The Neandertals and Us: What does it take to make us humans?

Liran Carmel
Department of Genetics
The Hebrew University of Jerusalem

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Key References

- Green RE, Krause J, Briggs AW, …, Reich D, Pääbo S. **A draft sequence of the Neandertal genome**. *Science* 2010 328:710-722. Link

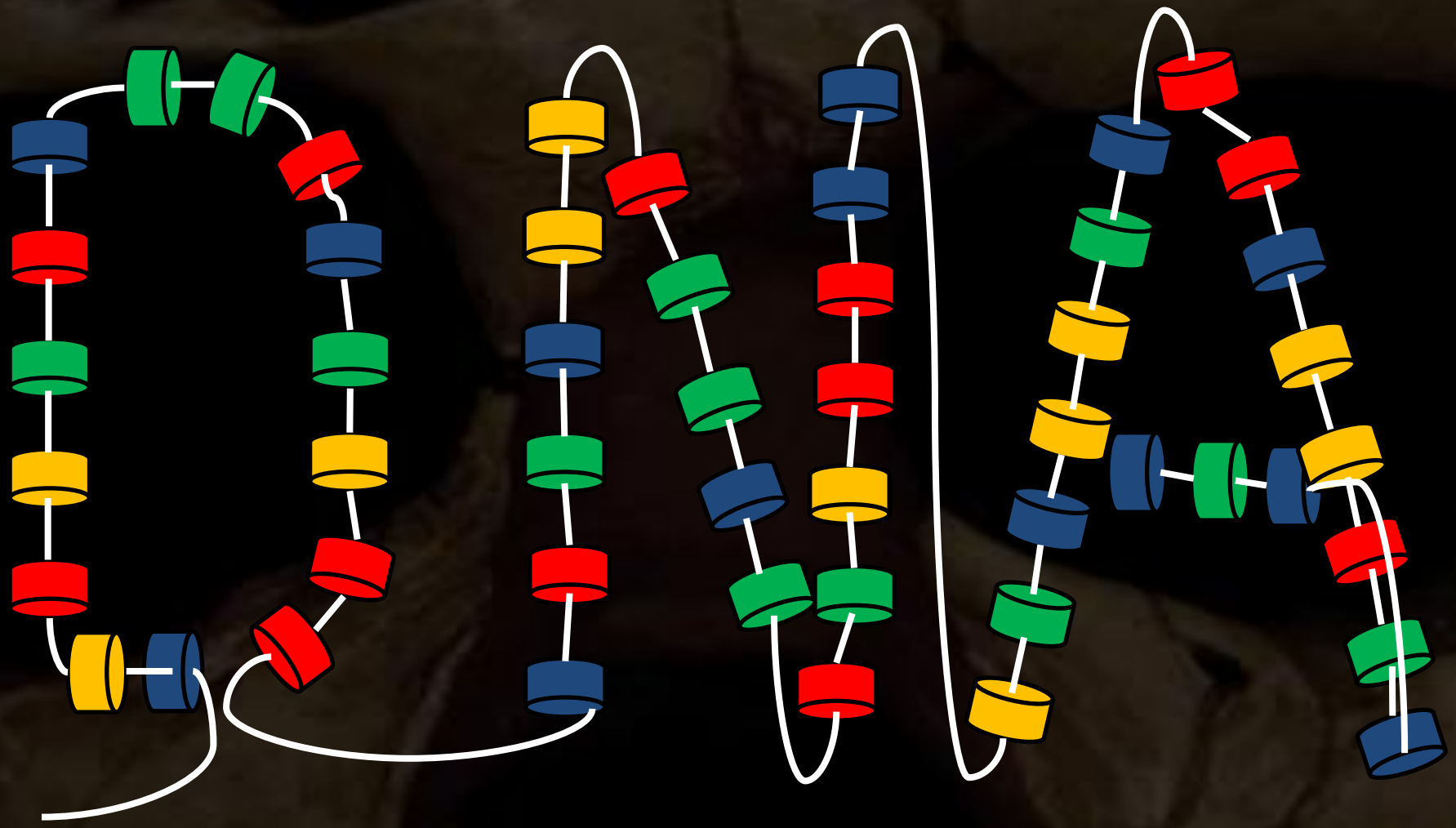
  The first draft of the Neanderthal genome, the result of many years of labor on the Neanderthal genome project.
- Meyer M, …, Slatkin M, Reich D, Kelso J, Pääbo S. **A high-coverage genome sequence from an archaic Denisovan individual**. *Science* 2012 338:222-226. Link

