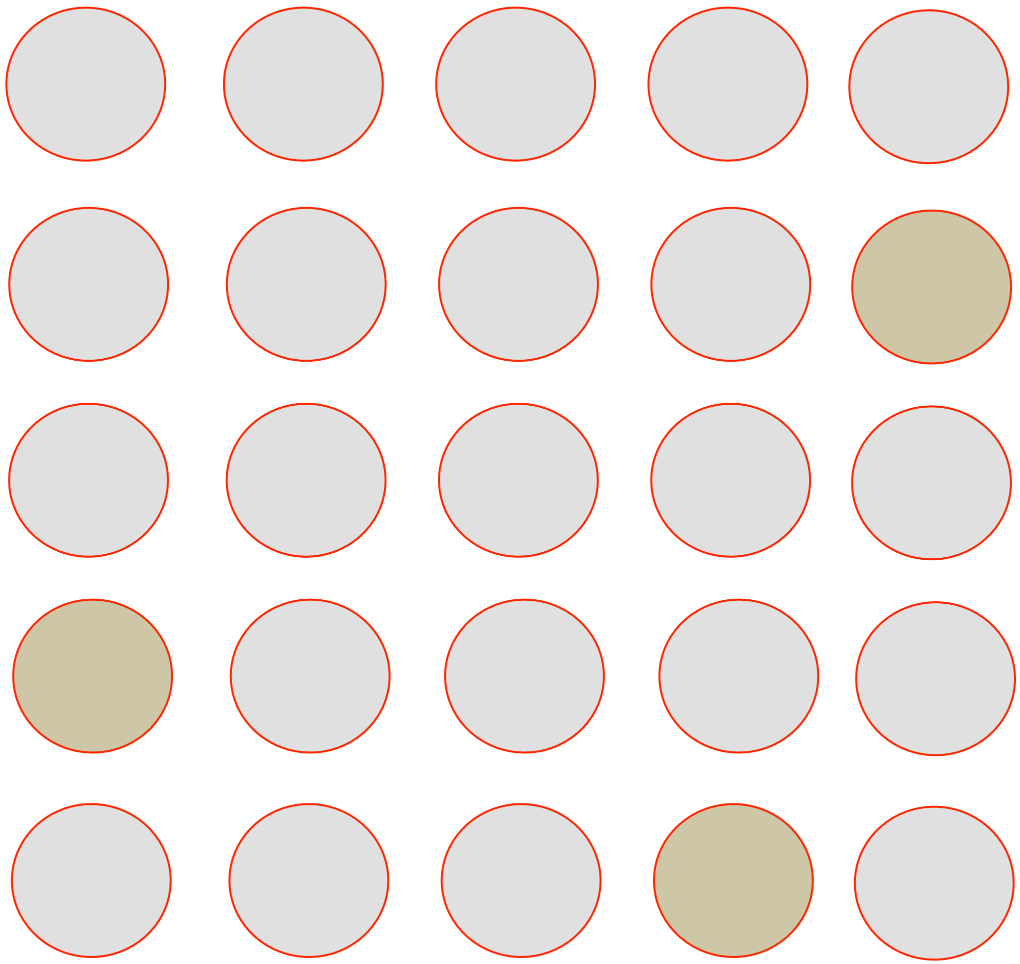
Pre-Botai Horse Domestication: David Anthony's Scenario



What Can We Learn About Early Domestication From Modern DNA?

Phylogeographic Expectations

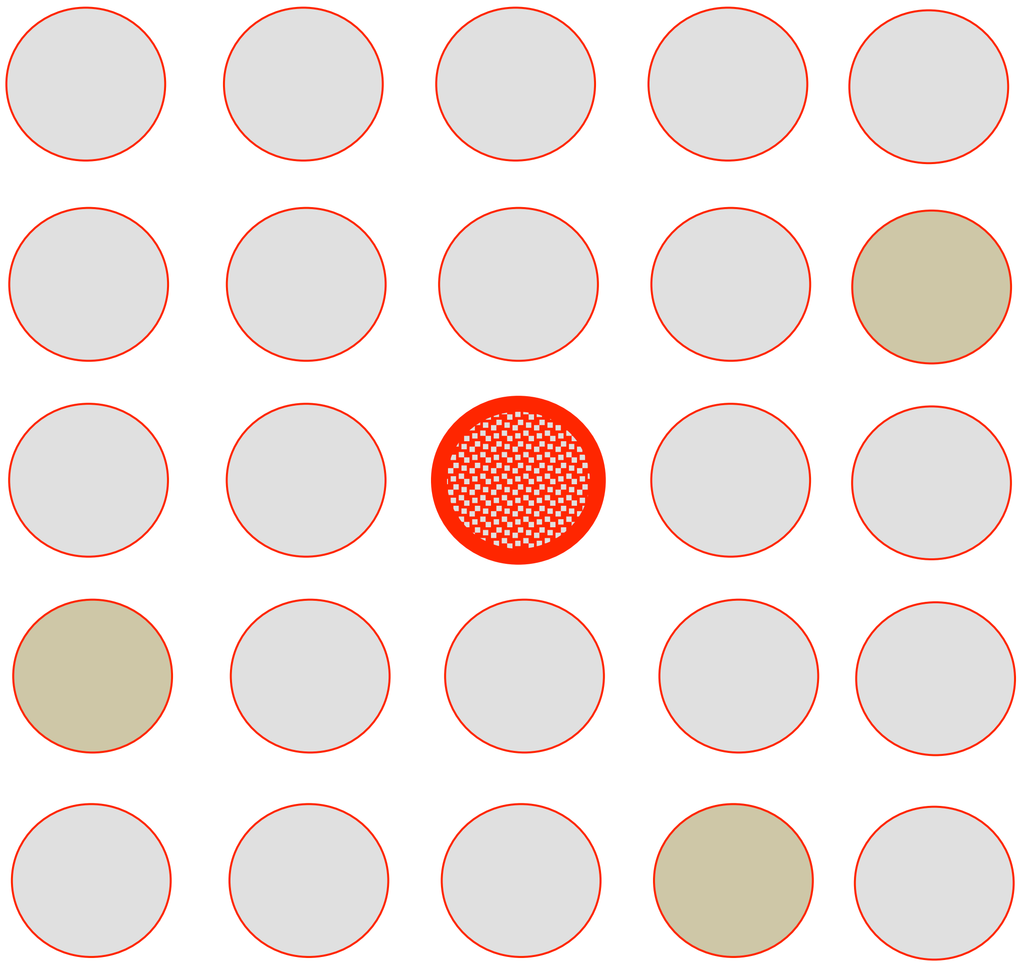
Rationale



Wild Populations

Phylogeographic Expectations

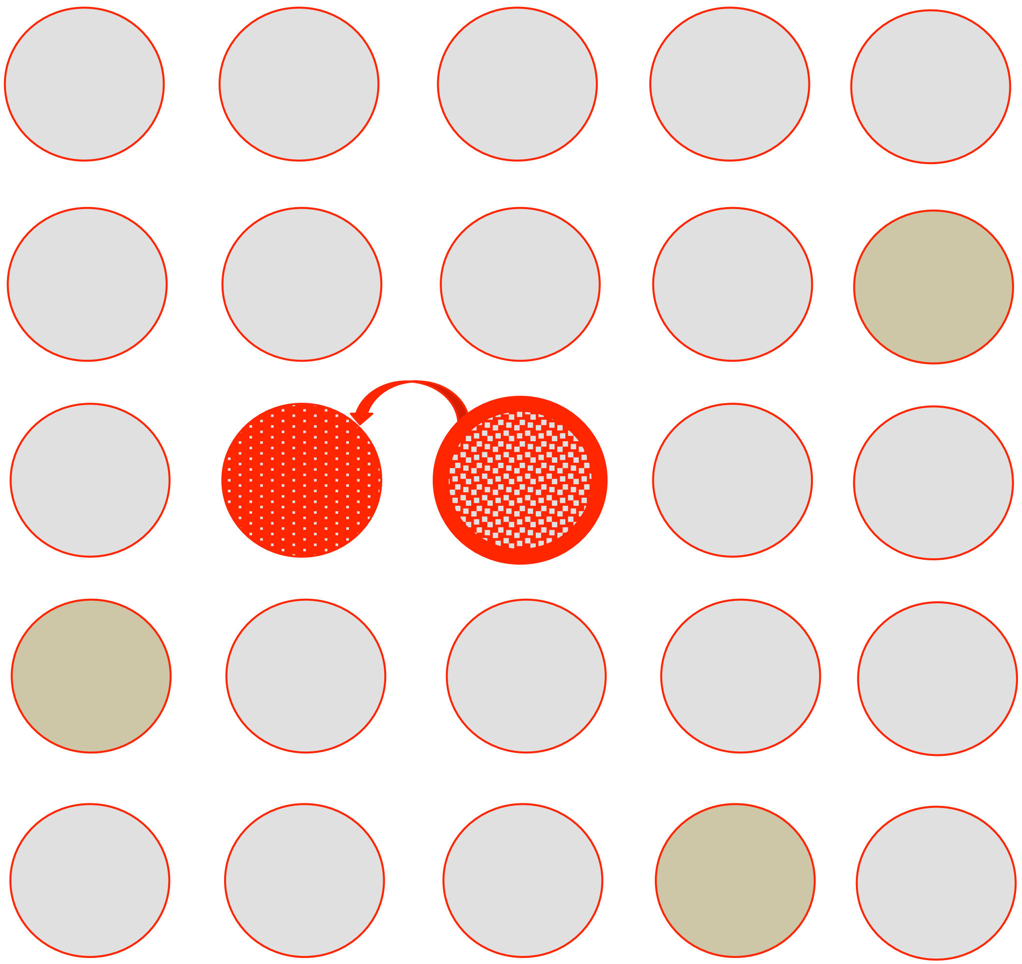
Rationale



Wild Populations, Domestication Centre

Phylogeographic Expectations

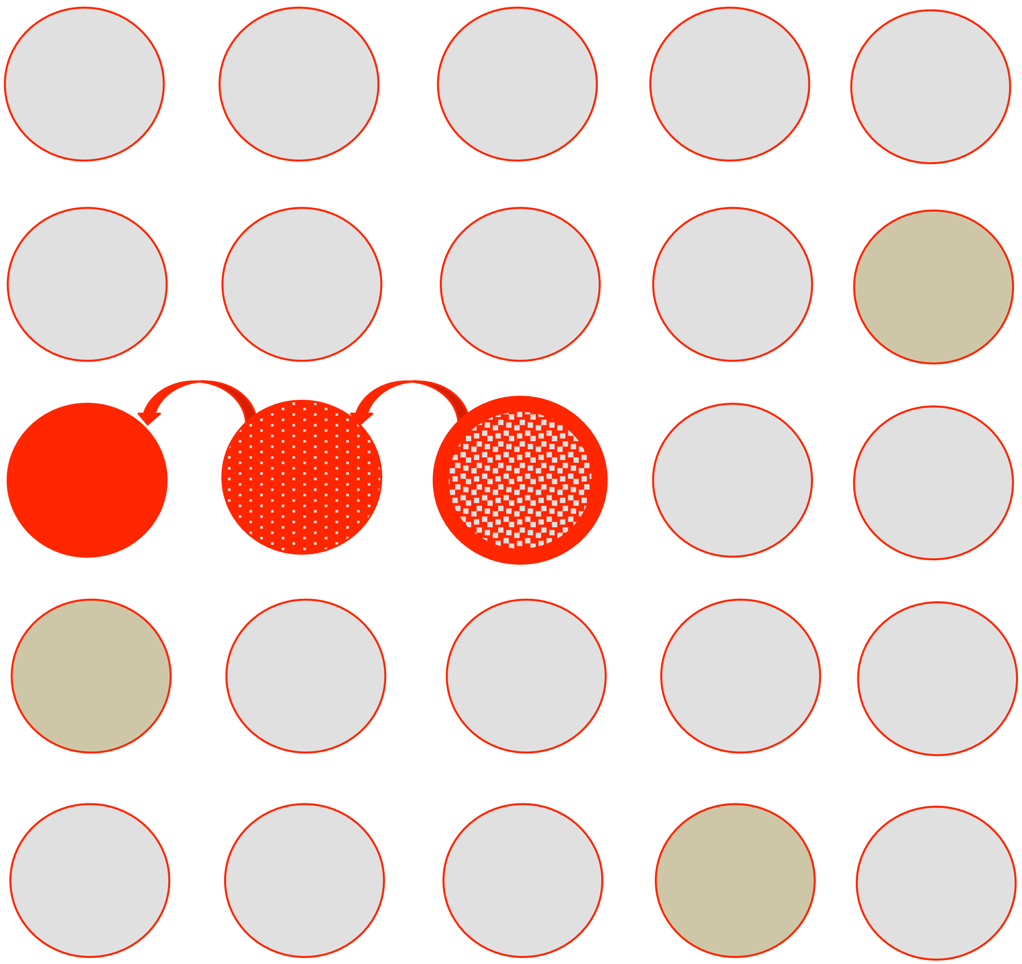
Rationale



Wild Populations, Domestication Centre, Demic Diffusion

Phylogeographic Expectations

Rationale



Wild Populations, Domestication Centre, Demic Diffusion

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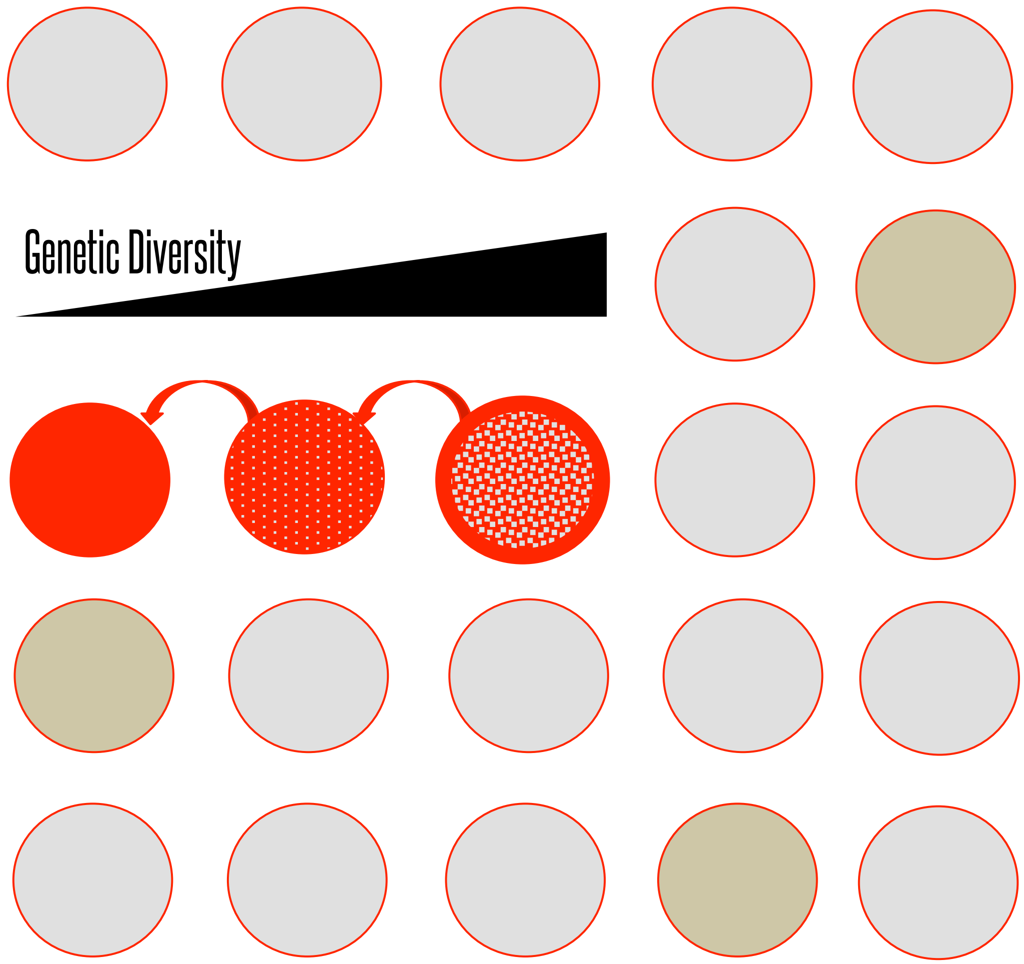

Wild Populations, Domestication Centre, Demic Diffusion

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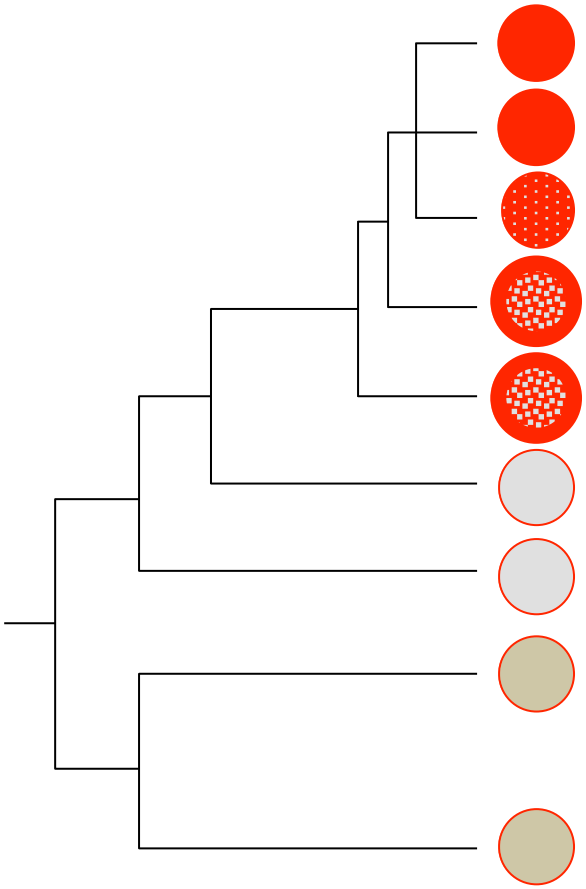
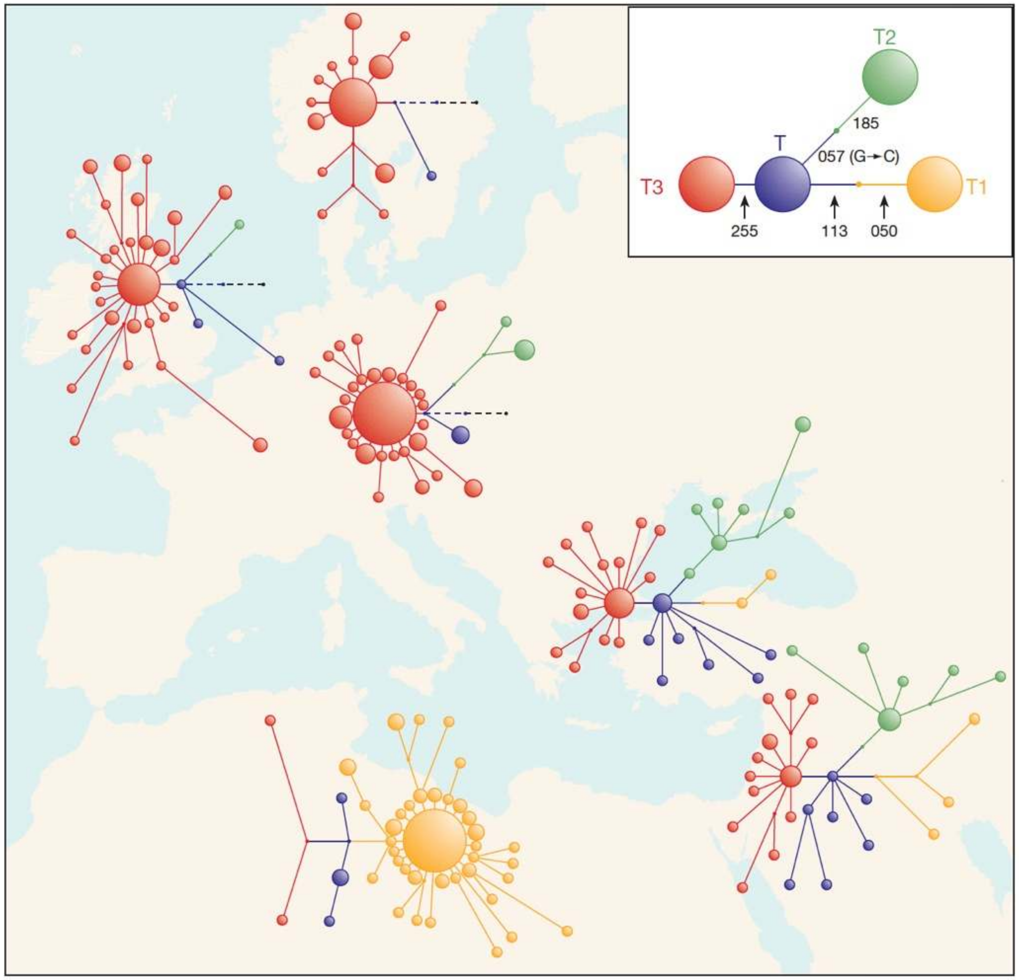
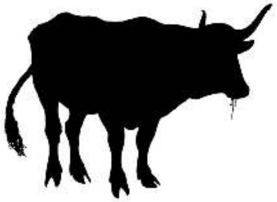


Phylogeographic Expectations

Example: European Taurine Cattle (240 bp, mtDNA Control Region)

