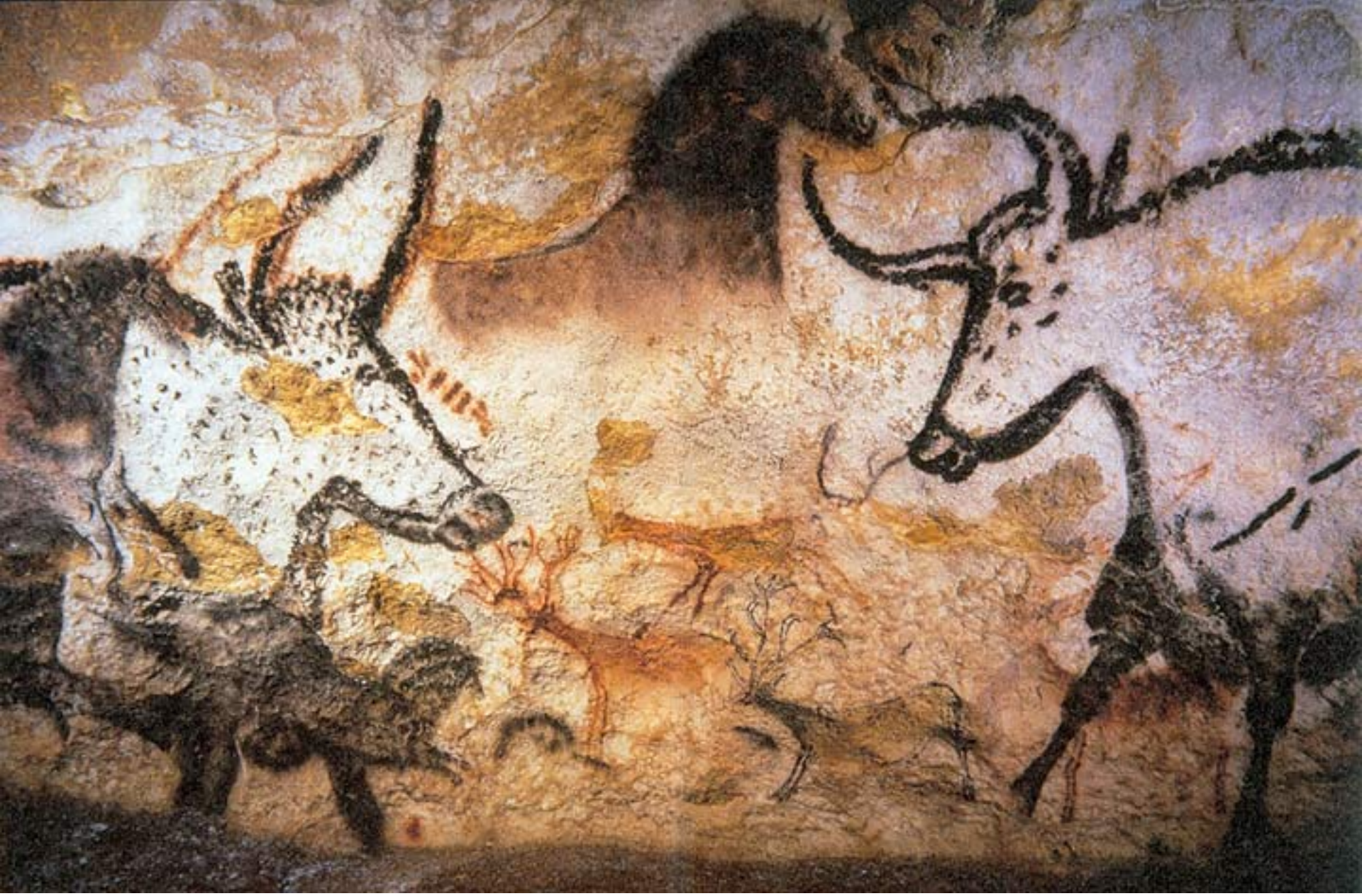
Tracking the evolution of complex traits over space and time with ancient DNA

Iain Mathieson
Department of Genetics
Perelman School of Medicine
University of Pennsylvania
mathi@upenn.edu

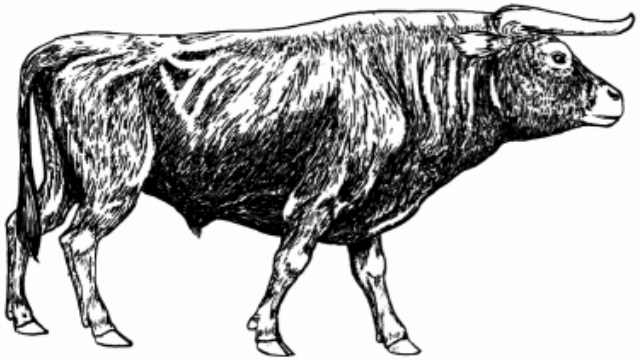


Lascaux cave paintings, France ~15,000 BCE

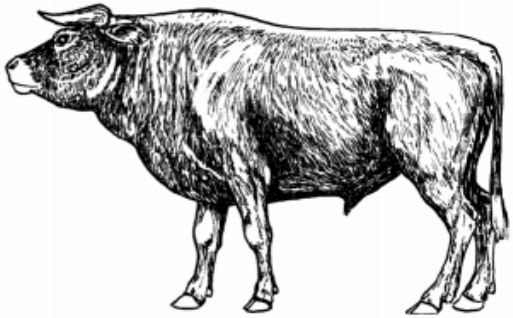
Image: Wikipedia user “Prof Saxx”

Reconstruction of an LBK house ~5,400 BCE

"There's certainly a big culture clash at that time," said Wolfgang Haak, a geneticist at the University of Adelaide and co-author of that paper. "Farmers are probably loud, noisy and stinky at the same time. They come with domestic farm animals and just take over the place."



Wild



Domestic

Images:

↑: Wikipedia
(user Kurt Stueber)

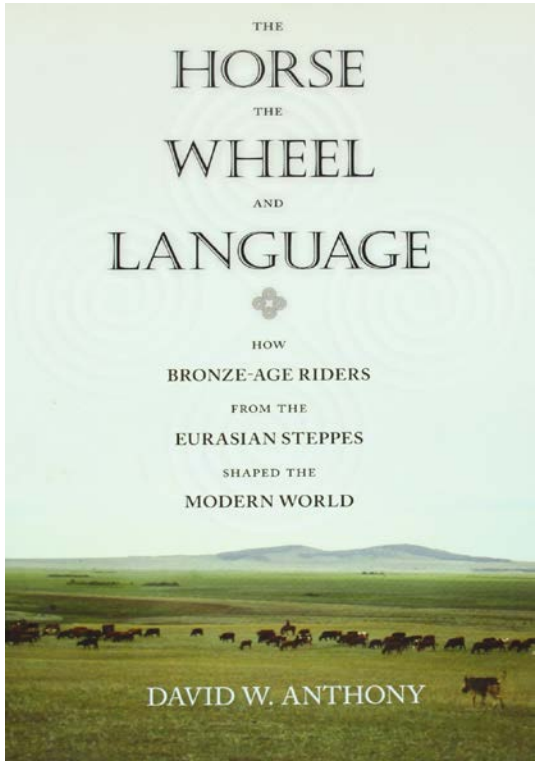
↖: Czekaj-Zastawny 2008
L. Wojcik

←: Bartosiewicz et al 2006

➔ Varna man, buried ~4,500 BCE with more gold than has been found in the entire rest of the world, up to that date. Image: Raiko Krauß

The Bronze Age brings dramatic changes in lifestyle and culture

What are the genetic changes associated with these shifts?

