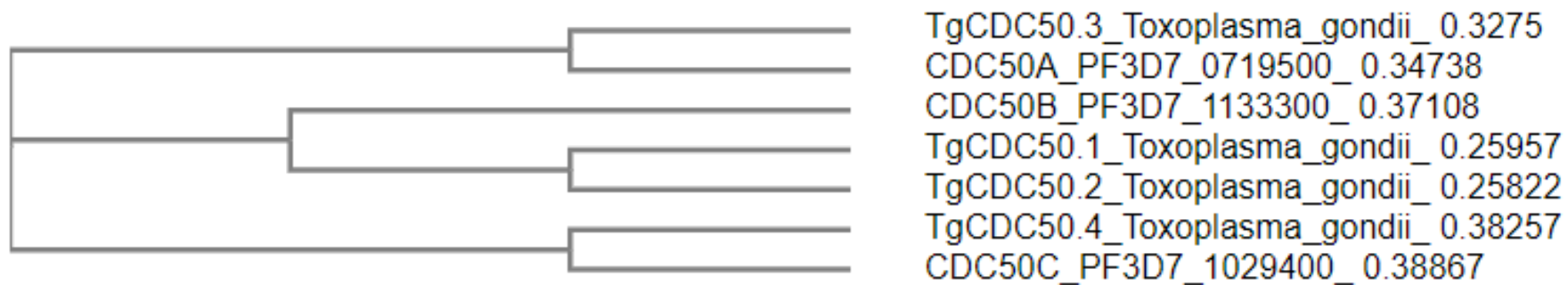


Figure S9

A)



B)

Alignment of *P. falciparum* CDC50s alongside Cdc50p and LEM3 from *S. cerevisiae* and cdc50a from *H. sapiens* showing the region surrounding the conserved Asn 180 (HsCdc50a) glycosylation site

ScCdc50p	L T N F Y Q N H R R Y V Q S F D T K Q I L G E P I K K D D L D T S C S P I R S R E D - K I I Y P C G L I A N S M E N D T F S Q V L S G I D D T E D - Y N L T N K H I S W S I D R - H R F K T T K Y N	237
ScLem3	L E K F A A N H R R Y V L S F S E D Q I R G E D A S 5 D A T G I N C K P L S K N A D G K I Y Y P C G L I A N S M E N D T F P L Q L T N V G D T S N N Y S L T N K G I N W E S D K - K R Y K K T K Y N	279
HsCDC50a	L S N F Y Q N H R R Y V K S R D D S Q L N G D S S A L L N P S K E C E P Y R R N E D - K P I A P C G A I A N S M E N D T L E L F L I G N D S Y P I P I A L K K K G I A W W T D K N V K F R N P P G G	220
PfCDC50A	I 5 N F Y Q N H K K Y L V S K S H N Q L M G T V Y T K D N E V S Q C G P I T K N H E G K I L H P C G L I A R S I F N D T F S V Y M D R E L H N M I K L D E S K E G I T W Y S D Y N K F K N P S D S E	332
PfCDC50B	V 5 G M Q Q N H Y K F V S G M K K E Q L N G N I F L K K E E L E E C Y P L I T F S E 5 K L L H P C G I F P W N V F T D S Y I F Y D K E P D E V P F P T P L P L K 5 I T I K Y Y R Q F Y K N P S P Q N	229
PfCDC50C	V S N F Y I N F K T F L S D E S H S L V N E K I P K K K K K N Q K C H I S D L K P E 3 K K I F P C G L V S A A I F N D K I A L S K N S V N Y D I D K F P I L H 3 F L T Y M K K H K Q F T N Y K I W I	335

