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Review

The SLC45 gene family of putative sugar transporters ☆

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Transporters in health and disease (SLC series)

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ABSTRACT

According to the classic point of view, transport of sugars across animal plasma membranes is performed by two families of transporters. Secondary active transport occurs via Na^+ symporters of the SLC5 gene family, while passive transport occurs via facilitative transporters of the SLC2 family. In recent years a new family appeared in the scenery which was called the SLC45 gene family of putative sugar transporters, mainly because of obvious similarities to plant sucrose transporters. The SLC45 family consists of only four members that have been denominated A1–A4. These members apparently have counterparts in all vertebrates. Moreover, their amino acid sequences reveal close homologies also to respective invertebrate proteins such as a recently detected sucrose transporter in *Drosophila*, and suggest a phylogenetic relationship also to corresponding proteins from plants, fungi and bacteria. This minireview describes the molecular features of its members with a focus on their possible role as sugar transporters.

Contents

1. A novel SLC family of putative sugar transporters

Transport of sugars across animal plasma membranes is accomplished by two groups of transport proteins, the SGLT family of Na^+ symporters that belongs to the large SLC5 family consisting of more than 200 members (Wright et al., 1994; Wright

Abbreviation: TMD, transmembrane domain(s).

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Table 1
A list of all members of the SLC45 gene family. For detailed information about the SLC gene tables, please visit: http://www.bioparadigms.org.

Human gene name	Protein or gene name(s)	Predominant substrates	Transport type/coupling ions	Tissue distribution and cellular /subcellular expression	Link to disease	Human gene locus	Sequence accession ID
SLC45A1	Past-A, DNB5	Glucose, galactose	H^+ symport	Brain, fetal kidney	Hypercapnia	1p36.1-p36.2	NM_001080397.1
SLC45A2	MATP, AIM1, underwhite			Skin, eye, melanocyte	OCA4, skin/hair/eye pigmentation, melanoma	5p13.3	NM_016180.3
SLC45A3	Prostein			Prostate, brain, kidney	Prostate cancer, huntington disease	1q32.1	NM_033102.2
SLC45A4				Brain, testis		8q24.3	NM_001080431.1

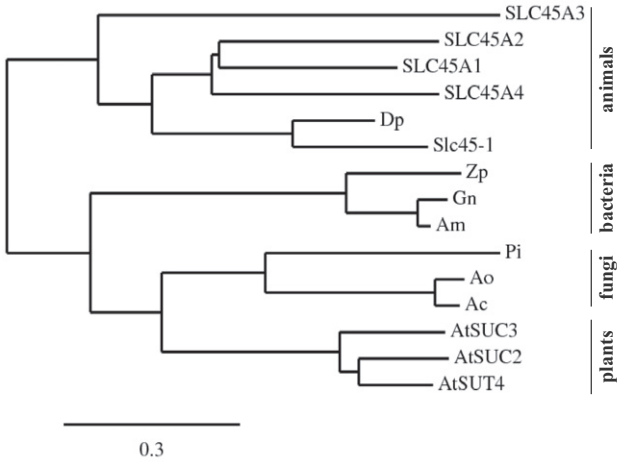

Fig. 1. Phylogenetic tree of SLC45 family like animal proteins and similar proteins from plants, fungi and bacteria. SLC45A1–4: *Homo sapiens* (NP_001073866.1, NP_057264.3, NP_149093.1, Q5BKX6.2); Slc45-1: *Drosophila melanogaster* (NP_648292.1); DP: *Daphnia pulex* (EFX86786.1); ZP: *Zunongwangia profunda* (YP_003585336.1); Gn: *Glaciecola nitratireducens* (AEP30121.1); Am: *Alteromonas macleodii* (ZP_04714820.1); Pi: *Piriformospora indica* (CCA68193.1); Ao: *Aspergillus oryzae* (XP_001818353.2); Ao: *Ajellomyces capsulatus* (EER44596.1); AtSUC2-4: *Arabidopsis thaliana* (NP_173685.1, NP_178389.1, AF175321.1). NCBI sequence accession numbers or UniProtKB/Swiss-Prot numbers are given in brackets. The tree was created using the ProtDist algorithm (Dereeper et al., 2008). Substitutions per position are indicated by the scale bar.

and Turk, 2004), and the GLUT or SLC2 family of facilitative transporters (Thorens, 1996; Thorens and Mueckler, 2010). Compared with these families, the novel SLC45 family (Table 1) is a small group which was named "putative" sugar transporter family mainly because one of its members had been shown to transport sugars (Shimokawa et al., 2002), and because all members exhibit an apparent amino acid sequence identity to plant sucrose transporters of slightly above 20%. A further reason for the term "putative" is that the four human members (A1–A4) show only 20–30% identity among each other. Nevertheless, based on derived amino acid sequences, all four members feature twelve transmembrane domains (TMD) with a large intracellular loop between TMD VI and VII, and have a signature sequence R-X-G-R-[K/R] between TMD II and III which is typical for plant sucrose transporters (Lemoine, 2000). For each of the human *SLC45* genes a corresponding gene appears to exist in other mammalia which is relatively conserved amongst the diverse species. Thus human A1 and A3 proteins are about 90% identical to their murine or bovine analogs while A2 and A4 show slightly above 80% identity among these species. Recently we detected an H^+/sucrose symporter in *Drosophila* which we called SCRT, **su**c**r**ose **t**ransporter (Meyer et al., 2011). This transporter shows a significant similarity to members of the human SLC45 family (Fig. 1), and therefore it was termed by FlyBase Slc45-1. Fig. 1 indicates the apparent phylogenetic relationship of the animal proteins not only with the plant counterparts, but also with those found in bacteria and fungi. In this minireview we will give a short survey on what is known about the members of the SLC45 family and the newly discovered insect member *Slc45-1*.

2. SLC45A1

The human *SLC45A1* gene was first published by Amler and colleagues as DNB5 (**d**eleted in **n**euro**b**lastoma-**5**) due to screening for putative tumor suppressors at chromosome 1p (Amler et al., 2000). In Northern blots they detected a strong signal at about 2.4 kb in fetal brain and kidney. In adult tissues a marked expression was found in brain, but transcripts were also detected in heart, muscle and kidney. Shortly afterwards the rat ortholog was detected, characterized and published as Past-A, **p**roton-**a**ssociated **s**ugar **t**ransporter-**A** (Shimokawa et al., 2002). The mRNA which encodes a 751 amino acids protein