

**Supplemental Figure 1. Lysine residues are conserved in the cytoplasmic tail of mammalian DO $\beta$  molecules.**

Amino acid sequences of the cytoplasmic tails of the homologues of HLA-DO $\alpha$  and  $\beta$  from 24 mammals are shown. The ubiquitination site at the residue corresponding to human DO $\beta$  lysine 225 is conserved across most mammalian species. The C-terminal parts of the putative transmembrane domains are highlighted in grey, lysine residues are shown in red, and Yxx $\Phi$  and dileucine motifs are in bold print. Sequences were obtained from the Ensemble database, Release 62. All species for which both  $\alpha$  and  $\beta$  chains were available are shown. In orangutan, mouse lemur, horse, dog and elephant, the DO $\beta$  STOP codon was not found in the database (...).

Species	Species name	DO $\alpha$	DO $\beta$
Human	<i>Homo sapiens</i>	...LVGTVLIIIMGYVSSVPR	...LVGIVIQLRAQ <b>KGYVRT</b> QMSGNEVSRAV <b>LLPQSC</b>
Chimpanzee	<i>Pan troglodytes</i>	...LVGTVLIIIVGTYVSSVPR	...LVGIVIQLRAQ <b>KGYVRT</b> QMSGNEVSRAV <b>LLPQSC</b>
Orang Utan	<i>Pongo pygmaeus</i>	...LVGTVLIIIMGYVSSARR	...LVGIVIQLRAQ <b>KGYVRT</b> QMSGNEVSRAV <b>LLPQ</b> [...]
Macaque	<i>Macaca mulatta</i>	...LVGTILIIIMGYVSSAPR	...LMGIIIQLRAQ <b>KGYVRT</b> QMSGDEVSRAV <b>LLPQPC</b>
Marmoset	<i>Callithrix jacchus</i>	...LVGTILIIIMGICVSSAPR	...LVGIVIQLRAQ <b>KGHVGTHMSGDEVSRAV</b> <b>LLPQSY</b>
Galago	<i>Otolemur garnettii</i>	...LVGTILII <b>KGTCQSSAPR</b>	...LVGIVIHLRAQ <b>KGYMEI</b> <b>QKSGDEVSRAV</b> <b>LPQPH</b>
Mouse Lemur	<i>Microcebus murinus</i>	...LVGTA LITGTRLSSAPGQ	...LLLGVLLRRRAQR[...]
Tarsier	<i>Tarsius syrichta</i>	...LVGTILII <b>IRGTCESHAPR</b>	...LVGIVIHLRARK <b>KGYMDT</b> QQSGDEVPTVMPWQPC
Large Flying Fox	<i>Pteropus vampyrus</i>	...LVGTVLIIITSTCLHSAPR	...LVGIAVHLRAQ <b>KGYAET</b> QLSGD <b>KVSRSLPPLTY</b>
Pika	<i>Ochotona princeps</i>	...LQGTVLILIATRMSRAPQ	...LVGIITYLRAW <b>KGCMET</b> QRSAAEVSRAGFPSQPY
Mouse	<i>Mus musculus</i>	...LLGTVLMIITGTRRPSIRR	...LVGVVIHLKAQ <b>KASVETQ</b> -PGNEASRESLHSQP.
Rat	<i>Rattus norvegicus</i>	...LLGTLLMVTATRMPSTRR	...LVGAVIHLKAQ <b>KASVETQ</b> -PGNEASRA <b>LLP</b> PPHY
Kangaroo Rat	<i>Dipodomys ordii</i>	...LMGTILIIILATTMADAHR	...LAGLIIHLRAW <b>KGSAAEQ</b> -AGHEVSR <b>ALLP</b> SQPY
Ground Squirrel	<i>Spermophilus tridecemlineatus</i>	...LMGTILIIITGTCMSSCPR	...LVGIIIHLRARK <b>GSVETQ</b> -SGD <b>KISRA</b> <b>ILQ</b> KPNS
Horse	<i>Equus caballus</i>	...LVGTILLIIISTCLSGAPR	...LVGIFIHLRARK <b>G</b> [...]
Pig	<i>Sus scrofa</i>	...LVGTVLIIITGRRRSSSPR	...LVGIIIHVRARK <b>GRVET</b> QLSGDEPH
Alpaca	<i>Vicugna pacos</i>	...LVGIVLIIITGSRLSRAPR	...LVGITVHVRARK <b>KGYET</b> QLSGD <b>KVLGAVCP</b> EQPH
Bottlenose Dolphin	<i>Tursiops truncatus</i>	...LVGVILIITGTCLSSTPR	...LVGIVIHTRARK <b>KM</b> -----VTVPRAVLRPQPH
Dog	<i>Canis lupus</i>	...LVGTIFIIRGTCLSSGPRYRGPO	...LVGTVICLRAQ <b>KGYET</b> QFSGDEVM[...]
Cat	<i>Felis catus</i>	...LVGFVGTVLILIIRGTCLSSAPR	...LVGTVICLRAQ <b>KGYMET</b> QLSGDEVSRAV-PSPPH
Nine-Banded Armadillo	<i>Dasypus novemcinctus</i>	...LAGLVVGTILIFAGTRLSSAPR	...LVGIIICLRAK <b>KGYMET</b> QLSDGVSR <b>ALLP</b> POLYQ
African Elephant	<i>Loxodonta africana</i>	...LVGTIFIISGTCLSSTPRCRGPR	...LVGIVIHFRCQ <b>KG</b> [...]
Hyrax	<i>Procavia capensis</i>	...LVGTIFIISGACLSSDPK	...LVGIFIYFRAQ <b>KGYVK</b> TQLSVD <b>KVSRSLP</b> QPYE
Lesser Hedgehog Tenrec	<i>Echinops telfairi</i>	...LLGTVLIIIHSTCCSSVLR	...LVGICIRLK <b>QAQRGHVET</b> TPQLHDEGSRSV-PIQSC