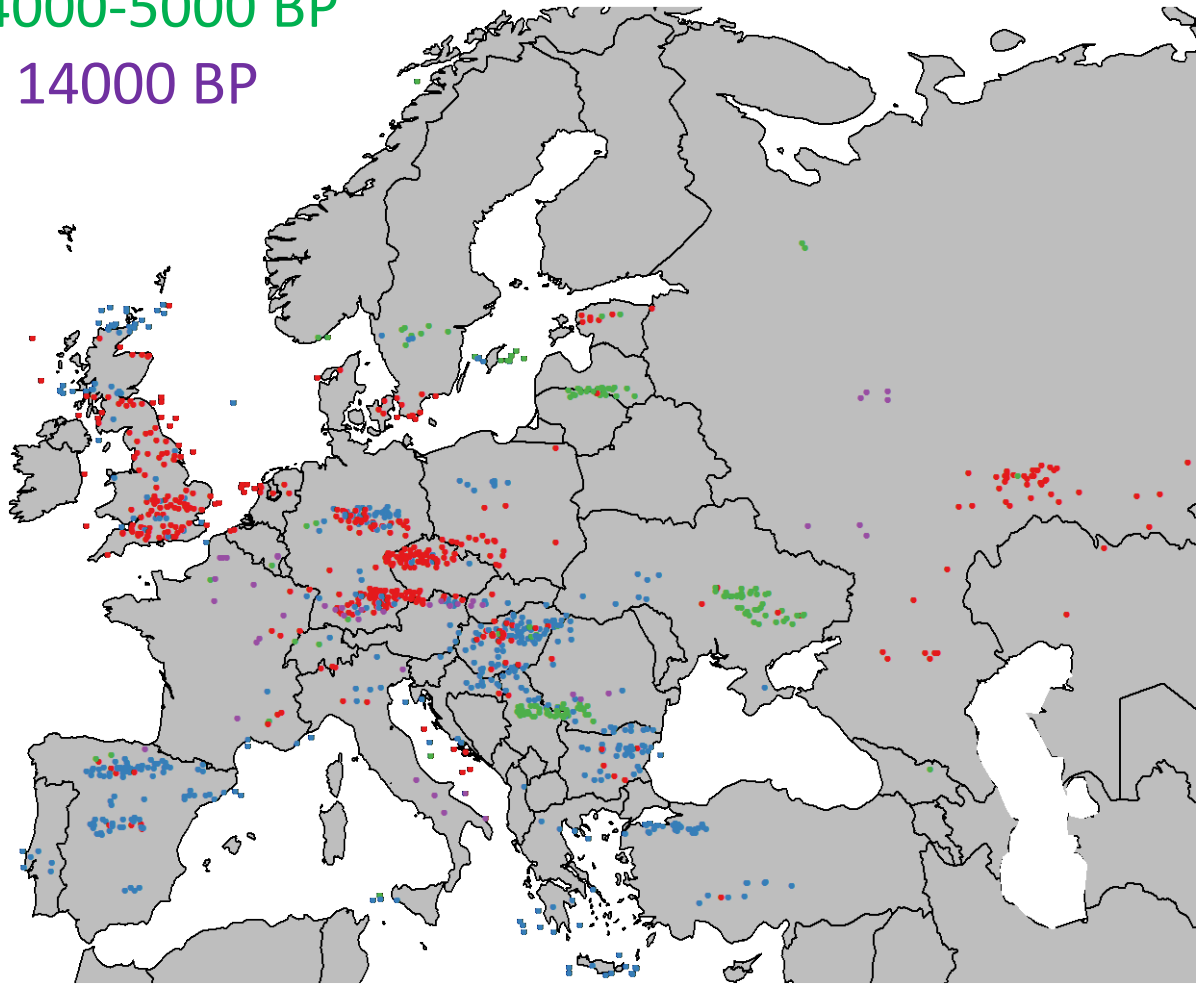


Steppe Ancestry < 4500 BP

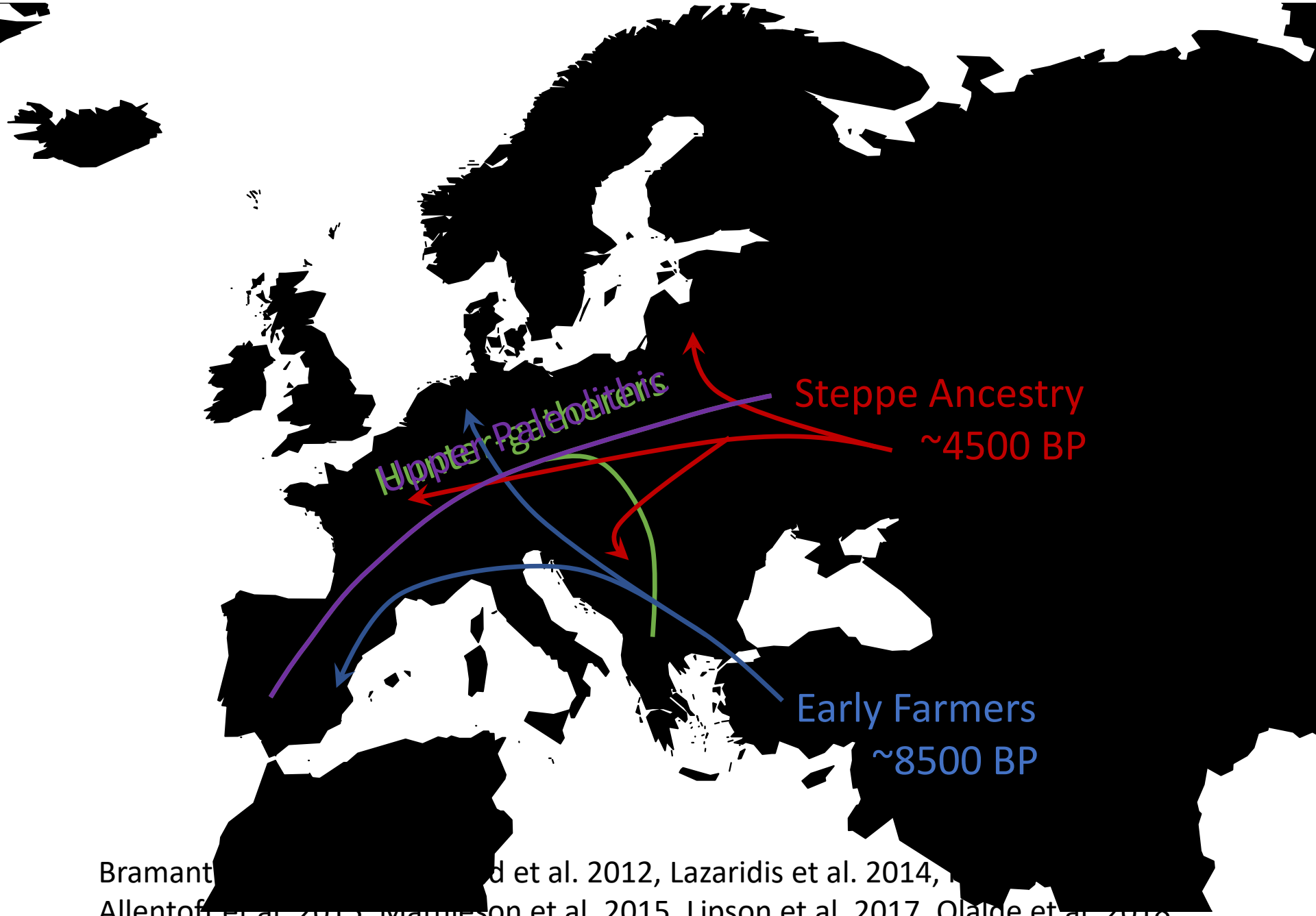
Early Farmer 8500-4500 BP

Hunter-gatherer 14000-5000 BP

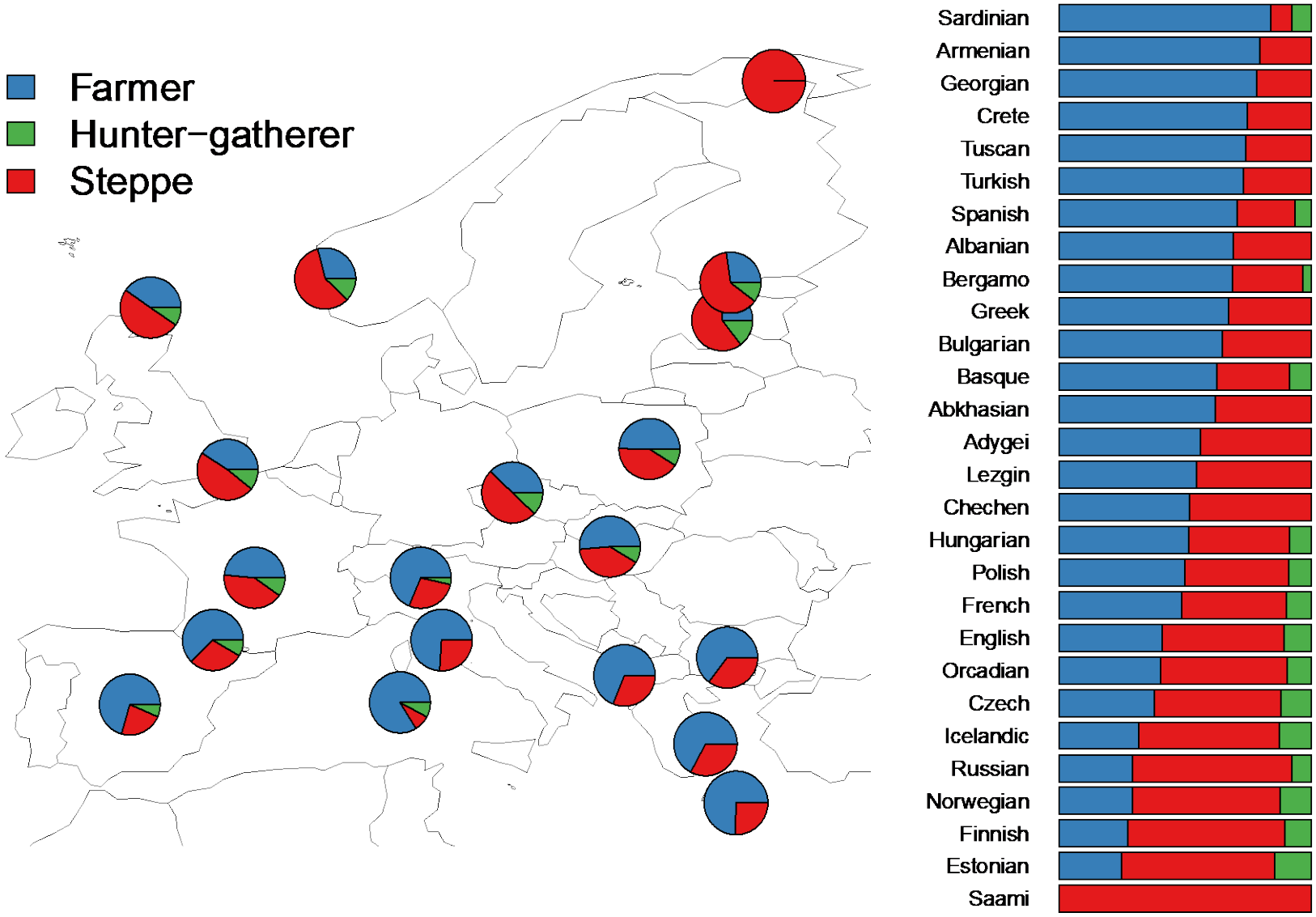
Upper Paleolithic > 14000 BP



Olalde et al. 2018, Mathieson et al. 2018, Lipson et al. 2017 Fu et al. 2016, Mathieson et al. 2015, Allentoft et al. 2014, Haak et al. 2014, & many others

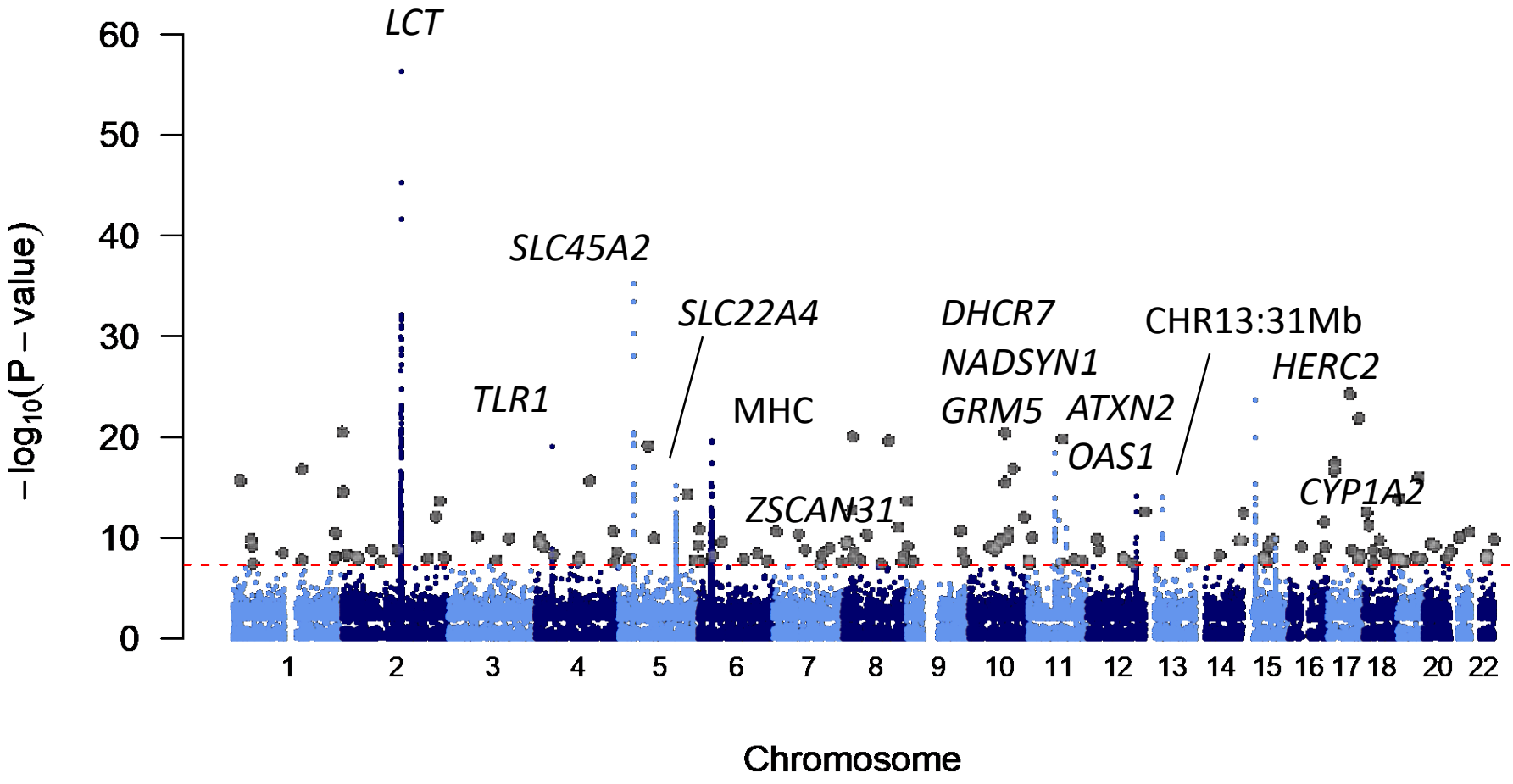


Bramant d et al. 2012, Lazaridis et al. 2014,
Allentoft et al. 2015; Mathieson et al. 2015, Lipson et al. 2017, Olalde et al. 2018



Lazaridis et al. 2014, Haak et al. 2015

14 genome-wide significant signals of selection



Mathieson et al. 2015

Diet

- *LCT*: Lactase persistence
- *NADSYN1/DHCR7*: Vitamin D metabolism
- *FADS1/2*: Decreased triglyceride levels
- *ATXN2/SHD2B3*: Associated with celiac disease, Type 1 diabetes
- *SLC22A4*: Ergothioneine uptake, celiac disease, IBD
- *CYP1A1*: Metabolism of exogenous substances; caffeine.