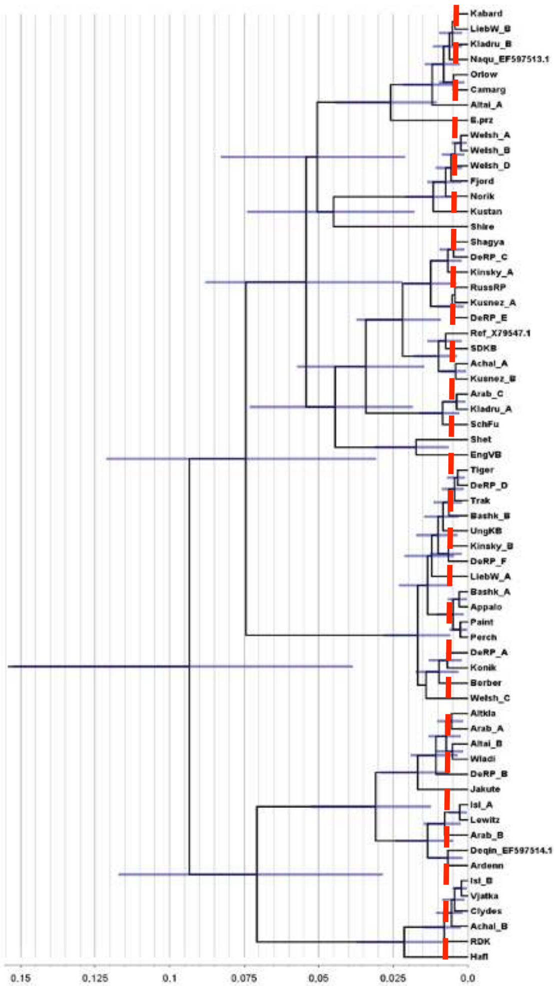




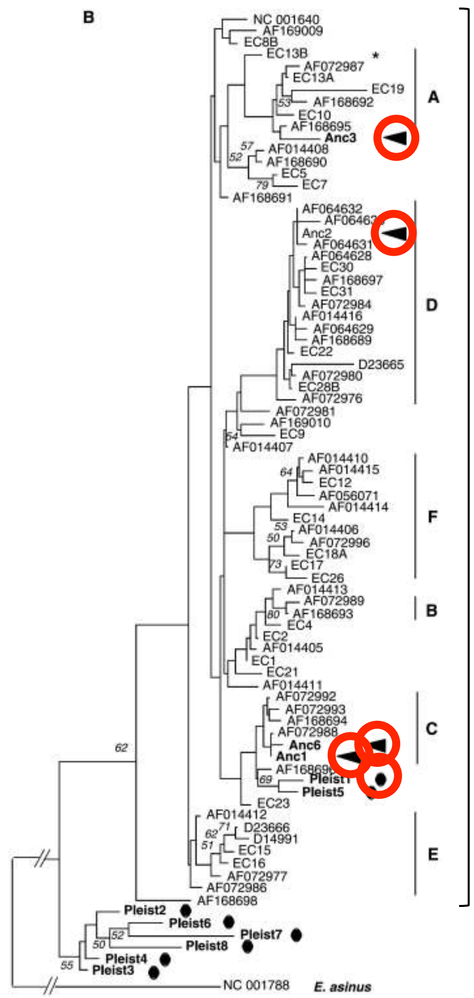
Troy et al. Nature 2001

Mitochondrial DNA

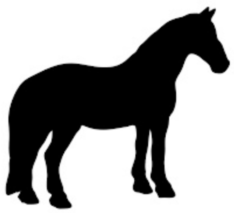
Median-Joining Networks & Neighbor-Joining Tree (355bp)



Lippold et al. BMC Evol Biol 2011

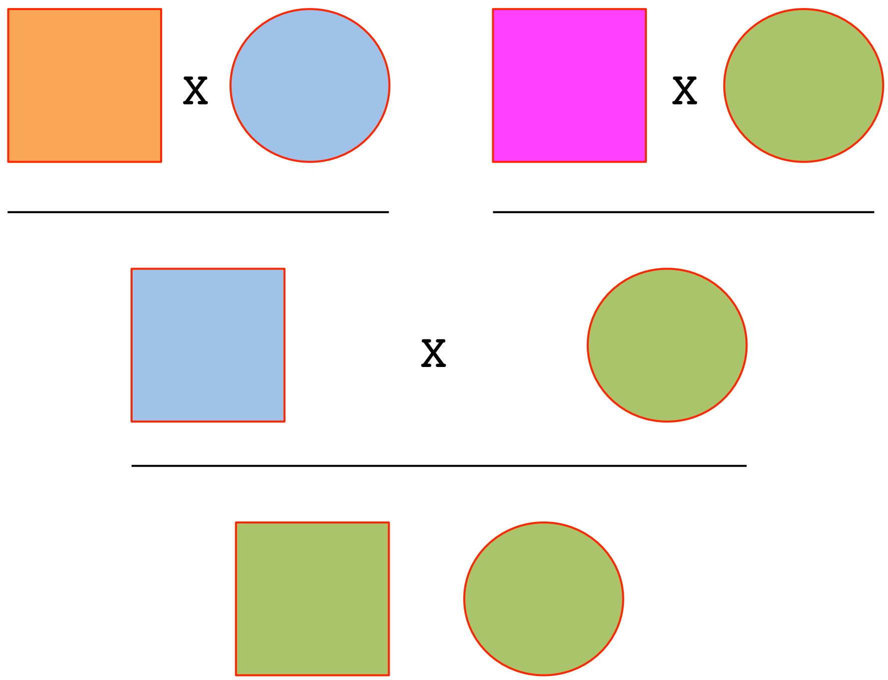


Vila et al. Science 2001



Mitochondrial DNA

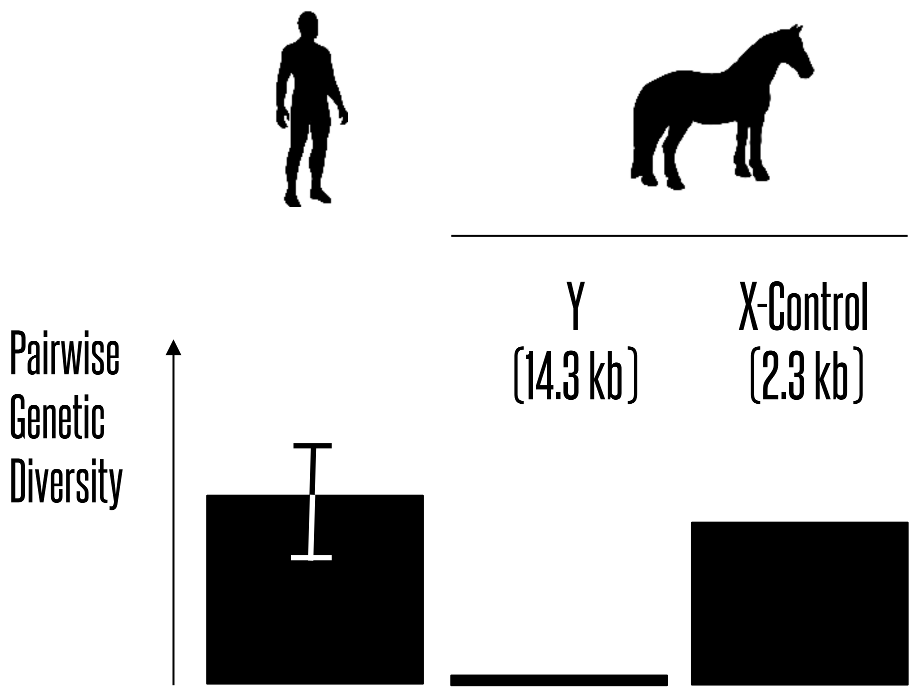
Maternal Heredity



Lots Of Mares Must Have Been Involved In The Domestication Process
Which Also Involved Substantial Restocking From The Wild

Paternal Lineages

Y-Chromosome (52 Stallions, 15 breeds)



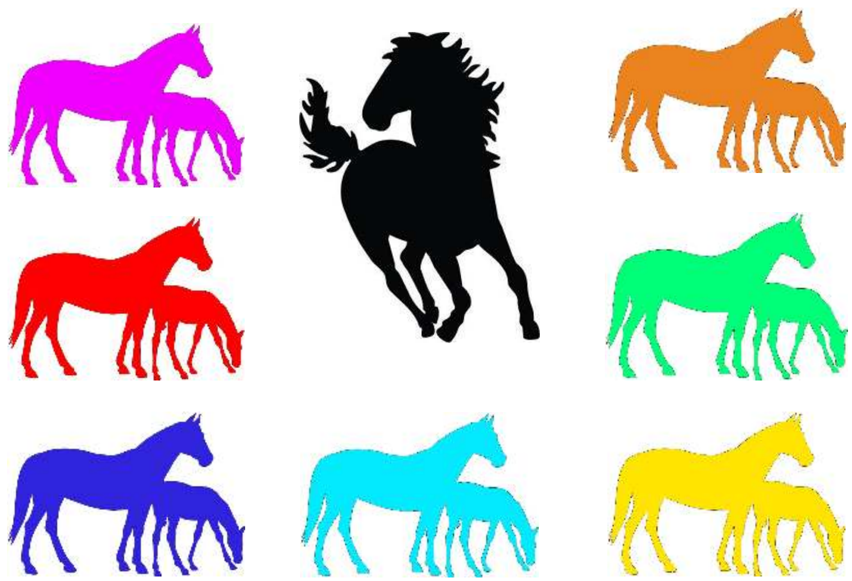
Ardennais,
Connemara,
Exmoor,
Fjord,
Gotland,
Icelandic,
Shetland,
North-Swedish,
Thoroughbred

Akhal Teké,
Arab,
Caspian Pony,
Khuzestan Arab,
Malwari,
Thai Pony

Lindgren et al. Nat Genet 2004

Horse Domestication Model

N Mares, ~1 Stallion



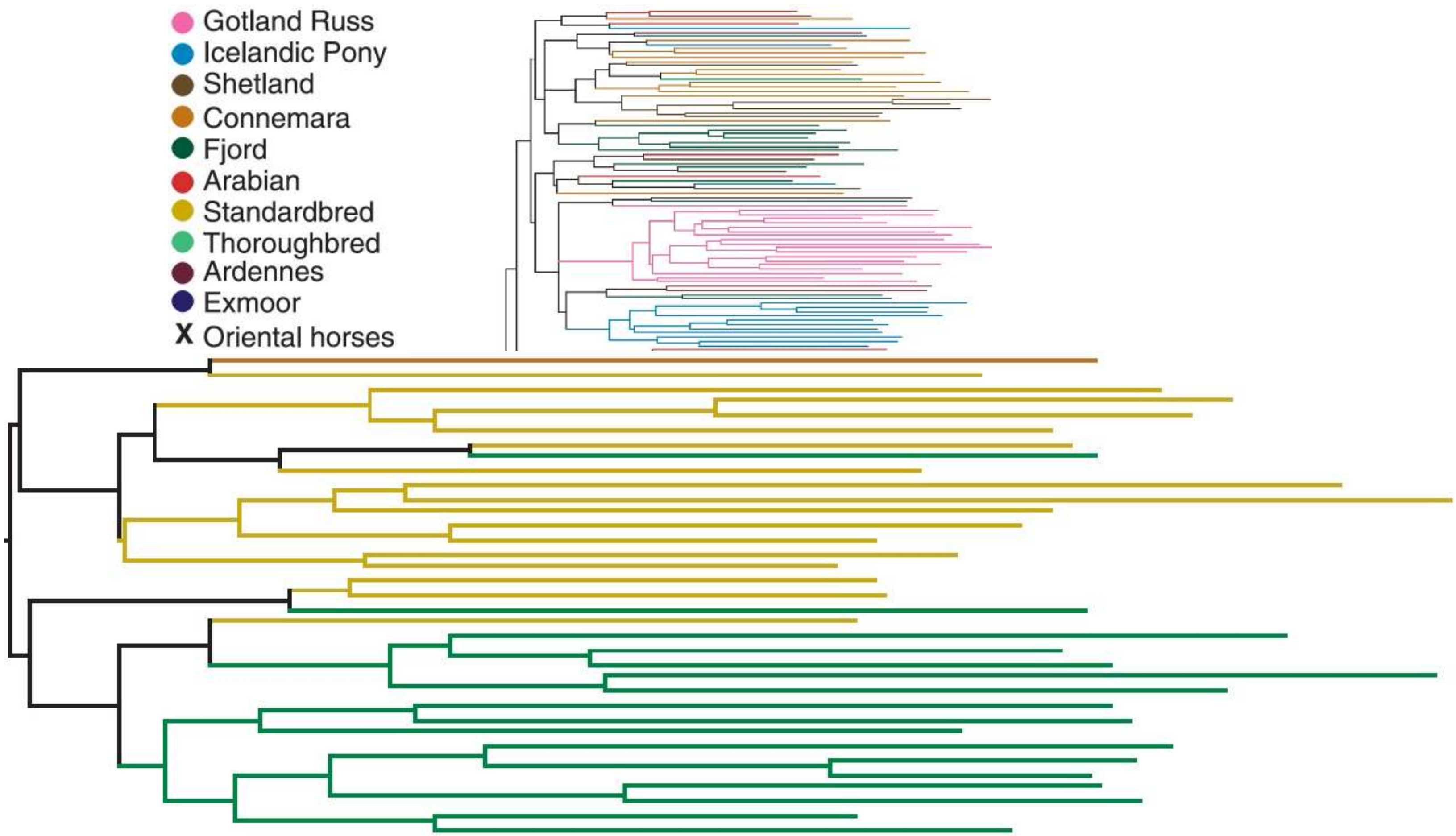
Microsatellites

Neighbor-Joining Tree (%Allele-Sharing in 10 Breeds)

Vila et al. Science 2001

Microsatellites

Neighbor-Joining Tree (%Allele-Sharing in 10 Breeds)

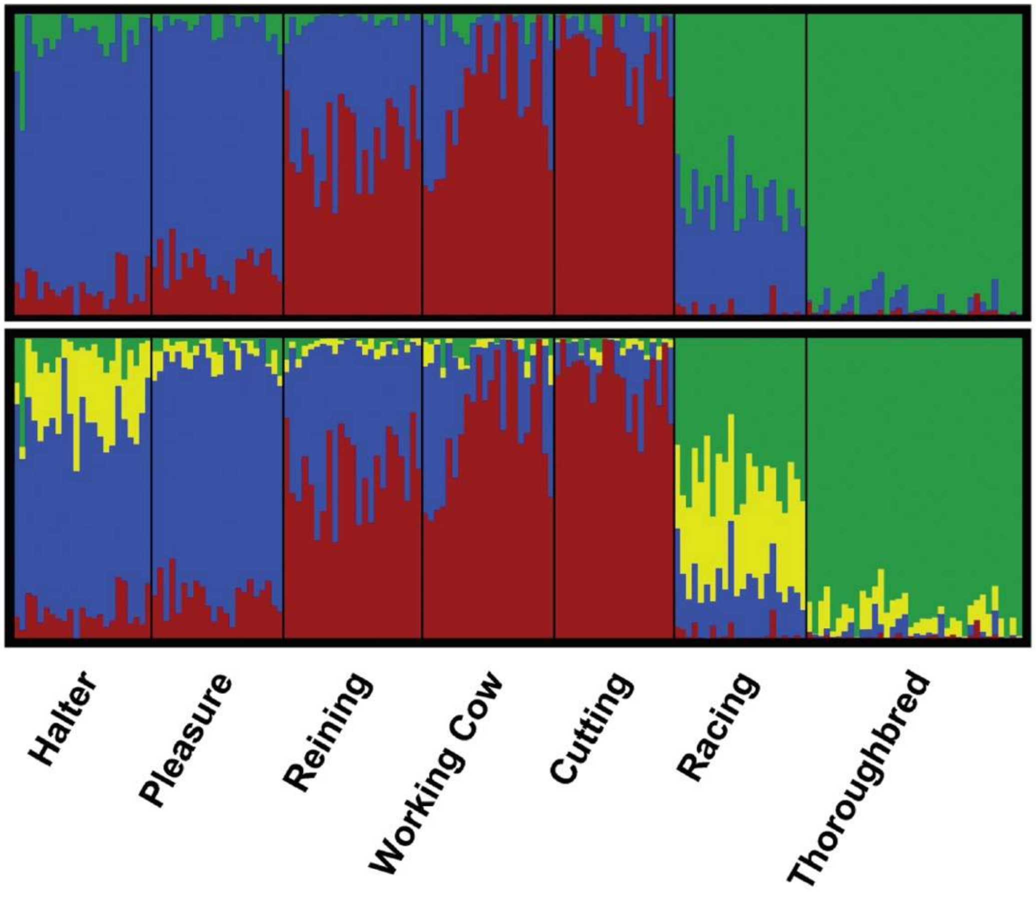


Vila et al. Science 2001

Single Nucleotide Polymorphisms

Revealing Breeding Management

American Standardbred Horses



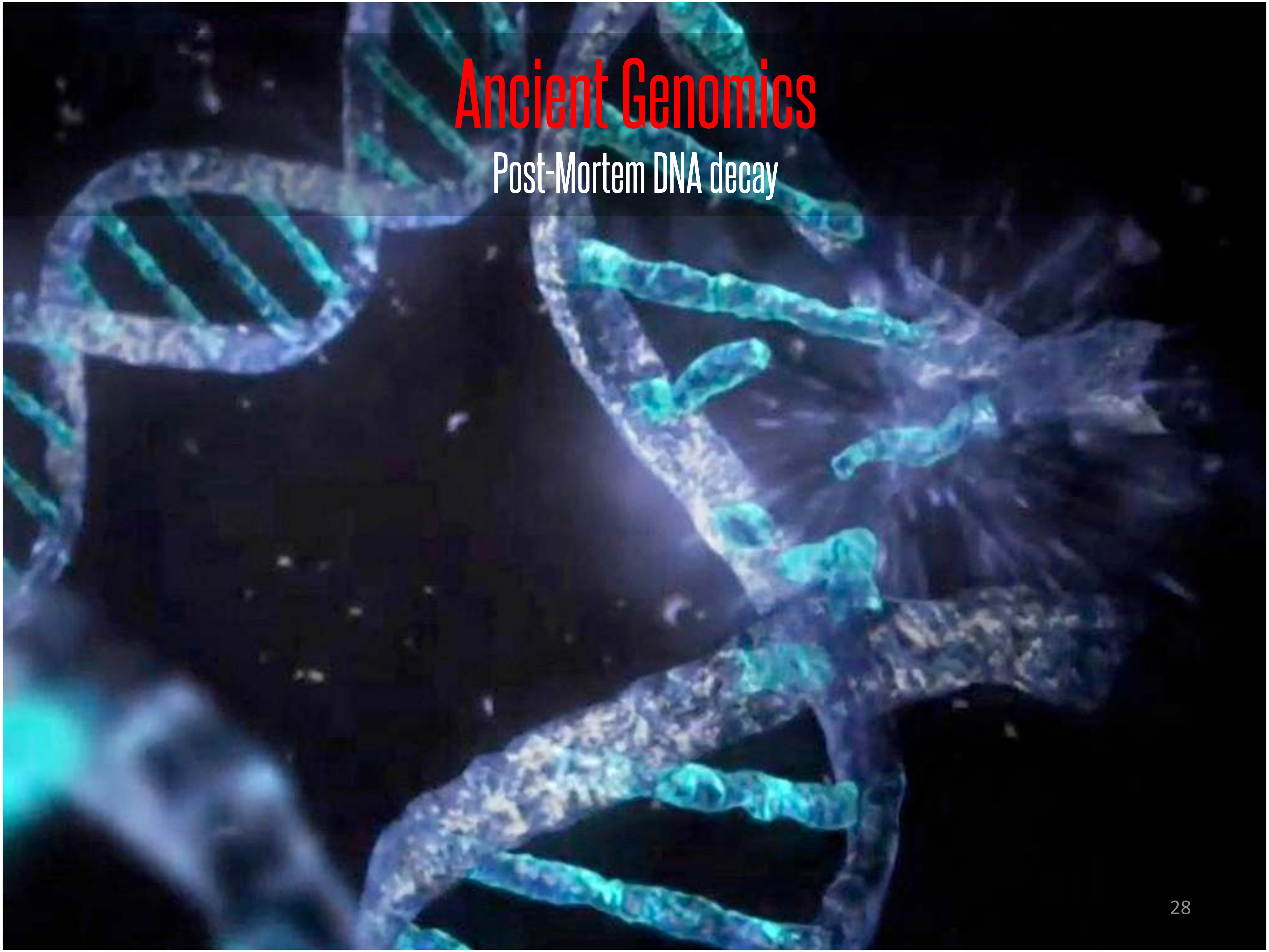
Petersen et al. J Hered 2014

What Can We Learn About Early Domestication From Modern DNA?

Not Much!

