Differential expression of glucose transporter GLUT8 during mouse spermatogenesis

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Abstract

GLUT8 is a facilitative glucose transporter expressed at high levels in the testis. In this study, we analyzed the GLUT8 expression in mouse testis during spermatogenesis by RT–PCR, Western blot and immunohistochemistry methods. Our results show that GLUT8 expression is limited to spermatids and spermatozoa in the testis. Expression begins when round spermatids are formed at postnatal day 24. The expression persists throughout spermiogenesis, and it is also detected in spermatozoa, but it is absent in more immature germ cells, Sertoli cells and interstitial tissue. GLUT8 immunoreactivity is always restricted to the acrosomic system in a manner that matches the acrosome system formation. The GLUT8 expression is mainly associated with the acrosomic membrane in the acrosome, although significant immunoreactivity is also found inside the acrosomic lumen. The specific GLUT8 location suggests that this transporter plays a pivotal role in the fuel supply of spermatozoa, and in the traffic of sugars during the capacitation and fertilization processes.

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Introduction

Glucose is the fuel and also an important metabolic substrate for most mammalian cells. The family of facilitative glucose transporter (GLUT) proteins is responsible for the entry of glucose into mammalian cells. At present, 13 members of the GLUT family with different substrate specificities, kinetics properties and tissue-expression profiles have been described (Uldry & Thorens 2004). On the basis of their structural and functional characteristics, and of their sequence alignment, GLUT family members have been classified into three subclasses (Joost & Thorens 2001, Wood & Trayhurn 2003). GLUT8 is a recently cloned member of class III facilitative transporters, which are expressed to a certain extent in heart, skeletal muscle, brain, spleen, prostate and intestine, but their expression levels are highest in testis (Carayannopoulos et al. 2000, Doege et al. 2000, Ibberson et al. 2000). GLUT8 is also expressed in the murine blastocyst, where it is important for blastocyst survival, and it seems to be regulated by the insulin/insulin-like growth factor-1 (IGF-1) signaling pathways through the IGF-1 receptor (IGF1-R) (Carayannopoulos et al. 2000, Pinto et al. 2002).

On the basis of its expression levels, GLUT8 appears to be one of the main glucose transporters in testis. GLUT8 has a high glucose transport activity (Doege et al. 2000, Ibberson et al. 2000) that is inhibitable by fructose (Ibberson et al. 2000). In spite of the fact that it is mainly expressed in testis, with a possible function of glucose and fructose transport, the precise localization of this protein in testicular cells remains unclear and controversial. It has been reported that GLUT8 expression is restricted to the type I spermatocytes in the rat (Ibberson et al. 2002), in the innermost cells within the seminiferous tubules and spermatozoa in mice and man (Schürmann et al. 2002), and in rat Leydig cells (Chen et al. 2003). It has also been reported that GLUT8 seems to be hormonally regulated in testis, since it is detected neither in testicular carcinoma nor under estrogen treatment (Doege et al. 2000).

The higher GLUT8 expression levels in the testis than in other tissues, in addition to the particular hexose metabolism of testicular cells, which bear a different glycolytic status according to their developmental stage, suggest an interesting yet unelucidated role for this transporter in this tissue. To clarify the concrete expression sites of GLUT8 in the testis, we have analyzed GLUT8 distribution in mouse testis of different ages by means of reverse
transcription (RT–PCR), Western blot and immunohistochemistry. Our results show that GLUT8 expression starts as soon as early spermatids are differentiated, and that the expression is present in all spermatids and spermatozoa, where is it found to be restricted to the acrosomal region. The concrete and specific localization of GLUT8 strongly suggests a physiologic role of this transporter not only in internal glucose movement, but also in the traffic of sugars during the capacitation and fertilization processes.

Materials and Methods

Animals

Handling, the equipment used and the killing of animals were all in accordance with European Council regulation 86/609/EEC on experimental animal protection. Male CD1 mice of 8–10 weeks of age and reproductive female mice were obtained from Harlan Iberica S.L. (Barcelona, Spain). Breeding pairs of CD1 mice were monitored daily for litters, and the day of birth was taken as day 0. All animals were maintained on a 12 h day–night cycle, at constant room temperature (22 °C), with free access to water and standard mouse fodder. All experimental protocols were approved by the ethics committee of the Cardenal Herrera-CEU University.

