'Resurrection' and structure-function analysis of extinct hemoglobin phenotypes: new life for ancient DNA

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Hemoglobin binds and carries O_2, though its ability to offload O_2 to respiring cells is hampered at cool extremities as heme deoxygenation is inherently endothermic (i.e. Hb–O_2 affinity increases as temperature decreases). Members of several tropical mammalian lineages (e.g. woolly mammoths, woolly rhinos, Steller's sea cows) provide ideal model systems to study blood adaptations in this regard, as they each independently colonized high-latitude environments during the Pleistocene Ice Ages. Unfortunately, as these 'living' processes do not fossilize, any information regarding the functional properties of extinct gene products, or their interplay with natural ligands, have remained beyond the range of scientific inquiry. We have overcome this limitation by sequencing and expressing hemoglobin from three woolly mammoths, and then performing *in vitro* tests on the resurrected product to reveal the genetic and structural basis of a novel solution to this problem, removing the need to maintain warm extremities for proper blood function and thereby minimizing energetically costly heat loss. We have utilized recent advances in targeted DNA enrichment and next generation sequencing technologies to test for parallel adaptive evolution in Steller's sea cows. This powerful new approach promises to add a significant new dimension to the study of natural selection.