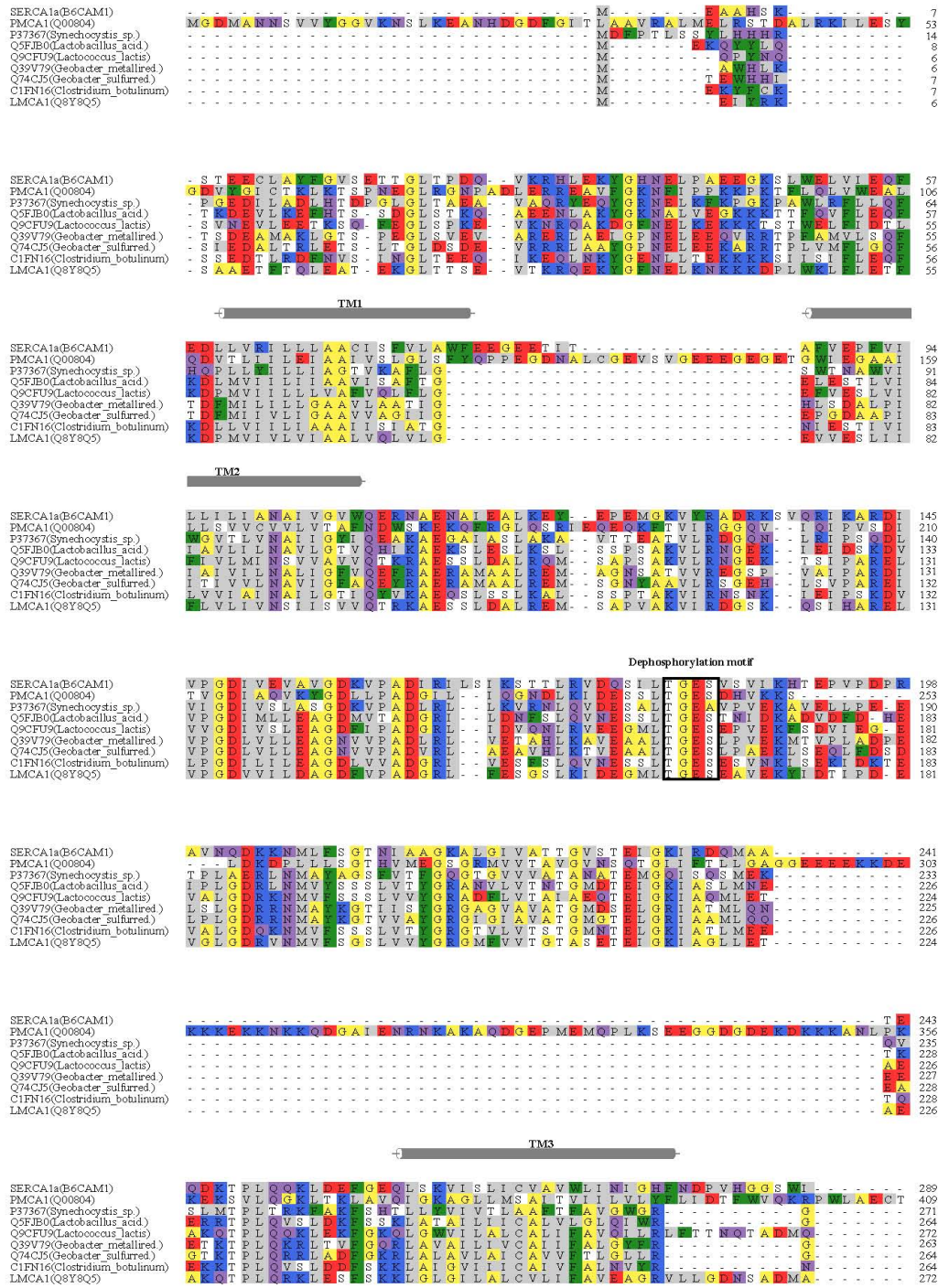


Figure S1



TM4  
 ↓ ↓ ↓ ↓

SERCA1a(B6CAM1)	PI I I Q V V K G I I G V T V L V V A V P E G L P A V I T T C L A L G T R R M A K K N A I V R S L P S	338
PMCA1(Q00804)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T I S L A S V N P M M K D N N L V R R H L D A	462
P37367(Synechocystis sp.)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	320
Q5FB0(Lactobacillus acid)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	313
Q9CFU9(Lactococcus lactis)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	321
Q39V79(Geobacter metallire)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	312
Q74CJ5(Geobacter_sulfured)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	313
C1FN16(Clostridium_botulinum)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	313
LMCA1(Q8Y9Q5)	PI I I Q V V K G I I G V T V L V V A V P E G L P L P V T V T L A I G V N R M M K D N N A I R K L L P A	321