Materials

All generic reagents were obtained from either Sigma or Roche.

Hybond membranes and enhanced chemiluminescence (ECL) detection system and antirabbit IgG secondary antibody were obtained from Amersham. Bradford and Wes-tern blotting reagents were from Bio-Rad.

Rabbit polyclonal antibody against actin was obtained from Sigma. Synthetic peptide (LEQVTAHFEGR) corresponding to the 11 C-terminal residues (467–477) of mouse GLUT8 with a terminal cysteine was prepared by Biorad. Synthetic peptide (467–477) of mouse GLUT8 was cross-linked to KLH by m-maleimidosobenzoic acid N-hydroxysuccinimide ester (MBS), and polyclonal antibodies against the peptide were produced in rabbit.

Tissue preparation

Groups (four animals per group) of male adult mice (8–10 weeks old), and male mice pups of 14 and 24 days of age were killed by cervical dislocation. After dissection, the left testis of each animal was fixed for immunohistochemical analysis. The other testes were frozen at −80 °C until subsequently used for protein and RNA extraction.

Reverse transcription–polymerase chain reaction (RT–PCR)

Total RNA was extracted from isolated testes with RNeasy Mini Kit and QIAshredder columns (Qiagen), as previously described (Mesonero et al. 2000). Reverse transcription was performed with 2 μg total RNA. cDNA was synthesized with Oligo dT and Superscript II Reverse Transcriptase (Invitrogen). PCR was performed with oligonucleotide primers specific for mouse GLUT8 (GenBank accession number NM0194881) and GAPDH (GenBank accession number BC083149), using a thermocycler GeneAmp PCR2700 (Applied Biosystems, FosterCity, CA, USA). Primer sequences (5′–3′) were as follows: GLUT8 forward ATCTCCGAAATCGCCTACC, GLUT8 reverse ATTAGGCCACATGACC, GAPDH forward CATCACATCTCCAGGAG, and GAPDH reverse CACGGAAGGCACATGCCAG. The amplification of GLUT8 (507 bp) and GAPDH (485 bp) were performed at 94 °C for 30 s, 58 °C for 30 s and 72 °C for 60 s, for 35 cycles. The PCR products were resolved on 1% agarose gels and visualized by ethidium bromide staining. Control reactions were performed with the primers in the absence of cDNA. PCR reactions were performed three times in two independent experiments.

Histologic and immunohistochemical methods

Testes were placed in Bouin’s fixative for periods from 6 h to overnight, depending on the size of the testis. After fixation, the tissues were dehydrated in increasing concentrations of ethanol, embedded in paraffin, serially sectioned (3 μm) with a HM 310 Microm microtome, and collected on polylysine-coated slides. Sections were deparaffined, rehydrated, incubated with 3% H2O2 in methanol for 20 min to quench endogenous peroxidase activity, and processed for immunohistochemical analysis with an anti-GLUT8 antibody. Immunohistochemistry for GLUT8 was performed by the immunoperoxidase procedure of the Vectastain Elite ABC kit (Vector Laboratories, Burlingame, CA, USA), according to the manufacturer’s instructions, with rabbit anti-GLUT8 polyclonal antiserum (dilution 1:50) and diaminobenzidine tetrahydrochloride (DAB) substrate (Vector Laboratories). Nonspecific antibody binding was blocked with 10% normal goat serum. Negative control sections were prepared by replacing the primary antibody with nonimmune serum from rabbit. Immunohistochemical analyses were performed at least twice in three independent experiments. Some sections were stained with hema-toxylin and eosin to identify cell morphology, or they were stained with PAS (periodic acid-Schiff staining) to identify the acrosome (Leblond & Clermont 1952, Russell et al. 1990). To study GLUT8 expression in spermatozoa, fresh mouse epididymides were incised with a scalpel, and samples of the content were obtained with sterile swabs and extended on slides. Then, GLUT8 immunoreactivity was investigated as on the testis sections.