	P-domain	Phosphorylation site	N-domain		
ATP8A1	INWDLDMHYEPTDAAMARTSNLNEELGQVKYIFSDKTGTLTCNV	MQFKKCTIAGVAYGHVPEPE	YGCSPDEWQNSQFGDEK-TFSDSSLLENLQN---NHPTAPIICEFLTMMAV	486	
Drs2p	IGSDLDLIYEKTDTPVVRTSSLVEELGQIEYIFSDKTGTLTRNIMEFKSCSIAGHCYIDKI-PEDKTATVE--DGIIEVGYR---KFDDLKKKLNDP---SDEDSPIINDFLTLLAT			632	
PfATP2	ISCDKNMIHKV113NAVPRRTSSLIEELGQIEYIFSDKTGTLTCNIMEFRKCAINGISYKGLTEIKRNLKKNLEIPVEPTMKFKKKT	PHVNIIDNDIINH7NHVN	LINFFLHLAI	747	
PfATP7	INWDNDMYSEKTGRHALSKAGQLEEMGNVTHIYSDKTGTLTCNV	MQLQNI	IGL2GTYGFDYFSNIKENITKSRHWGSQDPMDPVLEEYENEENVYSNVN159VQDQIYFLLLVLSL	895	
TgATP2A	INSRRVGS	SPD272EIVARTSDLNEELGQVSYVFS	DKTGTLTENMMEFRKCCI	QGIRYGDVEVEGEKVRLTQSGGREGLPQEREAPHVKVGDPTLRAALSDPD2MHSHTIDFFLHLAV	874
TgATP2B	IAQDESMFFHP402GAWPRTSDLNEELGQVSYIFSDKTGTMTSNVMEFRKCCVRGLSYGQGLTEVRRQALRRLGLPVPADPLPPPDEPTTPQVQMVDSALR8MHPYLVDFFLHLAI			972	
ATP8B1	INWDLQMYAEKDTPAKARTTTLNEQLGQIHYIFSDKTGTLTCNIMTFKKCCINGQIYGDHRDASQHNHNK--IEQVDFSWNTYADGKLAFYDHYLIEQIQSGKEPEVRQFFLLAV			533	
Dnf1	IYGDVLLYNAKLDYPCTPKSWNISDDLGVVEYIFSDKTGTLTCNVMEFKKCTINGVS	YGRAYTEALAGLRKRQ	GIDVETEG31VTFVSK	EFVRDLKGASGEVQQRCC-EHFMLLAL	776
PfGCα	IENDNHISTFE311WGLCLNSNMHGD	LVNDFIFTDKTGTLTCNMTFNMCS	IAGKTYGSK352KQNFPRPKSFRLNMN	SSVKGRCDFNDTKIYNDLNSQSWRGYYIDEFFKCMTL	1184
TgGC	IEGDIHIRGGG270WAEVHTPALNPNLGQVDFIFTDKTGTLTCNMTFMSCSVAGKIYGMA396YDNIDFPTGFRETMEGQIRRNCFYDASIFTDLARKDLRSHRINEFKCMAL			1256	

	N-domain	Adenine-binding			
ATP8A1	CHTAVPEREGDKIIYQAASPDGALVRAAQ	LNQVFTGRTPDSV--IIDSLGQEERYE	LLNVLEFTSARKRMSVIVRTPSGKLRLYCKGADTVIYDRLAETSK-YKEITLKHLEQFA	600	
Drs2p	CHTVIPEF2DGSIKYQAASPDGALVQGGADLGYKFIIRKPN	SVTVLLEETGEEKEYQLLNICEFNSTRKRMSAIFRFPDGS	IKLFCKGADTVILERLDDEANQYVEATMRHLEDYA	750	
PfATP2	NHAVICEK2EGVTTYSSSPDEEALVNAAKHFDITFLYRREGKY--GISIFGKIYEIDTLATIEFTSKRKMSSVICRIP103IMLFC	KGAGSII	LKLA--RTDVEITIEHMETYA	962	
PfATP7	CHSAMIR35QTQPQYDASSPDELALISTSLYLGC	FVNRPNLTT58MINNK644LSFEILDVFA	FDNVVRKMSLIVKNEKKEIFMLVKGADTSVLKLA	SKNQENIVDHEVQLHAF	1143
TgATP2A	NHSALAEH3TGHLCYSANSPDERAFVCAARHF	GVTFRARTPF	GV--ELNVLGRTVHVDILASFP	ESRRRRSSVLCQIS122VLLTKGADMVILPRLRRA51RRKAMETALEAYA	1160
TgATP2B	NHAVVLET2FGMTRYASASSPDEGALVYGARHF	GIEFLGQTPSGL--EVS	VLGRKLHVRVLASVEFSSKRKRSSMLCEIRY16IVLFTKGADTVILPPLKQ--RREETQMLNTMEEYA	1101	
ATP8B1	CHTVMVDRDQGLNYQAASPDGALVNAARNF	GFAFLARTQNTI--TISEL	GTERTYNVLAILDFNSDRKMSIIIVRTP	PEGNIKLYCKGADTVIYERLHR-MNPTKQETQDALDIFA	647
Dnf1	CHSVLVEA4PKKLDLKAQSPDEAALVATAR	DVGFVFGTKKGL--IIE	MQIQKEFEILNILEFNSSRKRMSCIVKIPGL7ALLICKGADSIISRLSRQSG5ILEKTALHLEQYA	904	
PfGCα	CHAVTP386FDAIKYQSSSLDEECLIIYSSS	FLGYRLVLRNKNTM--CIEIDG	SFNKWTIIGVNEFTNRRGKMSIVVK-PDS4SILYVKGSDSSILSLNLK140RYRRL	LEKQLRKFS	1821
TgGC	CNTVVP396VSIKIQASSPDEECLVSAASHM	GYTLVSRTN	NYA--ILNINQERRWQIIGVNEFTQKGRMSIVVRPQEW3SILYVKGADVAMLDLLSTS231DIALVEQH	LRKFS	1994