Phosphorylation Site

SERCA1a(B6CAM1)	V E T L G C T S V I C S K T G T L T T N Q M S V C K M I I K V D G D C S L N E S I T G S T V A P	391
PMCA1(Q00804)	C E T M G N A T A I C S K T G T L T T M N R M A V V Q A I N E L L A V L M L N D S S L S G C G L L	494
P37367(Synechocystis sp.)	V E A L G S A T V V C S K T G T L T T E N Q M T V Q A V A G G L L L L L L L L L L L L L L L L L	364
Q5FB0(Lactobacillus acid)	V E S L G S V S V I C S K T G T L T T Q N K M T V E S T L I G G L L L L L L L L L L L L L L L L L	345
Q9CFU9(Lactococcus lactis)	V E T L G S T S V I C T K T G T L T T Q N K M T V S D L	322
Q39V79(Geobacter metallire)	V E T L G S V T V I C S K T G T L T T L N R M T V E K V A M N G L L L L L L L L L L L L L L L L L L	344
Q74CJ5(Geobacter_sulfured)	V E T L G S V T V I C S K T G T L T T L N R M T V E K V A M N G L L L L L L L L L L L L L L L L L L	345
C1FN16(Clostridium_botulinum)	V E T L G S V T V I C S K T G T L T T Q N K M T V S D L	345
LMCA1(Q8Y9Q5)	V E T L G S T S V I C T K T G T L T T Q N K M T V S D L	353

SERCA1a(B6CAM1)	E G E V L K N D P I P I S S Q G D D G L V L	437
PMCA1(Q00804)	K H V K K V P E P P P P N I L S L	541
P37367(Synechocystis sp.)	K G E E V O V M G E E V N V L L D G L P P V L E E C I L T G M L C L L L L L L L L L L L L L L L L L L	413
Q5FB0(Lactobacillus acid)	L V L P N Q M L E N Q L H R L	381
Q9CFU9(Lactococcus lactis)	T Q G S K E L T L T Q A Q K L	389
Q39V79(Geobacter metallire)	V I T M P L A D A C G T M G G E A G R H L	384
Q74CJ5(Geobacter_sulfured)	L E G T D A G S S G V S A A T L	381
C1FN16(Clostridium_botulinum)	K L I T S E P I L N M S L S K R L	381
LMCA1(Q8Y9Q5)	G T E N P E S P E N S G E R R L	392

SERCA1a(B6CAM1)	G E A T E T A L T L V K M N V E N I T E V R N L S V E F R A N A C N S V I R Q L L L M K K E P T L E S	487
PMCA1(Q00804)	G N K T E C A L L G P L	578
P37367(Synechocystis sp.)	G D P T E E G A L L A S L	447
Q5FB0(Lactobacillus acid)	G D P T E A L L L A G L	425
Q9CFU9(Lactococcus lactis)	G D P T V V L L A G L	423
Q39V79(Geobacter metallire)	G D P T E E T A L S A A L	418
Q74CJ5(Geobacter_sulfured)	G D P T E E T A L L A G L	415
C1FN16(Clostridium_botulinum)	G D P T E V A L T N L	415
LMCA1(Q8Y9Q5)	G D P T E V A L T A L	426

Nucleotide binding

SERCA1a(B6CAM1)	S K D R K S M S V C S P A K S S R A A V G N K M V S G A P E G V I D R C N V R V G T T R V P M T G	539
PMCA1(Q00804)	O S V R K S M S T V L K N S D G S R L	626
P37367(Synechocystis sp.)	E S D R K S M S T V L K N S D G S R L	490
Q5FB0(Lactobacillus acid)	S R K L M S T L H L I H T V P T L	471
Q9CFU9(Lactococcus lactis)	D S E R K L M S T L N L H G Q K T L	469
Q39V79(Geobacter metallire)	D S E R K L M T T H E R S E G V L	461
Q74CJ5(Geobacter_sulfured)	D S E R K M C M T T H L T G D T V L	458
C1FN16(Clostridium_botulinum)	D S D R K L M S T L H L N I D N E V L	461
LMCA1(Q8Y9Q5)	D S D R K L M S T L E H L T N E N K A L	472