Immunoblotting

Western blotting was performed with 40 μg total protein. Protein concentration was determined by the method of Bradford and Western blotting reagents were from Bio-Rad.
Bradford (1976). Protein samples were analyzed by SDS–PAGE in 10% acrylamide gels, as described by Laemmli (1970), and the proteins were then transferred to Hybond-ECL membranes that were blocked for 2 h in 5% nonfat dried milk in Tris–buffered saline (TBS) (20 mM Tris–HCl (pH 7.5) and 500 mM NaCl). The blots were probed with rabbit polyclonal anti-GLUT8 antibody, used at a 1:800 dilution. The primary antibody was detected with antirabbit IgG antibody coupled to horseradish peroxidase (dilution 1:2000), using the ECL detection system. The blots were reprobed after stripping in 62.5 mM Tris–HCl (pH 6.7), 2% SDS and 100 mM β-mercaptoethanol for 60 min at 60°C. Nitrocellulose sheets were rinsed in TBS and then reblotted for 60 min in 5% nonfat dried milk in TBS before being probed with antiactin antibody (A5060; Sigma) at 1:300 dilution. The specificity of the primary antibody was demonstrated by its preadsorption with the corresponding control peptide. The amplitude of the signal was verified as being proportional to the amount of proteins loaded on the gels, at least within the investigated range (10–50 mg). Thus, the bindings of primary and secondary antibodies, as well as the ECL reaction, were not limiting.

Results

GLUT8 expression by Western blot analysis

We first analyzed the presence of GLUT8 in testis by Western immunoblots analysis using a polyclonal rabbit antiserum against a short C-terminus peptide of mouse GLUT8. As Fig. 1A illustrates, the antiserum detected a 42–45 kDa protein in adult testis. A second specific band was also detected at approximately 75 kDa. Other groups have also detected this second band in several expression systems, such as reticulocyte lysates and HEK293T cells (Ibberson et al. 2000) and COS-7-transfected cells (Doege et al. 2000, Schürmann et al. 2002), and in mouse liver and kidney tissues (Gorovits et al. 2003, Schiffer et al. 2005). Since glucose transporters tend to aggregate even under denaturing conditions, this band might represent a homodimer of GLUT8, because its intensity relative to the lower band depends in part on the cell lysis conditions, in particular on the addition of reducing agents (Ibberson et al. 2000). When the antiserum was blocked with the antigenic peptide, both specific signals (42 and 75 kDa) disappeared, indicating that this anti-GLUT8 antibody specifically detects the facilitative glucose transporter GLUT8.

After verifying the specificity of our antibody anti-GLUT8, we compared the expression of GLUT8 in adult, 24-day-old and 14-day-old mice. Since the higher band was always proportional to the intensity of lower band, we analyzed the protein expression of GLUT8 corresponding to the monomeric form of 42 kDa. No GLUT8 expression was detected in 14-day-old mice, whereas in 24-day-old and adult mice a band of the expected size was evident (Fig. 1B). The intensity of the band was higher in adult than in 24-day-old animals, suggesting that GLUT8 begins to be expressed at approximately this early stage.

GLUT8 immunohistochemical detection during mouse testis maturation

In order to confirm the absence of GLUT8 expression in prepuberal mouse testis, and to determine the stage of germ-cell differentiation at which GLUT8 first appears, we studied its expression in tissue sections obtained from mice of different ages on the basis of the type of germ cells found at each time. Tissues from 14-day-, 24-day-, and 8-10-week-old mouse testis were analyzed with the C-terminus anti-GLUT8 antibody by the experimental procedure described in Materials and Methods. Results are summarized in Table 1.

Immunochemical analysis of testicular sections in 14-day-old mice, in which the unique germ cells are spermatogonia and primary spermatocytes, showed no apparent
Table 1 Distribution of immunohistochemical staining of GLUT8 in mouse testis as a function of testicular development. Empty cells indicate that the cell type was not yet present in the sections of the corresponding age – no staining, ++ moderate staining, +++ intense staining. In 24-day-old sections, not all tubules were stained, probably as related to the degree of development of each tubule.

