

This is an electronic appendix to the paper by Lynch *et al.* 2004 Adaptive evolution of *HoxA-11* and *HoxA-13* at the origin of the uterus in mammals. *Proc. R. Soc. Lond. B* **271**, 2201-2207. (doi:10.1098/rspb.2004.2848)

Electronic appendices are refereed with the text. However, no attempt is made to impose a uniform editorial style on the electronic appendices.

Electronic Appendix A

A

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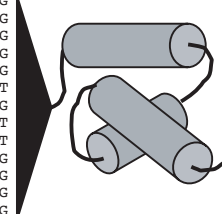
Bta  ??????????SNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVHEVTFREYAIEPATKWLPRGNLAHCYSAEELVHRDCLQAPSAA
Hsa  MDFDERGPCSSNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIEPATKWHPRGNLAHCYSAEELVHRDCLQAPSAA
Mmu  MDFDERGPCSSNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIEPATKWHPRGNLAHCYSAEELVHRDCLQAPSAA
Rno  MDFDERGPCSSNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIEPATKWHPRGNLAHCYSAEELVHRDCLQAPSAA
Dsp  ??????????????????SCTYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIEPATKWHPRGNLAHCYSAEELVHRDCLQAPSAA
Pca  ??????????????????VSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIEPATKWHPRGNLAHCYSAEELVHRDCLQAPSAP
Dvi  MDFDERVPCSSNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIEPSSKWHPRANLPHCYSAEELMHRDCLPASGSA
Oan  ??????????????PSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIDPSSKWHPRANLPHCYSAEELMHRDCLPATNTA
Tac  ??????????SNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIDPSSKWHPRANLPHCYSAEELMHRDCLPATNTA
Gga  MDFDERVPCSSNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIDPSSKWHPRANLPHCYSAEELMHRDCLPSTTTA
Gni  ??????????????????YVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIDPSSKWHPRANLPHCYSAEELMHRDCLPATNTA
Xtr  ??????????MYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIDTSSKWHHRNLPCHCYSAEELMHRDCLPASNTA
Lme  MDFDERVSCSSNMYLPSCYYVSGPDFSSLPFLPQTPSSRPMTYSYSSNLPQVQPVREVTFREYAIDTSSKWHHRNLPCHCYSTEELHRDCLATTAS
  
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Bta  GVEGDVLAKESSANVYHHTPAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--ASS-DYPGDKSAEKGPAAATSAAAAAAAT---GTPA
Hsa  GVEGDVLAKESSANVYHHTPAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--ASS-DYPGDKSAEKGPAAATSAAAAAAAT---GAPA
Mmu  GVEGDVLAKESSANVYHHTPAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--ASS-DYPGDKNAEKGPAAATSAAAVAA--AAT---GAPA
Rno  GVEGDVLAKESSANVYHHTPAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--ASS-DYPGDKNAEKGPAAATSAAAVAA--AAT---GAPA
Dsp  GVEGDVLAKESSANVYHHTPAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--ASS-DYPGDKSAEKGPAAATSAAAAAAAT---GAPA
Pca  GVEGDVLAKESSANVYHHTPAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--ASS-DYPGDKSSEKGPAAATSAAAAAAAT---GAPA
Dvi  SVG-DMLAKNSANVYHHTSTCTSSNFYSTVGRNGVLPQAFDQFFETAYGPPDNLATASSDYPGDKGTDKMPAAAAA-----APP
Oan  SVG-DMLAKNSANVYHHTSTVSS-NFYSTVGRNGVLPQAFDQFFETAYGAPENL--TSS-DYPGDKAGEKMPVATAAA-----AT
Tac  SVG-DMLAKNSANVYHHTSTVSS-NFYSTVGRNGVLPQAFDQFFETAYGAPENL--TSS-DYPGDKAGEKMPVATAAA-----AT
Gga  SMG-EVFGKSTANVYHHTSANVSS-NFYSTVGRNGVLPQAFDQFFETAYGTAENP--SSA-DYPPDKSGEKAPAAAGAT-----AA
Gni  SMG-EMFKNNTANVYH--PTTNVSS-NFYSTVGRNGVLPQAFDQFFETAYGTENL--SSA-DYSGDKNGEKMPATA-----TA
Xtr  SVG-EMFKNPNVYH--PNAVSS-NFYSTVGRNGVLPQAFDQFFETAYGTETESQ--PS--DYSVDKSCDKVAAAA-----AT
Lme  SIG-EIFGKGNANVYH--PGSSTSS-NFYNTVGRNGVLPQAFDQFFETAYGTENH--SS--DYSADKNSDKIPSA-----AT
  