	N-domain	P-domain	TGD motif			
ATP8A1	TEGLRTLCLFAVAEISESDFQEWRAVYQRASTSVQNRLLKLEESYELIEKNLQLLGATAIEDKLDQDVPETIETLMKADIKIWIITGDKQETAINIGH	SKLLKKNMGMI	VINEGSLD	717		
Drs2p	SEGLRTLCLAMRDISEGEYEWN	SIYNEAATLDNRAEKLEDEAANLIEKNLILIGATAIEDKLDQDVPETIHTLQ	EAGIKIWIITGDRQETAINIGMSCRLLSEDMNLLINEETR	867		
PfATP2	DEGLRTLCLIAQRELSEESFAEWYHLYKEASLSIKDREKLE	SVAEYIENDLILQGITGIEDKLDQEGVSS	TIEDLRMAGIHIWMLTGDKIETAMNIGIAANLIDNYSEQFIYTEEYIE	1079		
PfATP7	TSGLRTLVLGYKYLTENEFSDMYRNHINARKKSE2KEEY	LQEFYEEAENLLIIGCTGIDDKLQDDVPQVIQDLRD	AGMTICVILTGDKLETA	INIGHSINILNKQTYNAIFTETDPT	1261	
TgATP2A	GEGLRTLCLIAKRTIDEEEFARWYKEYQKEHTSRT2KEERLYQLAERLEVDLELQGV	TAVEDRLQDDVAMTIVKLRQAGIHVWMLTGDKTETALNVGISTFLVARD	TRLSRYLWNGRE	1278		
TgATP2B	ADGLRTLCLIAKREVDTEFFTFWQAYQQAERATVGRQEQIEAVAERLEVQLELQGITVEDKLDQAGVADTIEKLR	AGIKVWMLTGDQVETAINIGFATSLLTREM	QRTYVWEELD	1218		
ATP8B1	NETLRTLCLCYKIEIEKEFTENKFFMAASVASTNRDEALDKVYEEIEKDLILLGATAIEDKLDQDVPETISKLAKADIKIWIITGDKKETAENIGFACELLT	EDTTICYEGDINSL		764		
Dnf1	TEGLRTLCLIAQRELSWSEYEKWN	EYDIAASLANREDELEVVADSIERELILLGGT	AIEDRLQDGVPCIELLAEAGIKLWVITGDKVETAINIGFSCNLLNMEMELLVIKTTGDD	1021		
PfGCα	VKGLRSMIFAFRYLSSEETIKYKRM	YDDACSSIYNKEQRLKVAEEFERDLIYLGITGVKNGLQEKVPKTI	DILNQSGIRIWMILTGDNV	EYSLHVSFLCKFLNKHTKIFHAAL	ENSN	1938
TgGC	LQGLRTMALACRYLTQEEETETYKRLYTDACASVY	CRAERLEVAEDMERDLEYLGITGVRDKLQEQVPE	TLQLMMEAGIRVWMLTGDNV	EYALHICHSCRLLTSRTRIFHAAL	LEFSG	2111