SERCA1a(B6CAM1)	P V K E K I L S V I K E G T G R D T L R C L A L A T F D T P P K R E E M V L D S S R M E V E T D L	591
PMCA1(Q00804)	R D R D D I V K T V I E P M A S E G L R R V L A A R T V P H H H A I E H G N L L L L L L L L L L L L L L L L L L	674
P37367(Synechocystis sp.)	I D R G E I E S N V E P M A Q Q G L R R V L A A R T V P H H H A I E H G N L L L L L L L L L L L L L L L L L L	534
Q5FB0(Lactobacillus acid)	E D K K K L A Q N E H L S E N G L R V L A A R K E K L E E D L S P F L	511
Q9CFU9(Lactococcus lactis)	E L K E K L Q A Q N E A L S O K A L R V L A A R K E V S D N K T E L T L T L	512
Q39V79(Geobacter metallire)	P D V E K I L R L S E E M A E E G L R V L A V M R N V E O V P D R L S D R L	505
Q74CJ5(Geobacter_sulfured)	L D Q E I E R V T V E M A A R G L R V L A L A M R W E L P D R L S D E L	502
C1FN16(Clostridium_botulinum)	K D I N D I N N M L N R L L S S N G L R V L S G E K L D D K D L S L D D L	503
LMCA1(Q8Y9Q5)	E I L A K L K E T N E E L S N Q A L R V L A G E K R M P A D T T E L S L E L	515

SERCA1a(B6CAM1)	T V G V V G M L D P P K E V M G S I Q L C R D A G I R V I M I T G D N R K G T A I A I C R R I G I G E	644
PMCA1(Q00804)	R D R D D I V K T V I E P M A S E G L R R V L A A R T V P H H H A I E H G N L L L L L L L L L L L L L L L L L L	727
P37367(Synechocystis sp.)	I D R G E I E S N V E P M A Q Q G L R R V L A A R T V P H H H A I E H G N L L L L L L L L L L L L L L L L L L	587
Q5FB0(Lactobacillus acid)	E D K K K L A Q N E H L S E N G L R V L A A R K E K L E E D L S P F L	564
Q9CFU9(Lactococcus lactis)	E L K E K L Q A Q N E A L S O K A L R V L A A R K E V S D N K T E L T L T L	565
Q39V79(Geobacter metallire)	P D V E K I L R L S E E M A E E G L R V L A V M R N V E O V P D R L S D R L	558
Q74CJ5(Geobacter_sulfured)	L D Q E I E R V T V E M A A R G L R V L A L A M R W E L P D R L S D E L	555
C1FN16(Clostridium_botulinum)	K D I N D I N N M L N R L L S S N G L R V L S G E K L D D K D L S L D D L	556
LMCA1(Q8Y9Q5)	E I L A K L K E T N E E L S N Q A L R V L A G E K R M P A D T T E L S L E L	568

SERCA1a(B6CAM1)	N E E V A D R A T G R E F D L L P L A Q R E A C R R A C C A R V E P S H K S K I V E	689
PMCA1(Q00804)	G E E L L C L G K E F D L L P L A Q R E A C R R A C C A R V E P S H K S K I V E	778
P37367(Synechocystis sp.)	G D I L L A V T G L S L	629
Q5FB0(Lactobacillus acid)	G D I L L A V T G L S L	605
Q9CFU9(Lactococcus lactis)	G D M L L A V T G L S L	606
Q39V79(Geobacter metallire)	E S E L L V T G R E L A L	597
Q74CJ5(Geobacter_sulfured)	D G D A L L T G R E L A L	599
C1FN16(Clostridium_botulinum)	N D I L L A V T G L S L	597
LMCA1(Q8Y9Q5)	D D I L L A V T G L S L	609



