Amino acid transport across the plasma membrane

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23/11/2020
Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 74

This document contains 1 pathway and 36 reactions (see Table of Contents)
Amino acid transport across the plasma membrane

Stable identifier: R-HSA-352230

Compartments: plasma membrane

Amino acid transport across plasma membranes is critical to the uptake of these molecules from the gut, to their reabsorption in the kidney proximal tubules, and to their distribution to cells in which they are required for the synthesis of proteins and of amino acid derived small molecules such as neurotransmitters. Physiological studies have defined 18 "systems" that mediate amino acid transport, each characterized by its amino acid substrates, as well as its pH sensitivity and its association (or not) with ion transport. More recently, molecular cloning studies have allowed the identification of the plasma membrane transport proteins that mediate these reactions. Amino acid uptake mediated by 17 of these transporters is annotated here (Broer 2008).

Literature references


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SLC16A10-mediated uptake of aromatic amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352158

**Type:** transition

**Compartments:** plasma membrane

SLC16A10 mediates the reversible facilitated diffusion of phenylalanine, tyrosine, and tryptophan across the plasma membrane. The process is Na⁺-independent and not coupled to H⁺ transport. As measured by Northern blotting SLC16A10 is widely expressed in the body but especially abundant in kidney. In situ hybridization studies indicate that the gene product is abundant in kidney proximal tubules (Kim et al. 2001; Kim et al. 2002; Park et al. 2005).

**Literature references**


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SLC38A1 (ATA1)-mediated uptake of neutral amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352119

**Type:** transition

**Compartments:** plasma membrane

SLC38A1 (ATA1), associated with the plasma membrane, mediates the uptake of neutral amino acids, especially alanine, asparagine, glutamine, methionine, and serine in a sodium ion-dependent transport process. Northern blotting experiments indicate gene expression in placenta and heart, and at lower levels in other tissues including brain, lung, skeletal muscle, spleen, stomach and testis, but not kidney or intestine (Wang et al. 2000).

**Literature references**


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SLC38A2 (ATA2)-mediated uptake of neutral amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352108

**Type:** transition

**Compartments:** plasma membrane

SLC38A2 (ATA2), associated with the plasma membrane, mediates the uptake of neutral amino acids, especially alanine, asparagine, glutamine, glycine, leucine, methionine, proline, and threonine in a sodium ion-dependent transport process. Northern blotting experiments indicate gene expression in placenta and heart, and at lower levels in other tissues including brain, lung, skeletal muscle, spleen, stomach, testis, kidney, and intestine (Hatanaka et al. 2000).

**Literature references**


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https://reactome.org
SLC38A3-mediated uptake of glutamine, histidine, asparagine, and alanine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352174

**Type:** transition

**Compartments:** plasma membrane

SLC38A3 (SN1), associated with the plasma membrane, mediates the uptake of glutamine, histidine, and, with lower efficiency, alanine and asparagine. Uptake of one molecule of amino acid is coupled to the uptake of two sodium ions and the export of one H+. Northern blotting experiments indicate gene expression in liver and kidney, and at much lower levels in brain, lung, skeletal muscle, spleen, stomach, testis, kidney, and intestine (Fei et al. 2000; Nakanishi et al. 2001).

**Literature references**


Nakanishi, T., Sugawara, M., Huang, W., Martindale, RG., Leibach, FH., Ganapathy, ME. et al. (2001). Structure, function, and tissue expression pattern of human SN2, a subtype of the amino acid transport system N. *Biochem Biophys Res Commun*, 281, 1343-1348.

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SLC38A4 (ATA3)-mediated uptake of arginine and lysine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352136

**Type:** transition

**Compartments:** plasma membrane

SLC38A4 (ATA3), associated with the plasma membrane, mediates the sodium-independent uptake of arginine and lysine. SLC38A4 was first identified on the basis of its similarity to SLC38A1 and SLC38A2. Like those two transporters, it can mediate the sodium-dependent uptake of neutral amino acids in cultured cells transfected with an expression vector, but it does so very inefficiently and its role, if any, in neutral amino acid uptake in vivo is unclear. By Northern blotting, SLC38A4 is abundant in liver and undetectable in all other tissues tested, including heart, placenta, kidney, and intestine (Hatanaka et al. 2001).

