```
Lox  T TTC GGC TCA CTA CTA GGA GCA TGC CTA ATT ACA CAA ATC CTA ACA GGA TTA TTC CTA GCC ATA CAT TAT
Mam1 . ... ... ... ... ... ... ... ... ... ... ..c ..g ... ... ... ... ... ..t ... ... ... ... ...
Mam2 . ... ... ... ... ... ... ... ... ... ... ..c ... ... ... ... ..g ... ..t ... ..t ... ... ...
Ele  . ... ... ... ... ... ... ... ... ... ... ..c ... ... ... ... ... ... ... ... ... ... ... ..c

Lox  ACA CCC GAC ACA ATA ACT GCA TTT TCA TCT ATA TCC CAT ATT TGC CGA GAT GTA AAC TAC GGC TGA ATT
Mam1 ... ..t ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... ..c ... ... ... ... ...
Mam2 ... ..t ... ... ... ... ... ... ... ... ... ... ... ..c ... ... ... ..c ... ... ..t ... ...
Ele  ... ..t ... ... ... ... ... ... ... ... ... ... ... ..c ... ... ..c ..c ... ... ... ... ...

Lox  ATT CGA CAA CTA CAC TCA AAC GGA GCA TCC ATT TTC TTC CTC TGC CTA CAC ATT GGA CGA AAC ATC TAC
Mam1 ... ... ... ... ... ... ... ... ... ... ..t ... ... ... ... ... ... ... ... ... ... ... ...
Mam2 ... ... ... ... ... ... ... ... ... ... ..t ... ... ... ... ... ... ... ... ... ... ... ...
Ele  ... ... ... ... ... ... ... ... ... ... ..t ... ... ... ... ... ... ... ... ... ... ... ...

Lox  TAT GGG TCC TAC CTA TAC TCG GAA ACT TGA AAT ACC GGC ATT ATA TTA CTA CTA ATC ACC ATA GCC ACC
Mam1 ... ... ... ... ... ... ... ... ... ..c ... ... .
Mam2 ... ... ... ... ... ... ... ... ... ..c ... ... ... ... ... ... c.. ... ... ..a ... ... ... ...
Ele  ... ..a ... ... ... ... ..a ... ..c ... ... ..a ... ... ... ... ... ... ... ..t ... ... ... ...
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Alignment of DNA sequences obtained from the two Siberian mammoths (Mam 1 and 2) and one Asian elephant (Ele) with the published African cytochrome *b* sequence (Lox)[8] (GenBank accession number X56285); identity to this sequence is denoted by a full stop (.). The sequence was read from bases 96 to 378 of the cytochrome *b* gene[8].

species of elephantid, the African elephant *Loxodonta africana* and Asian elephant *Elephas maximus*[3]. Mammoth remains include not only bones and teeth from thousands of localities, but also whole carcasses frozen in Siberian and Alaskan permafrost.

We extracted DNA from bones of two frozen Siberian woolly mammoths, and subsampled both specimens for accelerator mass spectrometry (AMS) radiocarbon dating at the Institute of Geological and Nuclear Sciences, New Zealand. The first individual, the Khatanga mammoth, consisted of the partial carcass of an adult male excavated in 1977 from alluvial sand in the eastern Taimyr peninsula[4]. We cut a wedge of cortical bone from one humerus (no. 31829) at the Zoological Institute, St Petersburg. Previous conventional radiocarbon dating on a sample of trunk and skin yielded dates of ≥40,340 years BP (LU-750) and ≥53,170 years BP (LU-1057), respectively. Both these dates are consistent with the new bone AMS date of >47,000 years BP (NZA-3711). As the specimen is beyond the range of finite radiocarbon dating, the age of this mammoth must be 47,000 years or older.

The second mammoth sample was from a mandible (no. PIN 3657-181) excavated in 1975 by AVS from the Allaikha river, northeast Siberia[5]. It was found in permafrost 16 m below the surface in section ANV-1, beneath a horizon radiocarbon dated to >46,000 years BP on autochthonous plant vegetation remains (GIN-1681). We removed a piece of bone for DNA analysis, and a subsample yielded an AMS date of >47,000 years BP (NZA-3712). The predominant fossils in the fauna horizon were of the extinct lemming *Dicrostonyx simplicior*, an evolutionary precursor of the extant collared lemming *D. torquatus*. This suggests a late Middle Pleistocene age for the mammoth, not less than 150,000 years BP.