  The genome of the man from Denisova. This is the first high-coverage archaic genome, and the first time a new extinct human species is determined based on genetics alone.
- Prüfer K, …, Slatkin M, Reich D, Kelso J, Pääbo S. **The complete genome sequence of a Neanderthal from the Altai Mountains**. *Nature* 2014 505:43-49. Link

  The first high-coverage genome of a Neanderthal, based on a single individual whose bones were found at the same cave in which the Denisova bones were also found.
- Gokhman D, Lavi E, Prüfer K, Fraga MF, Riancho JA, Kelso J, Pääbo S, Meshorer E, Carmel L. **Reconstructing the DNA methylation maps of the Neandertal and the Denisovan**. *Science* 2014 344:523-527. Link

  The first work to provide a way to determine how genes worked in archaic genomes. The work analyzed gene activity patterns in Neanderthals and Denisovans, and found in what ways they differ from us.

What is DNA?



Revolution I: The genetic revolution

The human Genome Project

$4,000,000,000

and 13 years

$1,000

and 1 day

Comparative Genomics

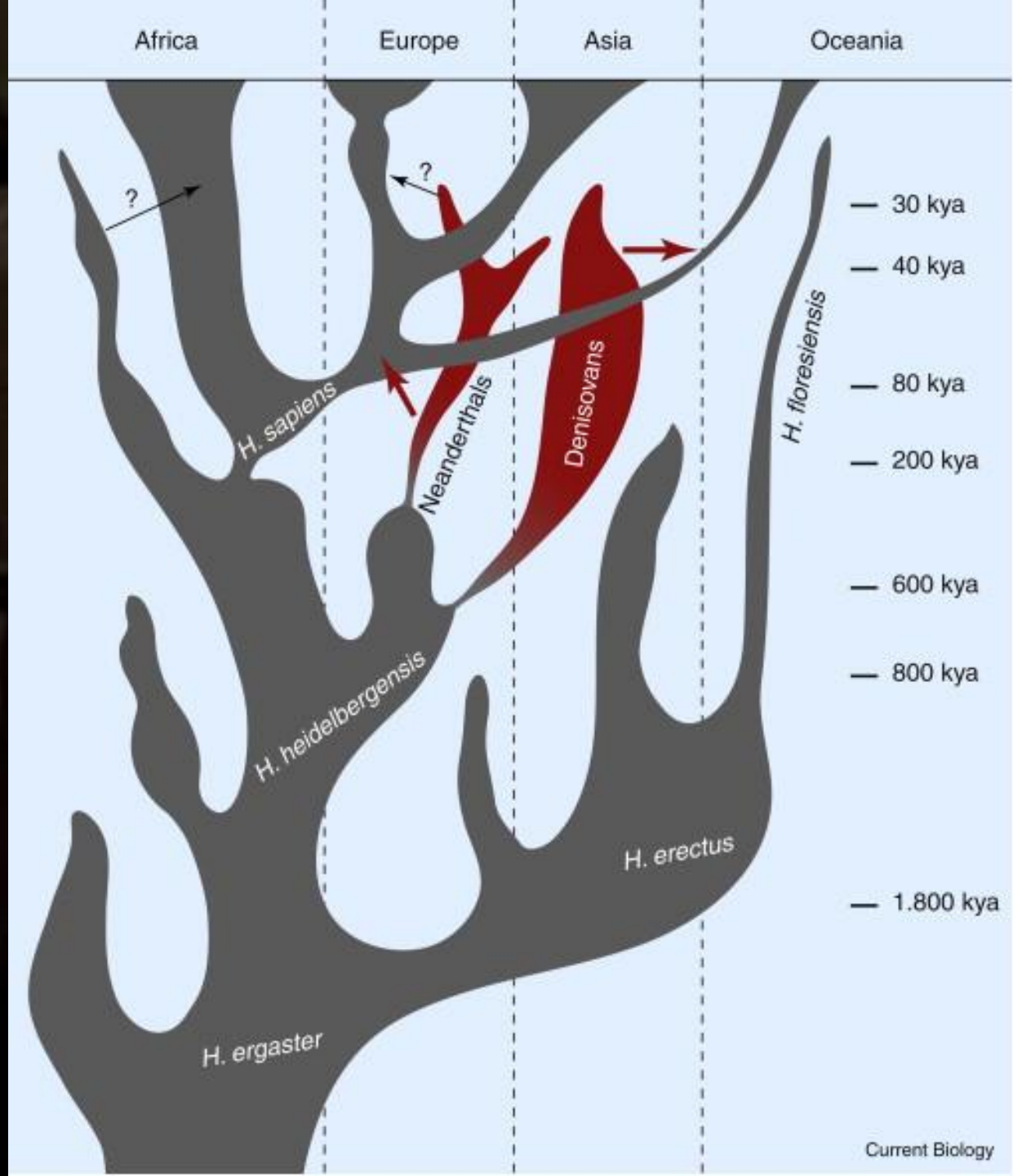
Revolution II: The ancient DNA revolution

