

17 **33** **35** **37** **38**
humART 1 MSSFEGQMAEYPTISIDRF-DRENLRA-RAYFLSHCHKDHMKGLRAPTLKRRLECSLKVY 58
muART 1 MSSFQGMAYEYPTISIDRF-DRENLKA-RAYFLSHCHKDHMKGLRAPSLKRRLECSLKVF 58
ratART 1 MSSFQGMAYEYPTISIDRF-DRENLKA-RAYFLSHCHKDHMKGLRAPSMKRRLECSLKVF 58
humSNM1 699 TCFYKPIPG-TGFTVDAF-QYGVVEGCTAYFLTHFHSDDHYAGLSKH-FTF----P---- 748
muSNM1 682 TCFYKRI PG-TGFTVDAF-QYGEIEGCTAYFLTHFHSDDHYAGLSKD-FTR----P---- 730
humSNM1B 1 MNGVL--IPH-TPIAVD-FWSLRRAGTARLFFLSHMHSDHTVGLSST-WAR----P---- 47
muSNM1B 1 MNGVV--IPQ-TPIAVD-FWSLRRAGSARLFFLTHMHCDHTVGLSST-WAR----P---- 47
scSNM1 229 VVDGF 233 246 LSHHSDHYI 255
smL1 72 LLDGG 76 103 LSHAHADHAG 112

115
humART 59 LYCSPVTKELLTSPKYRFWKRIISIEIETPTQISL-VDEASGEKEEIVVTLTPAGHCP 117
muART 59 LYCSPVTKELLTSPKYRFWENRIITIEIETPTQISL-VDEASGEKEEVVVTLTPAGHCP 117
ratART 59 LYCSPVTKELLTSPKYRFWENRIIAIEIETPTQVSL-VDEASGEKEEVVVTLTPAGHCP 117
humSNM1 749 VYCSEITGN-LLKN-KLHVQEYIHLPL--DTEC-I-VNGV---K--V-V-LLDANHCP 795
muSNM1 731 VYCSEITGN-LLKK-KLRVQEYIRQLPM--DTEC-V-VDSV---K--V-V-FVDANHCP 778
humSNM1B 48 LYCSPITAH-LLHR-HLQVSKQWIALEVG-ESHV-LPLDEIG--QETMTVTLLDANHCP 101
muSNM1B 48 LYCSPITAC-LLHR-RLQVSKHWIRALEVG-ESHV-LPLDEIG--QETMTVTLLDANHCP 101
scSNM1 316 ANHCP 320
smL1 179 AGHTP 183

136 **165**
humART 118 GSVMF LFQGNNGT-VLYTGFRLAQGEAARMELLSHGGRVKDIQSVYDITTFCDPRFYQI 176
muART 118 GSVMF LFQGSNGT-VLYTGFRLAKGEASRMELLSHGGRVKDIQSVYDITTFCDPRFYQI 176
ratART 118 GSVMF LFQGSNGT-VLYTGFRLAKGEVSRMELLSHGGRVKDIQSVYDITTFCDPRFYQI 176
humSNM1 796 GAVML LFYLPNGTIVLHTGDFRAD-PSMER-SLLA-D---QKVHMLYDITTYCSPEY-TF 848
muSNM1 779 GATML LFQLPNGAVILHTGDFRAD-PSMER-SRLA-G---RKVHTLFDITTYCSPEY-TF 831
humSNM1B 102 GSVMF LFEGYFGT-ILYTGFRTY-PSMLKEPALTLG---KQIHTLYDNTNCPAL-VL 155
muSNM1B 102 GSVMF LFEGYFGT-ILYTGFRTY-PSMLKEPALILG---KQIHTLYDNTNCPAL-VL 155
scSNM1 345 TGDFR 349 374 YLDTT 378
smL1 203 YADSL 207

humART 177 PSREELCS-GV-LELVRSWITRS PYHVWLNCKAAAYGYEYLFN--L-SEE-L----GVQ 226
muART 177 PSREQCLR-GI-LELVRSWITRS PHHVWLNCKAAAYGYEYLFN--L-SEE-L----GVQ 226
ratART 177 PSREQCLR-GV-LELVRSWITRS PKHVWLNCKAAAYGYEYLFN--L-SEE-L----GVQ 226
humSNM1 849 PSQQEVIRFAINTAFEAV--TLNPHALV-V-C-GTYSIG-K-EKVFLAIADVLGSKVGM 901
muSNM1 832 PSQQEVIQFAINTAFEAV--TLNPHALV-V-C-GTYCIG-K-EKVFLAIADVLGSKVGM 884
humSNM1B 156 PSRQEAH-QI-VQLIR---KHPQHNIK-I---GLYSLG-K-ES--L-LEQ-L----AL- 195
muSNM1B 156 PSRQEASQ-QI-VQLIR---QFPQHNIK-I---GLYSLG-K-ES--L-LEQ-L----AL- 195
scSNM1
smL1