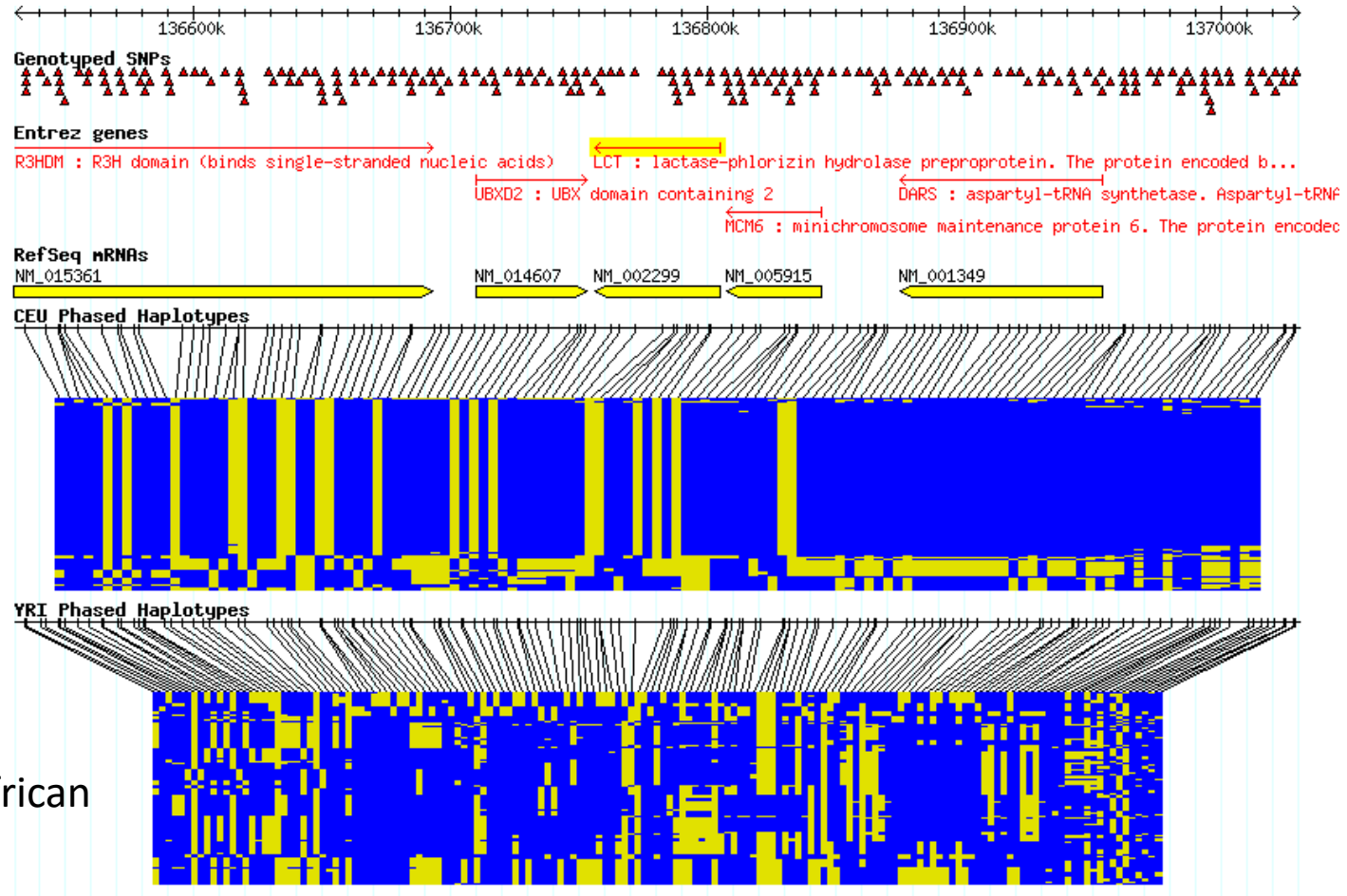
Pigmentation

- *SLC45A2, GRM5*: Light skin pigmentation
- *HERC2/OCA2*: Blue eye color

Immunity

- *TLR1/6/10*: Immunity, leprosy, TB and other mycobacterial resistance
- *OAS1/2/3*: Viral resistance; Neanderthal introgressed haplotype
- *ZSCAN32:* Autophagy
- *MHC*: Immunity, everything.

