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From Africa to the Arctic

how the woolly mammoth adapted to the cold

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Mammoths, African elephants, and Asian elephants diverged from one another about 7 million years ago in Africa. These members of the elephantid family were adapted to living in the hot tropical climates. This is why elephants today have large ears to maximize heat loss.

Figure 1

But mammoths migrated North at the same time as a sudden climate change saw temperatures plunge in the Arctic. And so 2 million years ago they adapted to survive the Arctic cold. To minimize heat loss, they developed small ears and tails, and a woolly undercoat that led to their common name of woolly mammoth.

On a molecular level, scientists have found that specific mammoth proteins contain amino acid changes that are not found in elephants. But it had not been possible to link these genetic changes to how the mammoth might have physiologically adapted to the cold. Until now.

Campbell et al. have found that amino acid changes in hemoglobin would have given the mammoth a unique genotypic adaptation to the cold. Hemoglobin is the oxygen-carrying protein found in red blood cells. In humans and in most mammals, an increase in temperature decreases the stickiness of oxygen to hemoglobin. This helps release additional oxygen where it is needed, to warm exercising muscles. However, Arctic mammals such as reindeer keep their limbs cold to minimize heat loss. Their hemoglobin is much less sensitive to changes in temperature as oxygen needs to be delivered to the tissues even when they are cold.

The genes encoding woolly mammoth hemoglobin acquired three nucleotide mutations that similarly helped oxygen delivery in its new Arctic environment. These three changes occurred on the HBB/HBD globin gene such that the chimeric β/δ globin chain had three amino acid substitutions: T12A, A86S and E101Q. African and Asian elephants, who remained in warmer climes, do not have these changes.

All three amino acid substitutions are on the same side of the hemoglobin protein. The T12A and A86S substitutions are exposed on the outer surface of the protein. Molecular modelling indicated that the E101Q substitution may be structurally important, as it occurs at the highly conserved interface between the two sliding αβ dimer subunits. To confirm their function, the three changes were spliced into cDNA of Asian elephants and the mammoth hemoglobin protein faithfully synthesized in *E. coli*. As expected, the substitutions had large phenotypic effect, thereby reducing the energy (heat) requirements for releasing oxygen.

The mammoth became extinct from mainland areas about 10,000 years ago, and the last mammoths died about 3700 years ago on Wrangel Island in the Arctic Ocean. Their extinction was possibly caused by hunting by man, further climate change, or a combination of the two. By sequencing and resurrecting phenotypic attributes of extinct species such as the woolly mammoth, we can discover functional differences that are not attainable by studying fossils. But just as we are discovering genetic factors that are beneficial in evolution, we may also discover genetic factors that played a part in the extinction of the woolly mammoth and other species.

This Coffee Break was reviewed by Kevin L. Campbell, Ph.D.

***Mammuthus primigenius* (woolly mammoth).**
The woolly mammoth lived in the late Pleistocene era across Asia, Europe, and North America. By using fossil DNA from preserved remains of woolly mammoth samples, scientists have decoded its mitochondrial genome, and are now sequencing other mammoth genes.

Image source: What Killed the Woolly Mammoth? Sedwick C *PLoS Biology* Vol. 6, No. 4, e99

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