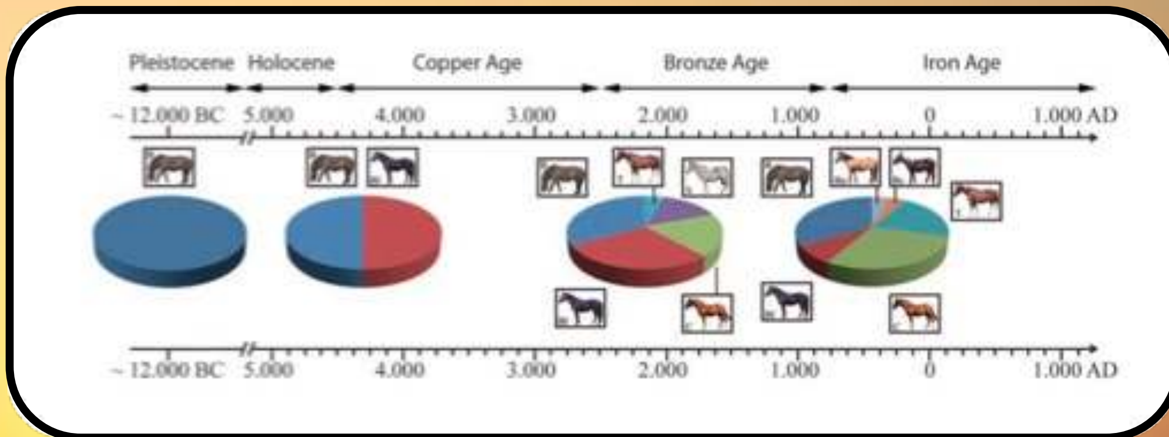
Ancient Genomics

Post-Mortem DNA decay



Coat Color Genes

Ancient DNA: Candidate Marker Genotyping

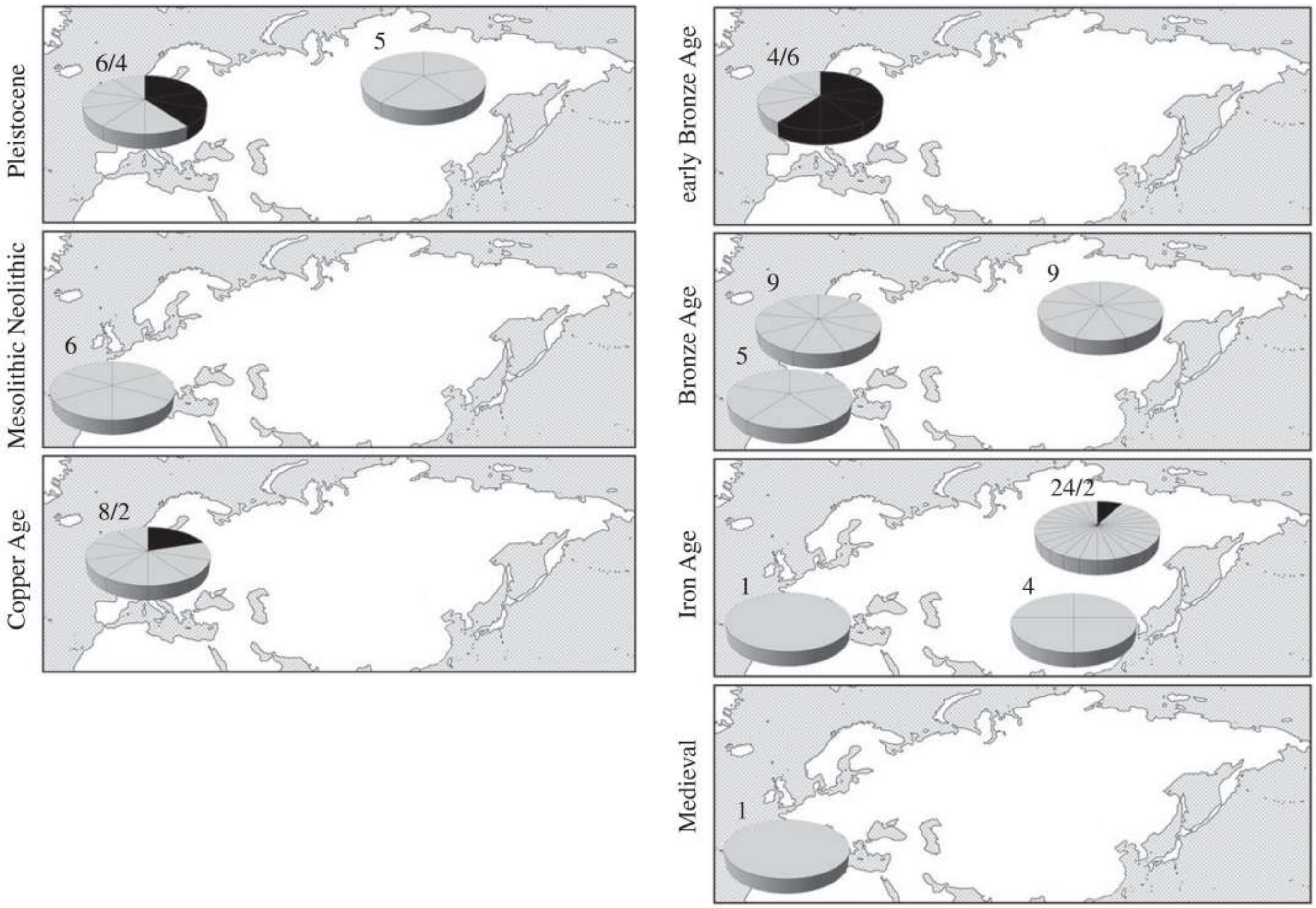


From Ludwig et al. Science 2009

ASIP, MC1R genes

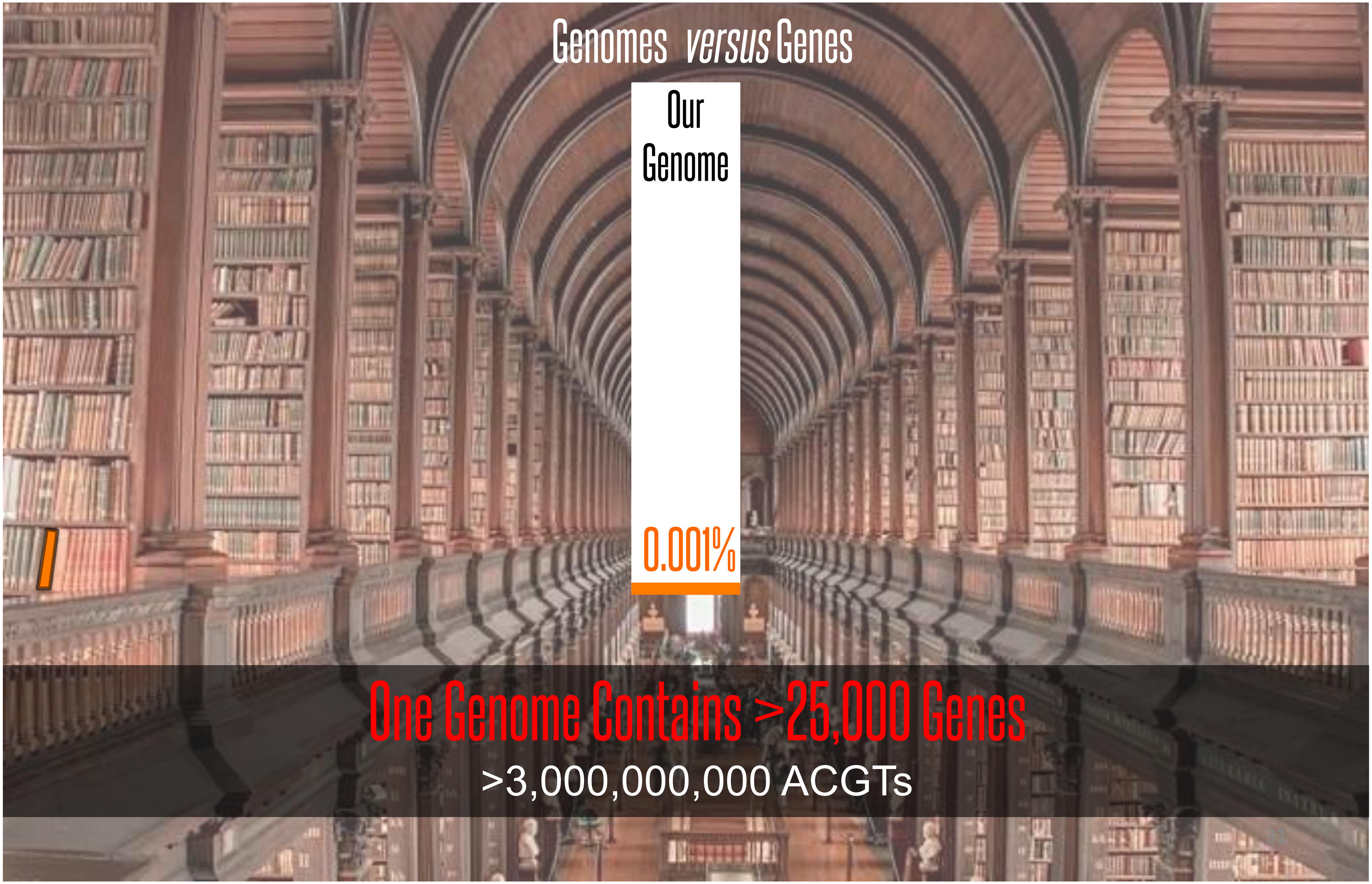
Coat Color Diversity

Spotted Horses (TRPM1) Through Space and Time



From Ludwig et al. Proc Roy Soc B 2015

Ancient DNA


Genomes *versus* Genes
Our Genome
0.001%
One Genome Contains >25,000 Genes
>3,000,000,000 ACGTs

Why Do We Need Genomes?

Many Additional Traits Have Been Selected


Gait


Speed/Endurance


Size/Color


Temper

Etc...

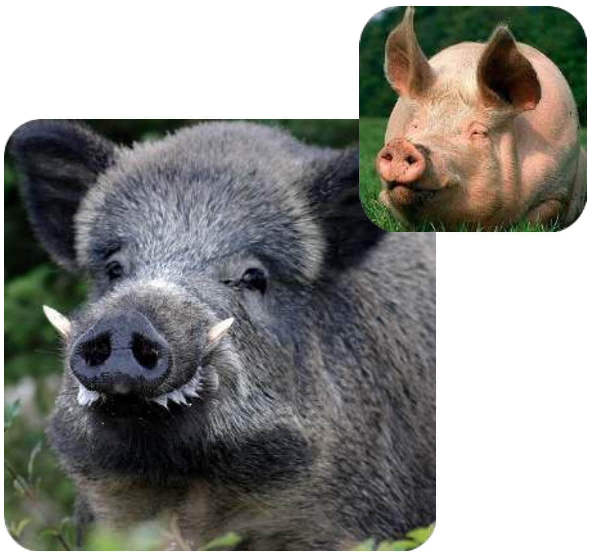
Historical Genomes

Late Pleistocene Genomes

Holocene Genomes

The Genomics Of Domestication

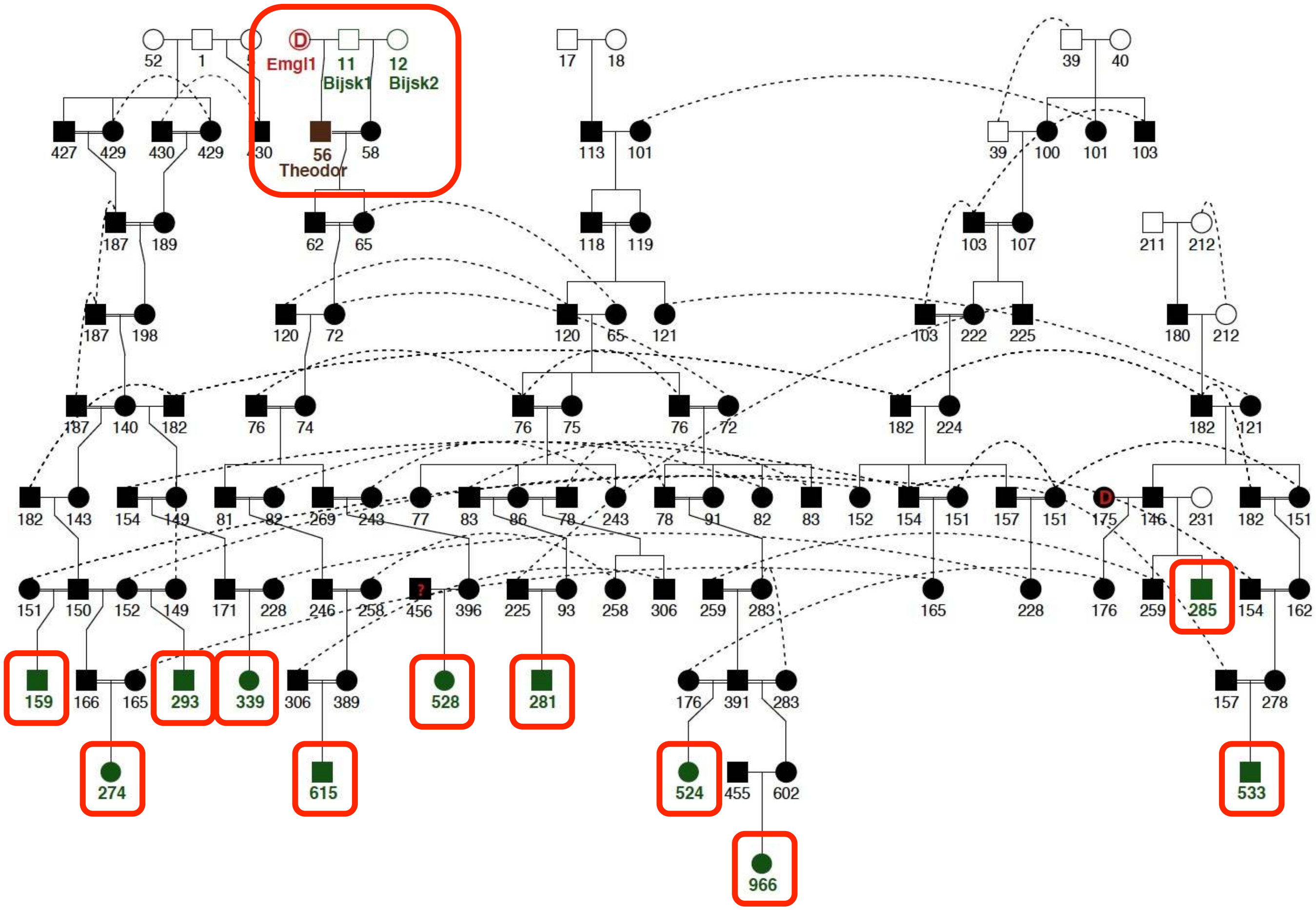
Comparing Genomes of Wild Animals and Domesticates




Der Sarkissian et al. Curr Biol 2015

Conservation/Comparative Genomics

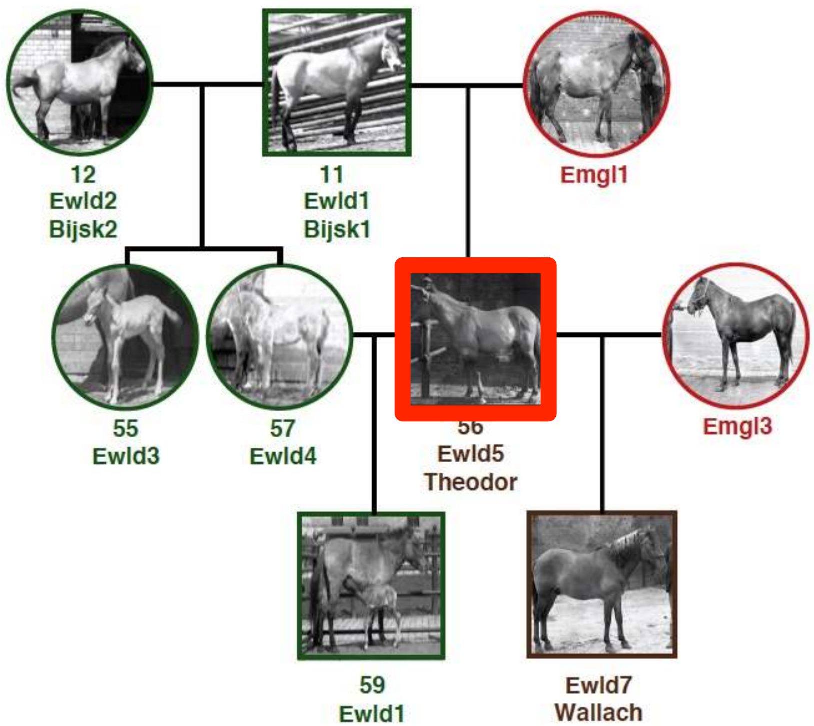
Extant Przewalski's horses



- Representing all founding lineages
- F1 Przewalski x Mongolian hybrid

Conservation Museomics

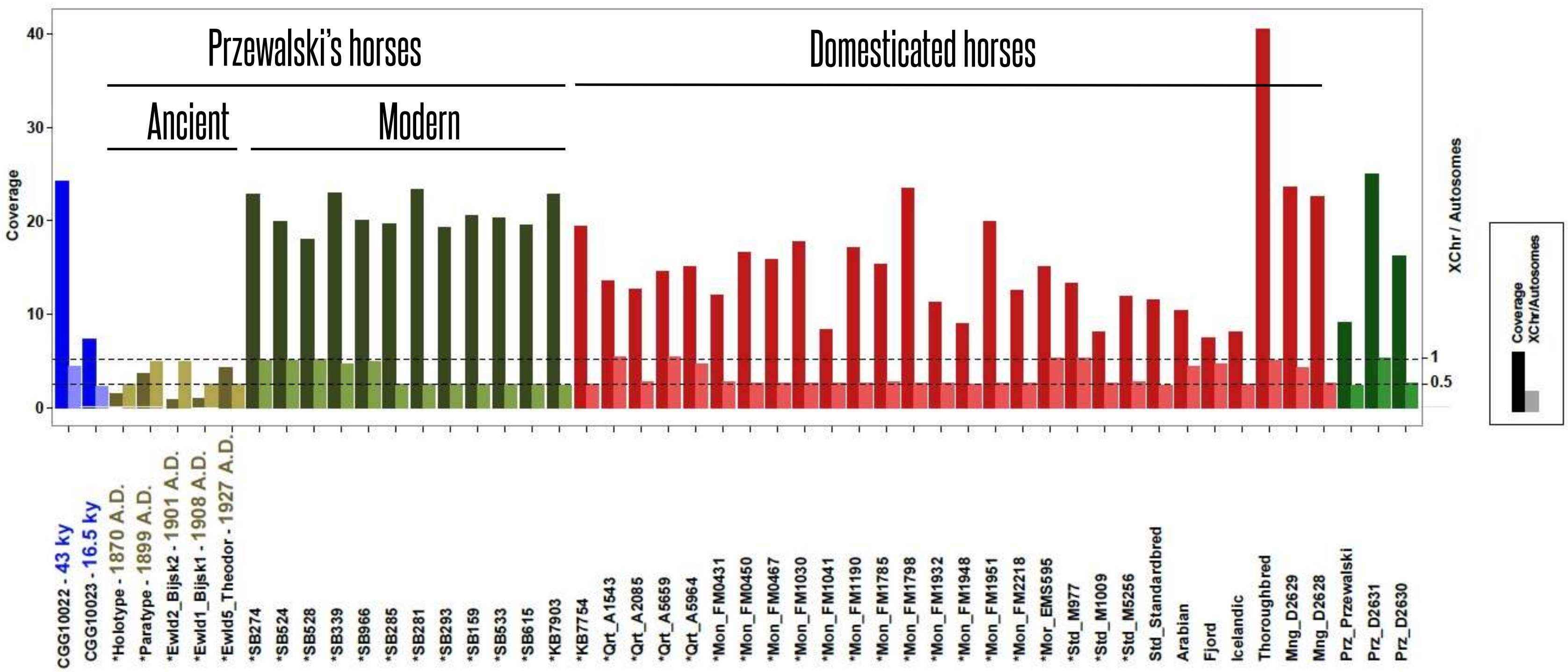
Ancient Founders of Captive Przewalski's horses – early 1900s



Putative F1 Mongolian x Przewalski's hybrids
19th Century AD Holotype & Paratype

Conservation Museomics

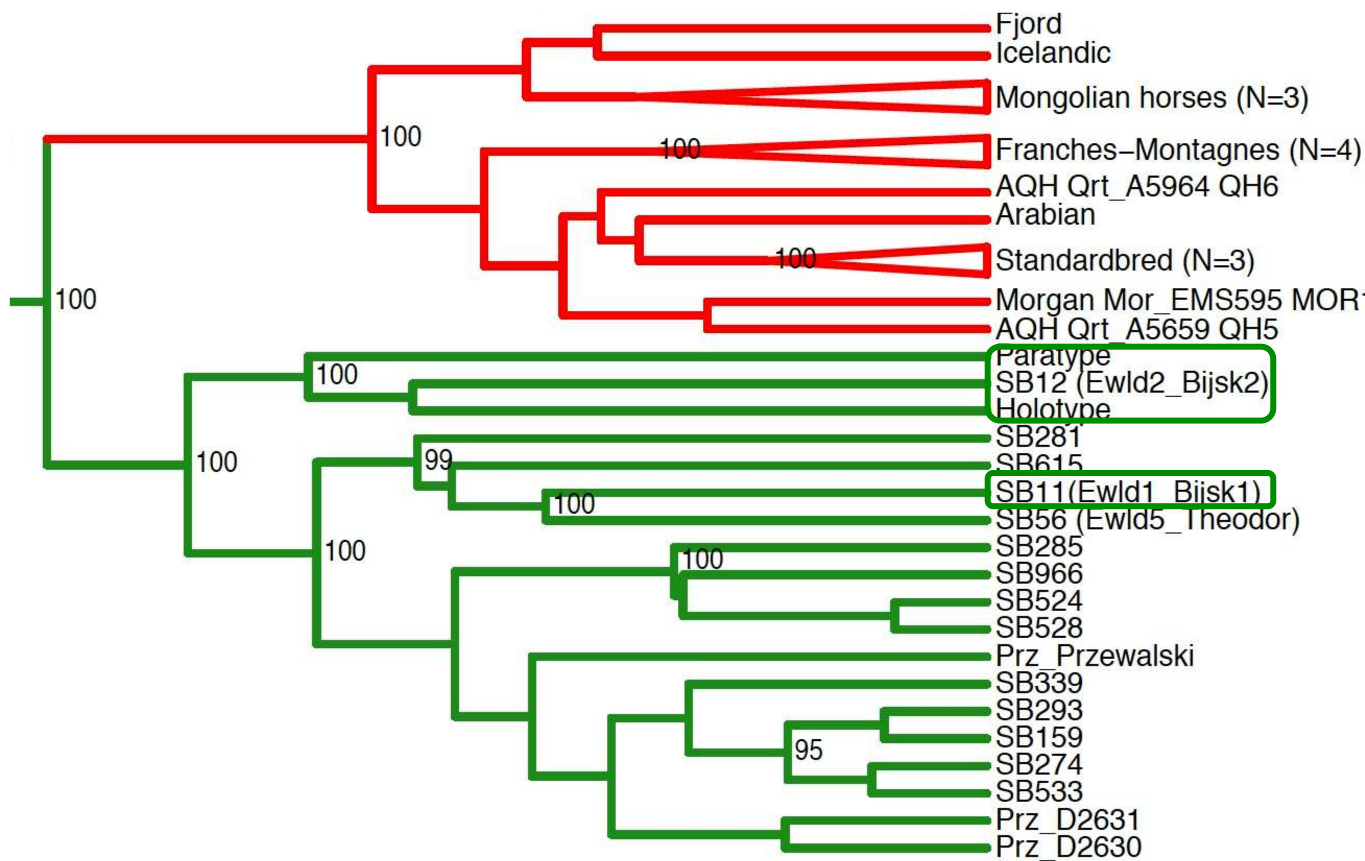
Overall Genome Dataset



- 5 Historical and 15 Modern Przewalski's horses
- 1 F1 Przewalski's x Domestic hybrid
- 28 Modern Domesticated horses