**Literature references**

Hatanaka, T., Huang, W., Ling, R., Prasad, PD., Sugawara, M., Leibach, FH. et al. (2001). Evidence for the transport of neutral as well as cationic amino acids by ATA3, a novel and liver-specific subtype of amino acid transport system A. *Biochim Biophys Acta*, 1510, 10-7.

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SLC38A5-mediated uptake of glutamine, histidine, asparagine, and serine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352182

**Type:** transition

**Compartments:** plasma membrane

SLC38A5 (SN2), associated with the plasma membrane, mediates the uptake of asparagine, glutamine, histidine, serine and, with lower efficiency, alanine and glycine. Indirect assays suggest that amino acid uptake is coupled to the uptake of sodium ion(s) and the export of H+. Northern blotting experiments indicate gene expression in brain and stomach, and at lower levels in liver, lung, and intestine (Nakanishi et al. 2001).

**Literature references**


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SLC43A1 (LAT3)-mediated uptake of large neutral amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352103

**Type:** transition

**Compartments:** plasma membrane

SLC43A1 (LAT3), associated with the plasma membrane, mediates the uptake of isoleucine, leucine, methionine, phenylalanine, and valine in a biphasic and sodium ion-independent transport process. Northern blotting experiments indicate gene expression in liver, pancreas, and skeletal muscle, and at lower levels in many tissues including kidney and intestine (Babu et al. 2003).

**Literature references**


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SLC43A2 (LAT4)-mediated uptake of large neutral amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352107

**Type:** transition

**Compartments:** plasma membrane

SLC43A2 (LAT4), associated with the plasma membrane, mediates the uptake of isoleucine, leucine, methionine, phenylalanine, and valine in a biphasic and sodium ion-independent transport process. Northern blotting and in situ hybridization experiments indicate gene expression in kidney and intestine (Bodoy et al. 2005).

**Literature references**


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SLC6A12 (BGT-1)-mediated uptake of GABA and betaine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352029

**Type:** transition

**Compartments:** plasma membrane, cytosol, extracellular region

The plasma membrane transport protein SLC6A12 (BGT-1) mediates the uptake of GABA (gamma-aminobutyrate) and betaine and, less efficiently, of diminobutyrate (DABA) and beta-alanine. Together with each amino acid molecule, 3 sodium ions and 2 chloride ions are taken up. In the body, SLC6A12 is expressed in the proximal tubules of the kidney and cells of the central nervous system (Rasola et al. 1995; Matskevitch et al. 1999).

**Literature references**


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**SLC6A15-mediated amino acid uptake**

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352059

**Type:** transition

**Compartments:** plasma membrane

SLC6A15, associated with the plasma membrane, mediates the uptake of a broad range of amino acids plus a sodium ion, transporting branched-chain amino acids and methionine most efficiently. The human protein is expressed in the brain (Takanaga et al. 2005).

**Literature references**


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SLC6A18 transports Gly from extracellular region to cytosol

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-351963

**Type:** transition

**Compartments:** plasma membrane

The protein SLC6A18 was first identified as an amino acid transporter based on sequence similarity to other members of the SLC6 protein family (Hoglund et al. 2005). It is annotated here as mediating glycine uptake based on the phenotype of mice homozygous for a null mutation in the homologous gene (Quan et al. 2004).

**Literature references**


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**SLC6A20 cotransports L-Pro, Na+ from the extracellular region to cytosol**

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352052

**Type:** transition

**Compartments:** plasma membrane

SLC6A20, associated with the plasma membrane, mediates the uptake of proline plus a sodium ion. The human protein is expressed in the intestine and kidney (Takanaga et al. 2005).

