

Denisovan Anatomy

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The puzzle of Denisovan anatomy

Fossils are identified as Denisovan by their DNA.

The known Denisovan fossils are too fragmentary to tell us much about anatomy

Is it possible to decipher anatomy from DNA?

The problem with GWAS

One approach to this problem uses genome-wide association studies (GWAS).

Variation in modern phenotypes is correlated with modern genetic variation to construct a *polygenic score*, which predicts phenotype from genotype.

Works well in recent past but not in ancient past, because most recent variants are not very old.

Using methylation to predict phenotype

Methyl groups are molecules that attach to DNA and inhibit transcription, which reduces the amount of protein produced.

Gokhman et al (2019) developed a way to predict ancient phenotypes from methylation patterns.

How to distinguish methylated from unmethylated parts of ancient DNA

All ancient DNA is damaged, to a greater or lesser extent.

The type of damage differs between methylated and unmethylated parts of a chromosome.

Gokhman et al estimated the methylation pattern from the damage pattern.

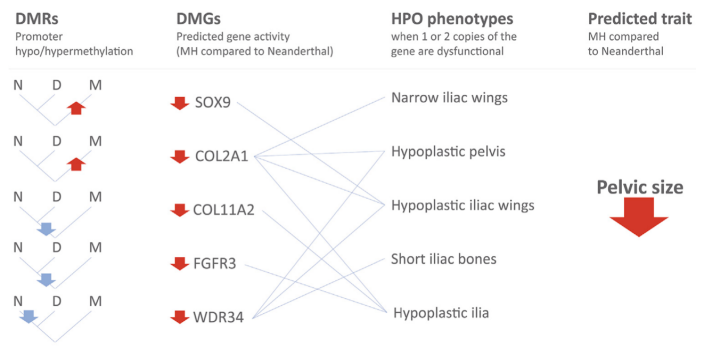
How to tell how methylation affects the phenotype

Methylation reduces *gene expression*—the amount of protein produced by a gene.

Other mutations may also reduce gene expression, and much is known about how gene expression affects phenotypes.

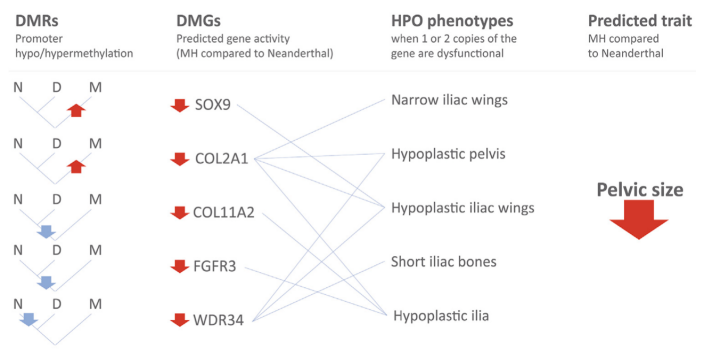
Gokhman et al made a list of genes that are methylated differently in modern humans, Neanderthals, and Denisovans. Then they searched the literature for information about how expression of these genes affects phenotypes.

An example: pelvic size



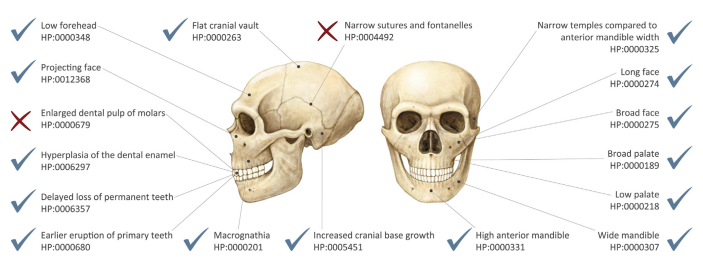
Methylation has increased in modern humans (MH) at the SOX9 gene ⇒ lower gene expression ⇒ smaller pelvis.

An example: pelvic size



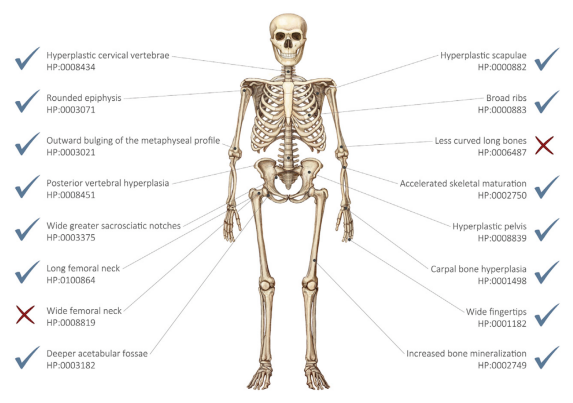
Four other genes also imply a smaller pelvis in MH than Neanderthals.