Conservation/Comparative Genomics

Quantifying The Effects of Captivity

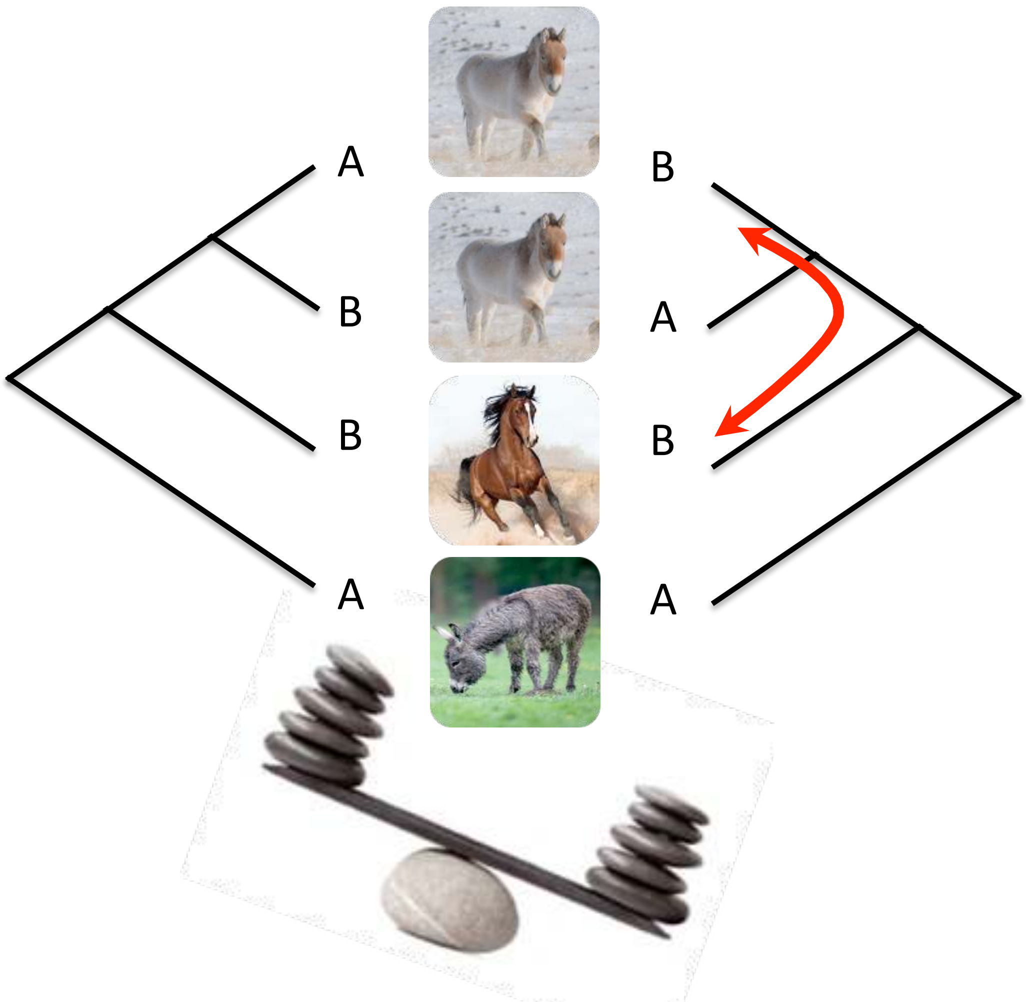


Loss of Phylogenetic Lineages

Comparative Museomics

Wild vs. Domesticates

D-Statistics



Comparative Genomics

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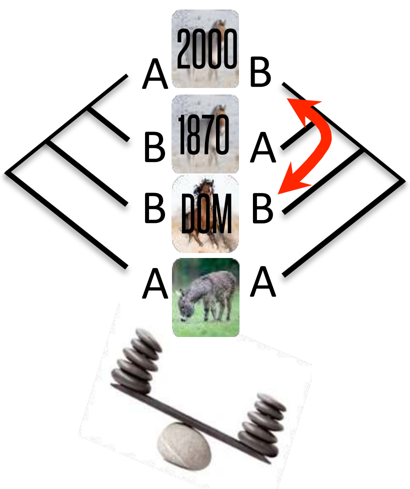
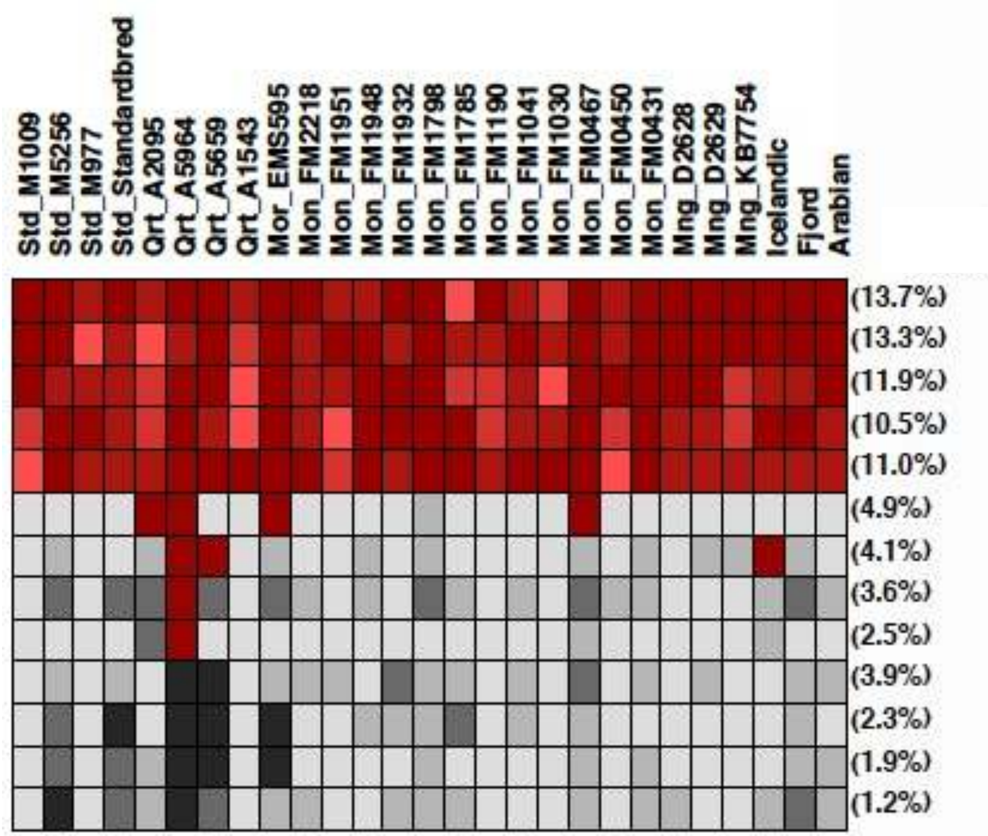
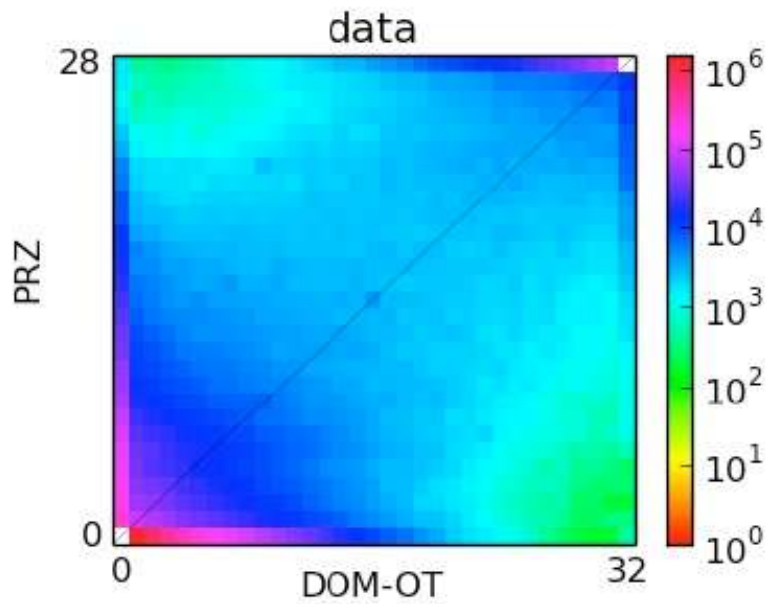


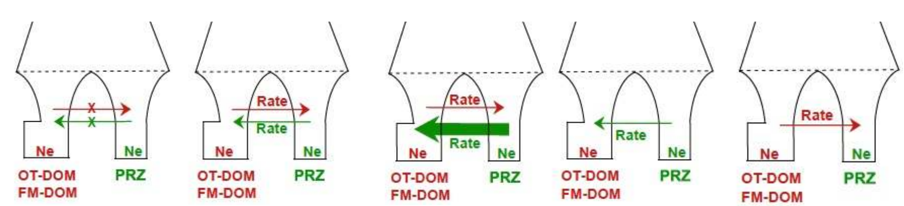


Evolutionary Genomics

Population Model

SFS-based δaδi Reconstructions





Evolutionary Genomics

Population Model

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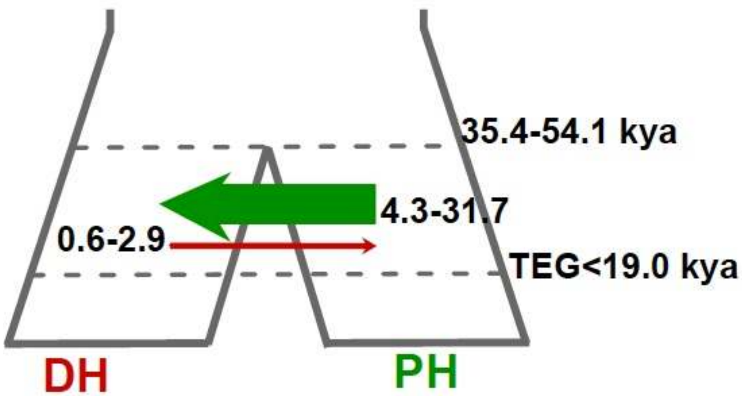
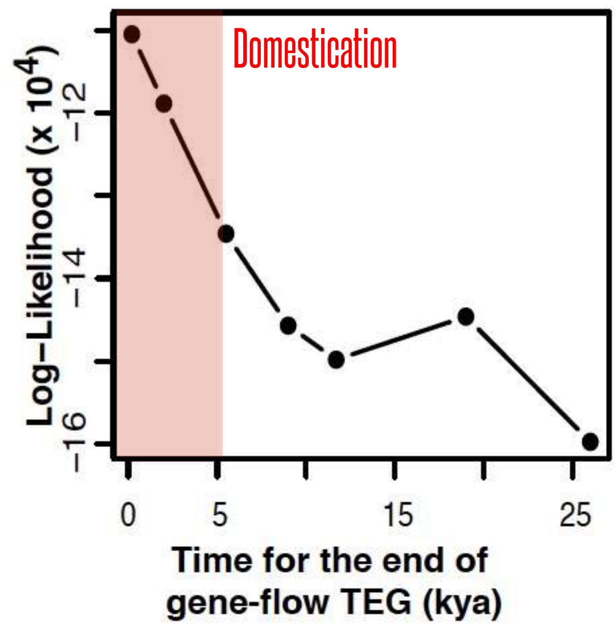
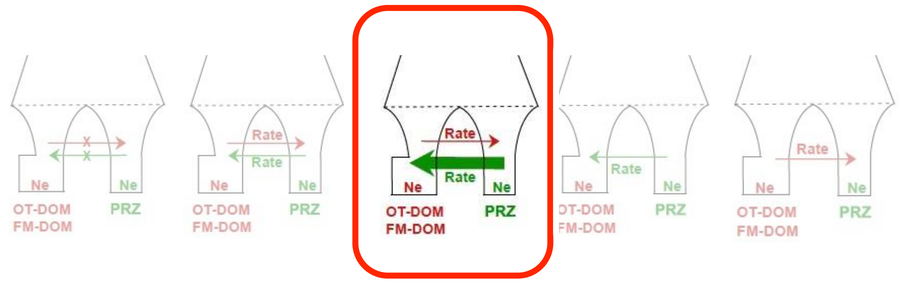


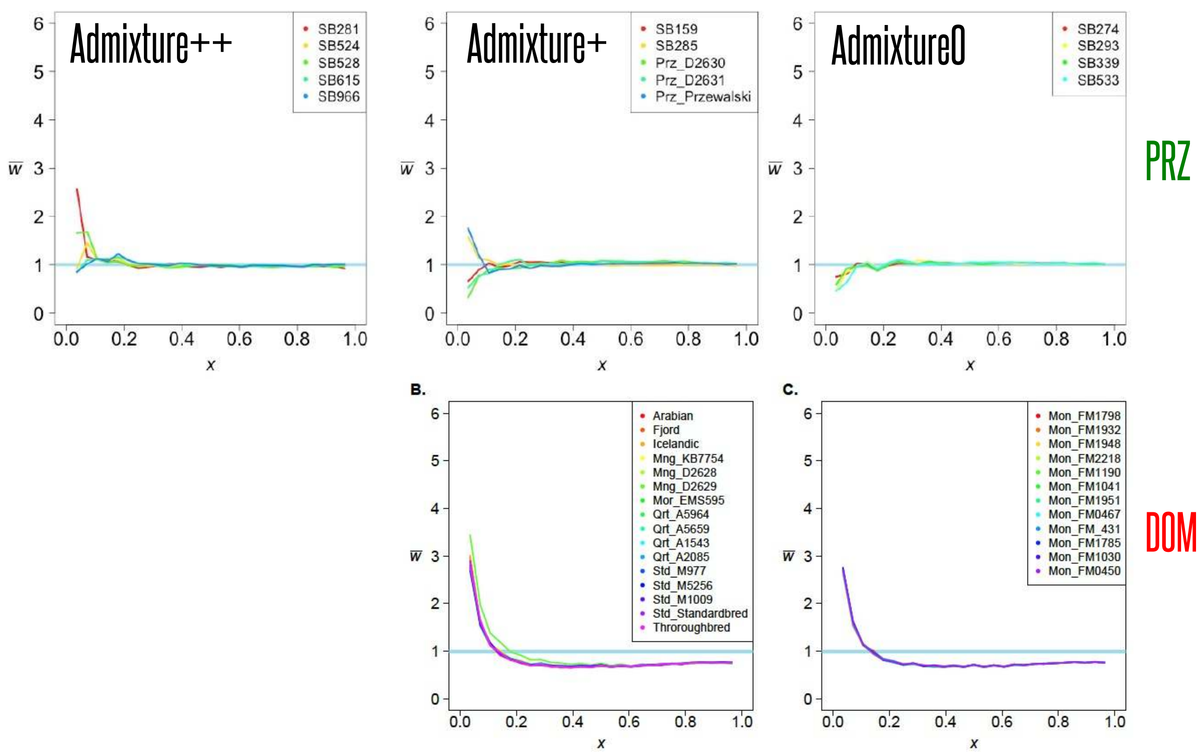




Evolutionary Genomics

Population Model

Genome Projections on Our Przewalski's horse Genome Panel

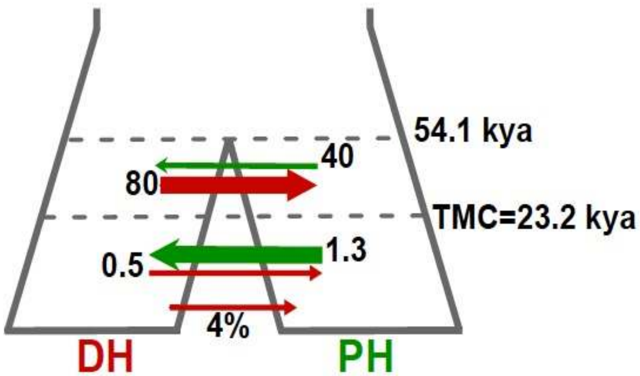


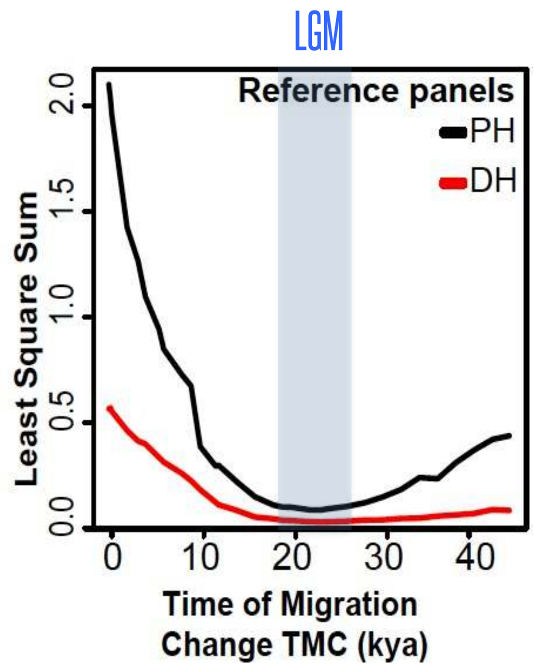
Categories of Derived Allele Frequencies

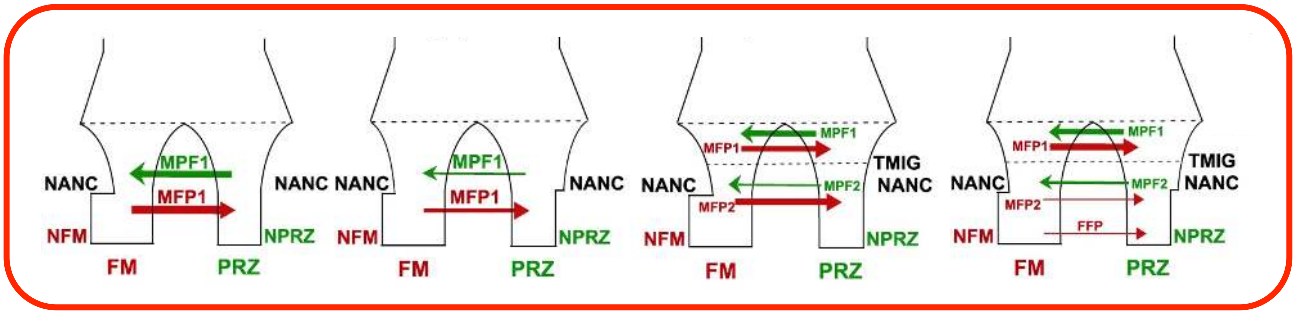
Evolutionary Genomics

Population Model

Genome Projections



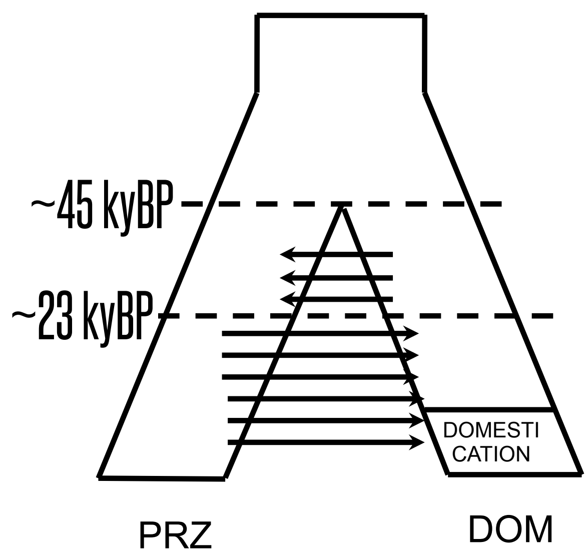




The Genomics of Horse Domestication

Summary 1

- Horse domestication involved significant restocking from the wild
- Przewalski's horses are NOT the ancestors of domesticated horses
- Understanding horse domestication, thus, requires temporal data



Der Sarkissian et al. Curr Biol 2015

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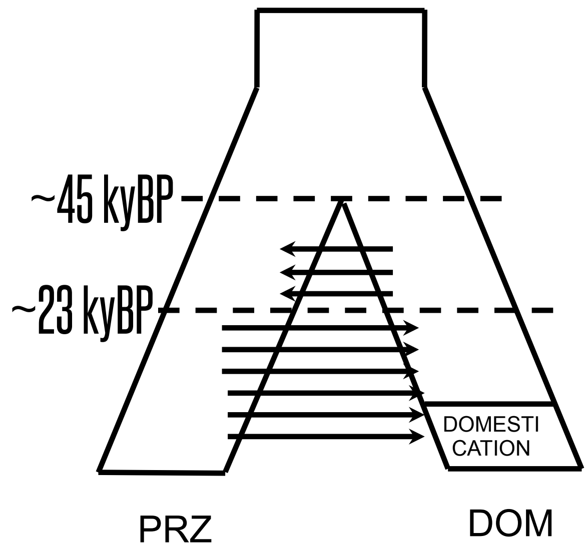