<table>
<thead>
<tr>
<th>Testicular cell types</th>
<th>14 days</th>
<th>24 days</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spermatogonia</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Spermatocytes I</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Spermatocytes II</td>
<td>–</td>
<td>++</td>
<td>+++</td>
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<tr>
<td>Round spermatids</td>
<td>–</td>
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<td>+++</td>
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<tr>
<td>Elongated spermatids</td>
<td>–</td>
<td>+++</td>
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<tr>
<td>Spermatozoa</td>
<td>–</td>
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GLUT8 immunoreactivity (GLUT8-IR) in any cell (Fig. 2B), thus confirming the absence of the GLUT8 protein expression at this age, as previously observed by Western blotting.

However, GLUT8-IR was evident in the testis of 24-day- and 8-10-week-old mice (Fig. 2E and H). Staining was confined to the seminiferous tubules and was absent from the interstitium. No signal was obtained when nonimmune serum was used instead of the primary antibody, (Fig. 2F and I) thereby confirming the specificity of the antibody reaction. Data also showed that GLUT8 was not expressed in all the testicular cells.

In 24-day-old mice, where spermatogonia, type I and type II spermatocytes, and round spermatids were present, evident GLUT8-IR was observed in the innermost part of some seminiferous tubules (Fig. 2E). Analysis at higher magnification showed that immunoreactivity was localized in round spermatids, while the other cells did not appear to express GLUT8 (Fig. 3A). GLUT8 immunostaining was restricted to a small area between the nucleus and cell membrane, presumably the acrosomic system.

In the testis of 8-10-week-old mice, which have already completed the first spermatogenic waves, and where all germ cells types (from spermatogonia to spermatozoa) may be identified, a heterogeneous staining in all seminiferous tubules was observed (Fig. 2H). Higher magnification of the sections showed that round and elongated spermatids were strongly immunoreactive with the anti-GLUT8 antibody (Fig. 3). GLUT8 expression was always restricted to the forming acrosomic system in round and elongated spermatids, depicting the changing shape of this structure. The immunoreactive structure showed two different aspects in round spermatids: in recently formed round spermatids, GLUT8-IR was limited to a granule situated close to the nucleus that matches the so-called Golgi phase of the acrosome formation (Fig. 3B). As development of round spermatids progressed, the GLUT8-expressing structure adopted a flattened cap shape covering approximately half of the nucleus (Fig. 3C). Strongly expressed GLUT8-IR was also observed in the head of elongated spermatids. The immunoreactivity in these cells was observed in a long area corresponding to the acrosome (Fig. 3D). In both round and elongated spermatids, the strongest immunoreactivity was localized apposed to the acrosomic membrane, but substantial immunoreactivity was also evident inside the acrosomic vesicle (Fig. 3D and E). GLUT8-IR localization in the acrosomic system was confirmed by PAS staining (Fig. 2J). No signal was observed with the anti-GLUT8 antibody in less mature germinal cells, either Sertoli cells or Leydig cells.

Finally, GLUT8-IR was analyzed in spermatozoa obtained from mouse epididymis. Once again, immunoreactivity was present in the acrosome of these cells (Fig. 3F).

mRNA expression of GLUT8 in mouse testis

The expression of GLUT8 mRNA in the testis was confirmed by RT–PCR, using specific primers that amplify and detect a sequence with an expected size of 507 bp. A single transcript for GLUT8 was identified in 24-day- and 8-week-old mice, while no amplification product was observed in 14-day-old mice (Fig. 4). These results corroborate those obtained by immunohistochemistry, and they show that GLUT8 mRNA is not expressed in early phases of mouse testis development.

This observation is consistent with the above immunohistochemical data, indicating that GLUT8 expression occurs only at late spermatogenesis stages, as illustrated in Table 1, which summarizes the stage-specific expression of GLUT8 in the germ cells.