Testing the method against skull traits



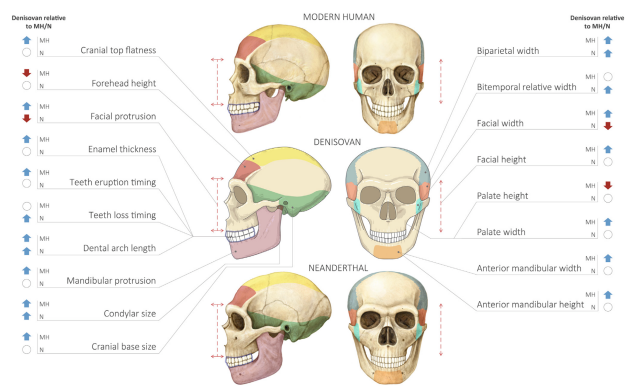
Method was correct for 15 of 17 differences between skulls of MH and Neanderthals.

Testing the method against other traits



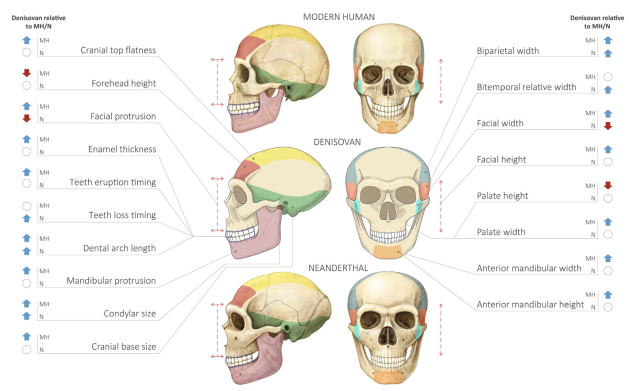
Correct for 14 of 16 other skeletal traits.

Predicted Denisovan skull traits



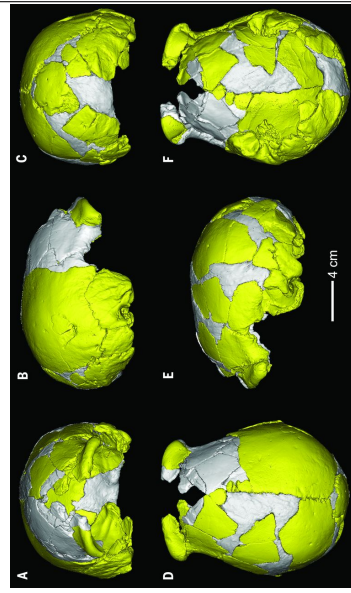
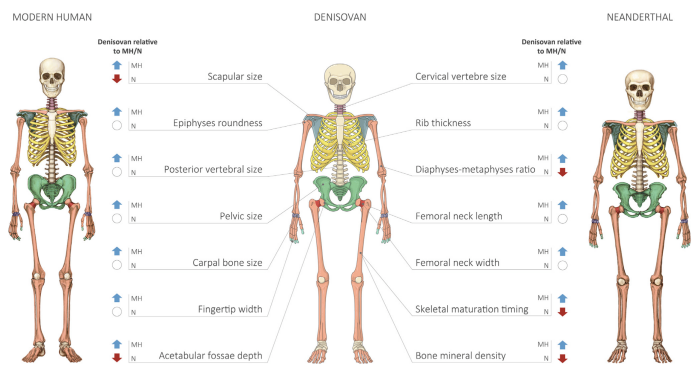
Example: predicted biparietal width is wider in Denisovans than in Neanderthals or MH.

Predicted Denisovan skull traits



Prediction: Denisovans had wider heads and flatter faces than Neanderthals.

Predicted Denisovan other traits

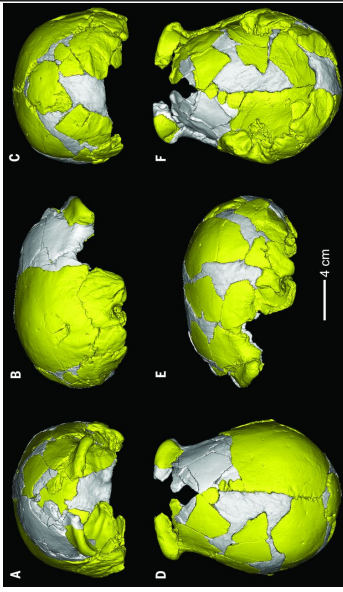


Xuchang skulls

100–130 kya, from China

Anatomy similar to Neanderthals, but it's too far east.

Right time and place for Denisovans, but we have no DNA.



8 traits differed from Neanderthals.

7 of the 8 were predicted to differ, based on methylation patterns in the Denisovan genome from Siberia.

For 4 of the traits, the direction of the difference could be predicted. All 4 differed in the predicted direction.

Summary

- ▶ Methylation of DNA suppresses gene expression.
- ▶ Also affects postmortem changes in DNA, allowing us to estimate methylation patterns in ancient DNA.
- ▶ Methylation patterns successfully predict known differences between MH and Neanderthals.
- ▶ Predict that Denisovans had wider heads and flatter faces than Neanderthals.
- ▶ Predicted Denisovan anatomy agrees remarkably with the Xuchang skulls from China.