**Literature references**


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**SLC6A6-mediated uptake of taurine and beta-alanine**

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-351987

**Type:** transition

**Compartments:** plasma membrane

The plasma membrane transport protein SLC6A6 mediates the uptake of taurine and beta-alanine. Together with each amino acid molecule, 2 sodium ions and 1 chloride ion are taken up. SLC6A6 is widely expressed in the body (Ramamoorthy et al. 1994).

**Literature references**


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https://reactome.org
SLC7A5:SLC3A2 transports neutral amino acids from extracellular region to cytosol

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-352232

Type: transition

Compartments: plasma membrane

SLC7A5, complexed with SLC3A2 in the plasma membrane, mediates the uptake of neutral amino acids. The process is Na+-independent and not coupled to H+ transport. As measured by Northern blotting SLC7A5 is widely expressed in the body. In situ hybridization studies indicate that the gene product is widely expressed in the body but not in the kidney (Pineda et al. 1999; Prasad et al. 1999).

Literature references


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SLC7A8-mediated uptake of neutral amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352191

**Type:** transition

**Compartments:** plasma membrane

SLC7A8, complexed with SLC3A2 in the plasma membrane, mediates the uptake of neutral amino acids. The process is Na+-independent and not coupled to H+ transport. As measured by Northern blotting, SLC7A8 is widely expressed in the body. In situ hybridization studies indicate that the gene product is abundant in kidney proximal tubules (Pineda et al. 1999; Park et al. 2005)

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SLC1A4-mediated exchange of extracellular alanine for cytosolic serine, threonine, or cysteine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352364

**Type:** transition

**Compartments:** plasma membrane

SLC1A4, associated with the plasma membrane, mediates the exchange of alanine and an extracellular sodium ion for a cytosolic sodium ion and any one of the four amino acids alanine, serine, threonine, or cysteine (Zerangue and Kavanaugh 1996).

**Literature references**


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SLC1A4-mediated exchange of extracellular cysteine for cytosolic alanine, serine, or threonine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352354

**Type:** transition

**Compartments:** plasma membrane

SLC1A4, associated with the plasma membrane, mediates the exchange of cysteine and an extracellular sodium ion for a cytosolic sodium ion and any one of the four amino acids alanine, serine, threonine, or cysteine (Zerangue and Kavanaugh 1996).

**Literature references**


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SLC1A4-mediated exchange of extracellular serine for cytosolic alanine, threonine, or cysteine

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-352347

Type: transition

Compartments: plasma membrane

SLC1A4, associated with the plasma membrane, mediates the exchange of serine and an extracellular sodium ion for a cytosolic sodium ion and any one of the four amino acids alanine, serine, threonine, or cysteine (Zerangue and Kavanaugh 1996).

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SLC1A4-mediated exchange of extracellular threonine for cytosolic alanine, serine, or cysteine

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352371

**Type:** transition

**Compartments:** plasma membrane

SLC1A4, associated with the plasma membrane, mediates the exchange of threonine and an extracellular sodium ion for a cytosolic sodium ion and any one of the four amino acids alanine, serine, threonine, or cysteine (Zerangue and Kavanaugh 1996).

**Literature references**


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SLC1A5-mediated exchange of alanine and glutamine across the plasma membrane

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-352379

Type: transition

Compartments: plasma membrane

SLC1A5, associated with the plasma membrane, mediates the exchange of extracellular alanine for cytosolic glutamine (Broer et al. 2000).

Literature references


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**SLC1A5-mediated exchange of glutamine and alanine across the plasma membrane**

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-352385

**Type:** transition

**Compartments:** plasma membrane

SLC1A5, associated with the plasma membrane, mediates the exchange of extracellular glutamine for cytosolic alanine (Broer et al. 2000).