Discussion

Spermatogenesis in mammals is characterized by a well-defined sequence of mitotic and meiotic divisions leading to the production of mature spermatozoa (McCarrey 1993). In newborn mice, male germ-cell precursors undergo self-renewal in the testis at days 1-7 postpartum. The early cell divisions lead to the development of types A and B spermatogonia, the latter of which undergo premeiotic replication, and enter meiosis as primary spermatocytes. Secondary spermatocytes proceed through a second meiotic division in which haploid germ cells are generated. These differentiate to form round spermatids, then elongated spermatids, and finally mature spermatozoa (spermigenesis). The first round of spermatogenesis is followed by additional waves, enabling continuous sperm production throughout the life of the animals (McCarrey 1993, Zindy et al. 2001). In this study, we show that GLUT8 expression in mouse testis first appears when round spermatids are formed (after day 20 postpartum) (McCarrey 1993), persists during spermiogenesis, and is present in spermatozoa isolated from the epididymis. However, it is not observed in spermatogonia or spermatocytes (Table 1).

GLUT8 expression is always restricted to the acrosomic region throughout spermiogenesis by adopting the changing shape of the forming acrosomic system, and it is...
apparently absent from other locations. Previous reports have shown the testis to be the organ that expresses the highest GLUT8 levels (Doege et al. 2000, Ibberson et al. 2000, Schürmann et al. 2002, Chen et al. 2003). However, certain differences with respect to the concrete cells that express the transporter have been described. Our results confirm those reported by Schürmann et al. (2002). In addition, we have identified the round and elongated spermatids inside the testicular tubules as the GLUT8-expressing cells. This is consistent with the fact that GLUT8 mRNA and GLUT8-IR are detected in 24-day-old mice, where round spermatids are present, and later, whereas in 14-day-old mice, a stage previous to spermatid differentiation, GLUT8 cannot be detected. Differences observed in other studies could be due to the different species studied (mouse versus rat), or to the techniques applied. Although no GLUT8 protein is detected before the spermatid stage, it cannot be ruled out that GLUT8 mRNA synthesis in the mouse could start at the previous stage to spermatocyte as in the rat (Ibberson et al. 2002). However, our results on GLUT8 mRNA analyses at different developmental stages show that no expression of GLUT8 mRNA is found at day 14 after birth, when leptotene, zygotene and pachytene phases are developed. Ibberson et al. (2002) indicated that GLUT8 is expressed specifically in the primary spermatocytes at these particular phases. Therefore, it is possible that GLUT8 has a species-differential cellular expression, and a similar pattern is presented in human and mouse (Schürmann et al. 2002).

It may be concluded from both this report and previous reports that GLUT8 is one of the main glucose transporters in the testis. Previous studies have shown the expression of GLUT1, GLUT2, GLUT3 and GLUT5 in testicular cells (Angulo et al. 1998, Burant & Davidson 1994). These transporters are also expressed in spermatozoa (Angulo et al. 1998).
et al. 1998). It is interesting to note that both glucose transporter expression and glucose metabolic pathways seem to be compartmentalized in the sperm cell. In spermatozoa, the different glucose transporters show precise localization, although there is a degree of variability in different species (Angulo et al. 1998). In addition to GLUT8, it has been shown that GLUT1 is expressed in human, rat and bull sperm heads, while only GLUT2 and GLUT5 are expressed in rat and bull, and only GLUT3 is expressed in bull (Angulo et al. 1998). Thus, GLUT1–3 and GLUT5 are expressed in bull sperm head, whereas only GLUT2 and GLUT5 are expressed in rat and only GLUT1 is expressed in human sperm head. On the other hand, hexose metabolism is also compartmentalized: in the sperm head, the glucose metabolic pathway is pentose phosphate, while ATP is generated through glycolysis in the principal piece, and, through oxidative phosphorylation, in the midpiece (Urner & Sakkas 2003). It is possible that this compartmentalization is related to GLUT expression, and that concrete GLUT transporters supply glucose for each metabolic pathway.

The high expression levels suggest that GLUT8 plays an important role in glucose metabolism in male germ cells. It is unlikely that this role would be in the transport of glucose into spermatids, since these cells do not use glucose directly as a fuel supply, but the lactate produced by Sertoli cells (Bajpai et al. 1998) and GLUT8 is located in the intracellular compartment. In spermatids, however, GLUT8 could act as a transporter between the citosol and the acrosomic compartment to provide the subsequent glucose molecules for both the glycosylation and deglycosylation processes (Clermont & Tang 1985, Bajpai et al. 1998). A similar function in the transport of glucose molecules between different intracellular compartments has been suggested for the hippocampus (Piroli et al. 2002). However, it is probable that GLUT8 function is even more complex in spermatozoa than in spermatids. Spermatozoa are transcriptionally inactive cells that have, then, to synthesize all the machinery that they will need.
Glucose seems to be the major energy source needed to maintain in vitro capacitation in mice and human spermatozoa, since this sugar induces much higher penetration rates and capacitation in mice and human spermatozoa, since this transporter might also play a role in the fuel supply of spermatozoa, and in the traffic of sugars during the capacitation and fertilization processes.