**Hinge motif**

SERCA1a(B6CAM1)	G L L - - - - -	S Q D E I T A M T	G D G V N D A P	A L K K A F I	G I A M G - S G T	V A V T A S F M V L A	736
PMCA1(Q00804)	G I I D S T V S	E Q R Q V V A V T	G D G T N D G P	A L K K A D G	G A M G I A G T	V A V E A S D I I L T	831
P37367(Synechocystis sp.)	A L - - - - -	Q E R G H I V A M T	G D G V N D A P	A L K K A D I	G I A M G I T G T	V A V E A S S D M L L T	677
Q5FB0(Lactobacillus acid)	A M - - - - -	Q N R K I V S M T	G D G V N D A P	A L K K A D I	G V A M G I T G T	V A V E A S S M I L A	653
Q9CFU9(Lactococcus lactis)	A M - - - - -	Q N R E Q V T A M T	G D G V N D A P	A L K K A M I	G I A M G - S G T	V A V E A S S M I L T	653
Q39V79(Geobacter metallire)	A L - - - - -	Q R G H I V A M T	G D G V N D A P	A L K K A D I	G I A M G I T G T	V A V E A S A M I L L	647
Q74CJ5(Geobacter_sulfured)	A L - - - - -	Q R G H I V A M T	G D G V N D A P	A L K K A D I	G I A M G I T G T	V A V E A S A M V L L	645
C1FN16(Clostridium_botulinum)	A M - - - - -	Q S K R I V A M T	G D G V N D A P	A L K K A D I	G I A M G I T G T	V A V E A S S M I L T	645
LMCA1(Q8Y9Q5)	A M - - - - -	Q S K R I V A M T	G D G V N D A P	A L K K A D I	G V A M G - S G T	V A V E A S A A M I L T	656

**TMS**

SERCA1a(B6CAM1)	D D N F S T I V	A A V E Q K A I	V N N M K Q I R	L I S S N V G E V V	V C I L T A A L G L P	E A L I P	789
PMCA1(Q00804)	D D N F T S I V	A A V M G R N V	D S I S K L Q	L T V N V V A V I V A	T G A C I T Q D S P L K A		884
P37367(Synechocystis sp.)	D D N F A S I E	A A V E Q R T V	Q N L R K K A I	M L L P V N G G E S M T I	V L S V L L A I N L P I L S		730
Q5FB0(Lactobacillus acid)	D D N F A T I T	A A V A M G R T V	E N I K N A I M	L L S G N L S A I I T V L	E S I G G S V P F A		706
Q9CFU9(Lactococcus lactis)	D D N F V S I V	A A V S I G V V L	D N I K A S P S	L S G N L G A I A I V	A V A V G V M P R T A		706
Q39V79(Geobacter metallire)	D D N F A T I V	A A V E G R R I	V A N I L K E I	I S I T S N A G T L V A I T	L A P F G L P L P L P		700
Q74CJ5(Geobacter_sulfured)	D D N F A T I V	A A V E G R R I	V A N I L K E I	T S I T S N I G T L V A I T	L A P F G L P L P L P		698
C1FN16(Clostridium_botulinum)	D D N F A T I V	A A V S I S N G R I	V A N I L K N S I	K L L S G N T S G I L A V L	S S L S A L P V P F A A		698
LMCA1(Q8Y9Q5)	D D N F V S I V	A A V G V G R T V	E N I K R S I A	L E A G N L G A I I A I L	A L V L D V I N P P F A		709

**TM6**      **TM7**

SERCA1a(B6CAM1)	V Q L L W V N L V T	G L P A T A L G E N P P	D L I M D R P P S P K E P L I S	G L L E E R Y M A I G G	842
PMCA1(Q00804)	V Q M L W V N L I M	T L A S L A L A T E P P T	S L L L G K P Y G R N K P L I S	R T M M K N I L G H A	937
P37367(Synechocystis sp.)	L Q V L W L N M I M	S I T M T V P L A E E A G S P	G I M Q Q A P R N P N E P L I T	K L L L H R I L L V S L	783
Q5FB0(Lactobacillus acid)	V Q L L F I N L V T	S P A I A I G M E P G A P	V L D S P P P K P V G I G	R N L V T K I T L Q G I	759
Q9CFU9(Lactococcus lactis)	V Q L L F I N L V M	S P A I A I G M E K A P	V L M R A P K Q L N E G I	A N G M R V I L I R G S	759
Q39V79(Geobacter metallire)	I Q I L W L N L L C	S L P G L A L A G E P A E R	V M R P P V D P K R E G I S	A G G G F V L G Y G E	753
Q74CJ5(Geobacter_sulfured)	I Q I L W L N L L C	S L P G L A L A G E P A E R	V M S R P P V D P K R E G V	A G G G F Y A A G Y G L	751
C1FN16(Clostridium_botulinum)	V H L L F I N L L T	S L P A I A I G M E K S T R	V V L N E K P P D S K E S I	N G G V S I L V F G E	751
LMCA1(Q8Y9Q5)	L Q L L F I N L L E	S L P A I A I G M E K A P	V M R R K P R I N E G I	A G G T M R A V I S R G V	762

