

ASHBi SEMINAR

How gene regulation shaped the evolution of modern and archaic humans

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Time: Noon–1:00PM

Venue: Zoom Online Meeting

To study human evolution, it is imperative to compare our genetics to that of our closest extinct relatives – the Neanderthal and Denisovan. Particularly important is gene regulation, as regulatory changes are thought to be the main driver of phenotypic differences between closely related organisms. However, ancient samples are degraded, and mapping their gene regulatory marks is largely impossible. To address this, we developed a method to reconstruct a key gene regulatory mark – DNA methylation – from ancient samples. We used these reconstructed DNA methylation maps to identify regulatory differences between modern and archaic humans. We found that genes affecting the voice box have gone through particularly extensive changes. We then turned to use these maps to shed light on the little-understood Denisovan. We present a method for reconstruction of anatomical profiles using DNA methylation patterns and data from monogenic diseases. We then apply it to the Denisovan and offer a putative morphological profile. We conclude that DNA methylation can be used as a tool to reconstruct anatomical features, including some that do not survive in the fossil record. Finally, we use massively parallel reporter assays (MPRAs) to measure the regulatory effects of each of the 14,000 single-nucleotide variants that separate modern from archaic humans. Overall, 1,791 (13%) of these loci showed active regulatory activity, and 407 (23%) of these drove differential expression between human groups. Differentially active sequences were associated with vocal tract and brain anatomy and function. Together, these works provide insight into the recent evolution of human gene regulation.

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