Adaptation to agriculture

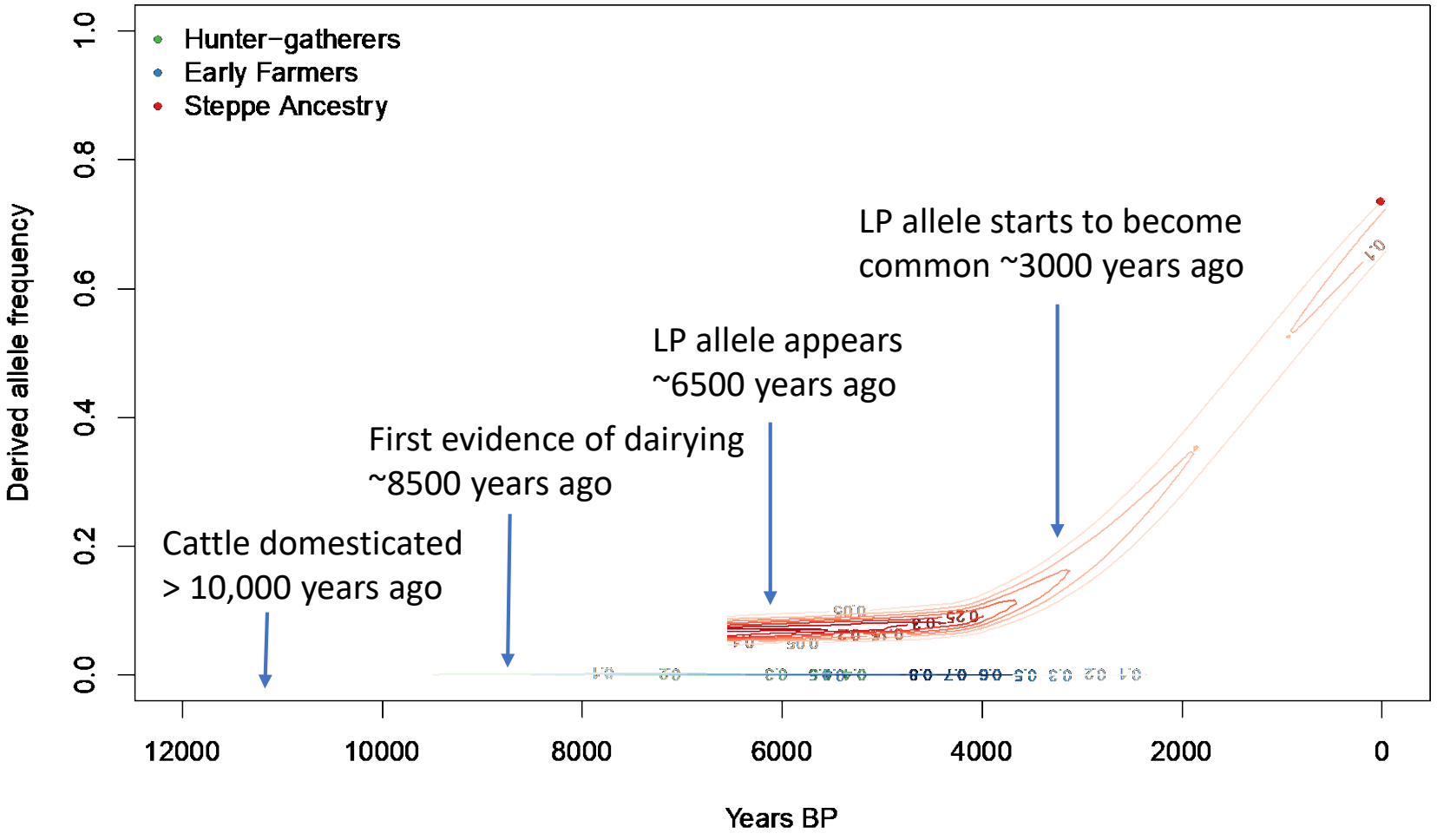


Northern European

West African

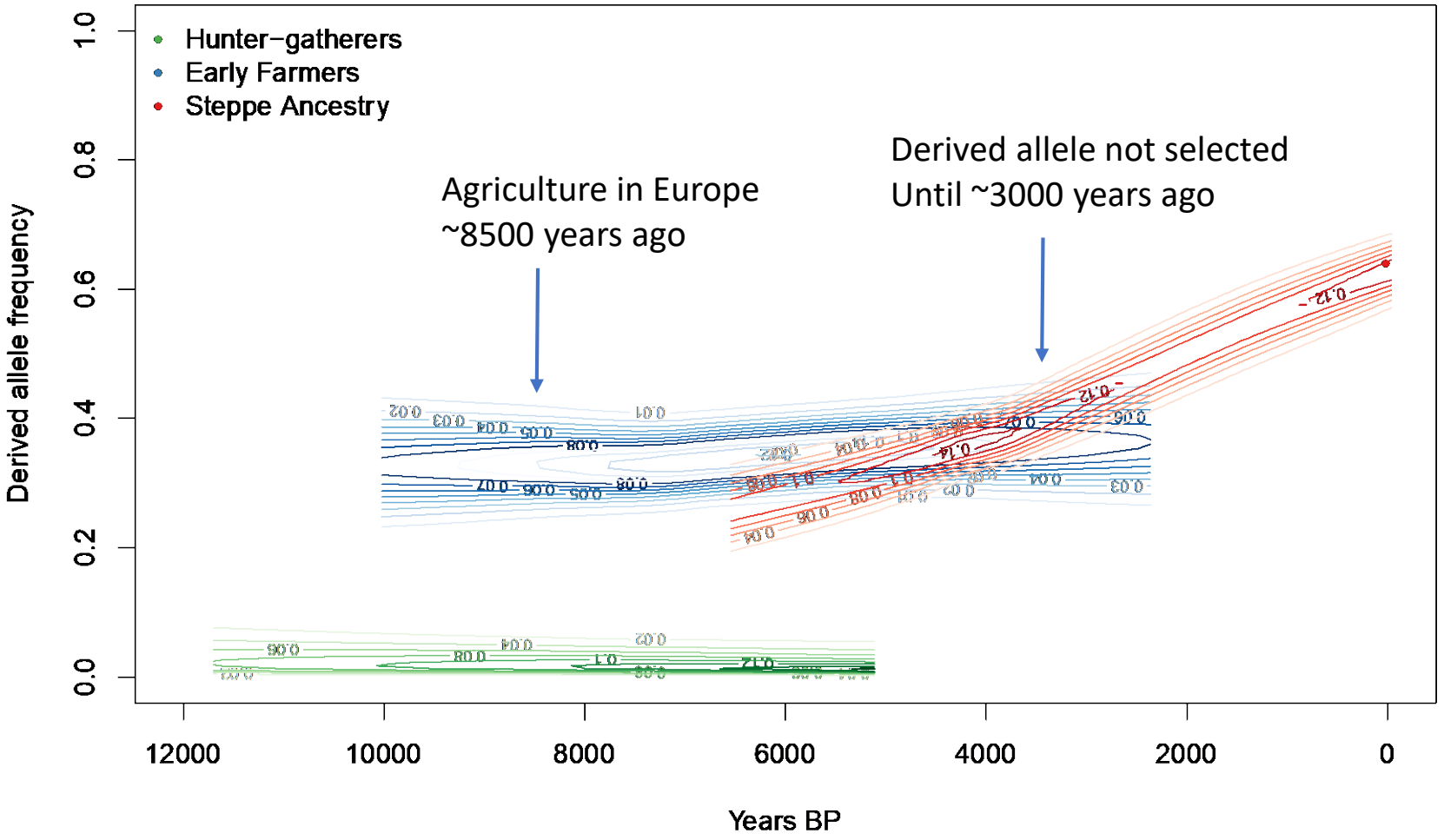
Figure: Gil McVean

Lactase persistence postdates cattle domestication



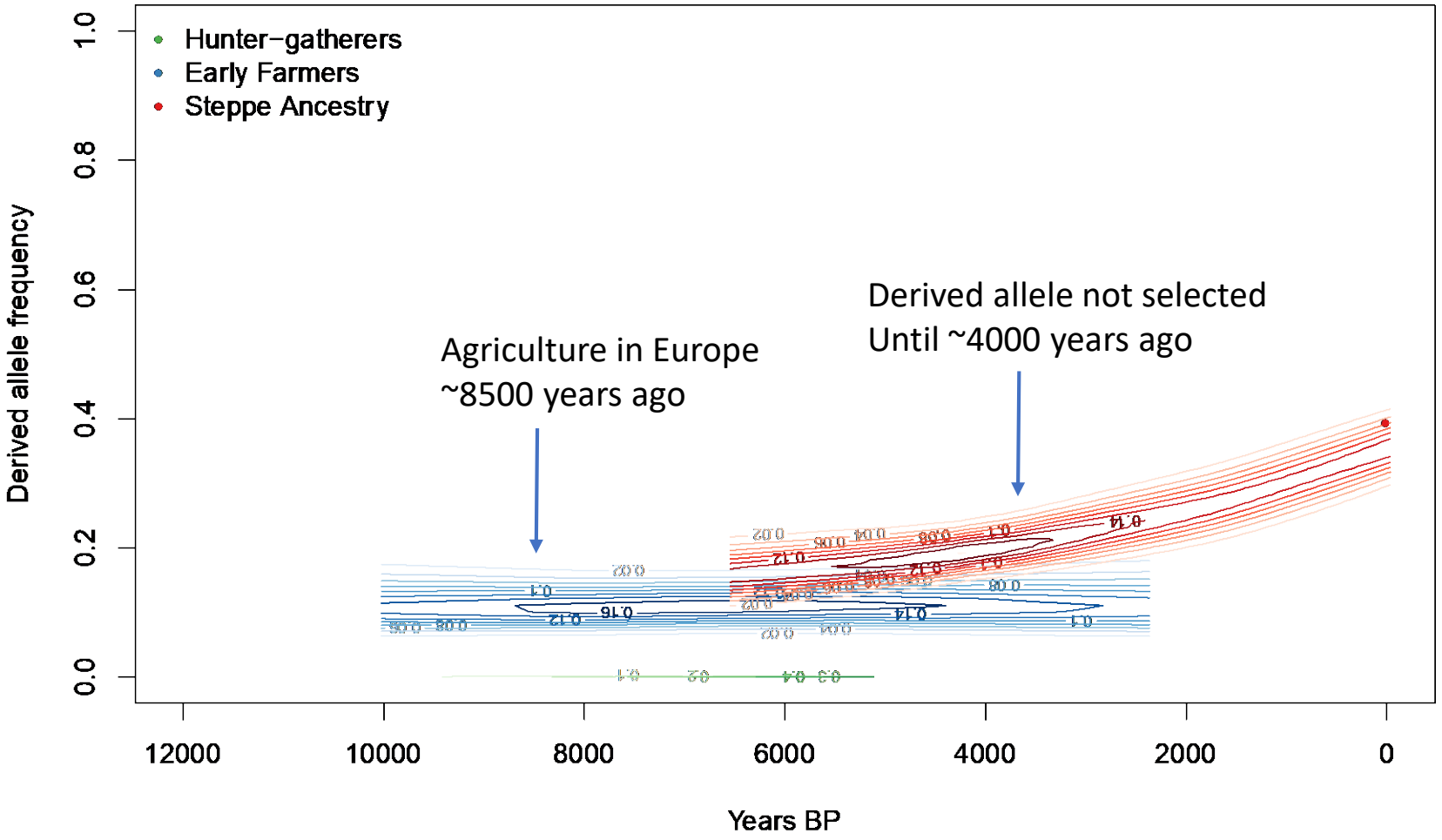
Mathieson & Mathieson 2018

FADS1 variants post-date agriculture