Photo Credit©Andreas F. Voegelin, Antikenmuseum Basel, and Sammlung Ludwig

Otzi the iceman


© South Tyrol Museum of Archaeology

Beyond Sapiens: who are you, Neandertal?



Did Neandertals have language (FOXP2)?

Are Scottish people Neandertals (MRC1)?

Test yourself: are you a bit Neandertal?

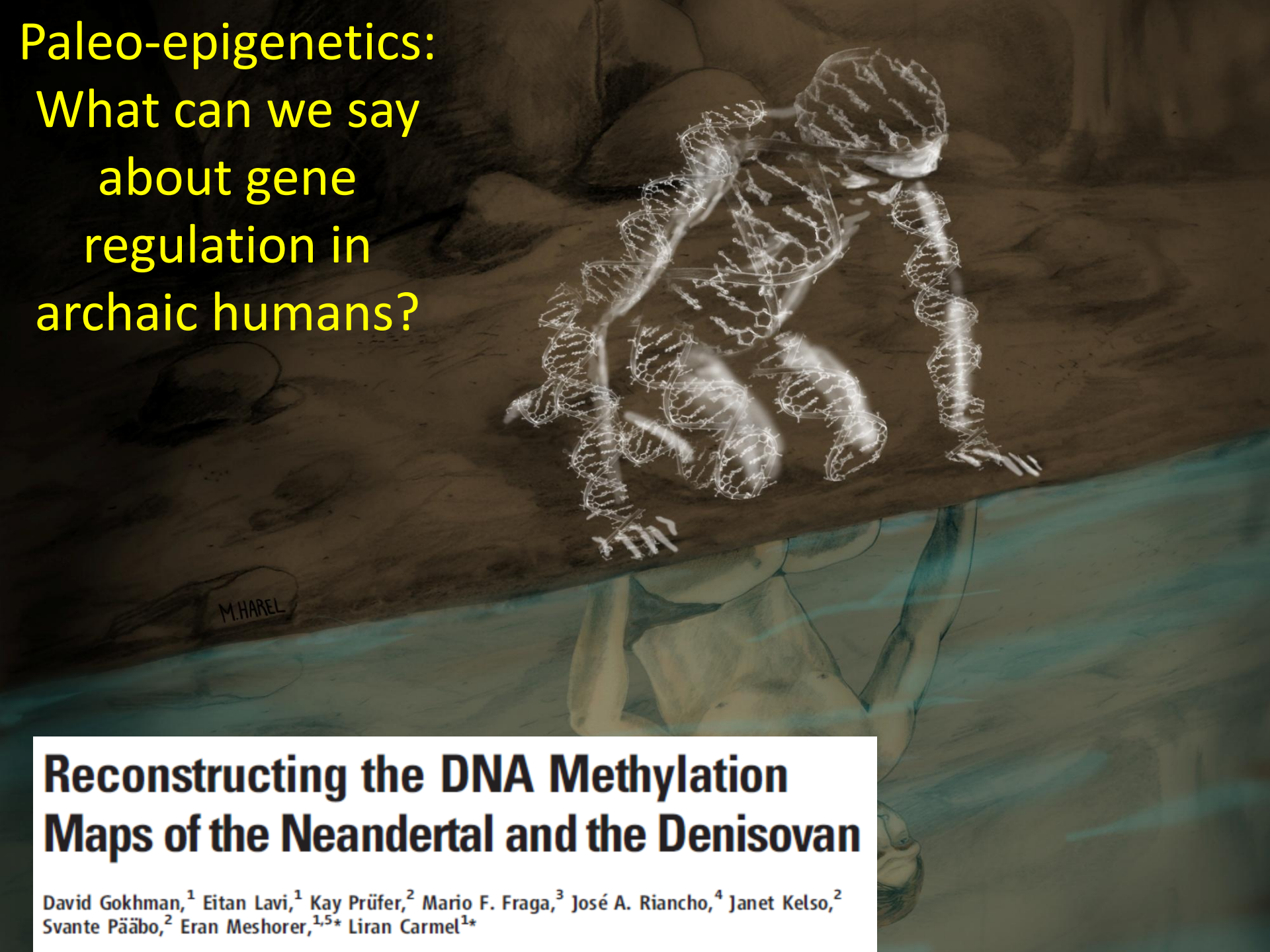
Sequence or Regulation?

