

```

      M1
D.melanogaster 205 tssdprdirmidp-----rdp-----
D.ananasae    200 tasdprdirmidp-----rdp-----
Apis mellifera 623 emrdprdrhmsldp-----rehir-----vmdpmar-----dpr-----mtd
human TNRC6A   688 gesqsrdrk-idq-----htllqsisvnrtdldp--rvlsnsgwgqtpikqntaw-d
human TNRC6B   583 sdshnsgrrs-yrpthpdcqavlqtllsrtdldp--rvlsntgwqgtqikqdtvw-d
human TNRC6C   417 gegrrrdkgi-idq-----gh-iq--lprndldp--rvlsntgwqgtpvkqntaw-e

```

```

      M2
irgdprgisgrlngts--emwghhpqmshnqlgqinkmvgqsvata-----stsvg-tsgsgigpg--
irgdprgisgrlngts--emwghhpqmthnqmqnmklvgqsvtsa-----gtgvggstgpg-ipg--
irgdprgisgrlnganadamwgpppphhqmghq-----hps
tetsprgerktdngt--eawgssatqtfnsgacidktspngndtssvsgwgdpkpa-----lrwgdsk--gsncq
ieevprpegksdkgt--egwesaatqtknsggwgdapsqs--nqmksgwgelsas-----tewkdp-----knt
feesprserkndngt--eawgcaatqasnsggkndgsimnstntssvsgwvnappaavpantgwgdsnn--kapsgp
.  **      : * :      * . . : .

```

```

ggweddsaatg-----mvksnqwgnc k--eekaawndssqk-nkqgwgdggkssqgwsvsasdnwets-rnnhwe
ggwndyknnn-----ssnwggg rpdektpsswneneps-kdqggwggrqrpnqwssgk-ngwgeevd-----
gwggdsisstavstaaaaksghwsgaanedksptwgeppkksqhwgdgqrsnpawsagg-gdwadsssvlghlgd

```

```

      M3
-----gggps-tv-----
-----ggpn-sv---pv-----
-----gp-pa-ki---l-----
ankkssggsdsdrsvsgwnelgtssftwgnninp--nnssgwdessktpts-gwgdppksnqslgwgd--sskp
-qtknswessaskpvsgwgeggqneigtwnggnaslaskgwedck-rspawnetgrqpn-----swnkqhqqqqp
gkkngsgwdadnrsgwndtrsgnsgwnstntkanpgtnwetlkpppq-qnwaskpq-----

```

```

      M4a      M4b
-----sgniptqwgpa---q-pvsvg---vsg--p-kd-mskqisgweepsppppqrrsipnyddgtslwgqqtr
-----stniatqwgpa---q-avgs-----kd-iskqisgweepsppppqrrsipnyddgtslwgqqpr
-----npsninqwaa-----ppkdim-pgkgtgweepsptqrrnvpnyddgtslwgnpa
vsspdwnkqqdivgswgip---patgkppgtgwlggpipapak-eeeptgweepsesirrkm-eiddgtsawgdpsk
pqqqp-ppqeasgswggpppppgnvrpsnsswsggppatpk-deepsgweepsqsirrkm-diddgtsawgdpns
-----dnnvsnwgga---a-svkqtgtgwiggppvkkdsseatgweepspsirrkm-eiddgtsawgdpsn
.  . *      : : * * * * * . * . : : * * * * * * * :

```

```

      M5
----vpaa---sghwkdmt-dsigrsshlmrgqstggia--gvgnsnvpvganpsnp-----
----vpsa---sghwkdin-dsinrgghlmrgqnsvgigit--gvgnsnvpvganpnnpn-----
nqrtipgsk--vshwkdiptnlgrg-----mqcp-----
----ynyk---nvn-----mwnknvpgnsrsdqqa-----
----ynyk---nvn-----lwdknsgggparepnlp-----
----ynnk---tvn-----mwdrnnpviqstttnttttttttttttttttttntthrvet
:

```

```

-----issvvgpqaripsvggvqhkpd-gg---amwhsgnvgrnnvaavttwgddthsv-nvgapssgv
-----insvigpqarlasvggvqhkpd-gs---tmwhsnnvsgrnpvtgvtswedhnv-svgaptagav
-----pgmpqnrmpgqgm--kpdvsg---pmwghpgapgrn-----gswaegphda-----
-----qvhqlltpasaisnk-----eas-sgsgwgepwgepstpat-tvdngtsawgkpidsppswgepiaaas
-----tpmts-----k-sa-----swkstppa---pdngtsawgepnesspgwgemdtga
ppphqagtqlnrspllggrkvssgwgem-pnv-h-sktenswgepspst-lvdngtaawgkpppssgwgdhpaepp
* . . . . . * . . . . . : * . . . . .

```

```

ssnnwvddksnstlaqnswsdpapvgvsgnkqsk 490
pvsnwvdeksntslvqnswtdagsvgvswggkqtk 483
--gswddpktps----twneaqlnpgtwggpsah 850
sttwgss--svgpqalsksgksmqdgwcgddmp 1132
sttgwnt--panapnamkpnskmqdgwgesdgp 1003
vafgraga--pvaasalckpaskmqegwsggd- 884

```

Figure S1. Complete version of the alignment of NED across the species that is schematically represented in Figure 3A. Alignment was performed with a T-Coffee tool (41). Mutated residues are shown with red (always to alanine; mutants analyzed in Figures 3 and 4). The numbers correspond to amino acid position. Asterisks mark residues identical in all sequences, colons mark conservative substitutions, dots mark semi-conservative substitutions.