SERCA1a(B6CAM1)	V V G A A T V G A A A M V E M	A E D G P G V T	H Q L T H F M Q C T	E D H P H E G L D C H I E A P E	895
PMCA1(Q00804)	V Q L V V V T L L L A G E K	E D I D S G R N A P L H A P P S E			970
P37367(Synechocystis sp.)	L N N I L I G M	E M V N R T D D L A			805
Q5FB0(Lactobacillus acid)	I I S V G V I T A M I	G R N T S P A V			779
Q9CFU9(Lactococcus lactis)	L I G I A A I I S Q	V G Q K T S P E M G			780
Q39V79(Geobacter metallire)	L I G A V A L A Q A	A L R K G L P W			773
Q74CJ5(Geobacter_sulfured)	V I G A A A L A Q A	A L R M L P W			771
C1FN16(Clostridium_botulinum)	L I A I A T I T A	H I G L S S G P V G T			772
LMCA1(Q8Y9Q5)	L I G I A V I I S Q	I G M Q I S P E M S			783

**TMS**      **TM9**

SERCA1a(B6CAM1)	P M T M A L S V L V T I	E M C N A L N S L -	S E N O S L - - - -	M M P P V V N I W L L G S I C L S	940
PMCA1(Q00804)	H V T I V N I V L M Q L	E N I N A R K I H G E R N V		E G I N N A I C T I V L G T	1066
P37367(Synechocystis sp.)	A T M A I Q A L A A A V I	L L S I S - - -	L G S L G V I T G	R Q T T R A S I L L L G I A V A	856
Q5FB0(Lactobacillus acid)	A C T M A E S T L T A	L L H G F N C R -	S Q E S T - - - -	K R I G E K M N M P S L A A A V G	823
Q9CFU9(Lactococcus lactis)	- V A M A F T T L I L A	T L Q T A A R - - -	S Q S Q N I - - - -	L K L G T T N K V L M A V T C	824
Q39V79(Geobacter metallire)	- Q T M V F T L V L N R	M A V L S V R - -	S D R Q S L - - - -	R I G L L S N L P L C G A I V I T	817
Q74CJ5(Geobacter_sulfured)	- Q T M V F T L V L N R	M A V L S V R - -	S D R T S L - - - -	L R I G I M S N E P L V G A I V I T	815
C1FN16(Clostridium_botulinum)	A S T M A P A T L C I G	L H G F N C R -	G V K S I - - - -	A L G L S N R S W I A A G I G	816
LMCA1(Q8Y9Q5)	- V A M A F T T L I L A	T L Q T A A R - -	S N V Q T A - - - -	G A G E S N R S W I G A V L L C	827

**TM10**

SERCA1a(B6CAM1)	M S L H L I L I V D P L P M I	K L - K A L E L T O W L M V L K I	S L P V I G L D E I L K K I A - - -	988
PMCA1(Q00804)	E V V Q I I I V Q A G K P -	S S C - S E L S V E Q W L M S I	L G M G T L L G Q L I S T I P T S R L	1066
P37367(Synechocystis sp.)	L A L Q I G S L P M N V L P E T	A P M E W Q Q A I C L L P M I	P M V P V A I L A N R L D P - - -	905
Q5FB0(Lactobacillus acid)	T L L L A L I L W P A L H V L A V I	T P L P N S D M L L L A L M P T I	L I Q I W I A N - - - -	871
Q9CFU9(Lactococcus lactis)	L A L S L T T - L P N L R E I	S I P A A L G S Q M I V A A G L A V I	A V I C M E I L K S I K - - -	872
Q39V79(Geobacter metallire)	L L Q L M V V T P L L N P I F S T	- A P L S G A L L I T V G L A V G M I	L V S L H K V L K - - - -	865
Q74CJ5(Geobacter_sulfured)	L C L Q L A V V T P A L N P L F H T	- E P L S G A L V A T V V L A M G M V L S	L O Q V L I - - - -	863
C1FN16(Clostridium_botulinum)	L L L L N A V L L V P P L Q S L	F H V I P L S G A N I G H I L L A	L M P T L I Q I K V I K - - -	864
LMCA1(Q8Y9Q5)	L V L G I T V L P G A K E I	S I P A S G L H R S T I A A G L A L A A V V M M	E I I K V V Q - - - -	875