Human-Chimp Comparison

Proteins are more than 99% identical

DNA is around 98.8% identical

Paleo-epigenetics: What can we say about gene regulation in archaic humans?



Reconstructing the DNA Methylation Maps of the Neandertal and the Denisovan

David Gokhman,[1] Eitan Lavi,[1] Kay Prüfer,[2] Mario F. Fraga,[3] José A. Riancho,[4] Janet Kelso,[2] Svante Pääbo,[2] Eran Meshorer,[1,5]* Liran Carmel[1]*

DNA methylation

AAAGCGGCGCACTTCAGGCATAAAAGGATGGATTTTTGACAA

TCCCCGATGTCCAAGCTATGGTCCCTTAACAGCAATGCTAGGG

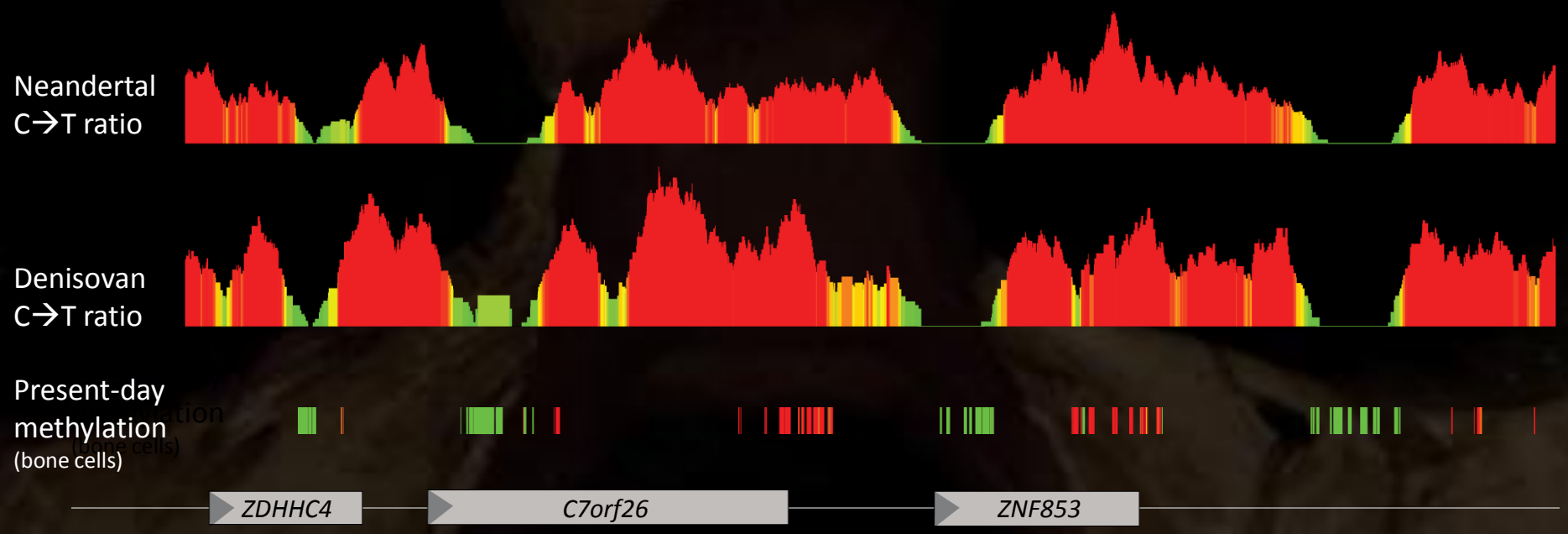
AGCAATAAACATAACCATCCACAGTGAATTGATCCGAAGGGG

GTCGGCATCGGAAGCTTGAAATTGAGAAGCGGGGAGTTACC

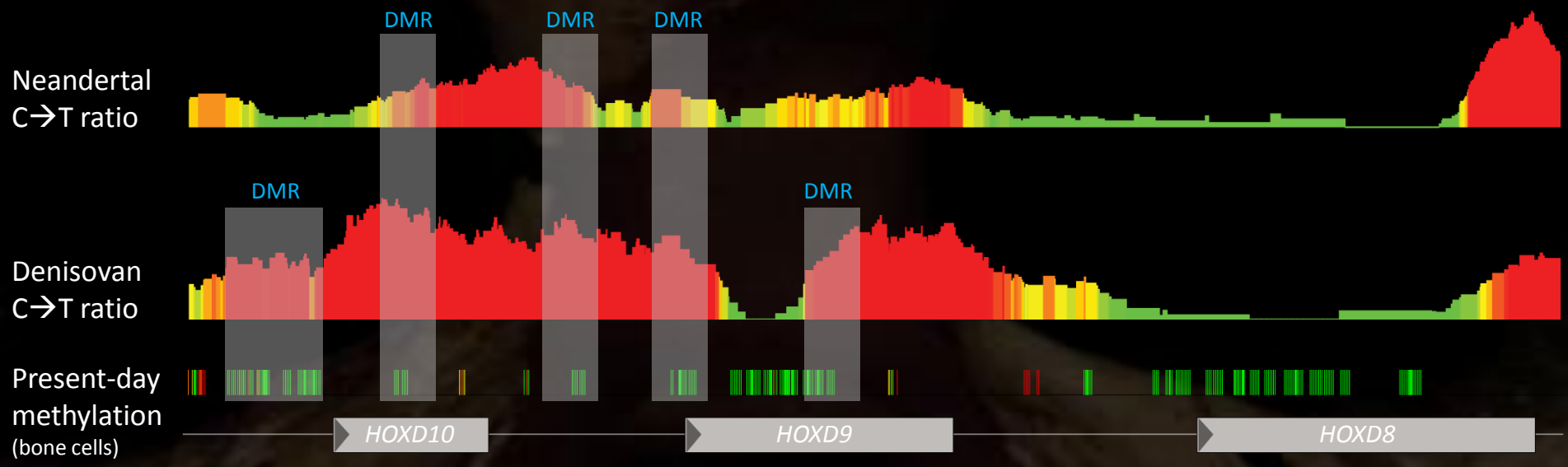