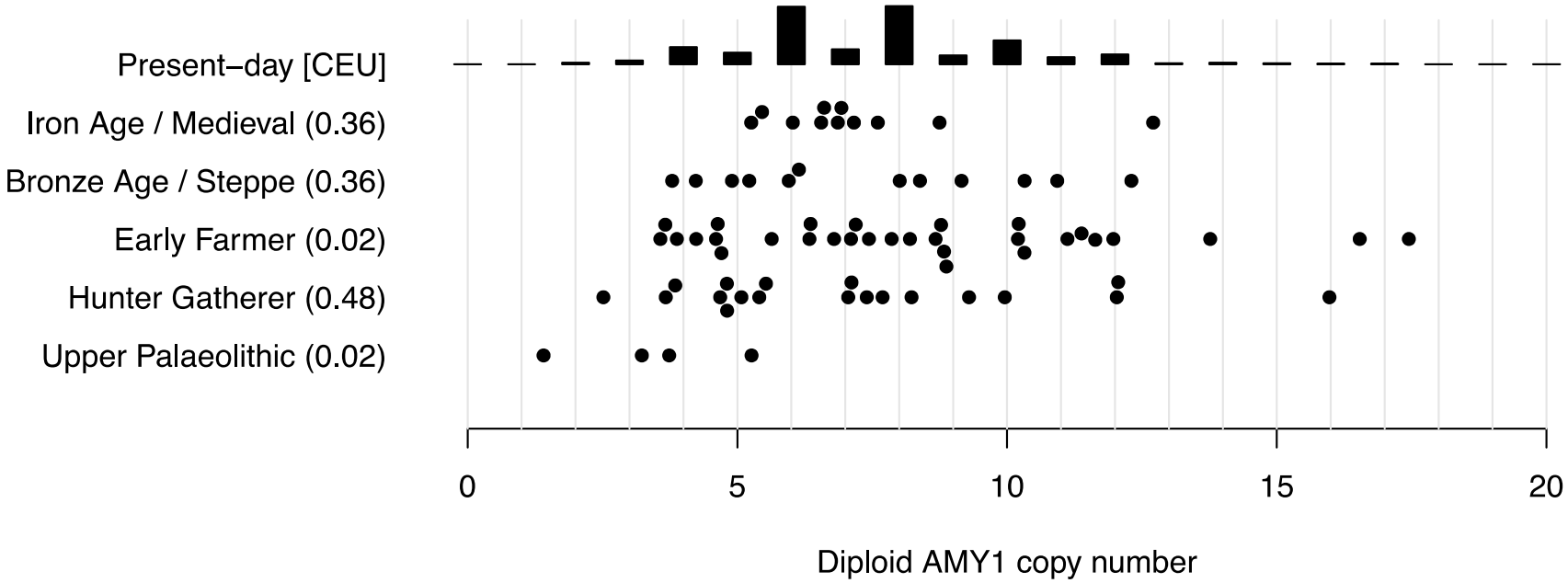
Mathieson & Mathieson 2018

SLC22A4 selection post-date agriculture



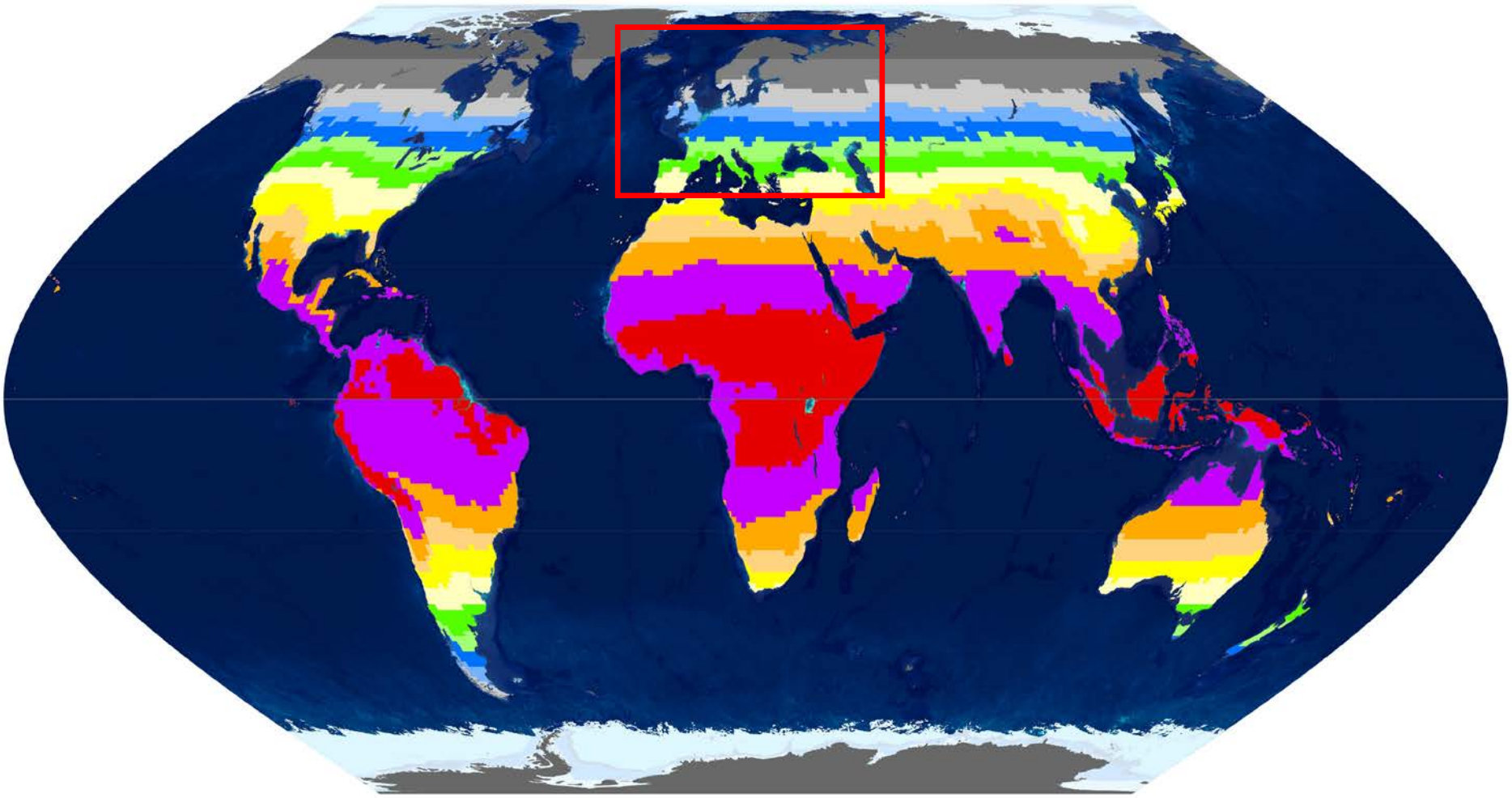
Mathieson & Mathieson 2018

Amylase copy number pre-dates agriculture



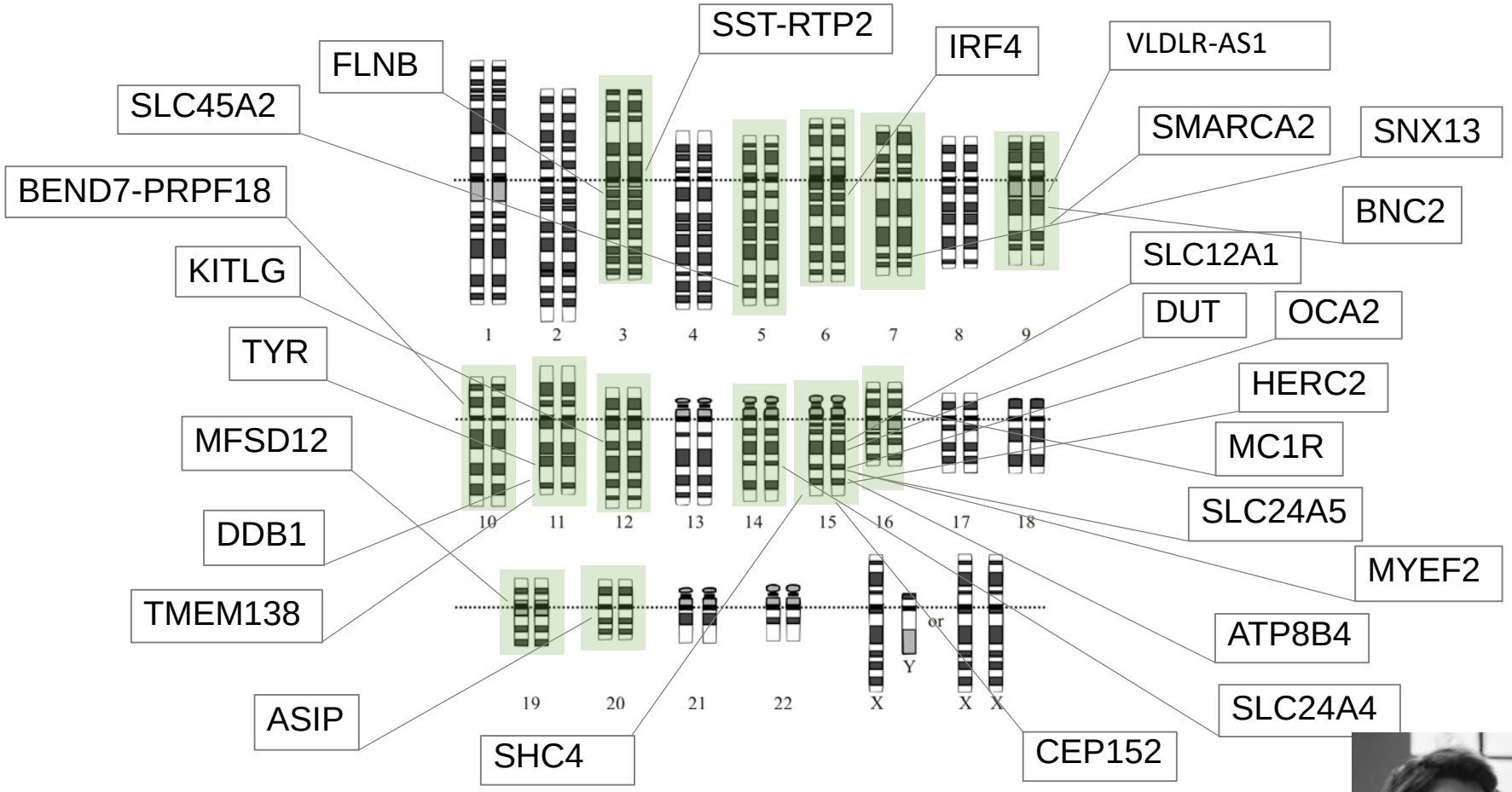
Mathieson & Mathieson 2018

Evolution of pigmentation