Der Sarkissian et al. Curr Biol 2015

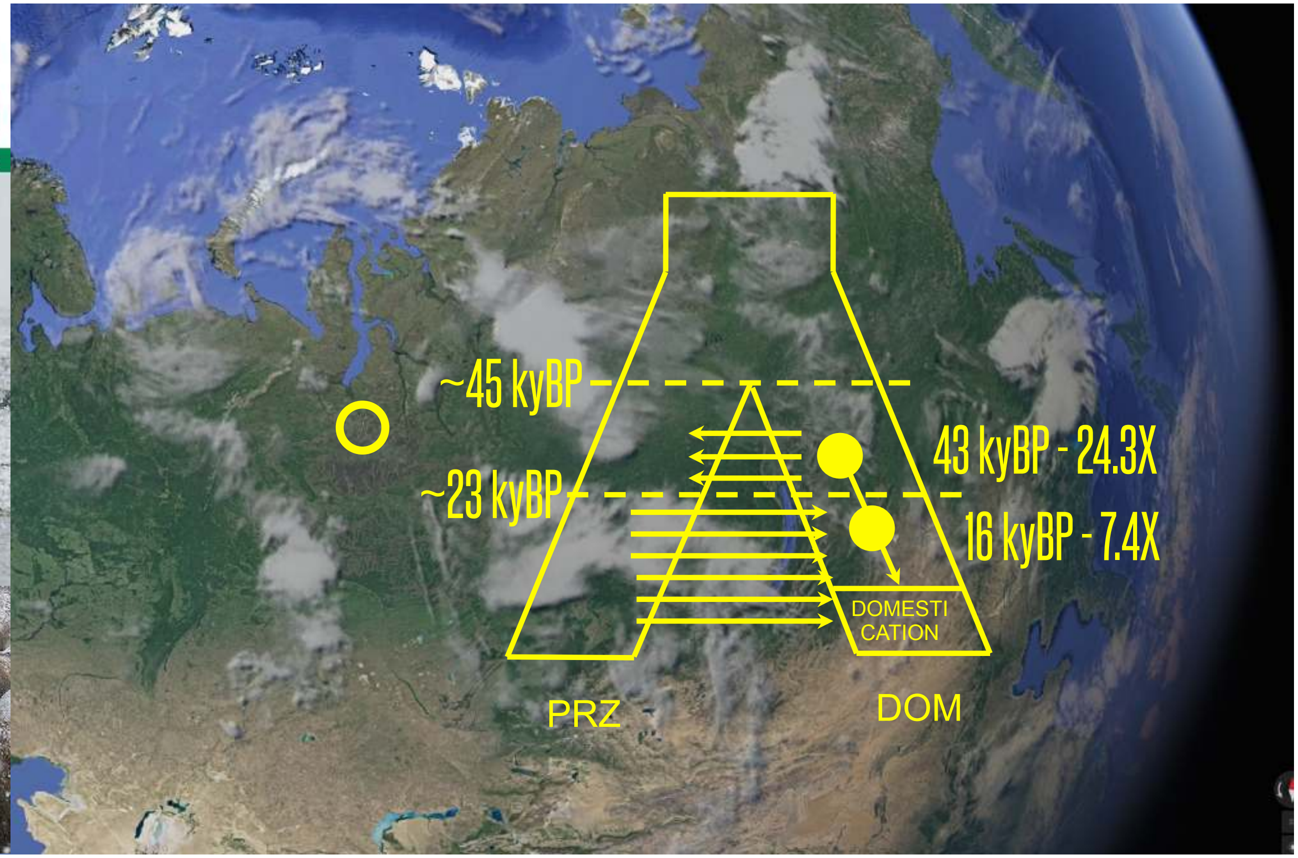
Historical Genomes

Late Pleistocene Genomes

Holocene Genomes

Sequencing Ancient Horse Genomes

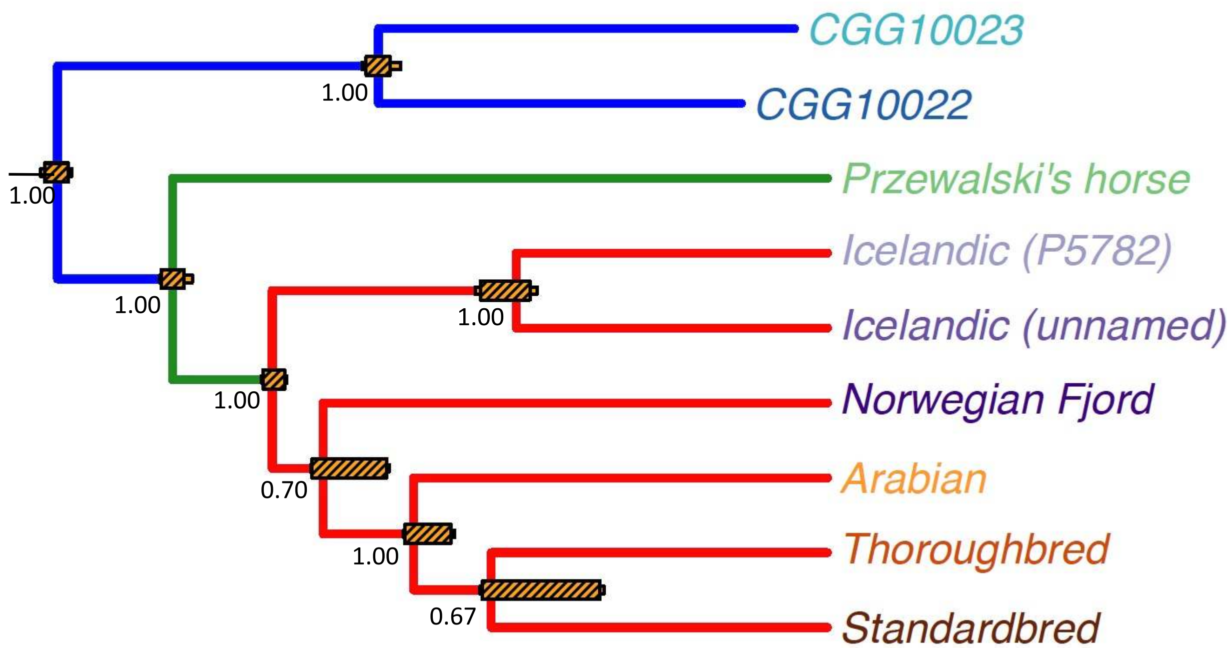
Overall Approach



Schubert et al. PNAS 2014

The Population Model Underlying Domestication

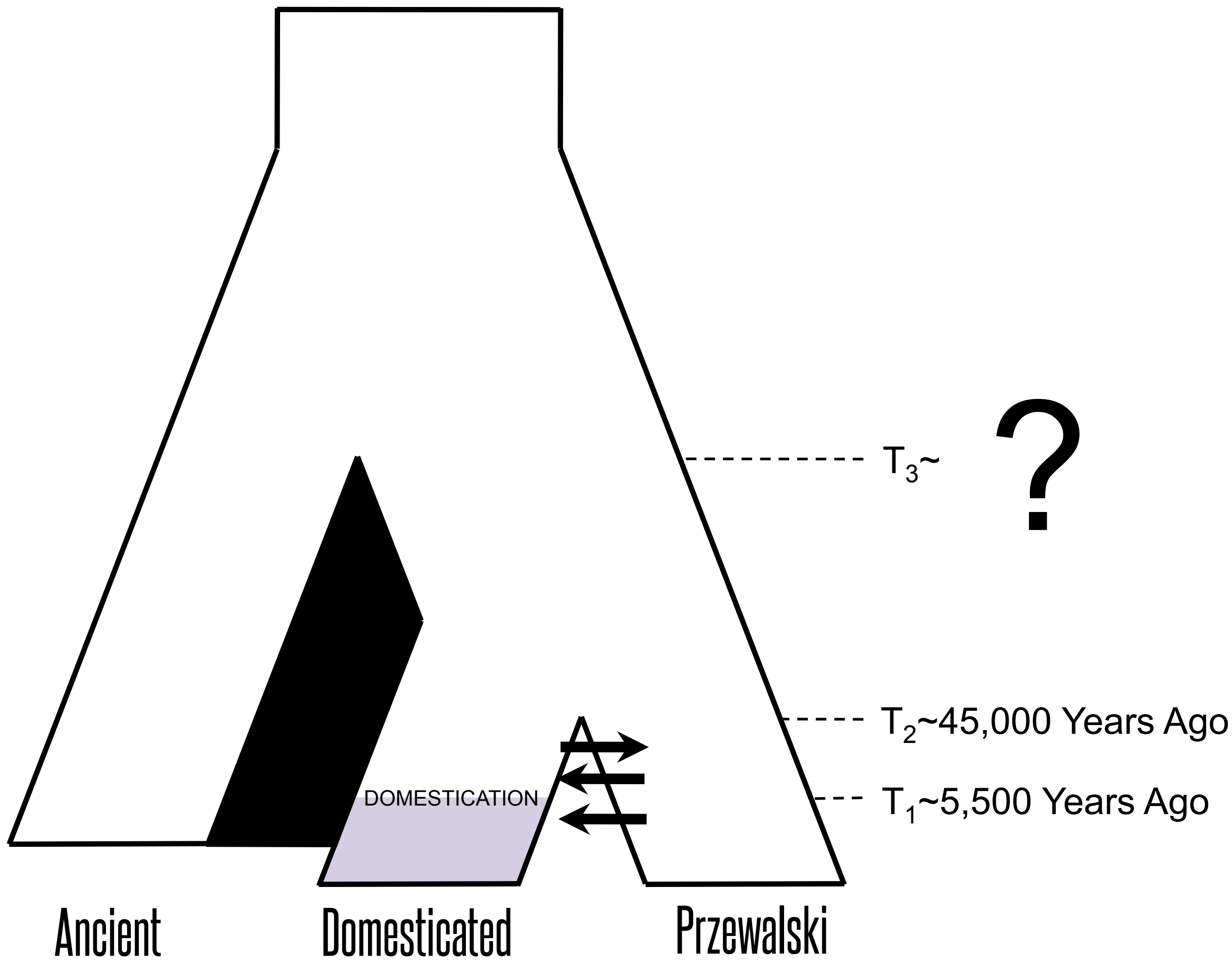
Phylogenetic Relationships



Whole-Exome ML-tree (20,374 Genes, each Partitionned as $1^{st}+2^{nd}$, 3rd)
TreeMix (2,686,345 SNPs)

The Population Model Underlying Domestication

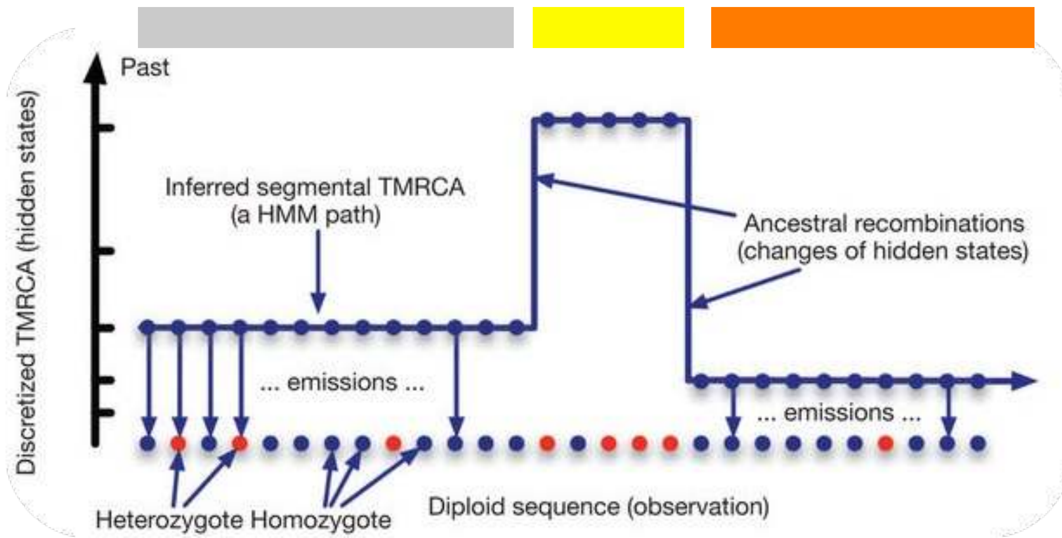
Population Admixture



The Population Model Underlying Domestication

Dating Population Splits through Demographic Trajectories

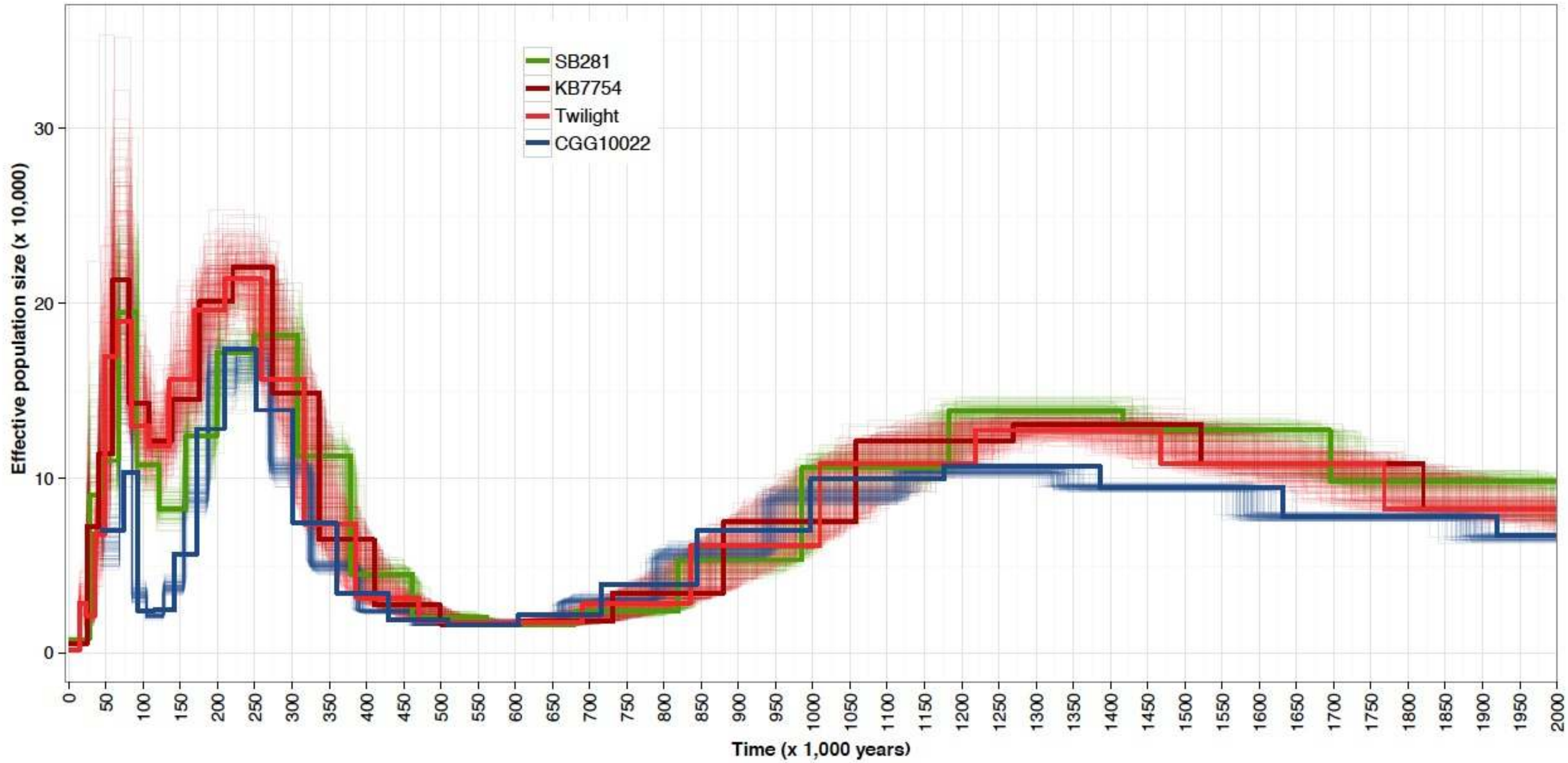
$H_{e,1} \sim Ne_1$ $H_{e,2} \sim Ne_2$ $H_{e,3} \sim Ne_3$



<u>P</u>airwise <u>S</u>equential <u>M</u>arkov <u>C</u>oalescent
From Li & Durbin Nature 2011

The Population Model Underlying Domestication

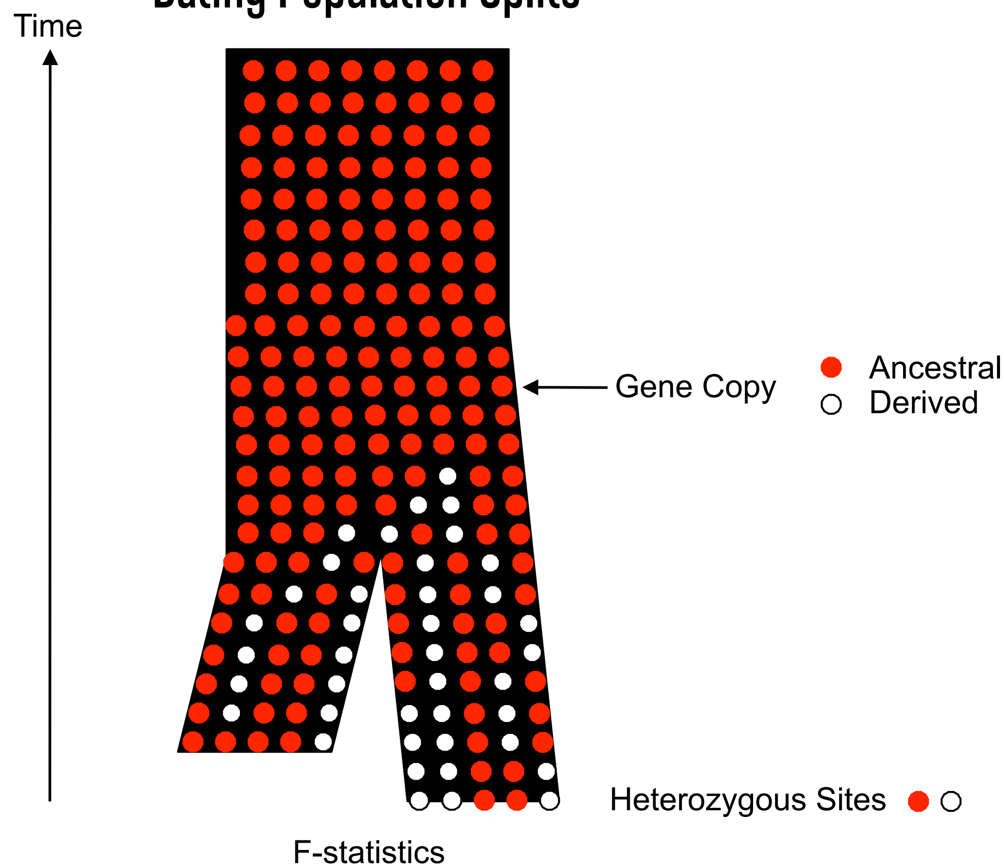
Dating Population Splits



PSMC Demographic Profile

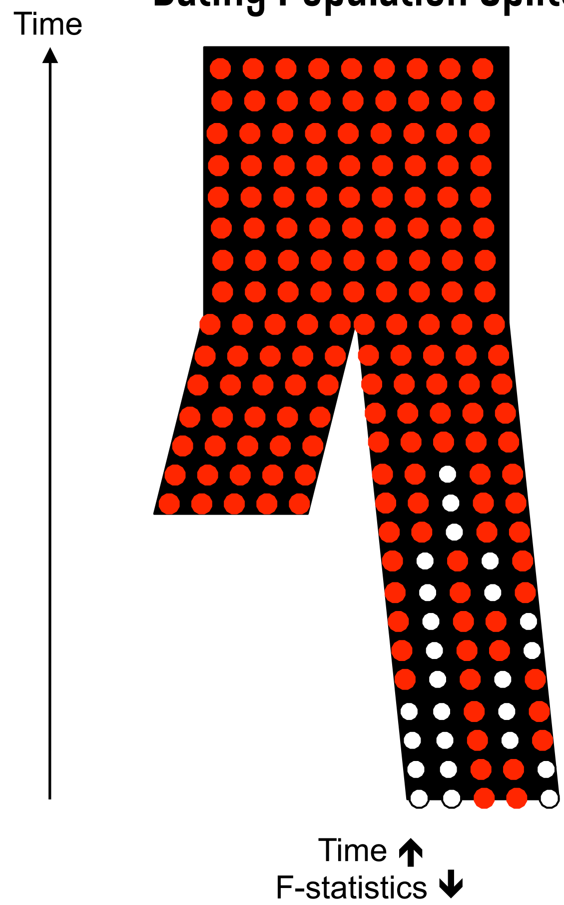
The Population Model Underlying Domestication

Dating Population Splits



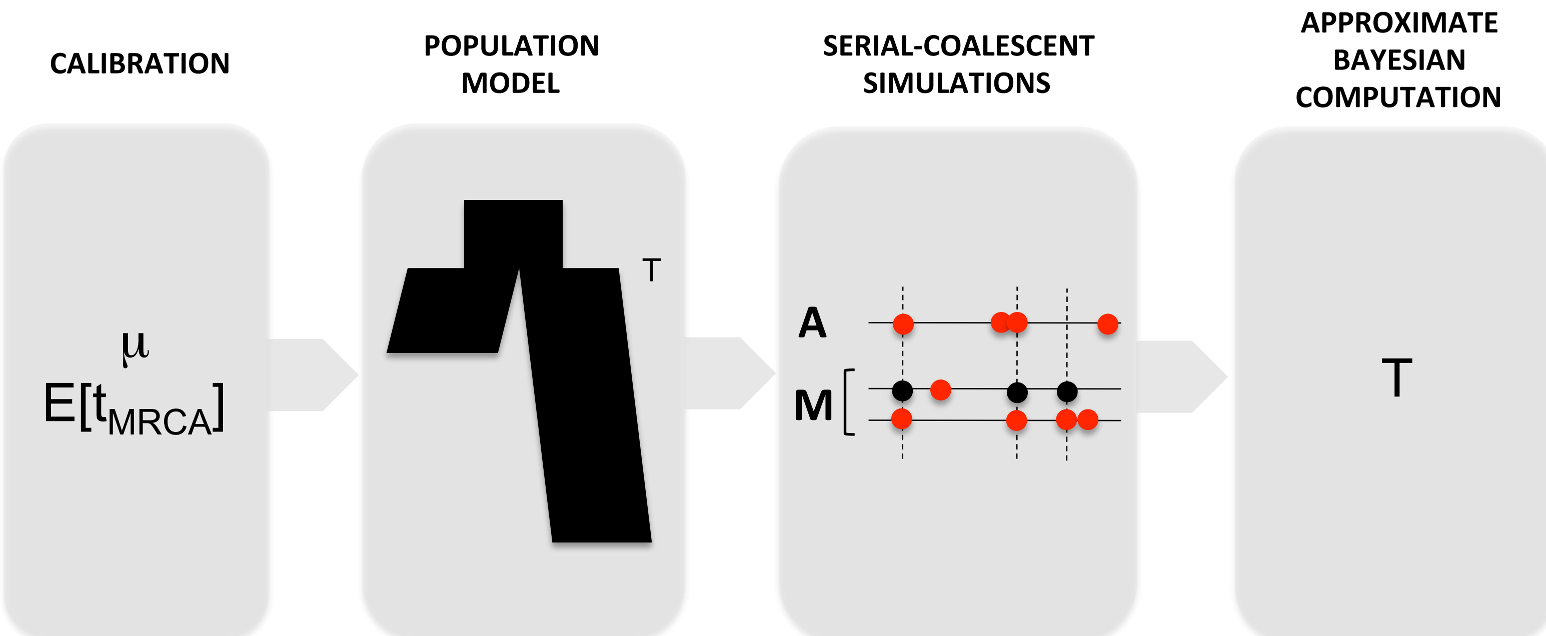
The Population Model Underlying Domestication