GGTCAATACGAGCATACAGACAATCGTCGTCGATACTCTCCAG

CCGACTGAAAACGGGAGAAAAAACCACTGGAAATGGCAGTA

Gene activity patterns in modern and archaic humans are generally very similar



But sometimes they are not – the HOXD example



HOXD – the genes behind limb evolution

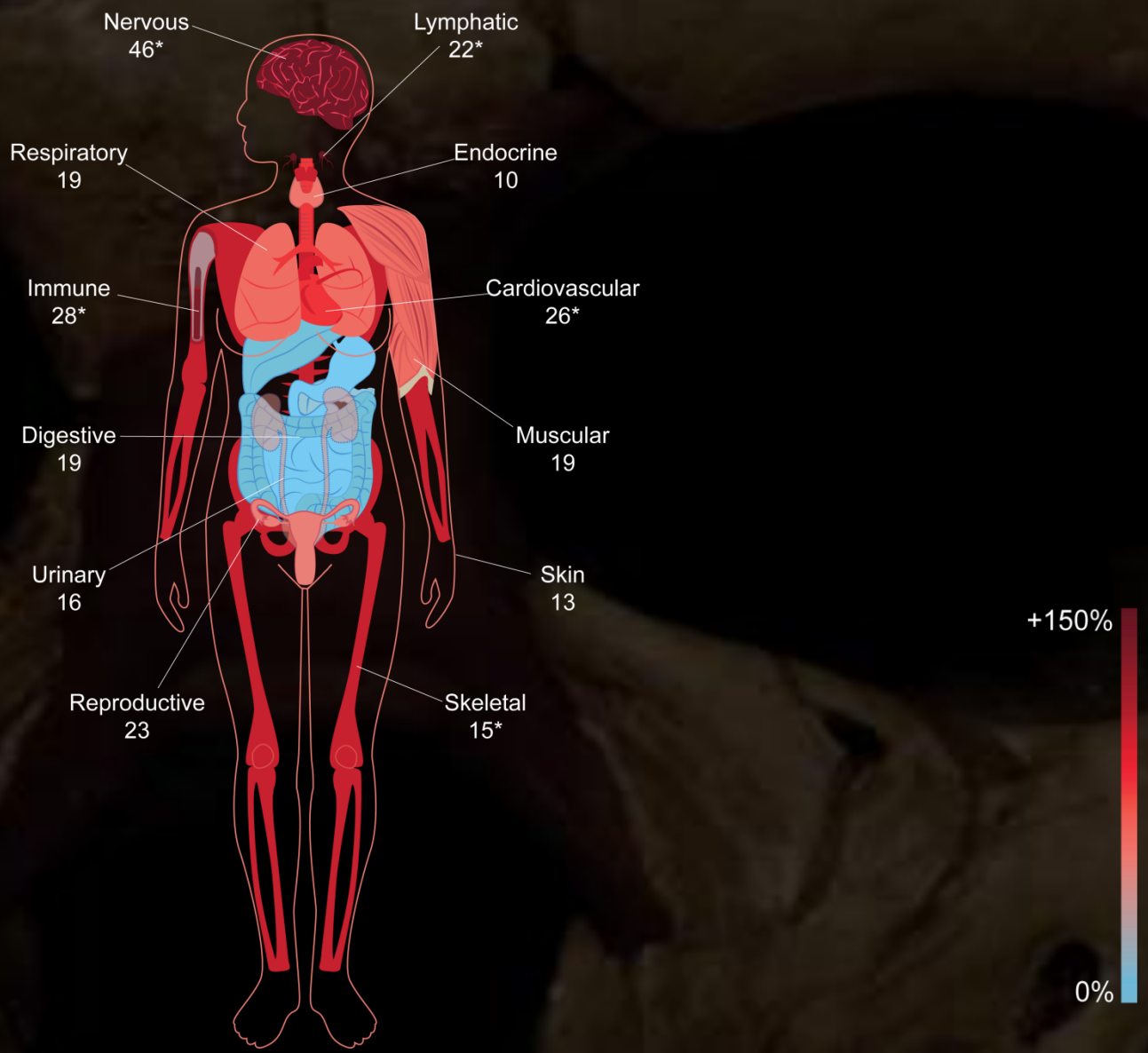
Phenotypes of HOXD9/10 inactivity:

- Curved femur
- Shorter limbs
- Robust fingers
- Broader elbow
- Curved radius
- Broader knee joints
- Thickened kneecaps

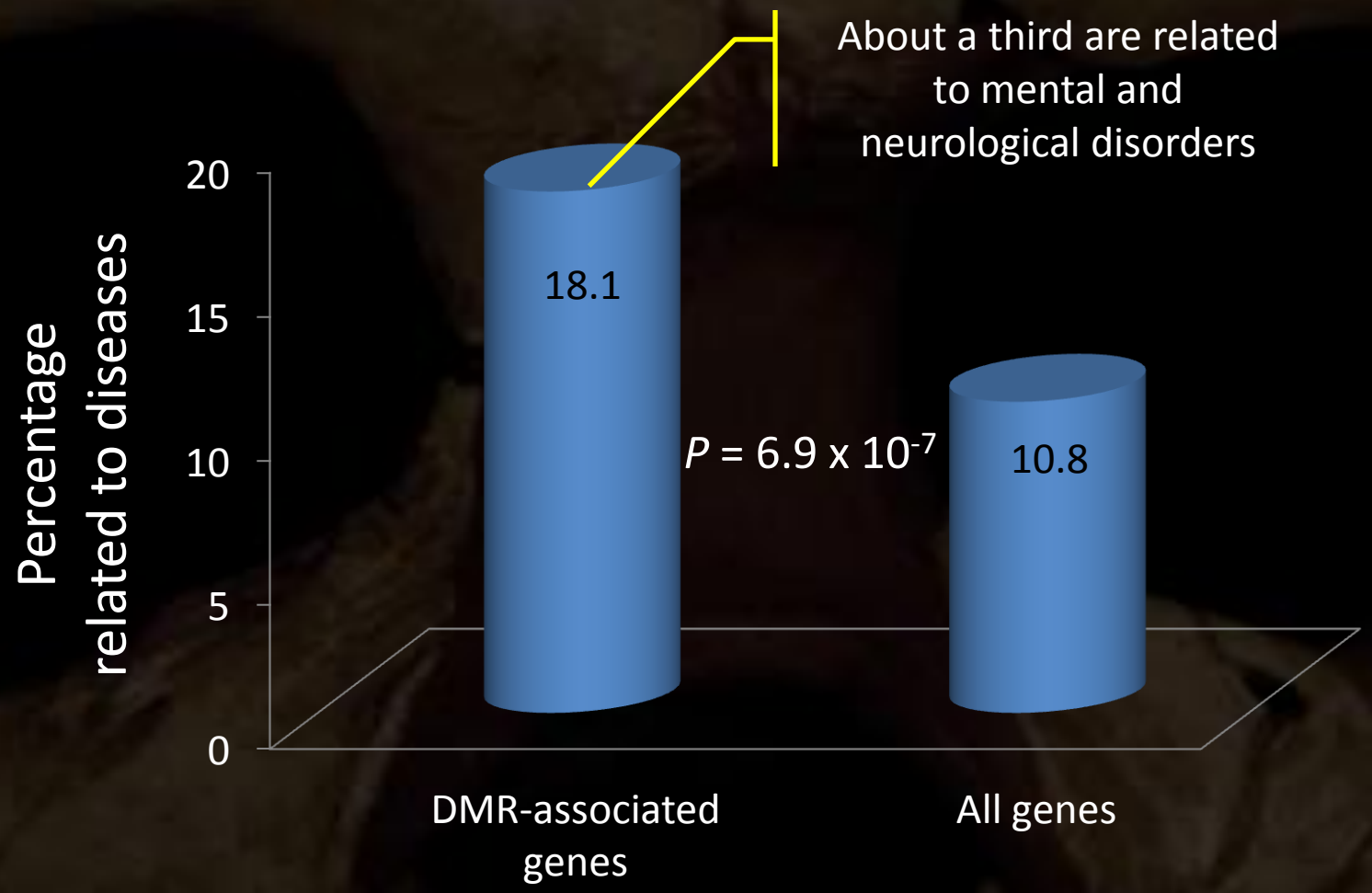
Neandertal Present-day human

Photo by K. Mowbray

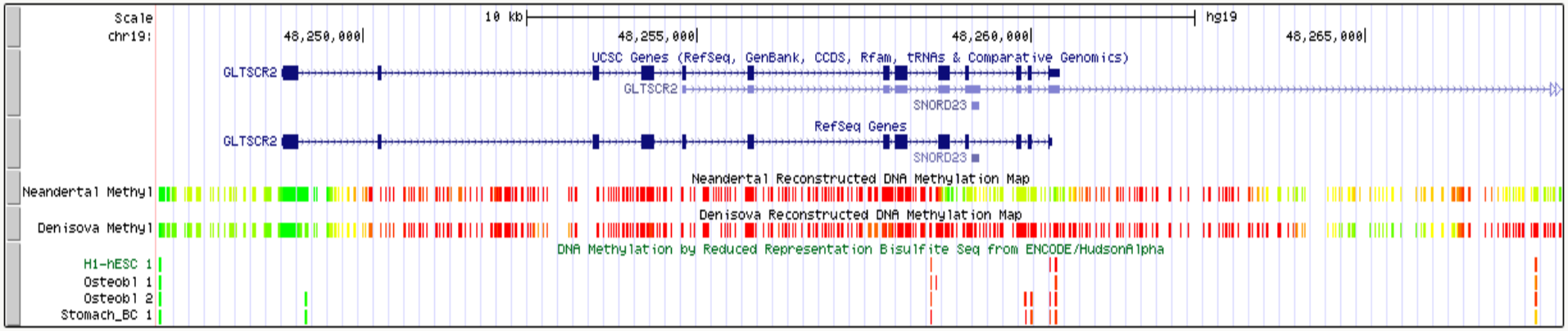
Genes whose activity pattern is unique to modern humans – what do they do?



Genes whose activity pattern is unique to modern humans – how they affect us?