	P-domain	Phosphate-binding/ Mg ²⁺ coordination	
ATP8A1	GTRETLRSR-----CTTLGDALRKENDFALIIDGKTLKYALTFGRVQYFLDLALSCKAVICCRVSP ¹ LQKSEVEMVKKQVKVVTLAI GDGAND VSMIQTAHVGVGISGNEGL		824
Drs2p	DTERNLLEK-----INALNEHQLSTHDMNTLALVIDGKSLGFALPELEDYLLTVAKLCKAVICCRVSP ¹ LQKALVVKMVKRKSLLAI GDGAND VSMIQAAHVGVGISGMEGM		977
PfATP2	45NF IKNFFCAKNKSGLLLNPDKYNMLINTLN ¹ VLVVDG ² SVIDL ³ LLSEKMERKFFYLADKCSSVICG ⁴ RVSPY ⁵ QKGAIVSSANRLLNKITLAI GDGAND RNMINTANIGIGIRGQEGV		1239
PfATP7	85NSFLESSESFCHNNNEMDKTKGKEKVHYSQFSITITGEALDVIMK-DLKIKFYTLARSASTLIACRVTPKQKSLLVKENSANFP ² TSLAI GDGAND VGMILMANVGVGIAGKEGL		1463
PfATP2A	33KWSGHPREAEDSRAETGSEGGDQAVREPPEALIVDGEALTF ¹ LFE ² ERQCAFIRLCCACRAVICCR ³ LAPHQKGA ⁴ VVSLVKKTTQKVTLAI GDGSND CNMLLQAHIGVIRGNEGN		1427
TgATP2B	10EAQEMSI LAKHQKSGRGEAKGSPGRERQAHALVVDGEALQQMLEPDMQLFVSVCTNCVTVICSRVTPH ¹ QKGA ² VVSLIKRHLQKITLAI GDGAND CNMIQSADIGIGLKGEEGM		1343
ATP8B1	LHARMENQRNRGGVYAKFAPPVQESFFPPGGNRALIIITGSWLNEL ¹ 37QRQNFVDLACECSAVICCRVTPKQKAMVVDLVKRYKKAITLAI GDGAND VNMIKTAHIGVIGISGQEGM		916
Dnf1	VKEFGSEPS ¹ EIVDALLSKYLKEYF ² 16EFPKGN ³ YAI ⁴ VDG ⁵ DALKLALY ⁶ 2DIRRKL ⁷ LLCKNCRAVLCC ⁸ RVSP ⁹ QKA ¹⁰ AVV ¹¹ KLVD ¹² SLD ¹³ VM ¹⁴ TLAI GDGSND VAMIQSADVGIAGEEGR		1153
PfGCα	AKKLR ¹ REGMALYELF-----QLEKEEK ² PYENL ³ LLV ⁴ GN ⁵ GRNL ⁶ Q ⁷ TFLN ⁸ 2DLQ ⁹ TH ¹⁰ FLNMA ¹¹ CTCDV ¹² VIA ¹³ CRITAK ¹⁴ QAF ¹⁵ LV ¹⁶ QLIK ¹⁷ NRLY ¹⁸ 3NTLAI GDGAND IAMIQEANIGVIMTSDCI		2053
TgGC	RKAKREGVMLYELFR-----KARRLK ¹ RSDEHIC ² LVVT ³ GNL ⁴ RTFLN ⁵ 2DLQ ⁶ TY ⁷ FLNMA ⁸ CCSDV ⁹ VVAA ¹⁰ RVTP ¹¹ SQKA ¹² EMV ¹³ RLV ¹⁴ KKRLT ¹⁵ 3ITMAV GDGGND VAMLQEAHVGVAIRGKDSA		2225