Dating Population Splits



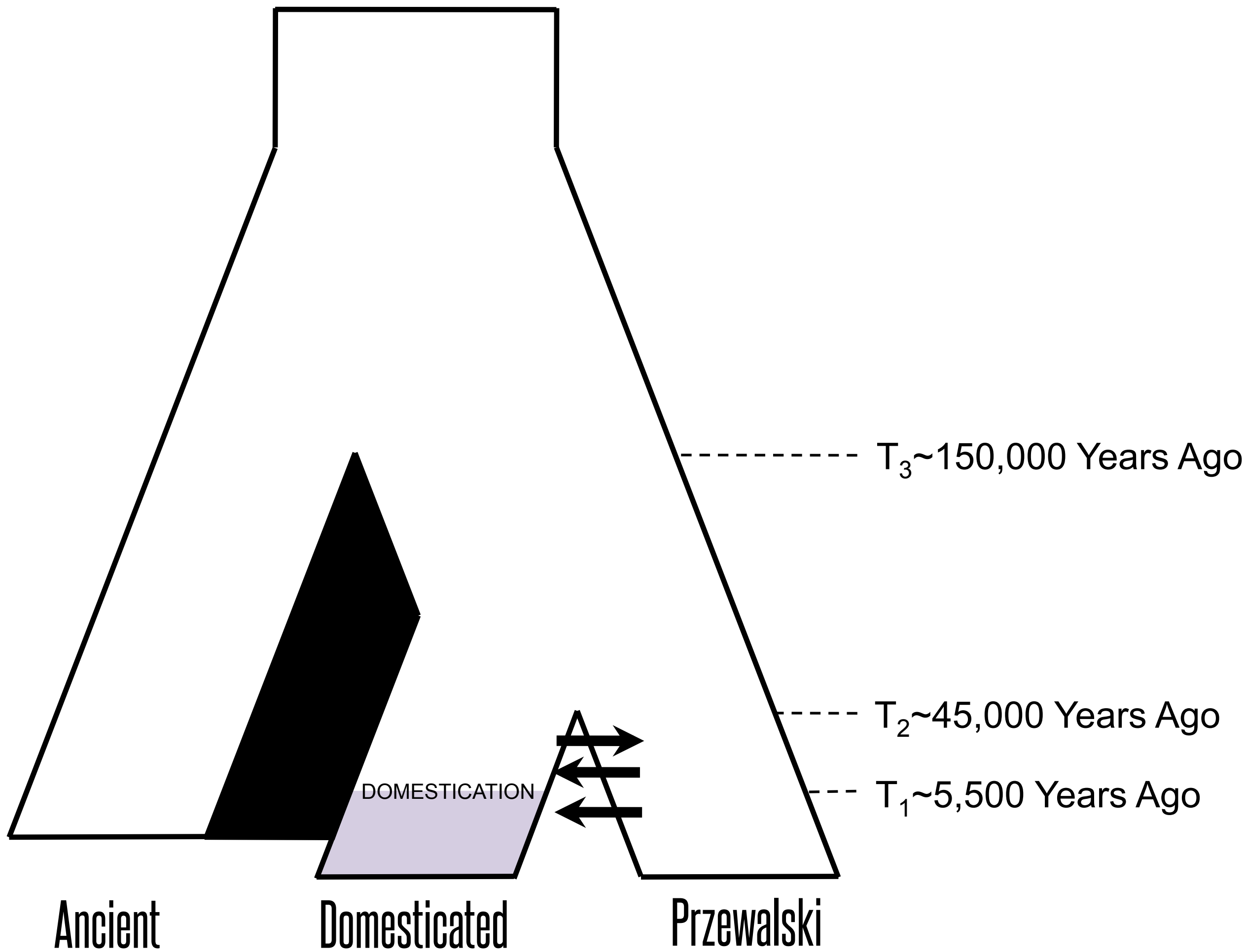
The Population Model Underlying Domestication

Dating Population Splits



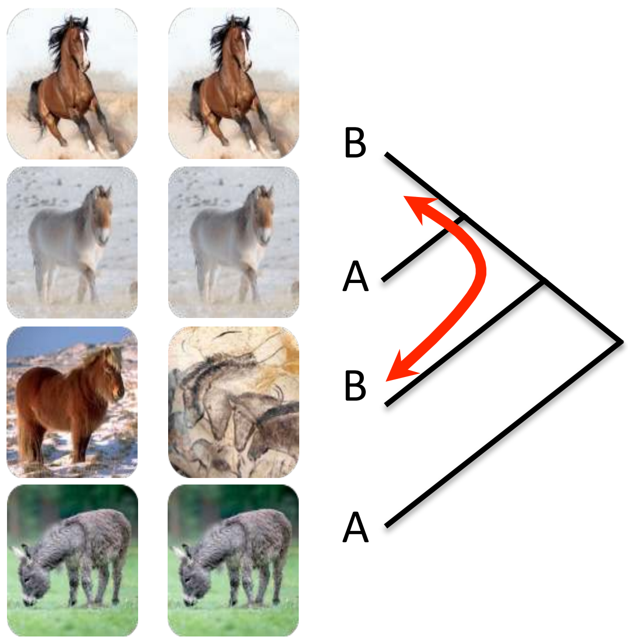
The Population Model Underlying Domestication

Population Admixture



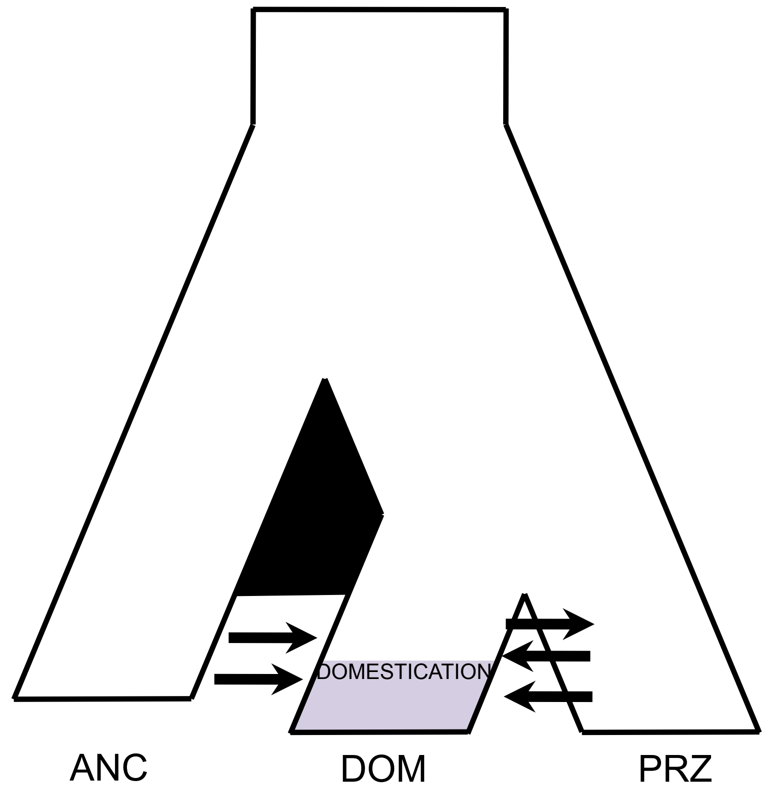
The Population Model Underlying Domestication

Admixture: D-statistics



(I) (II)

$$\%\mathrm{GenomeAdmixed} = \frac{(\#ABBA-\#BABA)_{II}}{(\#ABBA-\#BABA)_{I}} \geq 12.9\text{-}17.8\%$$



Population Model 2

Candidate Domestication Genes

Scans for Positive Selection

Locomotion

•ACTA1, C-SKI, MYBPC1, SGCD (Myopathies)
•VRK1, TCTN1, CNTN6 (Balance, Motor coordination)
•COL22A1 (Myotendinous, Articular junctions)

Cardio-Vascular

•ACAD8, BRAF, FANCA, SGCD, CACNA1D (Cardiomyopathies)
•NR3C2, SCPeP1, WNK2, CACNA1D (Regulation of Blood Pressure)

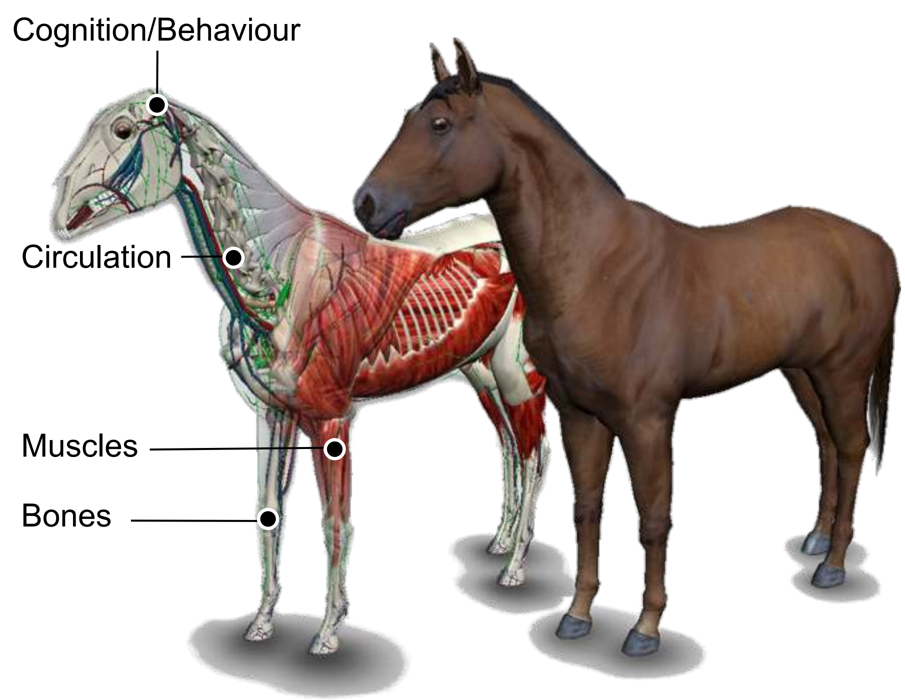
Skeleton

•ACSF3, B3GALTL, GNPTAB, NIPBL, POP1 (Skeletal dysplasia, Shortened Limbs)

Cognition/Behaviour

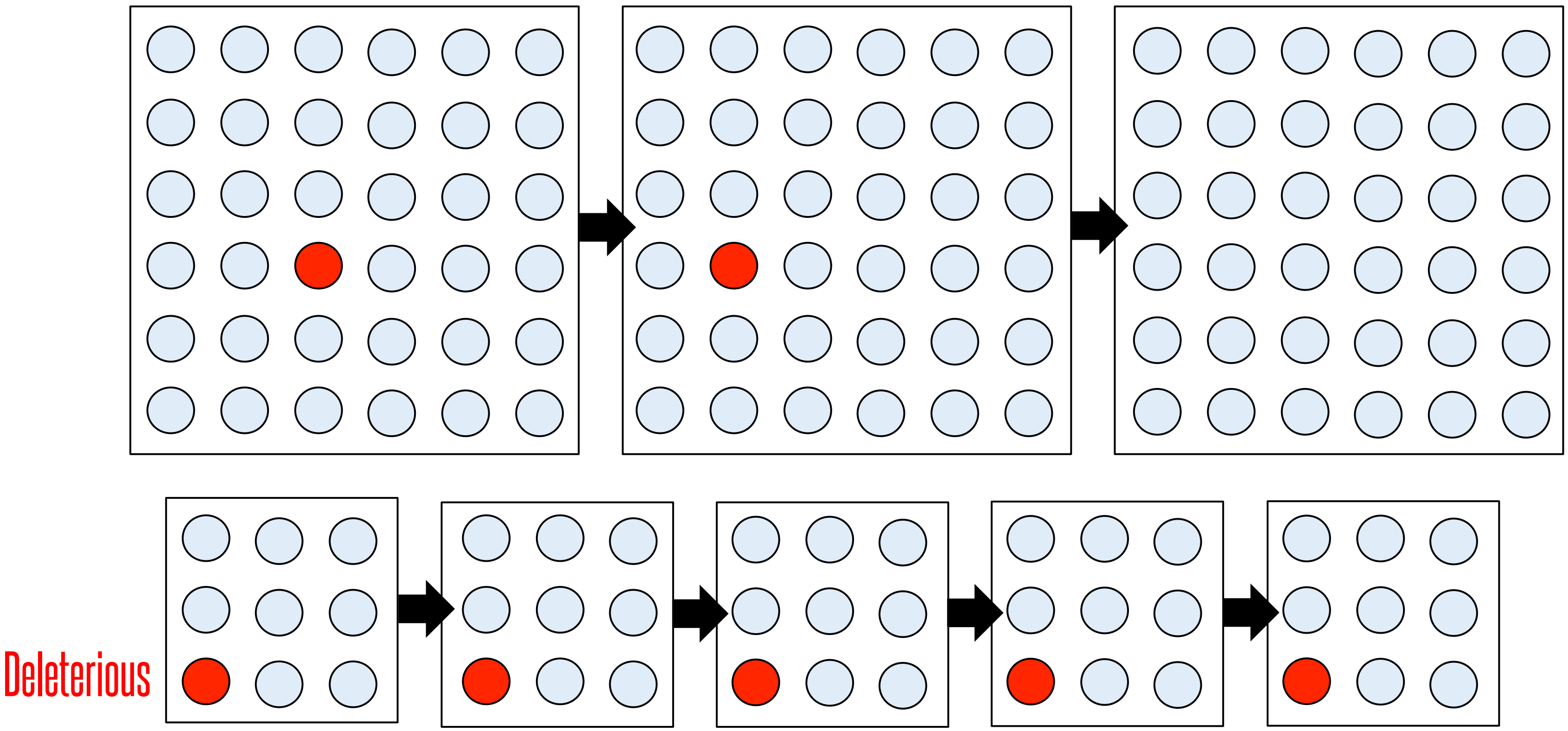
•NINJ1, NTM (Neural growth)
•MATN2, DCC, ASTN1 (Axon and Glial Guidance)
•DLGAP1 (Synapse Plasticity)
•ALK, NUMB (Neurogenesis)
•B3GALTL, GNPTAB, NIPBL, VDAC1 (Psychomotor retardation, **Learning disability**)
•VDAC1 (**Fear response**)
•CACNA1D, GRID1 (**Social behavior** and Schizophrenia)

125 Genes



The Cost of Domestication

Demography & Purifying Selection



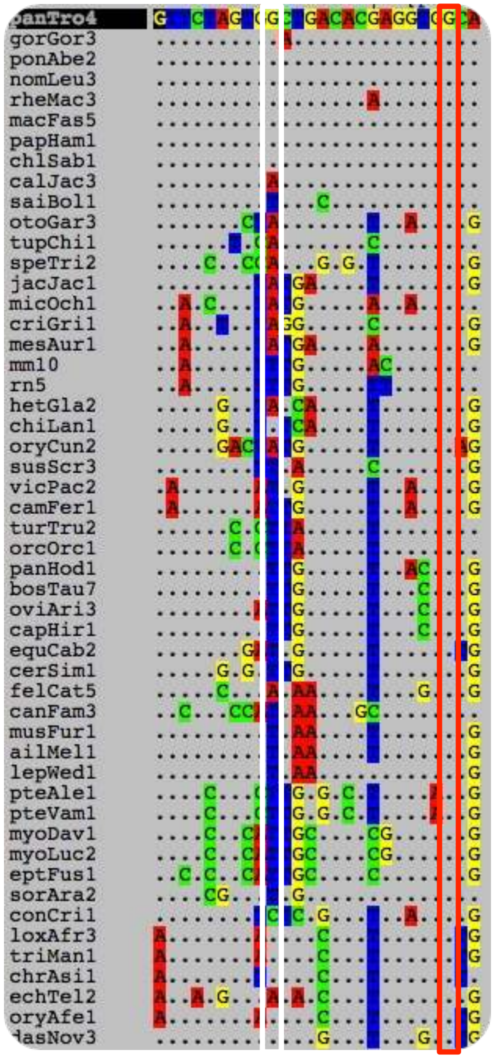
The Cost of Domestication

Quantifying Mutation Loads

GERP
(Conservation) Scores

Deficits of substitutions ~ a measure of constraint that reflects the strength of past purifying selection

From Davydov et al. PLoS Comp Biol 2010



The Cost of Domestication

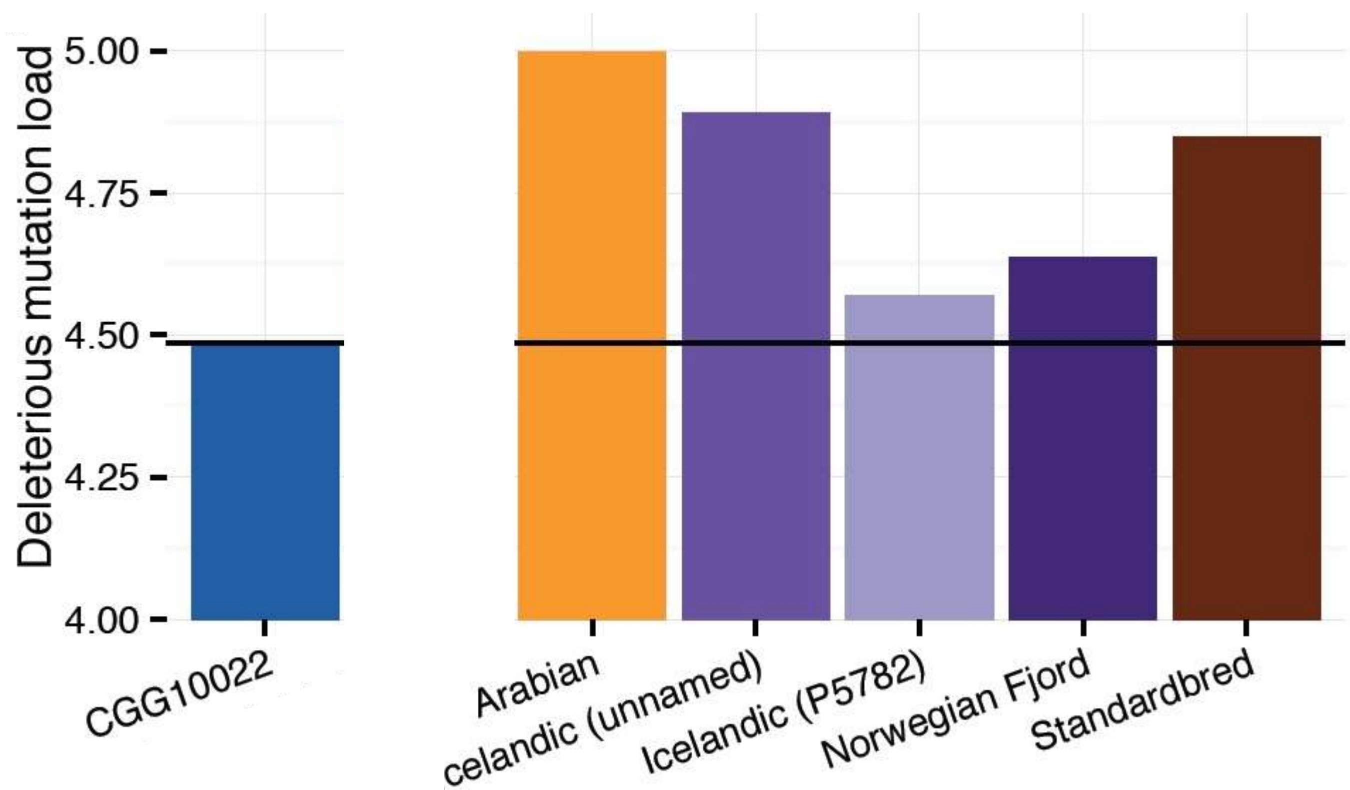
Quantifying Mutation Loads

$$\text{Load}_k = \frac{\sum_{i}^{n} \#\text{DerivedAllele} \times \text{GERP}_i}{n}$$

Conditioned on:
- Homozygous Sites
- GERP≥2 (i.e. Non-Neutral)

The Cost of Domestication

Demography & Purifying Selection: Genetic Loads

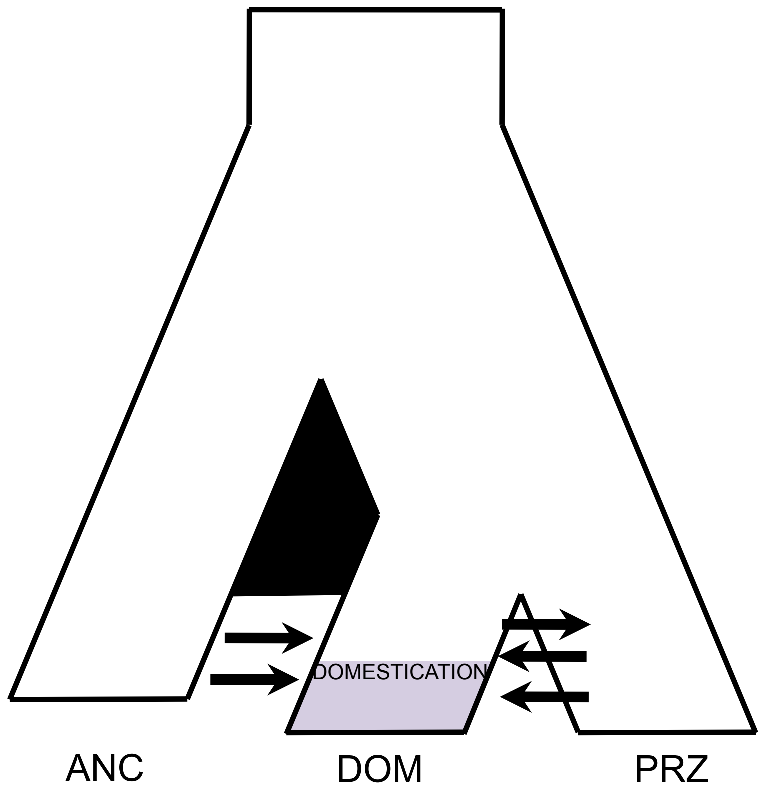


Kolmogorov-Smirnov (Holm-Correction)

The Genomics of Horse Domestication

Summary 2

- We discovered a now extinct population of Wild Horses
- This population significantly contributed to the genetic makeup of domesticated horses
- Locomotory, Physiological, Developmental and Behavioral Genes were domestication targets
- Horse domestication was costly and enhanced deleterious mutation loads