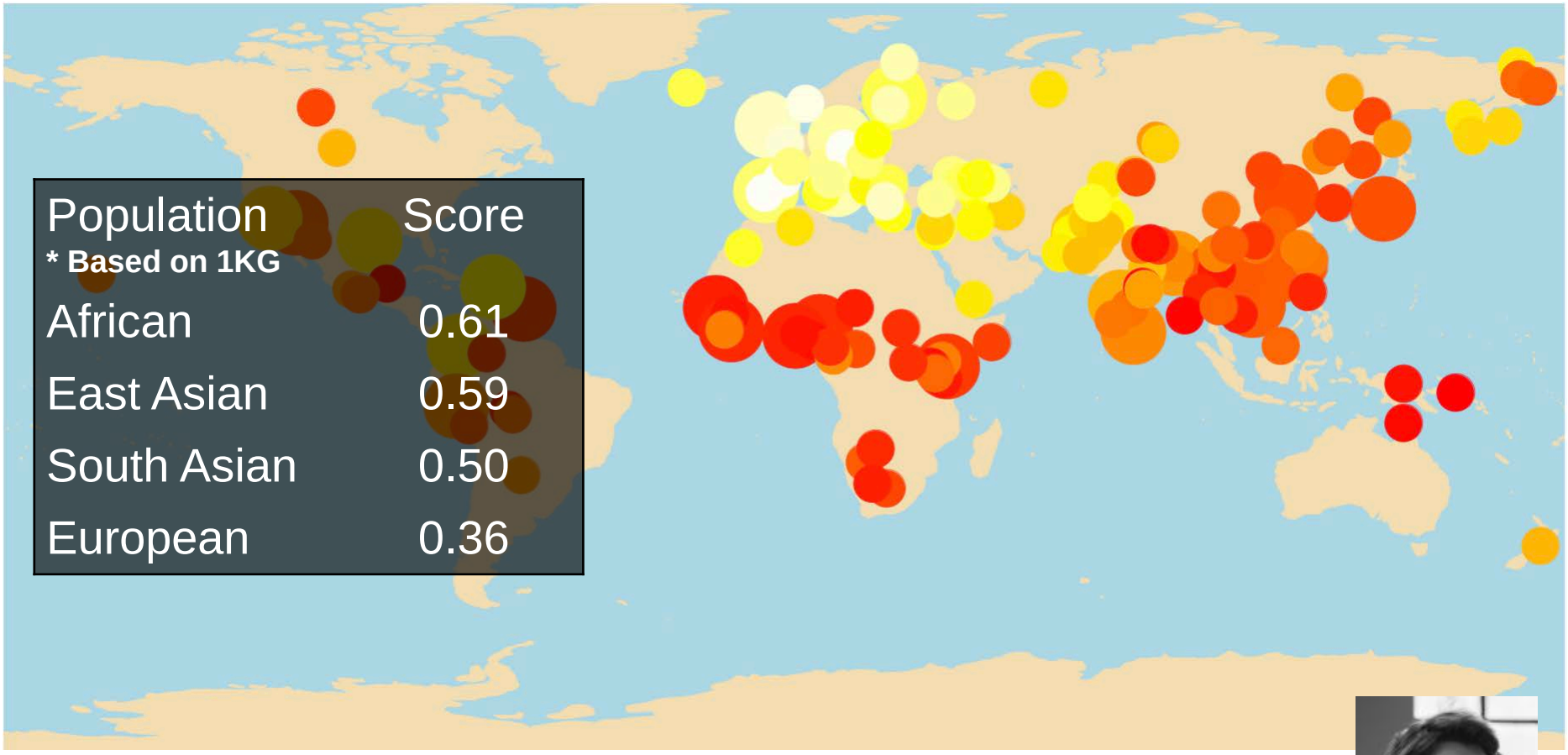
Jablonski & Chaplin 2009

54 pigmentation-associated variants



Dan Ju

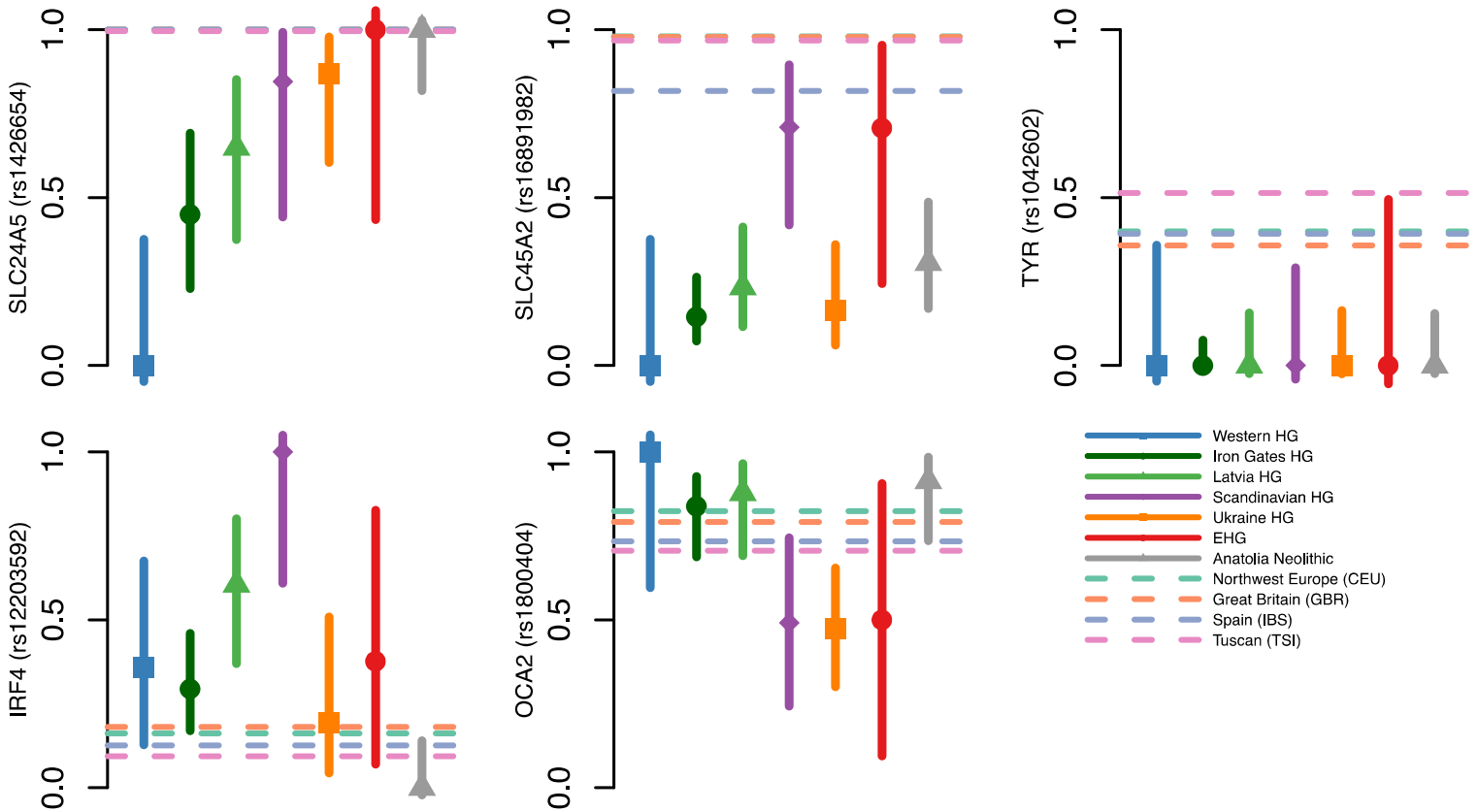
Score: proportion of pigmentation-increasing variants



Population * Based on 1KG	Score
African	0.61
East Asian	0.59
South Asian	0.50
European	0.36