**Literature references**


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**SLC36A1-mediated uptake of glycine, proline, and alanine**

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375417

**Type:** transition

**Compartments:** plasma membrane

SLC36A1 (PAT1), associated with the plasma membrane, mediates the uptake of glycine, alanine, and proline coupled to the uptake of a proton. Northern blotting experiments indicate gene expression principally in the intestine (Chen et al. 2003).

**Literature references**


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SLC36A2 cotransports Gly, L-Pro with H+ from extracellular region to cytosol

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375405

**Type:** transition

**Compartments:** plasma membrane, cytosol, extracellular region

SLC36A2 (PAT2), associated with the plasma membrane, has been shown in a limited set of tests in vitro to mediate the uptake of glycine and proline coupled to the uptake of a proton (Boll et al. 2003). PAT2 is most abundantly expressed in kidney and muscle.

**Literature references**


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SLC36A4 transports extracellular L-Pro to the cytosol

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-8870354

**Type:** transition

**Compartments:** plasma membrane, extracellular region, cytosol

Plasma membrane-associated SLC36A4 (solute carrier family 36 member 4, also known as PAT4 - proton-coupled amino acid transporter 4) mediates the uptake of extracellular L-Pro (L-proline) (Pillai & Meredith 2011).

**Literature references**


**Editions**

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SLC6A14 cotransports SLC6A14 ligands, Cl-, 2Na+ from extracellular region to cytosol

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375487

**Type:** transition

**Compartments:** plasma membrane

SLC6A14, associated with the plasma membrane, mediates the uptake of multiple basic and nonpolar amino acids as well as beta-alanine. Uptake of one amino acid molecule is accompanied by uptake of two sodium ions and a chloride ion. As assessed by Northern blotting, SLC6A14 is expressed at high levels in lung but only at low levels, if at all, in intestine or kidney (Sloan & Mager 1999, Anderson et al. 2008).

**Literature references**


**Editions**

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SLC6A19 cotransports neutral amino acids, Na+ from extracellular region to cytosol

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375473

**Type:** transition

**Compartments:** plasma membrane

SLC6A19 mediates the uptake of neutral amino acids across the plasma membrane. Uptake of an amino acid molecule is accompanied by uptake of a sodium ion. The protein is abundant in cells in the small intestine and kidney. Its deficiency is associated with Hartnup disorder, the failure to take up neutral amino acids efficiently from the gut lumen and to reabsorb them in the proximal kidney tubule (Kleta et al. 2004, Seow et al. 2004).

**Literature references**


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SLC7A1 (CAT-1)-mediated uptake of cationic amino acids

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-375776

Type: transition

Compartments: plasma membrane

SLC7A1 mediates the uptake of cationic amino acids across the plasma membranes of non-epithelial cells (Broer 2008; Closs et al. 1997; Furesz et al. 2002; Kamath et al. 1999).

Literature references


Editions

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SLC7A2, isoform A (CAT-2A)-mediated uptake of cationic amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375790

**Type:** transition

**Compartments:** plasma membrane

SLC7A2, isoform A, mediates the uptake of cationic amino acids across the plasma membranes of non-epithelial cells (Broer 2008; Closs et al. 1997).

**Literature references**


**Editions**

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SLC7A2, isoform B (CAT-2B)-mediated uptake of cationic amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375768

**Type:** transition

**Compartments:** plasma membrane

SLC7A2, isoform B, mediates the uptake of cationic amino acids across the plasma membranes of non-epithelial cells (Broer 2008; Closs et al. 1997; Furesz et al. 2002).

**Literature references**


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SLC7A3 (CAT-3)-mediated uptake of cationic amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-375770

**Type:** transition

**Compartments:** plasma membrane

SLC7A3 mediates the uptake of cationic amino acids across the plasma membranes of non-epithelial cells (Vekony et al. 2001).

**Literature references**


**Editions**

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SLC7A10-mediated uptake of small neutral amino acids

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-376200

**Type:** transition

**Compartments:** plasma membrane

SLC7A10, complexed with SLC3A2 in the plasma membrane, mediates the uptake of small neutral amino acids. The process is Na⁺-independent. As measured by Northern blotting SLC7A10 is widely expressed in the body (Nakauchi et al. 2000).