We extracted DNA from the two mammoth bones (0.7 g bone) as described previously[6], in parallel with three forensic and three prehistoric human bone samples, and an extraction blank with no bone. DNA was amplified from the bone extracts using the PCR with the highly conserved primers L14841 and H15149, which define a 375-base-pair fragment of the cytochrome *b* gene[7]. All the bone extracts yielded phylogenetically meaningful DNA sequences. We performed amplification reactions in a laboratory where elephant DNA had not been handled before. Following amplification, we determined the DNA sequences of both strands and compared them with the previously published African elephant cytochrome *b* sequence[8] (see figure above), as well as with the orthologous sequences of eight African and six Asian elephants (one of which is shown in the figure). Preliminary phylogenetic analysis of the sequences from all these individuals shows that the mammoths fall within the elephantid clade, with the close divergence times for the three genera reflected in a tight clustering of the *Mammuthus*, *Loxodonta* and *Elephas* sequences.

Previous studies using protein analysis have failed to resolve the trichotomy between the three genera. Using a radioimmunoassay, Lowenstein and colleagues found the albumins of *Mammuthus*, *Loxodonta* and *Elephas* to be 99% immunologically homologous, consistent with an evolutionary divergence between 3 and 5 million years ago[9]. Our results are unable to resolve this trichotomy conclusively, although parsimony and maximum likelihood analysis with dolphin and rhinoceros as outgroups suggest that *Mammuthus* and *Loxodonta* could be sister taxa in a monophyletic clade, in contrast to the anatomical evidence. Sequencing data from additional informative mtDNA regions and a larger number of individuals, from both the living and extinct genera, are needed before the evolutionary relationships of the elephantids can be fully understood.

Erika Hagelberg
Mark G. Thomas
Charles E. Cook Jr
Department of Biological Anthropology, University of Cambridge, Cambridge CB2 3DZ, UK
Andrei V. Sher
Institute of Evolutionary Animal Morphology and Ecology, 117071 Moscow, Russia
Gennady F. Baryshnikov
Zoological Institute, 199034 St Petersburg, Russia
Adrian M. Lister
Department of Biology, University College London, London WC1E 6BT, UK

1. Lindahl, T. *Nature* **362**, 709–715 (1993).
2. Lindahl, T. *Nature* **365**, 700 (1993).
3. Lister, A. M. *Trends Ecol. Evol.* **4**, 362–363 (1989).
4. Vereshchagin, N. K. & Nikolaev, A. I. *Trudy Zoologicheskovo Instituta* **111**, 3–17 (1982).
5. Kaplina, T. N. *et al. Bull. Comm. Quat. Res.* **50**, 73–95 (1980).
6. Hagelberg, E. & Clegg, J. B. *Proc. R. Soc.* B**244**, 45–50 (1991).
7. Kocher, T. D. *et al. Proc. natn. Acad. Sci. U.S.A.* **86**, 6196–6200 (1989).
8. Irwin, D. M., Kocher, T. D. & Wilson, A. C. *J. molec. Evol.* **32**, 128–144 (1991).
9. Shoshani, J., Lowenstein, J. M., Walz, D. A. & Goodman, M. *Paleobiology* **11**, 429–437 (1985).

Peptide design

SIR — Jameson *et al.*[1] reported the rational design of a modified cyclic peptide from the CDR3 region of CD4 receptors of T cells which displayed considerable therapeutic effects both *in vitro* and *in vivo* in the experimental mouse model for allergic encephalomyelitis. The significant *in vivo* biological activity of this reverse-sequence peptide probably results from the fact that it contains all D-amino acids.

Brady and Dodson[2] summarized, in an associated News and Views article, how such a peptide analogue with reversed peptide bonds can introduce stability to proteolysis and at the same time stereochemically preserve the topological surface of the side chains in the original L-amino-acid sequence.

Readers should be made aware that this general approach to modification of the peptide backbone has a rather rich history in the areas of peptide medicinal chemistry and bioorganic chemistry. Cyclic retro-inverso peptides[3] and linear, partial retro-inverso pseudopeptides[4] have long been used as relatively stable peptidomimetics for numerous bioactive peptides. A recent review by Chorev and Goodman[5] provides entry into the literature of retro-inverso isomers in peptide design and synthesis.

David B. Glass
Departments of Pharmacology and Biochemistry, Emory University School of Medicine, Atlanta, Georgia 30322, USA

1. Jameson, B. A., McDonnell, J. M., Marini, J. C. & Korngold, R. *Nature* **368**, 744–746 (1994).
2. Brady, L. & Dodson, G. *Nature* **368**, 692–693 (1994).
3. Prelog, V. & Gerlach, H. *Helv. chim. Acta* **47**, 2288–2294 (1964).
4. Goodman, M. & Chorev, M. *Acc. chem. Res.* **12**, 1–7 (1979).
5. Chorev, M. & Goodman, M. *Acc. chem. Res.* **26**, 266–273 (1993).