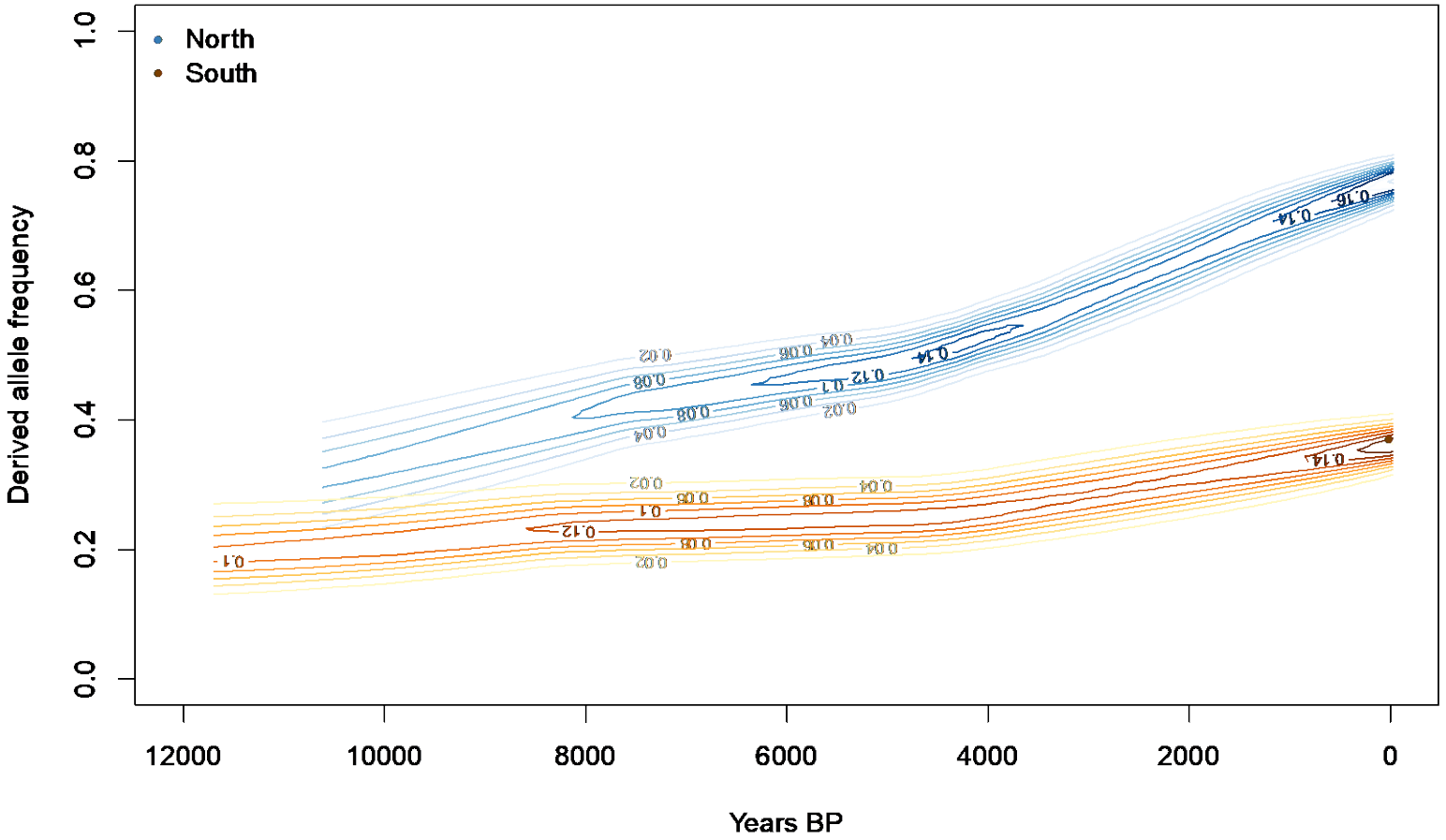
Dan Ju

Variation in pigmentation in Europe 10,000 BP



Mathieson et al. 2018

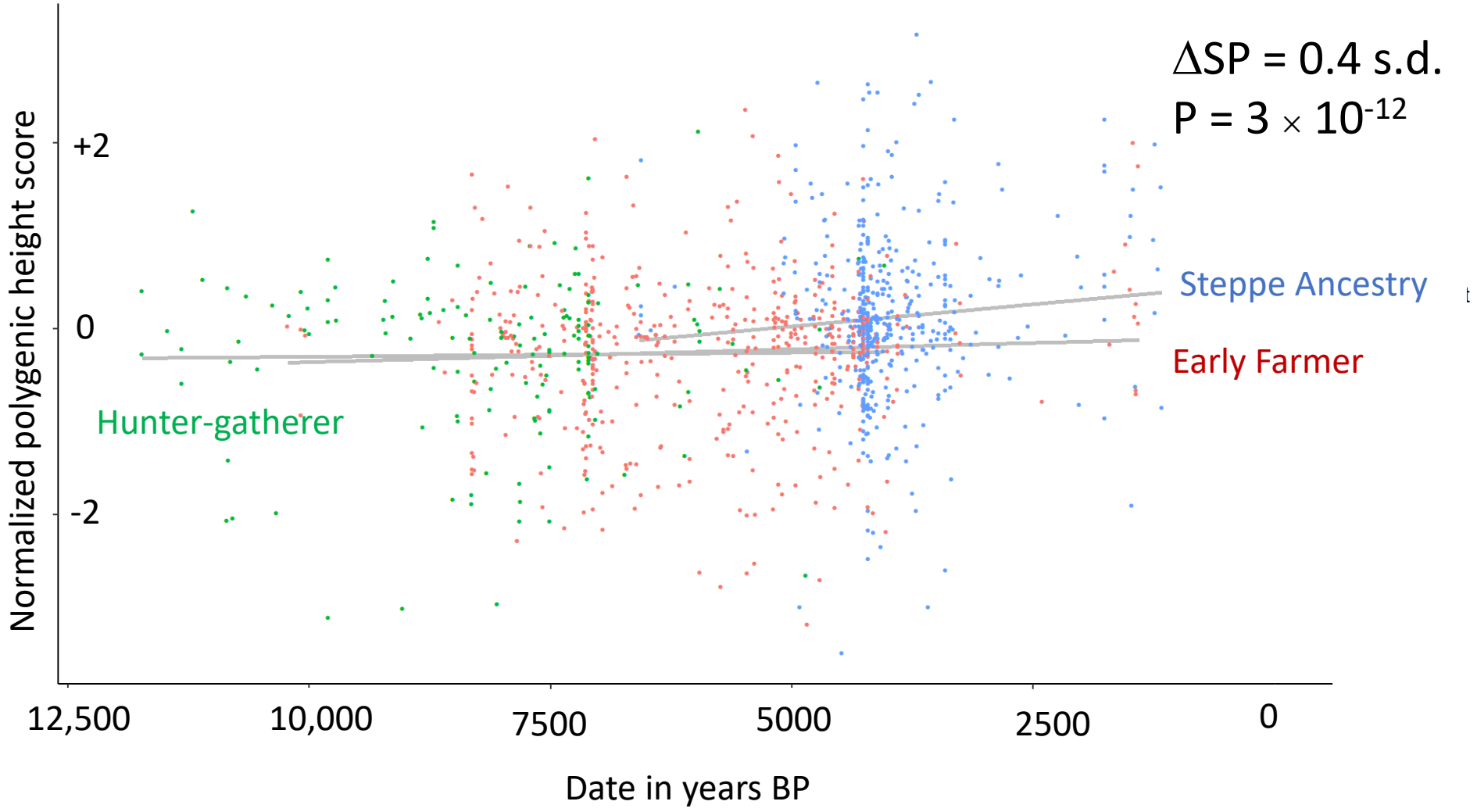
HERC2 [OCA2] Eye color–associated rs12913832



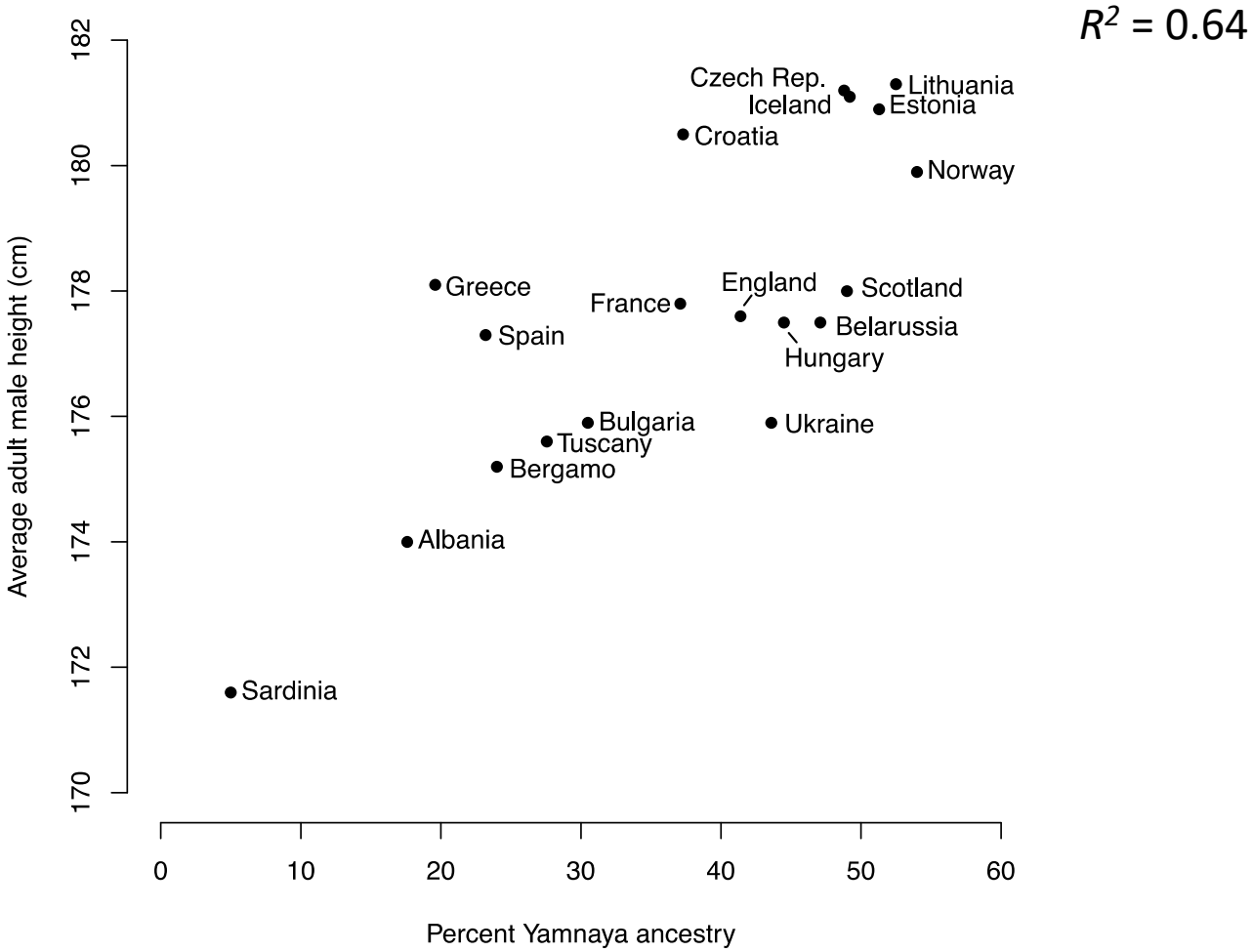
Dan Ju

Evolution of stature

Differences in genetic height among ancient populations (N=1107)



Steppe ancestry predicts present-day height



Skoglund & Mathieson 2018

Collaborators & Funding

Penn

Dan Ju

Other institutions

Sara Mathieson (Swarthmore)

Pontus Skoglund (Crick Institute)

David Reich (Harvard)

Christopher Ruff (Johns Hopkins)


Questions?