**Literature references**


**Editions**

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</table>
SLC7A11-mediated exchange of extracellular cysteine and cytosolic glutamate

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-378513

Type: transition

Compartments: plasma membrane

SLC7A11 as a heterodimer with SLC3A2 in the plasma membrane mediates the exchange of glutamate and cysteine. Under physiological conditions, cytosolic glutamate concentrations are high and cysteine concentrations are low, so glutamate is exported and cysteine imported. SLC7A11 is widely expressed in the body (Bassi et al. 2001; Gasol et al. 2004).

Literature references

Bassi, MT., Gasol, E., Manzoni, M., Pineda, M., Riboni, M., Martin, R. et al. (2001). Identification and characterisation of human xCT that co-expresses, with 4F2 heavy chain, the amino acid transport activity system xc-. Pflugers Arch, 442, 286-96.


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SLC7A6 (y+LAT2)-mediated exchange of extracellular leucine for cytosolic arginine

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-379426

Type: transition

Compartments: plasma membrane

SLC7A6 as a heterodimer with SLC3A2 in the plasma membrane mediates the exchange of arginine for leucine and a sodium ion. The physiological concentrations of arginine and leucine are expected to favor arginine export. By the criterion of Northern blotting, SLC7A6 is expressed in a variety of tissues (Broer et al. 2000).

Literature references


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SLC7A7:SLC3A2 exchanges L-Arg for L-Leu, Na+ across the plasma membrane

**Location:** Amino acid transport across the plasma membrane

**Stable identifier:** R-HSA-379415

**Type:** transition

**Compartments:** plasma membrane

SLC7A7 as a heterodimer with SLC3A2 in the plasma membrane mediates the exchange of arginine (L-Arg) for leucine (L-Leu) and a sodium ion (Na+). The physiological concentrations of arginine and leucine are expected to favor arginine export. By the criterion of Northern blotting, SLC7A6 is predominantly expressed in the kidney (Pfeiffer et al. 2000).

**Literature references**


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SLC7A9:SLC3A1 exchanges L-Arg, CySS-, L-Lys for L-Leu

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-379432

Type: transition

Compartments: plasma membrane

SLC7A9 as a heterodimer with SLC3A1 in the plasma membrane mediates the exchange of arginine (L-Arg), lysine (L-Lys), or cystine (CySS-) for leucine (L-Leu) and other neutral amino acids. The physiological concentrations of these amino acids favor neutral amino acid export and arginine/lysine/cystine import. Defects in SLC7A9 and SLC3A1 cause cystinuria. In the body, this transport process is prominent in the kidney (Mizoguchi et al. 2001).

Literature references


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SLC25A29 transports basic amino acids from cytosol to mitochondrial matrix

Location: Amino acid transport across the plasma membrane

Stable identifier: R-HSA-8959781

Type: omitted

Compartments: cytosol, mitochondrial matrix, mitochondrial inner membrane

Members of the solute carrier family 25 (SLC25) can transport carboxylates, amino acids, nucleotides and cofactors across the inner mitochondrial membrane, thereby connecting cytosolic and matrix functions. The main physiological role of mitochondrial basic amino acids transporter (SLC25A29) is to carry basic amino acids into the mitochondrion. It transports arginine (L-Arg), lysine (L-Lys), homoarginine (h-omoArg), methylarginine (methylArg) and, to a much lesser extent, ornithine (L-Orn) and histidine (L-His) (Porcelli et al. 2014).

Literature references


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  - SLC38A3-mediated uptake of glutamine, histidine, asparagine, and alanine
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SLC7A9:SLC3A1 exchanges L-Arg, CySS-, L-Lys for L-Leu

SLC25A29 transports basic amino acids from cytosol to mitochondrial matrix

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