	P-domain	TM5	TM6	
ATP8A1	QAANSSDYSIAQFKYLKNLLMIHGAWNYNRVSKCILCYFKNIVLYIIIEIWF ¹ AFVNGFSGQILFERW ² CI ³ GLYNV ⁴ MFTAMP ⁵ PLTLGIFERSCRKENMLKYP ⁶ ELYKTSQNALDFNTKVF			941
Drs2p	DAARSADIAVGQFKFLKLLLVHGSWSYQRI ¹ SVAILYSFYKNTALYMTQFWYVFANAFSGQSIMESW ² MSFYNL ³ F ⁴ FTVW ⁵ PPFVIGVFDQFVSSRLLERYP ⁶ QLYKLGKQGF ⁷ F ⁸ SVYIF			1094
PfATP2	QAFNSSDYGISQFRFLKNLLLVHGRLSYRRI ¹ SKLVVYMFYK ² NMVLIFPLFIFGSI ³ LSYSGKIYF ⁴ EFLHL ⁵ FNVLFTA ⁶ IPVVIH ⁷ AVLDQD ⁸ ISLNTAMEK ⁹ PNLYKLGIIHHYYFNIRTF			1356
PfATP7	QAARSSDFTISEFKYLKLLLVHGRRESLRNNSFLVYFCIFRNVSFCLCSMILI ¹ FWTGYSAIDAWN ² PWTKQIINIAFTSL ³ PVIF ⁴ FVALDKQLPHN ⁵ ILN ⁶ NPLLY ⁷ 61Y ⁸ GTHYL ⁹ FVYLLF			1644
TgATP2A	QAFNCSDFGVTQFRLLLP ¹ LLL ² VHGRWCYRRI ³ TTVILYIIYKN ⁴ FL ⁵ LVLP ⁶ LVYFG ⁷ FLCLFSGQRFY ⁸ PEVLA ⁹ QTYN ¹⁰ PVLTAMP ¹¹ ITLYGVLEQ ¹² IDERASL ¹³ KFP ¹⁴ QLYR ¹⁵ LGQADS ¹⁶ FLN ¹⁷ LRTC			1544
TgATP2B	QAFNCSDDYGLVQFRLLLP ¹ LLL ² THGSWN ³ YRRI ⁴ SKLVLYMFYK ⁵ NLV ⁶ LVLP ⁷ FFF ⁸ GYISL ⁹ FSGQK ¹⁰ FYFE ¹¹ FLYQ ¹² MNVVFTA ¹³ IPITLYGVFDQ ¹⁴ VD ¹⁵ DKL ¹⁶ LAL ¹⁷ KYP ¹⁸ QLYR ¹⁹ CGQID ²⁰ LYL ²¹ NL ²² RVF			1460
ATP8B1	QAVMSSDYSFAQFRYLQRL ¹ LLL ² VHGRWSYIR ³ MCKFL ⁴ RYFFYK ⁵ NAFTLV ⁶ HFWYSFFN ⁷ GYSAQ ⁸ TAYEDW ⁹ FTLY ¹⁰ NVLYTSL ¹¹ PVLLMGLLD ¹² QDV ¹³ SDKLS ¹⁴ LRFP ¹⁵ GLYIV ¹⁶ GQRDLL ¹⁷ FNYKRF			1033
Dnf1	QAVMSSDYAIGQFRYLARLVLVHGRWSYKRLAEMIPEFFYKNMIFALALFWYGIYND ¹ FDGS ² LYEYTYMMFYN ³ LAF ⁴ TS ⁵ LPVIFL ⁶ GILD ⁷ QDV ⁸ NDTIS ⁹ LVV ¹⁰ P ¹¹ QLYR ¹² VGIR ¹³ KEWN ¹⁴ QRKFL			1271
PfGCα	ISAGYSDYCIKKFCYLRKLLFY ¹ GSKHLYT ² ISII ³ LYWN ⁴ FFKN ⁵ ILLIL ⁶ PIFFYQAYAS ⁷ WCVKI ⁸ PEL ⁹ LYTF ¹⁰ FSIF ¹¹ FWVF ¹² IP ¹³ IYYM ¹⁴ FLQHN ¹⁵ LYND ¹⁶ ILYNI ¹⁷ PLFYALSRRRYNMNCFK ¹⁸ F			2170
TgGC	AA ¹ 3AYADYSFTEFRFLQRL ² LVHGR ³ LSLMRVSTVIL ⁴ WSFFKSLCIGLPTFLFQ ⁵ QAFWSAVEVYD ⁶ PLLMI ⁷ VDFFW ⁸ TLP ⁹ GI ¹⁰ IHGYS ¹¹ DQDL ¹² PTHLL ¹³ PSV ¹⁴ PVLYTP ¹⁵ GRRRLY ¹⁶ FNGFRF			2344