humART 227 VH-VNKLDMFRNMPDILHHLTT-DR-NTQIHACRHPKAEYFQ-WS-KLP-CGITSRNRI 280
muART 227 VH-VDKLDMFKNMPDILHHLTT-DR-NTQIHACRHPKAEFCFQ-WN-KLP-CGITSQNK 280
ratART 227 VH-VDKLDMFKNMPDILHHLTT-DR-NTQIHACRHPKAEYFQ-WN-KLP-CGMASKTKT 280
humSNM1 902 QEKYKTLQCL-NIPE-INSLITDMCSSLVHLLPMMQ-IN-FKGLQSHLKKCG--GKYNQ 955
muSNM1 885 QEKYKTLQCL-NIPE-VSSLITDMCDSLHLLPMMQ-IN-FKGLQSHLKKCG--GKYDQ 938
humSNM1B 196 -E-FQTWVVL-SPRR-LE-LV--QL-LGLADVFTVEEKAGRIHAVD-HMEIC----H-SN 241
muSNM1B 196 -E-FRTWVVL-SPQR-LE-LV--QL-LGLADVFTVEEAGRIHAVD-HTEIC----H-SA 241
scSNM1
smL1

319
humART 281 PLHISIKPSTMW-FGERSRKT-NVI--VRT-GESSYRACFSFHSYSEIKDFLSYICPV 335
muART 281 ALHTISIKPSTMW-FGERTRKT-NVI--VRT-GESSYRACFSFHSFSEIKDFLSYICPV 335
ratART 281 VLHTISIKPSTMW-FGERTRKT-NVI--VRT-GESSYRACFSFHSYSEIKDFLSYICPV 335
humSNM1 956 ILA---FRPTG-WTHSNKFTRIADVI PQTKG-NISYIGIPYSEHSYLEMKRFVQWLKPK 1010
muSNM1 939 ILA---FRPTG-WTHSNNTSTADII PQTRG-NISYIGIPYSEHSYLEMKRFVQWLKPK 993
humSNM1B 242 ML-----R----WNQTHPTTAILPSTRKIHSSHPDIHVIPYSDHSYSELRAFVAALKPC 292
muSNM1B 242 ML-----Q----WNQSHPTAIFPSTRKVRSPHPSIYTPYSDHSYSELRAFVAALRPC 292
scSNM1 609 SEHSS 613
smL1 244 TPEFG 248

humART 336 NAYPNVI--PVGT-TMDKVVEILKP-LCRSSQSTEPKYK 370
muART 336 NVYPNVI--PVGL-TVDKVMDFLKP-LCRSPQ-SVPKYK 370
ratART 336 NAYPNVI--PIGL-TVDKVMDFLKP-LCRSSQCAEPKYK 370
humSNM1 1011 KIIPTVN---VGT-WKSR-ST-MEK-YFREWK-LEAGY- 1040
muSNM1 994 KIIPTVN---VGS-FRSR-NT-MEK-YFKEWR-LEAGY- 1023
humSNM1B 293 QVVPIVSRRPCGG-FQDSLSPRISVPLIPD-S-VQQ-Y- 326
muSNM1B 293 QVVPIVHQKPCGEFFQDSLSPRLAMPLIPH-S-VQQ-Y- 327
scSNM1
smL1

Figure Sup_1. The Human ARTEMIS Protein

Conserved Residues in the Metallo- β -lactamase/ β -CASP Domain of ARTEMIS and Related Proteins. GenBank accession numbers of the sequences used were NM_022487 for human (hum) ARTEMIS, BAC34960 for murine (mu) ARTEMIS, AAM89124 for rat ARTEMIS, NM_014881 for human SNM1, AAF64472 for murine SNM1, NM_022836 for human SNM1B, BAC33550 for murine SNM1B, P30620 for yeast (sc) SNM1 and AJ251815 for *Stenotrophomonas maltophilia* (sm) L1. Highly conserved residues chosen for mutagenesis are indicated by black boxes. The numbering of mutagenized amino acids refers to positions in the human ARTEMIS protein (also see Callebaut et al. 2002).