

hs TMC1-1
hs TMC1-2
mm TMC1-1
mm TMC1-2
dr Tmc1-1
dr Tmc1-2
hs TMC2-1
hs TMC2-2
mm TMC2
dr Tmc2a
dr Tmc2b-1
dr Tmc2b-2

4 9
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 -----MGSKMKVIKIVVEEK-----
 -----MLQIQVVEEK-----
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 -----MSHQVGLKEELAS-----GGVGRKVSGS--
 -----MPCRHTLGCPLVSLKELSS--RNHLGRLISHGRGHFPGEAVGTRT
 -----MSPQLKSLDEEGD-----
 -----MPKKSDDTRKRLQVGIEMDQ-----VDSAEED
 -----MCVLLDVGWKWGD-----
 -----MPRRKSDIEITMDDVGMEMDAE-----FDSGSDVDSKRR

14 24 34
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 -----EEDTEESSSEEEEDKLP-----
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 GKRRRERNGETRRKASEKRTNEGESKKAEEKKHEKGRHTARKAGEKHGRQRKR
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 -----K SARRPRTKQTSRAACPQDGHRAQSSSRKDPAGKSPRPGSSRKR--
 KKSKGKGGKAAAGKRGKASGDEDEDEDPPPKGRRRANKKPKAPVDEED--
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36 46 56
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 -----RESLRPKRKRTRDVINEDDPEPEP
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60 70 80
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 ED-----EETRKAREKERRRRLKRGAE EEE-----
 ED-----EETRKAREKERRRRLKRGAE EEE-----
 ETK-----QHLKEEKRRKKRKPETTSSESEKSESASESES
 ETK-----QHLKEEKRRKKRKPETTSSESEKSESASESES
 EK-----EIPRREEKSRQKPPSSSLASSAGGES
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 -----IDEEELERLKAELDENRQI IATVKCKPWKMEKKI EVLKAEKK
 -----M IATVKCKPWKMEKKI EVLKAEKK
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 KNSPAVGLVGLSLTPEEL ENLKEAVEERKLLITQLKGPVPMRRLKLVLRSE
 -----LSEEEALQILEQVEEKKLI IATMRKSPWMAKLLTELREAQ
 -----LSEEEALQILEQVEEKKLI IATMRKSPWMAKLLTELREAQ
 -----LSEEEALQILEQVEEKKLI IATMRKSPWMAKLLTELREAQ
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127 137 147 157 167 177
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187 197 207 217 227
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237 247 257 267 277
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 AEEEKAMDFSVLWDFEGYIKYSALFYGYNNQRTIGWLRYLPMAYFMVGVSV
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287 297 307 317 327
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346 356 366 376 386
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396 406 416 426 436
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446 456 466 476 486
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503 513 523 533 543
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553 563 573 583 593
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603 613 623 633 643
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712 722 732 742 745
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 VILVMV-LAIYYLNATAKGGQKAAALDLKMKMQAL ENKMR--NKKMA----
 VILVMV-LAIYYLNATAKGGQKAAALDLKMKMQAL ENKMR--NKKMA----
 VILVMV-LAIYYLNATAKGGQKAAALDLKMKMQAL ENKMR--NKKMA----
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 VVLLMV-LAIYYLNSVSKLSRANALRKKIQLVREVEKSH--KSVK GKATAR
 VVLLMV-LAIYYLNSVSKLSRANALRKKIQLVREVEKSH--KSVK GKATAR

750 760
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 YSEDITKN-----SKNATQILHTKEEPTSHSSSQIQLDCKAAGP
 DLEDLLPNRPPPPSPRENIEAKNQGQGGKSAKV--KPGTAG-----GV
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853 863 873 883 893 903
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 HVQKDVSLAAANP--RAPVTRAPGRPGPLPQPP-----GAGRGGRGQPP
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953 963 973 983 993
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 VILVMV-LAIYYLNATAKGGQKAAALDLKMKMQAL ENKMR--NKKMA----
 FLLLLLV-LAIYYLQSTSKTYKRVNMLKLLKQAQNEENKMR--NKKMA----
 FLLLLLV-LAIYYLQSTSKTYKRVNMLKLLKQAQNEENKMR--NKKMA----
 AII LLMF-LAIYYLNSVSKLSRANALRKKIQLVREVEKSH--KSVK GKATAR
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 AVLLMV-LAIYYLNSVSKLSRANALRKKIQLVREVEKSH--KSVK GKATAR
 VVLLMV-LAIYYLNSVSKLSRANALRKKIQLVREVEKSH--KSVK GKATAR
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1053 1063 1073 1083 1093 1103
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 DLEDLLPNRPPPPSPRENIEAKNQGQGGKSAKV--KPGTAG-----GV
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hs TMC1-1
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 hs TMC2-2
 mm TMC2
 dr Tmc2a
 dr Tmc2b-1
 dr Tmc2b-2

TMC sequence alignment. Protein sequences correspond to: *hs TMC1-1* (NCBI ID: NP_619636.2), *hs TMC1-2* (NCBI ID: XP_016869745.1), *mm TMC1-1* (NCBI ID: NP_083229.1), *mm TMC1-2* (NCBI ID: XP_036017315.1), *dr Tmc1-1* (NCBI ID: NP_012299610.1), *dr Tmc1-2* (NCBI ID: XP_021331607.1), *hs TMC2-1* (NCBI ID: NP_542789.2), *hs TMC2-2* (NCBI ID: NP_005260717.1), *mm TMC2* (NCBI ID: NP_619596.1), *dr Tmc2a* (NCBI ID: NP_001289166.1), *dr Tmc2b-1* (NCBI ID: NP_001289152.1), and *dr Tmc2b-2* (NCBI ID: XP_017211636.1). Secondary structures underneath the sequences are based on AF2 models of *hs TMC1*. Interface residues between TMC-NT/IL1 and CIB proteins were based on our AF2 model (for NT) and on Liang et al. (blue brackets).