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Bta  TSSSDSGAGG---C--REAAAA-----EKKERRRPE-----SSSPE?????????????G
Hsa  TSSSDSGGGG---C--RETAATA-----EKKERRRPE-----SSSPSSSGHTEDEKAGGSSG
Mmu  TSSSDGGGGG---C--QEAATA-----EKKERRRPE-----SSSPSSSGHTEDEKAGGSSG
Rno  TSSSDGGGGG---C--QEAATA-----EKKERRRPE-----SSSPSSSGHTEDEKAGGSSG
Dsp  TSSSDGGGGGGGG---C--REAAAA-----EKKERRRPE-----SSSPSSSGHTEDEKAGGSSG
Pca  TSSSDSGG---C--REAA-----EKKERRRPE-----SSSPSSSGHTEDEKAGGSSG
Dvi  TSSSDAGGG---CGRDNAAAAAATAAATAA-----EKKERRRPE-----SSSPSSSGNNEKSSGSSG
Oan  TSSSDGG---C--GRDAATAAAVASAAAAASAASAAVAEKKDRRRRTE-----SSSPSSSGNNEKSSGSSG
Tac  TSSSDGG---C--GRDAATAAAVASAAAAASAASAAVAEKKDRRRRTE-----SSSPSSSGNNEKSSGSSG
Gga  TSSSEGG---C--G--GAAAAAG-----KERRRPE-----SSSPSSSGNNEKSSGSSG
Gni  TSSSEGG---C--SREAAAA-----EKKERRRPE-----SSSPSSSGNNEKSSGSSG
Xtr  TSSSEA-----C--REP-----EKKERR--AESGRSSSSSSQSSSGNNEKANSSSG
Lme  TSRSET-----C--RET-----DEKERR--EE-----SSSPSSSGNNEKSSSSG
  
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B

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Hsa  MTASVLLHPRWIEPTVMFLYDNCGLVADELNKNMGGAAAAAAGAGGGGFPHPAAAAGCNFVAAAAAANQCRNLMHAHPALPAPLAPC
Mmu  MTASVLLHPRWIEPTVMFLYDNCGLVADELNKNMGGAAAAAAGAGGGGFPHPAAAAGCNFVAAAAAANQCRNLMHAHPALPAPLAPC
Mdo  ??????????????????CGGLVADELNKNMGGAAAAAAGAGGGGFPHPAAAAGCNFVAAAAAANQCRNLMHAHPALPAPLAPC
Gga  ??????????????MFLYDNS--L--DEINKNMDG-----F-----HAGSNFAAAAA-----NPCRNLMAHPALPAPLAP
Xla  MTASVLLHPRWAE--VMFLYDNS--L--EEMKNKMDG-----F-----PVSS-FAA-----NPCRNLIGHHAPL--P

Hsa  AASAYSAEPGEAPSAIAAAAAAASSSGGPGPAGPAGAAA--EFA-KQCSPCSAAQSSSGAALPYGYFGSGYYPCCARMGHPNNAIKSCP-
Mmu  AASAYSAEPGEAPSAIAAAAAAASSSGGPGPAGPAGAAA--EFA-KQCSPCSAAQSSSGAALPYGYFGSGYYPCCARMGHPNNAIKSCA-
Mdo  AASAYSAEPGEAPSAIAAAAAAASSSSSGGPGPTGAAGAEFV-KQCSPCSAAQSSSGAALPYGYFGSGYYPCCARMGHPNNAIKSCAA
Gga  SAAAYTSS--EAPAGMA-----EPVAVKQCSPCSAAVQSSSGAALPYGYFGSGYYPCC-RMTHH-NAIKSCA-
Xla  PSSAYPSS--EVPVSAIA-----EFS-KQCNPCSA-VQSTPNGS-LPYGYFGSGYYPCC-RMSHH-NGIKSCS-

Hsa  --QPPSAAAAA---FADKYMDTGPAA---EEFSSRAKEFAFYHQGYAAGPYHHHQVMPGYLDMFVVPVGLGGPESRHEPLGLPMESYQPWALPNGWN
Mmu  --QPASAAAA---FADKYMDTGPAA---EEFSSRAKEFAFYHQGYAAGPYHHHQVMPGYLDMFVVPVGLGGPESRHEPLGLPMESYQPWALPNGWN
Mdo  AAQPASAAAAAFAADKYMDTAGPAAAAEEFSSRE????????????????????????????????????????????????????????????
Gga  --QPAST---FADKYMDTSVSG---EEFTSRAKEFAFY--QGYAAGPY--QVPVGYLDMFVVPVITGGPGEPRHDSLL--PMDSYQPWAIITNGWN
Xla  --QPSS---FADKYMDTSGSAG---KDFPSRAKEFAFY--QSYPLGPY--QVPVGYLDMFVVPVITGSTGKRHEPL--PMDGYQAWPITNGWN

Hsa  GQMYCPKEQAQPPHLWKSSTLPDVVSHPSDASSYRRG
Mmu  GQMYCPKEQTQPPHLWKSSTLPDVVSHPSDASSYRRG
Mdo  ?????????????????????????????????????????????????????????????????????????????????????????????
Gga  GQVYCPKEQSQPPHLWKSSTLPDVVSHPSDANSYRRG
Xla  GQVYCAKDQAQPTHLWKSSTLPDVV-HQSDSSYRRG
  
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Figure 3. Amino acid alignment of *HoxA-11* (A) and *HoxA-13* (B) sequences used in this study. Amino acid sites that were under directional selection in the stem lineage of therians are light blue, sites that were selected in the stem lineage of eutherians are red, and sites in yellow were replaced in the stem lineage of therians but were not identified to be under directional selection. The positions of the homeodomain are shown as grey cylinders. Bta, *Bos taurus*; Hsa, *Homo sapiens*; Mmu, *Mus musculus*; Rno, *Rattus norvegicus*; Dsp, *Dyspus sp.*; Pca, *Procavia capensis*; Dvi, *Didelphis*

virginiana; Mdo, *Monodelphis domestica*; Oan, *Ornithorynchus anatinus*; Tac,
Tachyglossus aculeatus; Gga, *Gallus gallus*; Gni, *Geochelone nigra*; Xtr, *Xenopus*
tropicalis; Xla, *Xenopus laevis*; Lme, *Latimeria menadoensis*.