**Calmodulin-binding domain**

SERCA1a(B6CAM1)	K F Q R E V V H G T Q K R E I	G E E P L A E D V E S I V H A E R P	R R S W O I F V R G F N R I O T O M I	988
PMCA1(Q00804)	- - - - -	- - - - -	- - - - -	1119
P37367(Synechocystis sp.)	- - - - -	- - - - -	- - - - -	905
Q5FB0(Lactobacillus acid)	- - - - -	- - - - -	- - - - -	871
Q9CFU9(Lactococcus lactis)	- - - - -	- - - - -	- - - - -	872
Q39V79(Geobacter metallire)	- - - - -	- - - - -	- - - - -	865
Q74CJ5(Geobacter_sulfured)	- - - - -	- - - - -	- - - - -	863
C1FN16(Clostridium_botulinum)	- - - - -	- - - - -	- - - - -	864
LMCA1(Q8Y9Q5)	- - - - -	- - - - -	- - - - -	875

SERCA1a(B6CAM1)	V V N A Q S R S S I	Q G A L R R Q P I S I A S	Q H H I R V V N A R S S L	V E G L E R P S K S S I H N	988
PMCA1(Q00804)	- - - - -	- - - - -	- - - - -	- - - - -	1172
P37367(Synechocystis sp.)	- - - - -	- - - - -	- - - - -	- - - - -	905
Q5FB0(Lactobacillus acid)	- - - - -	- - - - -	- - - - -	- - - - -	871
Q9CFU9(Lactococcus lactis)	- - - - -	- - - - -	- - - - -	- - - - -	872
Q39V79(Geobacter metallire)	- - - - -	- - - - -	- - - - -	- - - - -	865
Q74CJ5(Geobacter_sulfured)	- - - - -	- - - - -	- - - - -	- - - - -	863
C1FN16(Clostridium_botulinum)	- - - - -	- - - - -	- - - - -	- - - - -	864
LMCA1(Q8Y9Q5)	- - - - -	- - - - -	- - - - -	- - - - -	875

SERCA1a(B6CAM1)	- - - - - R N L L G - - - - -	994
PMCA1(Q00804)	MT H P E R I E S P H I P L I D D T A E D D A P T K R N S S P P P S P N K N N L V D S G I H L	1225
P37367(Synechocystis_sp.)	- - - - - R K F - - - - -	905
Q5FJB0(Lactobacillus_acid)	- - - - - G V P S K H - - - - -	875
Q9CFU9(Lactococcus_lactis)	- - - - - R I Q P F S - - - - -	878
Q39V79(Geobacter_metalired.)	- - - - - R W R I G S S R - - - - -	871
Q74CJ5(Geobacter_sulfurred.)	- - - - - R S E K A D I N F E N K G G K V K E K Q V A - - - - -	871
C1FN16(Clostridium_botulinum)	- - - - - N K - - - - -	889
LMCA1(Q8Y8Q5)	- - - - -	880

SERCA1a(B6CAM1)	- - - - -	994
PMCA1(Q00804)	T I E M N K S A T S S S F G S P L H S L E T S L	1249
P37367(Synechocystis_sp.)	- - - - -	905
Q5FJB0(Lactobacillus_acid)	- - - - -	875
Q9CFU9(Lactococcus_lactis)	- - - - -	878
Q39V79(Geobacter_metalired.)	- - - - -	871
Q74CJ5(Geobacter_sulfurred.)	- - - - -	871
C1FN16(Clostridium_botulinum)	- - - - -	889
LMCA1(Q8Y8Q5)	- - - - -	880

Figure S1: Multiple sequence alignment selected  $\text{Ca}^{2+}$  ATPases from rabbit and eubacteria generated by aligning 52 sequences of type IIa and IIb P-type ATPases in MUSCLE(1). The following amino acid groupings are indicated by colour schemes: positively charged (RK) shown on blue background; polar (QN) shown in purple; hydrophobic (CLIVM) with gray background; aromatic (FWY) with green background; small (TS) with a white background and tiny (AG) with yellow background. The dephosphorylation motif (TGES), phosphorylation motif (DKTGT), nucleotide binding motif (KGA), hinge motif (GDGXND) and calmodulin binding domain are highlighted in boxes. The residues involved in binding  $\text{Ca}^{2+}$  at site I and II are marked by black arrowheads. The structural elements of the transmembrane helices of SERCA1a (PDB: 1T5T) (2) are depicted in gray above the alignment.