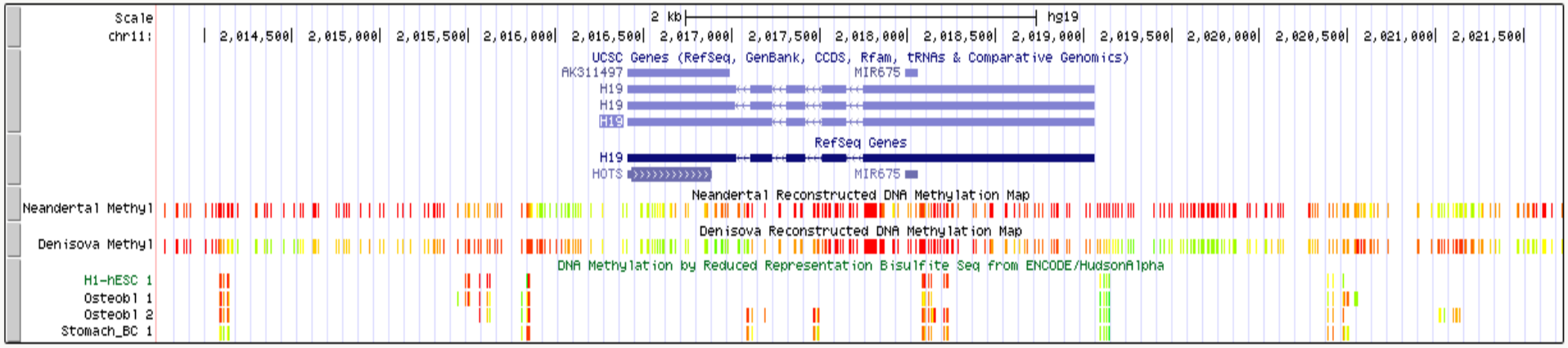


GLTSCR2 – A Gene for aggressiveness?



H19 - Gene for accelerated growth?

Beckwith-Wiedemann Syndrome



What's next?

- Method that do not damage precious ancient DNA samples
- Gene regulation of an extinct species
- The epigenetic history of our species

Acknowledgements

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