

SUPPLEMENTARY INFORMATION

SLC41A1 is essential for magnesium homeostasis *in vivo*

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Human SLC41A1	1	-----MSSKPE-----PKDVHQLNG--TGPSASPCSSD-----GPGREPL
Mouse SLC41A1	1	-----MSSKPE-----PKDIHQPNQ--TGPTPSPCSSD-----GPGREPL
Rat SLC41A1	1	-----MSSKPE-----PKDIHQPNQ--TGPTPSPCSSD-----GPGREPL
Zebrafish Slc41a1	1	MVLWLKDQDKLSDMSTGTETRIEMKKEGVPPAYHHSNGSVHPEVILEDSPEEVPQTPGEYEL
Human SLC41A1	34	AGTS---EFLGPDGAGVE--VVIESRANAKGVREEDALLENGSQSNESDDVSTDRGPAPPS
Mouse SLC41A1	34	AGTS---EFLGPDGVEV--VVIESRANAKGVREEDALLENGSQSNESDDVSTDRGPAPPS
Rat SLC41A1	34	AGTS---EFLGPDGAGVE--VVIESRANAKGVREEDALLENGSQSNESDDVSTDRVPAPPS
Zebrafish Slc41a1	61	TEVTSLPDCGDQENERPDMVVLDCRANAKGVREEDALLENGSQSNESDDTSTDQSPVPPA
TMD1		
Human SLC41A1	90	PLKETSFSIGLQVLPFLLAGFGTVAAGMVLDIVQHWVEVFQKVTEVFILVPALLGLKGNL
Mouse SLC41A1	89	PLKETSFSIGLQVLPFLLAGFGTVAAGMVLDIVQHWVEVFQKVTEVFILVPALLGLKGNL
Rat SLC41A1	91	PLKETSFSIGLQVLPFLLAGFGTVAAGMVLDIVQHWVEVFQKVTEVFILVPALLGLKGNL
Zebrafish Slc41a1	121	PLKETSFSIGLQVLPFLLAGFGTVAAGMVLDIVQHWVTEVFTEVFILVPALLGLKGNL
TMD2 PX ₆ GN		
Human SLC41A1	150	EMTLASRLSTAANIGHMDTPKELWRMITGNMALIQVQATVVGFLASIAAVFGWIPDGHF
Mouse SLC41A1	149	EMTLASRLSTAANIGOMDTPKELWRMITGNMALIQVQATVVGFLASIAAVFGWIPDGHF
Rat SLC41A1	151	EMTLASRLSTAANIGOMDTPKELWRMITGNMALIQVQATVVGFLASIAAVFGWIPDGHF
Zebrafish Slc41a1	181	EMTLASRLSTAANIGOMDTAKDMWKMTMGNTALIQVQATVVGFLASIAAVTFGWIPGNE
TMD3 TMD4		
Human SLC41A1	210	SIPHAFLLCASSVATAFIASLVLGIMIGVIIIGSRKIGINPDNVATPIAASLGDLITLAL
Mouse SLC41A1	209	SIPHAFLLCASSVATAFIASLVLGIMIGVIIIGSRKIGINPDNVATPIAASLGDLITLAL
Rat SLC41A1	211	SIPHAFLLCASSVATAFIASLVLGIMIGVIIIGSRKIGINPDNVATPIAASLGDLITLAL
Zebrafish Slc41a1	241	RMGHATLLCASSVATAFIASIALGLIMIGVIIASRKVGINPDNVATPIAASLGDLITLAL
TMD5 P(D/A) ₄ PX ₆ D ↑ TMD6		
Human SLC41A1	270	LSGISWGLYLELTHWRYIYPLVCAFFVALLPVWVVLARRSPATREVLVYSGWEPVIIAMAI
Mouse SLC41A1	269	LSGISWGLYLELTHWRYIYPLVCAFFVALLPVWVVLARRSPATREVLVYSGWEPVIIAMAI
Rat SLC41A1	271	LSGISWGLYLELTHWRYIYPLVCAFFVALLPVWVVLARRSPATREVLVYSGWEPVIIAMAI
Zebrafish Slc41a1	301	LAGISTGLYKELEFNNYANPNVCAFFVALTPVWVLIARRTPSTREVLVYSGWEPVIIAMAI
TMD7		
Human SLC41A1	330	SSVGGLILDKTVDSPNFAGMAVFTPVINGVGGNLVAVQASRISTFLHMNGMPGENSEQAP
Mouse SLC41A1	329	SSVGGLILDKTVDSPNFAGMAVFTPVINGVGGNLVAVQASRISTFLHMNGMPGENSEETP
Rat SLC41A1	331	SSVGGLILDKTVDSPNFAGMAVFTPVINGVGGNLVAVQASRISTFLHMNGMPGENSEETP
Zebrafish Slc41a1	361	SSVGGLILDKTVDSPNFAGMAVFTPVINGVGGNLVAVQASRISTFLHMNALPIVEPNPAP
TMD8 TMD9		
Human SLC41A1	390	RRCPSPCCTFFSPDVNSRSARVFLFLVPGHLVFLYTIISCMQGGHTTLTLIFIFIYMTAA
Mouse SLC41A1	389	RRCPSPCCTFFSPDVNSRSARVFLFLVPGHLVFLYTIISCMQGGHTTLTLIFIFIYMTAA
Rat SLC41A1	391	RRCPSPCCTFFSPDVNSRSARVFLFLVPGHLVFLYTIISCMQGGHTTLTLIFIFIYMTAA
Zebrafish Slc41a1	421	RCPTPWGCTFFGSGVNSRSARVFLFLVAPGHLVFLYTIISMRGGHTTLTYIFIAFYIAAA
TMD10		
Human SLC41A1	450	LLQVLILLYIADWMVHMMWGRGLDPDNFSIPYLTALGDLGTLGLALS FHVWLIGDRDT
Mouse SLC41A1	449	LLQVLILLYIADWMVHMMWGRGLDPDNFSIPYLTALGDLGTLGLALS FHVWLIGDRDT
Rat SLC41A1	451	LLQVLILLYIADWMVHMMWGRGLDPDNFSIPYLTALGDLGTLGLALS FHVWLIGDRDT
Zebrafish Slc41a1	481	LLQVLILLYIADWMVHMMWGRGLDPDNFSIPYLTALGDLGTLGLALS FHVWLIGDRDT
Human SLC41A1	510	DVGD
Mouse SLC41A1	509	DVGD
Rat SLC41A1	511	DVGD
Zebrafish Slc41a1	541	DVGD

Online Resource 1. Conservation of SLC41A1 proteins between zebrafish and mammals. Alignment of the zebrafish Slc41a1 protein (GenBank accession no. XP_002663867) and its mammalian counterparts: human SLC41A1 protein (GenBank accession no. NP_776253), mouse SLC41A1 protein (GenBank accession no. NP_776290), and rat SLC41A1 protein (GenBank accession no. NP_001102325). Identical amino acids are

boxed in black, conservative substitutions in gray. The predicted transmembrane α -helices in the SLC41A1 proteins are indicated by TMD1-TMD10. The residues conforming the two functionally relevant motifs for the transport of Mg^{2+} , PX_6GN and $\text{P(D/A)X}_4\text{PX}_6\text{D}$, are indicated. The residue mutated to generate a dysfunctional SLC41A1, and located in the pore region, is indicated by an arrow.