Figure S2

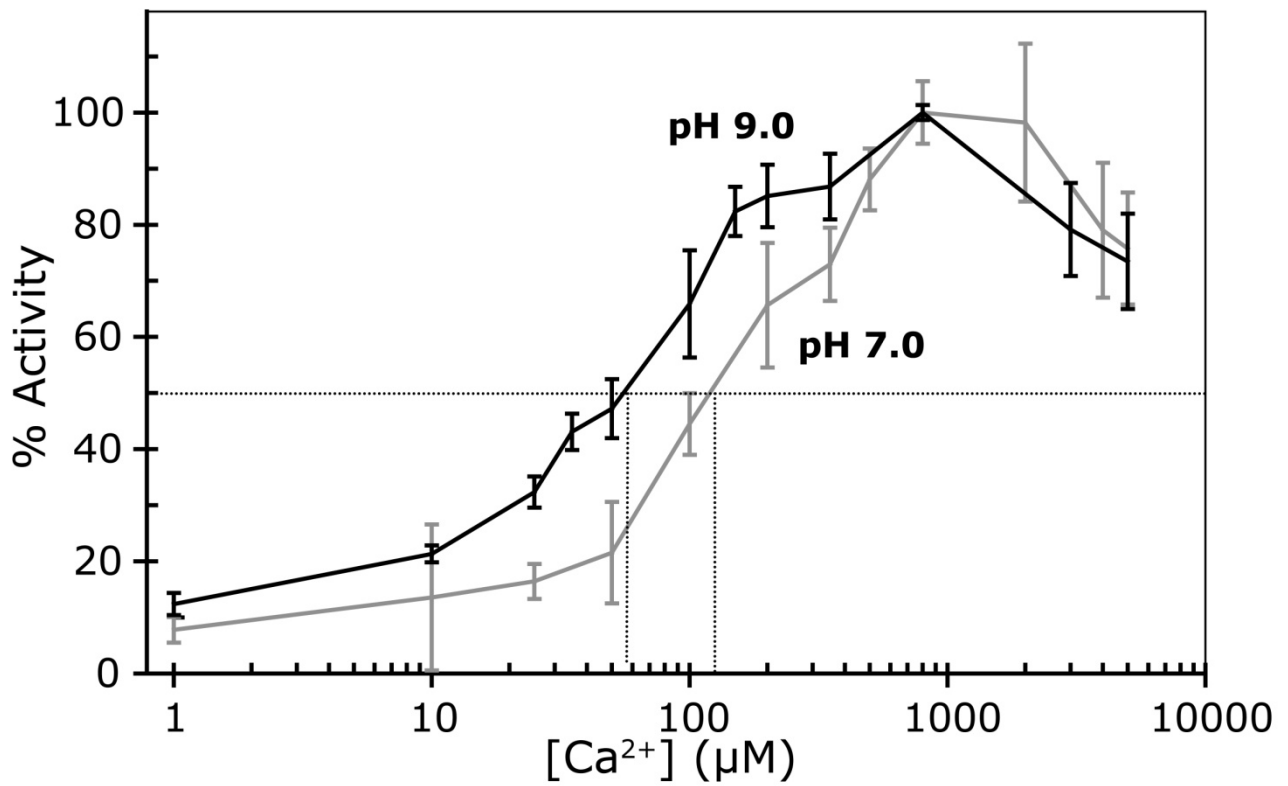


Figure S2. The ATPase activity of LMCA1 measured as a function of Ca<sup>2+</sup>-concentration at pH 7 (grey line) and 9 (black line).

1. Edgar, R. C. (2004) *Nucl Acids Res* **32**, 1792-1797
2. Sorensen, T. L., Moller, J. V., and Nissen, P. (2004) *Science* **304**, 1672-1675