	TM7	TM8	TM9	
ATP8A1	WVHCLNGLFHSVILFWFPLKALQYGTAFNGKTS ¹ SDYLLGNF ² VYTFVVI ³ TVCLKAGLET ⁴ SYWTFW-SHIAI ⁵ WGSIAL ⁶ LWV ⁷ VFFGIYSSLWPAIPMAPDMSG ⁸ EAML--FSSGV ⁹ FWMGL			1055
Drs2p	WGWIINGF ¹ FHSAIV ² FIGTIL ³ IYRYGFALNMHGELADHWSWGVTVYTTS ⁴ VII ⁵ VLGKAALV ⁶ TNQWTKFTLIAIPGS ⁷ LLFWLIFFP ⁸ YAS--IFPHANISREYYGV ⁹ VKHTYGS ¹⁰ GVFWLTL			1209
PfATP2	ISWVMNSLFHGSVVFLIPLYFLSYINI ¹ PTSDGIPYDIWTVGCATYFLT ² VLIVNFKILFET---YYLNILPIS ³ GIALSIFSFVLLVTA ⁴ FSFMCVGSIHLLGT-----IVYLVQ			1460
PfATP7	AIWLATVETVIMLHFSTSQILYTHHVI ¹ AVNIVVLMNTWFF ² ISHVVLWIELIATFFFWF---IISNTKFFLDI ³ GADELHGT ⁴ FEKAHSSG-----NYYASL			1759
TgATP2A	ISWILLGVVHAAIFVVGLYAFGYIIPGSPGQPFDMVMVGTVMMAANCLVANLAILFYS---FSVSAV ¹ TWCGIA ² FSLFSCLV ³ LFFA ⁴ ASTATVGGISTGAI ⁵ FL ⁶ LKASPTICLY ⁷ VLV			1658
TgATP2B	LKWM ¹ LNGVWQAIVIFVVP ² TFV ³ FGCNAVPTTGR ⁴ TMDLW ⁵ VGTV ⁶ MFMMN ⁷ MIVV ⁸ NIKV ⁹ LLET---YLT ¹⁰ TI ¹¹ IWAG ¹² FYISL ¹³ LACLLFV ¹⁴ FL ¹⁵ SSW ¹⁶ PGFAGSV ¹⁷ LGCV ¹⁸ FYLFIDAAACAVIAT			1574
ATP8B1	FVSLHGVLTSMILFFIPLGAYLQTVGQDGE-APS ¹ DYQSFAV ² TIASALVI ³ TVNFQIGL ⁴ TSYWTFVNA ⁵ SIFGSIALYFGIM ⁶ DFH ⁷ SAGIH ⁸ VLFP ⁹ SAFQFTGTAS ¹⁰ NLRQ ¹¹ PYI ¹² WLT ¹³ I			1149
Dnf1	WYM-LDGLYQSICFFFPYLVYHKNMIVT ¹ S ² NGLGLD ³ HRYFVG ⁴ VYVTTIA ⁵ AVISCNTYVLLH ⁶ QYRWDW---FSG ⁷ FLIALSCLV ⁸ VFAWTGI ⁹ WSSAIASREFFKAAARIY ¹⁰ GAPS-FWAV ¹¹ F			1382
PfGCα	LPWIFEAIFYSMIYFFAYAA ¹ LKENS ² HLNN-GEVITINT ³ FGNIC ⁴ FIGCLLISILR ⁵ LFLE ⁶ GLWS ⁷ SPSILITCF ⁸ GCF ⁹ LVF ¹⁰ FP ¹¹ SL ¹² LFIC ¹³ FAYLS ¹⁴ NEYIREVFRQT ¹⁵ FLWAP ¹⁶ LYVLLI ¹⁷ LWF			2286
TgGC	ILWTV ¹ EGIIYSFLIF ² YLLQAT ³ WMDGNT ⁴ FHD-GQVLG ⁵ FHSYGI ⁶ LL ⁷ LFGS ⁸ LL ⁹ QSNVRI ¹⁰ IILE ¹¹ TS ¹² LWTP ¹³ TL ¹⁴ FT ¹⁵ IVL ¹⁶ CTIM ¹⁷ F ¹⁸ PTV ¹⁹ LLYS ²⁰ VTGW ²¹ PRRYMELAGR ²² VVFAW ²³ PMLY ²⁴ FLI ²⁵ PLWV			2460

TM10

ATP8A1	LFIPVASLLLDVYKVIKRTAFKTLVDEVQELEA	1089
Drs2p	IVLPIFALVRDFLWKYYKRMYPETYHVIQEMQK	1243
PfATP2	SLRFWLVIILGLFTALLRDYVFKVYKRNFNPEIY	1494
PfATP7	TIISLYISILPLIILMTYQFIKKPTMEQIVLEQLK	1793
TgATP2A	ACSLSLGLLWFKRSFRVAFRPELYDVLQRHEYLG	1692
TgATP2B	VAVTSLCLARDWLWKAFRVNCAPLYHLIQQREY	1608
ATP8B1	ILAVAVCLLPVVAIRFLSMTIWPSESDKIQKHRK	1183
Dnf1	FVAVLFCLLPFRFTYDSFQKFFYPTDVEIVREMWQ	1416
PfGCα	STCIISYIFINFTKSILFPNIYNVNVNHWLFEQYQ	2320
TgGC	SIGILVQLLLQVFTSSLPNISGSVKQYLAQKQA	2494