Schubert et al. PNAS 2014

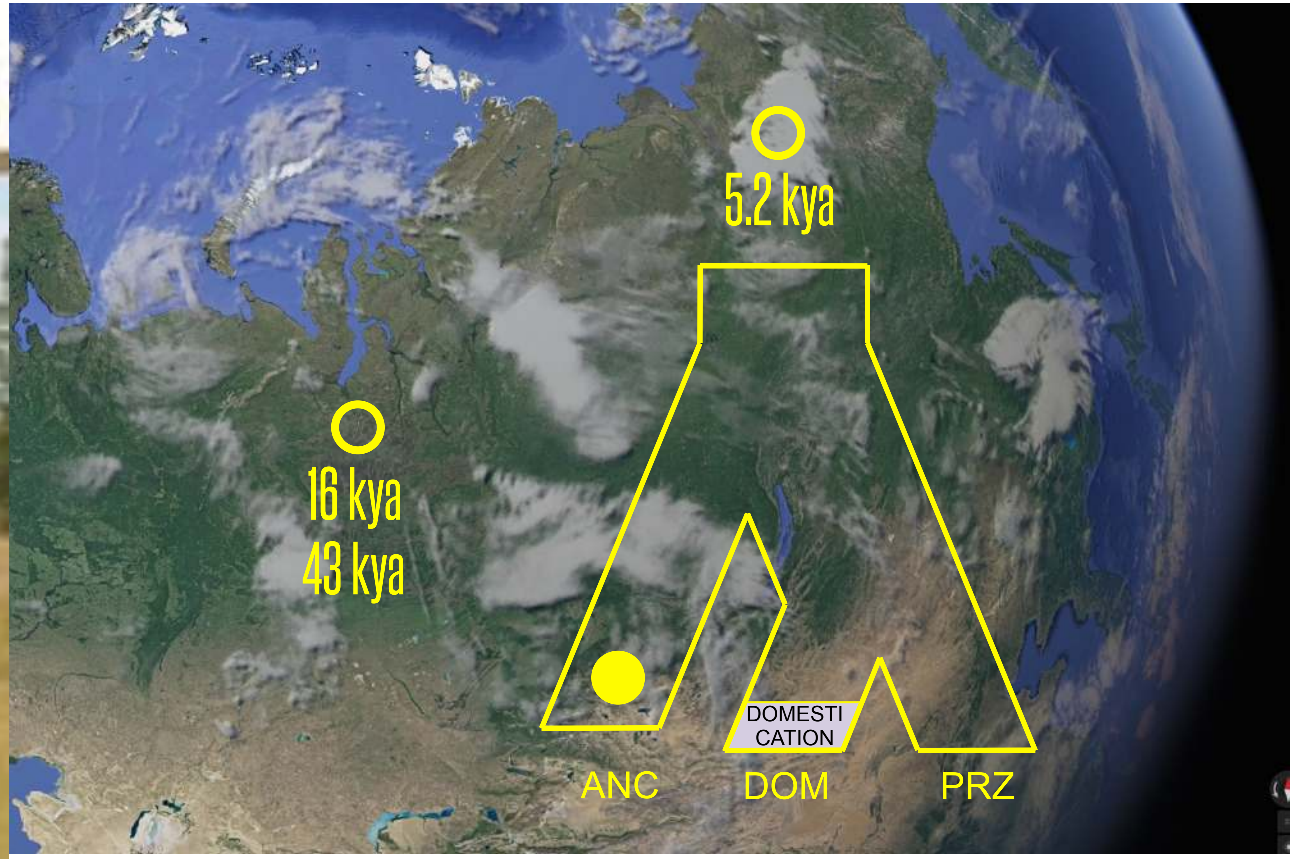
Historical Genomes

Late Pleistocene Genomes

Holocene Genomes

The Genomics of Cold Adaptations

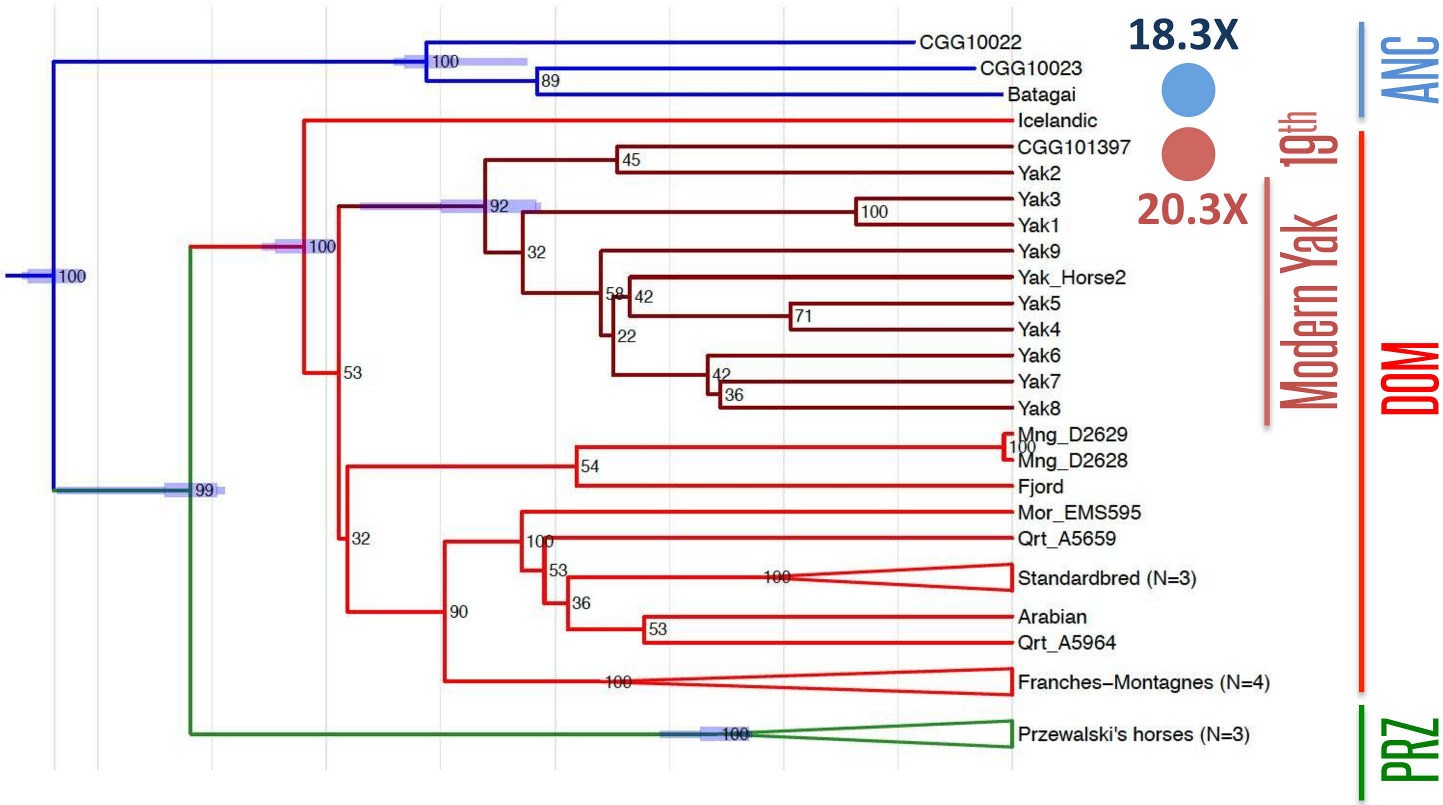
Evolutionary Origins of Yakutian Horses



Librado et al. PNAS 2015

The Genomics of Cold Adaptations

Evolutionary Origins of Yakutian Horses

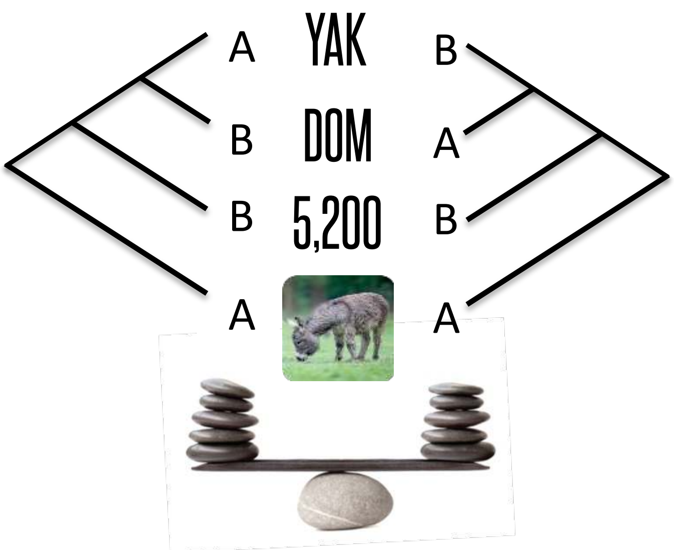


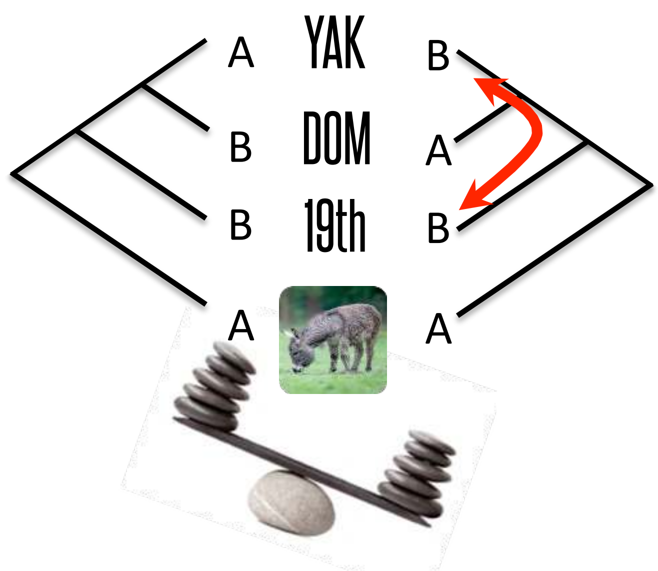
Whole-Exome (ExaML), SNP (TreeMix)

The Genomics of Cold Adaptations

Evolutionary Origins of Yakutian Horses

Admixture Tests



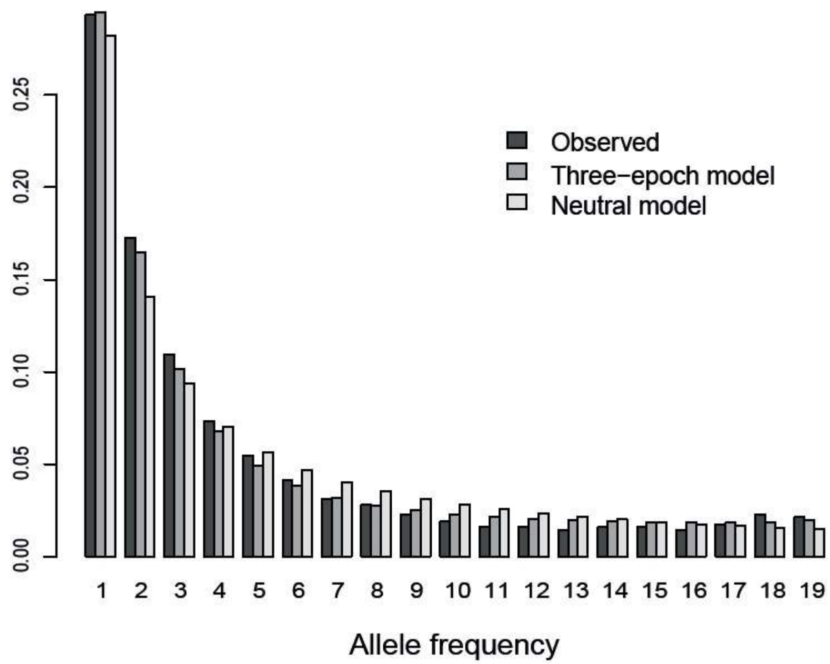


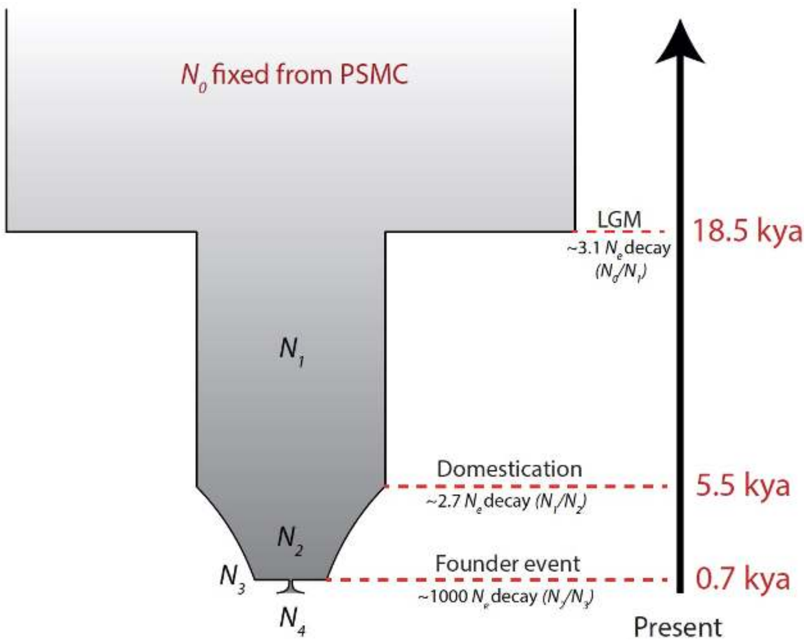
(f3- and) D-statistics

The Genomics of Cold Adaptations

Evolutionary Origins of Yakutian Horses

Demographic Model





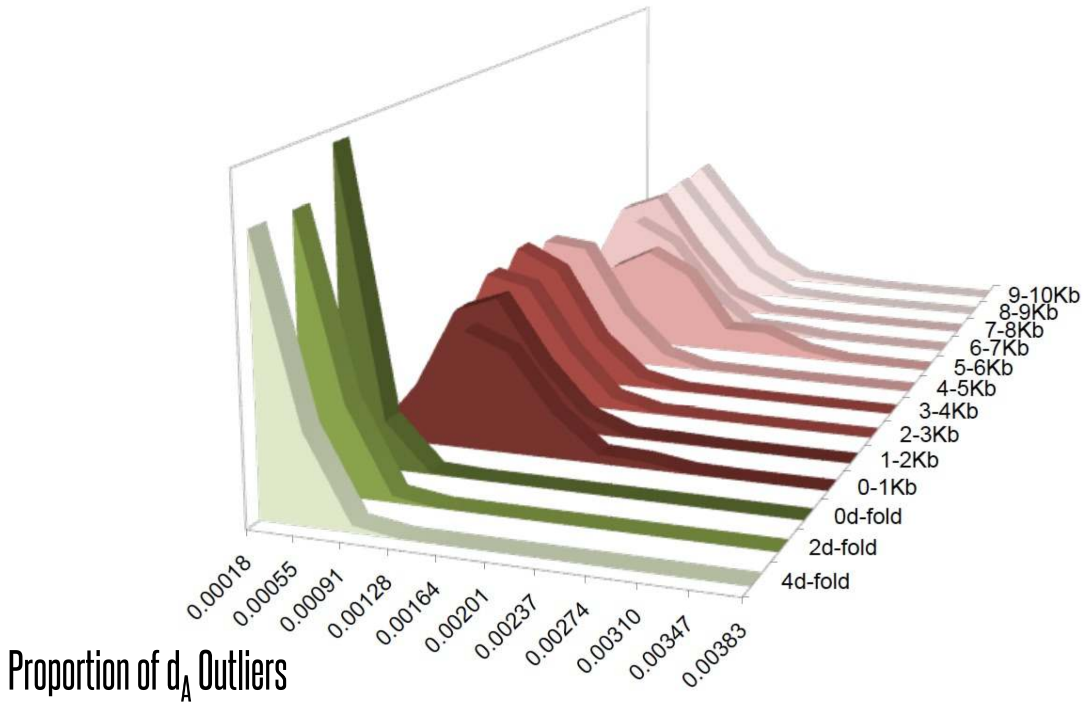
dadi Analyses (SFS-based)

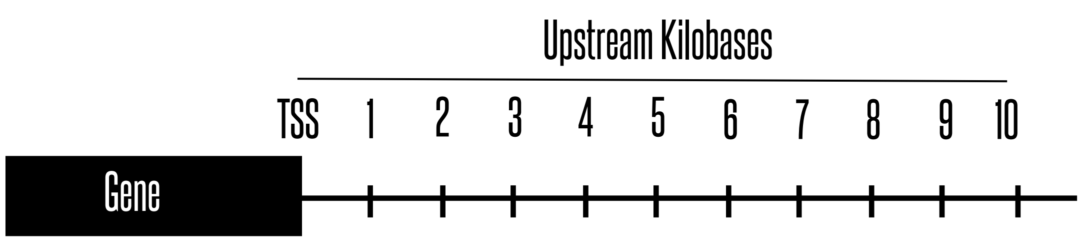
The Genomics of Cold Adaptations

Yakutian Horses: An extremely fast adaptive history

The Genomics of Cold Adaptations

The Genetic Makeup of Yakutian Horses



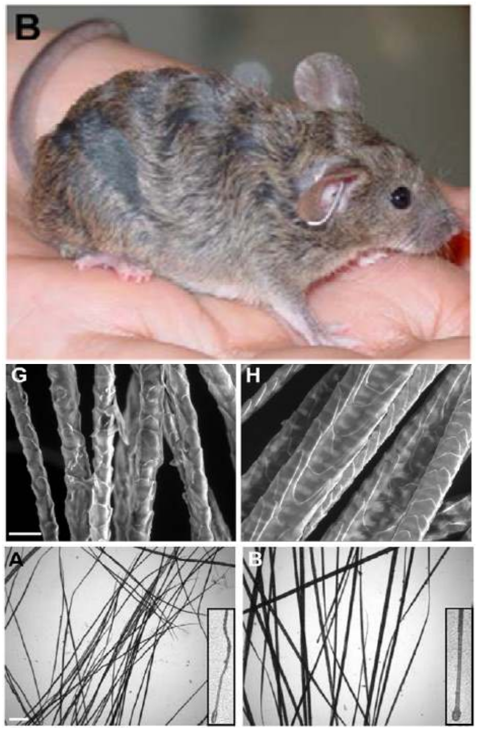


dA differentiation index

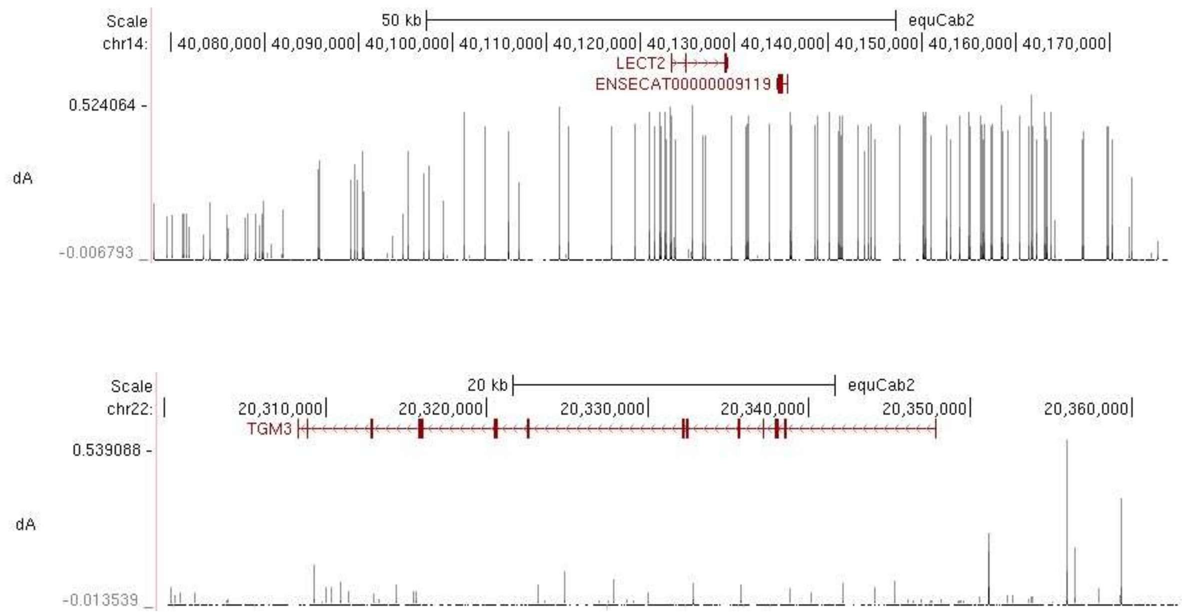
The Genomics of Cold Adaptations

The Genetic Makeup of Yakutian Horses

TGM3



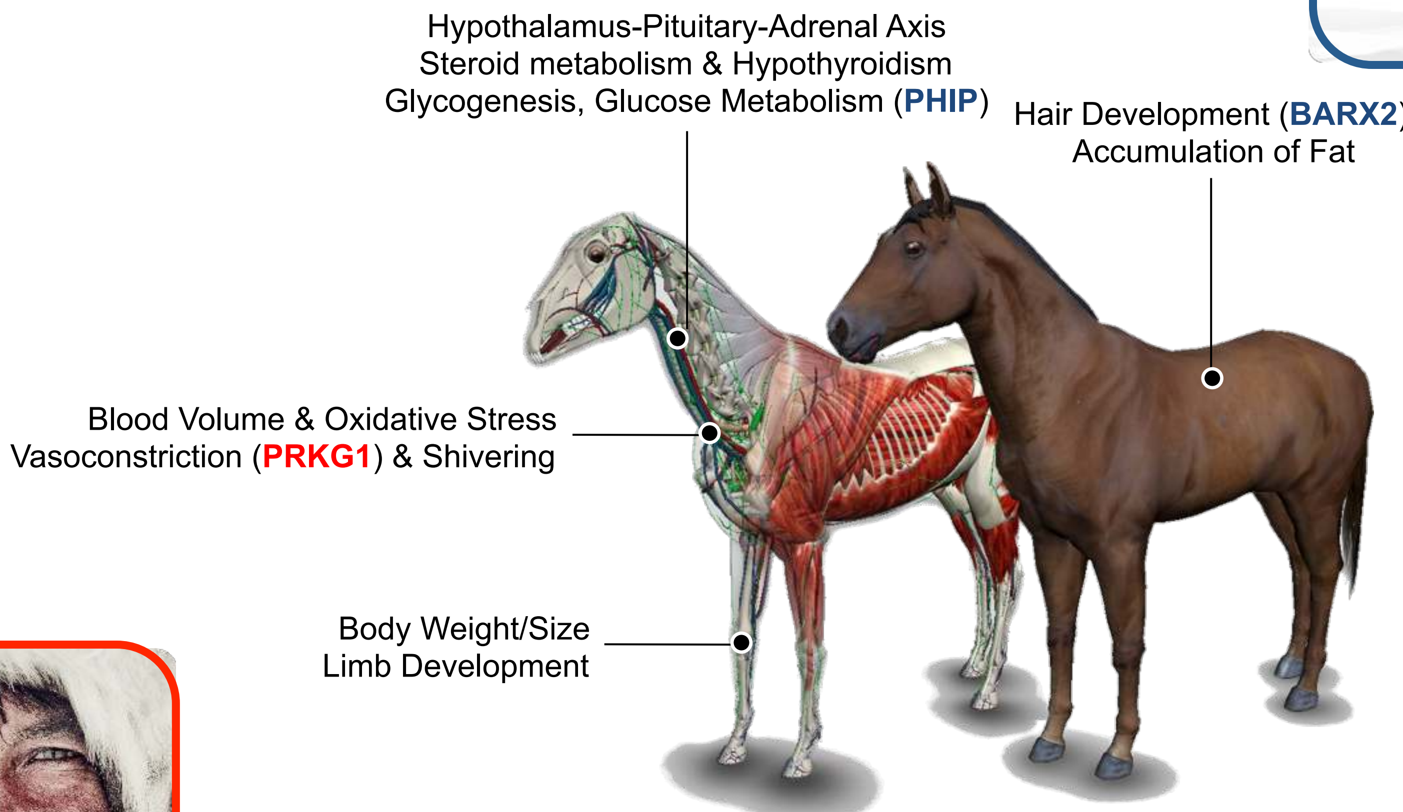
From John et al. PLoS One 2012



LECT2 and TGM3, 2 opposite cases of differentiation

The Genomics of Cold Adaptations

The Genetic Makeup of Yakutian Horses



Metabolic, Morphological and Physiological Traits

The Genomics of Cold Adaptations

Summary 3

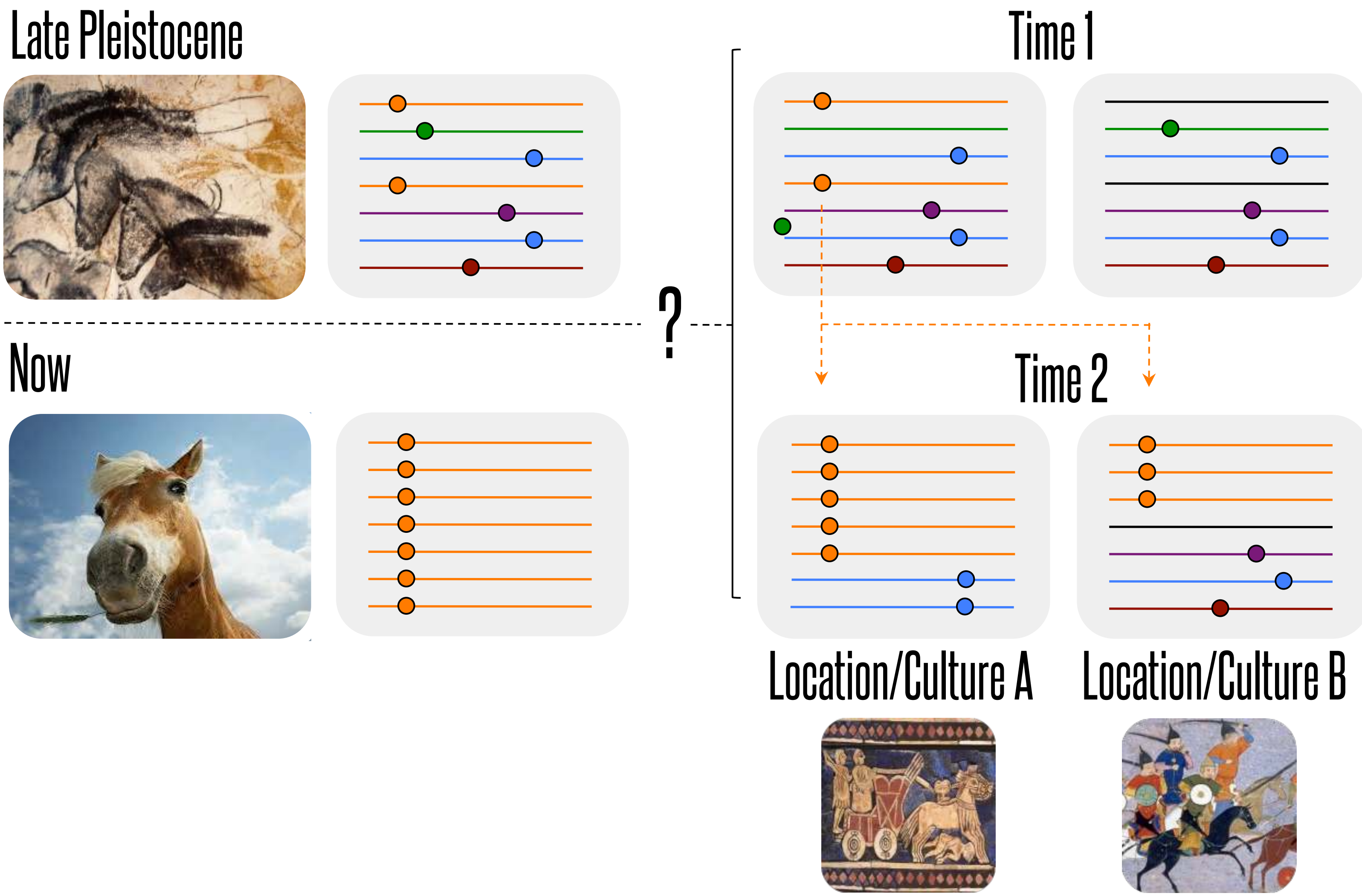
- The third extinct population of wild horses survived at least until 4.4 kya, and extended to Far-Eastern Siberia
- Yakutian horses represent the descent of a recent founder event from domestic livestocks
- Regulatory changes drive rapid adaptation to extreme environments

Librado et al. PNAS, Minor Revisions

Ongoing Work

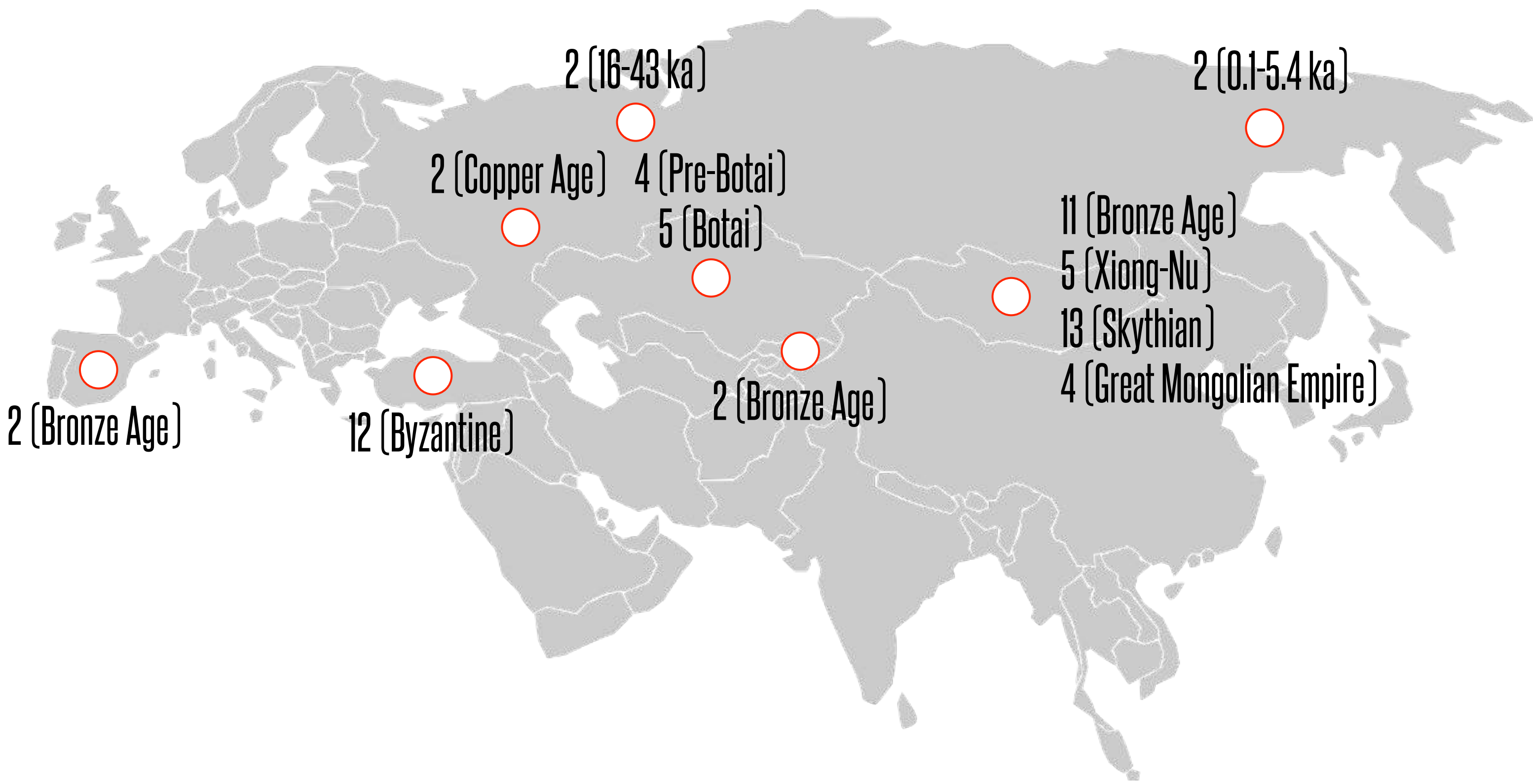
Candidate Domestication Genes

Scans for Positive Selection (& Admixture)



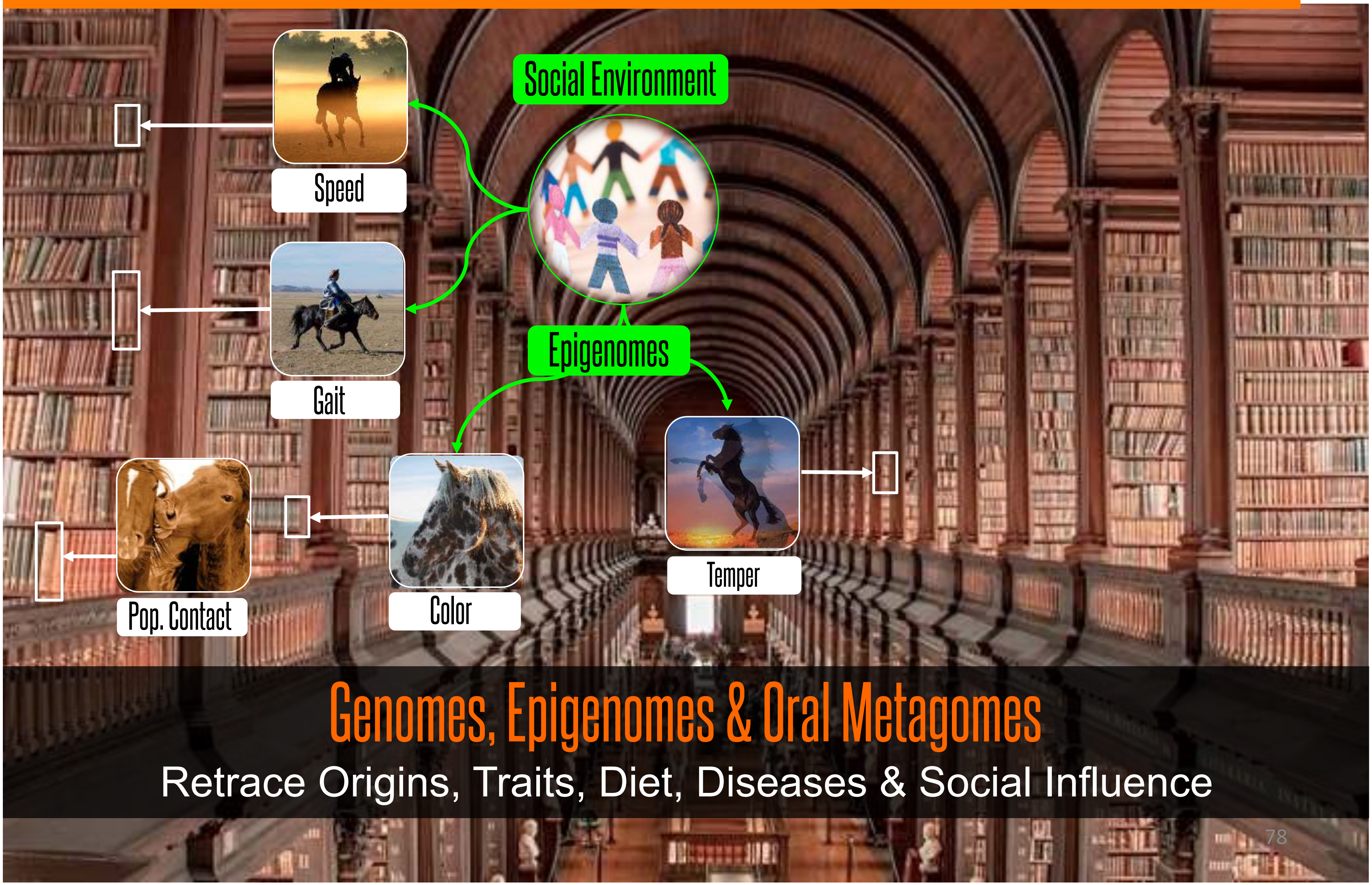
Candidate Domestication Genes

Scans for Positive Selection (& Admixture)



64 Medium (2-6X) to High (25X) Quality-Genomes

Providing Unprecedented Levels Of Information

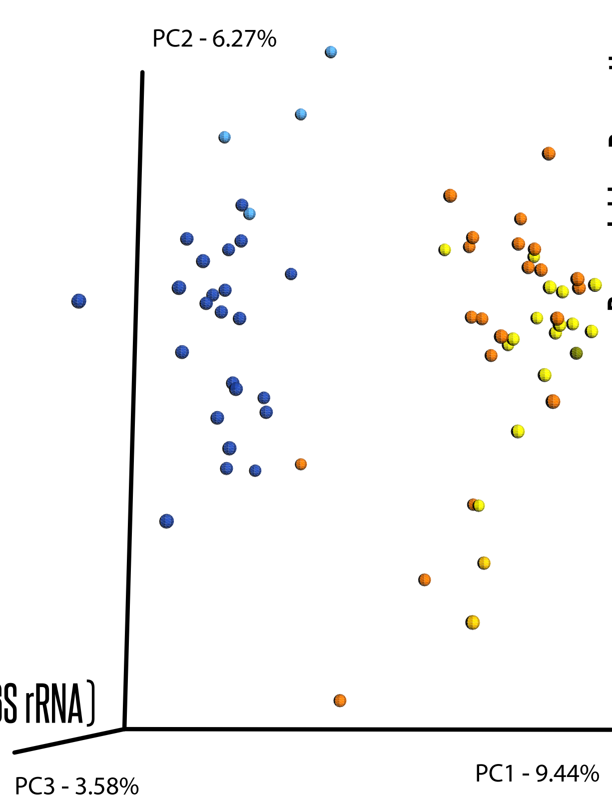


Evolutionary History

Gut Microbiomes: Preliminary Data

When

?

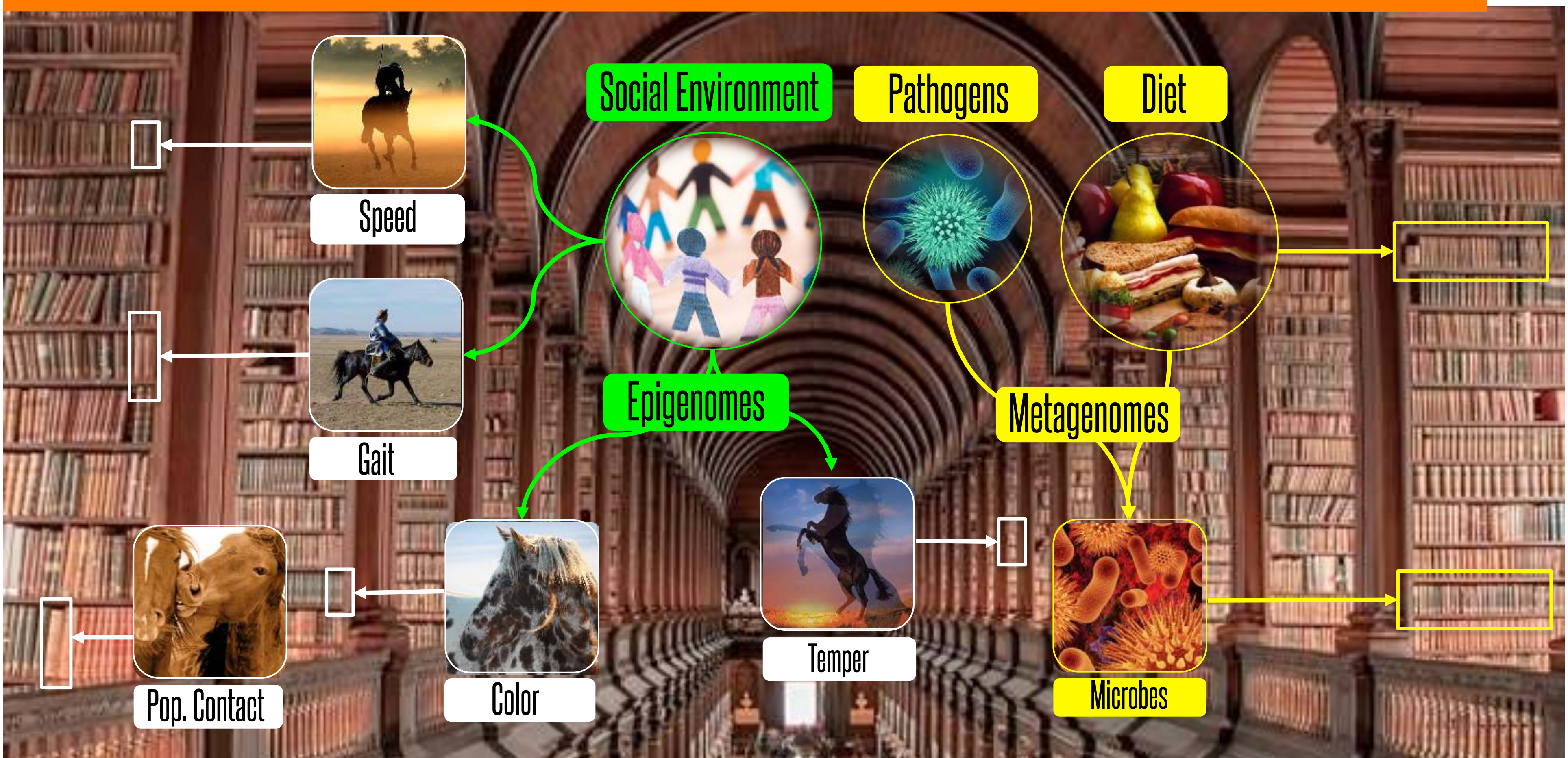


Unweigthed Unifrac-distances (16S rRNA)

The Gut Microbiome of Domesticated and Przewalski's Horses

Is Differentiated, Supporting Domestication-Driven Changes

Providing Unprecedented Levels Of Information



Genomes, Epigenomes & Oral Metagomes

Retrace Origins, Traits, Diet, Diseases & Social Influence

Horses As A Unique Opportunity To Merge

Acknowledgements

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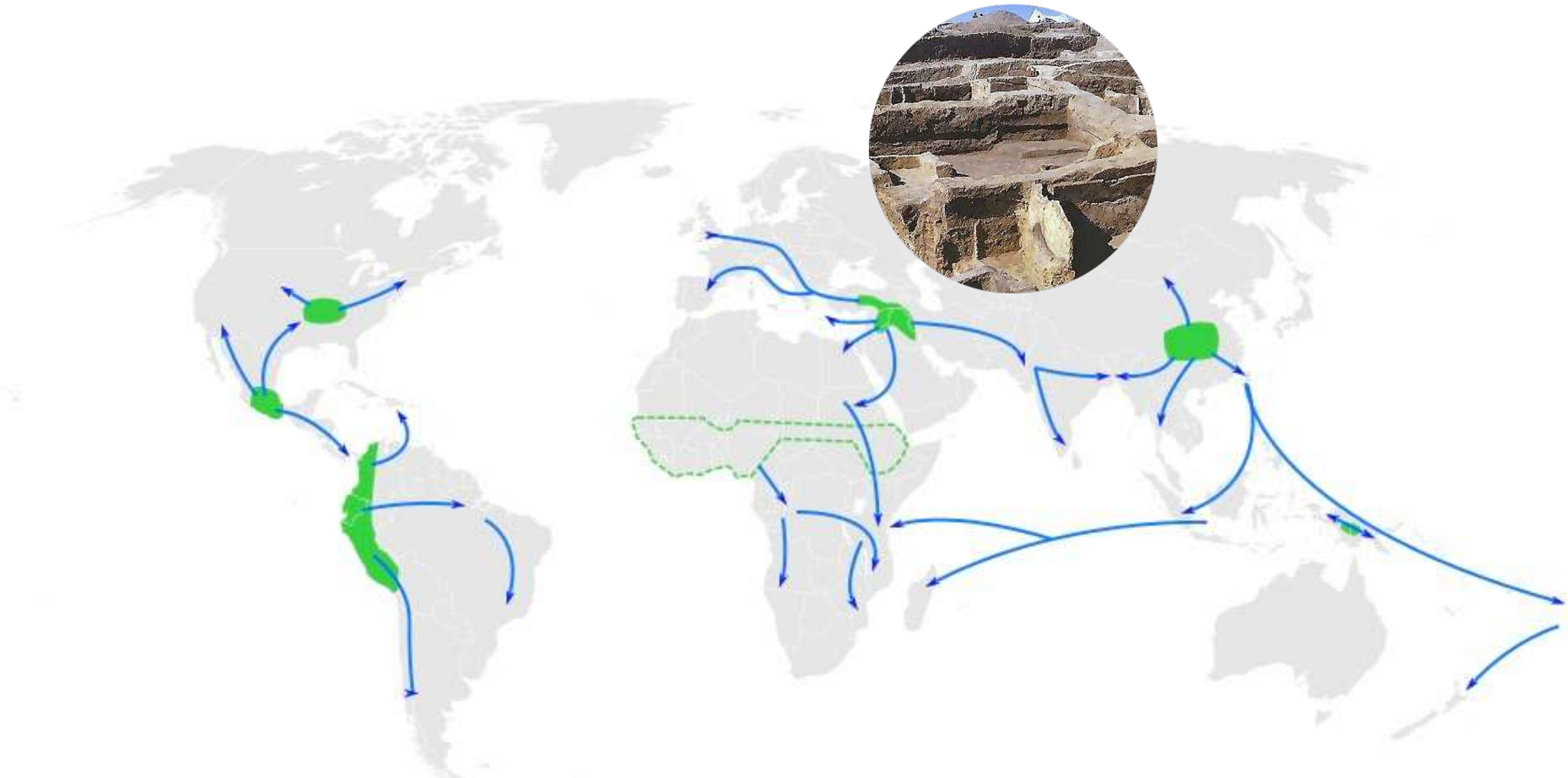
The Process of (Animal) Domestication

The First Agricultural Revolution(s)



Huntering-Gathering ⇨ **Farming**

- Storage economy
- Demographic Expansion
- Sedentarism
- Societal differentiation