Figure 4 Mouse testis GLUT8 mRNA expression during development. First-strand cDNA synthesis and subsequent PCR of testis mRNA from 14-day-old, 24-day-old and adult mice. GLUT8 amplification was performed as described in Materials and Methods, and GAPDH was amplified as a control. No GLUT8 expression was detected from 14-day-old mouse testis. A representative gel is shown.

at the previous spermatid stage. It is remarkable that other sperm glucose transporters, begin to be expressed at the spermatid stage (Angulo et al. 1998). In contrast to spermatids, glucose is necessary for the sperm function, and it has to be metabolized by spermatozoa for zona pellucida penetration and sperm–oocyte fusion, and to ensure that tyrosine phosphorylation occurs during capacitation (Urner & Sakkas 2003). Capacitation of mammalian spermatozoa is a functional process that requires the consumption of significant amounts of energy. Glucose seems to be the major energy source needed to maintain in vitro capacitation in mice and human spermatozoa, since this sugar induces much higher penetration rates and capacitation-like changes than do other monosaccharides, such as fructose or mannose (Travis et al. 2004).

GLUT8 must be translocated from the acrosome to the cell membrane for glucose transport into the sperm cells. GLUT8 translocation from subcellular compartments to the cell membrane has been reported in insulin-treated blastocysts through insulin-like growth factor receptor-1 (IGFR-1) activation (Carayannopoulos et al. 2000, Pinto et al. 2002). A similar change in GLUT8 localization could occur in sperm cells during the capacitation or sperm–oocyte interaction, and GLUT8 could be located in the cell membrane under accurate stimuli to allow glucose entry into the cell. IGF-1 is a candidate as such a stimulus since it is found in the seminal plasma, and its receptor IGFR-1 is present in the sperm acrosome (Naz & Padman 1999). It has also been shown that both the sperm plasma membrane and the acrosome represent cytologic targets for insulin (Silvestroni et al. 1992). Recent studies (Aquila et al. 2005) have shown that insulin is expressed in, and secreted from, human ejaculated spermatozoa, with higher secretion in the capacitated sperm, suggesting that insulin plays a role in capacitation. Since GLUT4, the most important and studied insulin-regulated transporter, has not been detected in the testis or spermatozoa (Burant & Davidson 1994, Angulo et al. 1998, Schürmann et al. 2002), GLUT8 is the best candidate for regulation by members of the insulin-IGF system in testis. However, more studies are necessary to determine the precise role of GLUT8 in testicular cells. The developmentally regulated expression accompanying its cellular location and its function in other tissues suggest that this transporter might also play a role in the fuel supply of spermatozoa, and in the traffic of sugars during the capacitation and fertilization processes.

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References


Carayannopoulos MO, Chi MM, Cui Y, Pingsterhaus J, McKnight RA, Mueckler M, Devaskar SU & Moley KH 2000 GLUT8 is a glucose transporter responsible for insulin-stimulated glucose uptake in the blastocyst. PNAS 97 7313–7318.


Joost HG & Thorens B 2001 The extended GLUT-family of sugar/polyol transport facilitators: nomenclature, sequence characteristics and potential function of its novel members. Molecular Membrane Biology 18 247–256.


Pirollo GG, Grillo CA, Hoskin EK, Znamensky V, Katz EB, Milner TA, McEwen BS, Charron MJ & Reagan LP 2002 Peripheral glucose administration stimulates the translocation of GLUT8 glucose transporter to the endoplasmic reticulum in the rat hippocampus. Journal of Comparative Neurology 452 103–114.


Uldry M & Thorens B 2004 The SLC2 family of facilitated hexose sugar/polyol transport facilitators: nomenclature, sequence characteristics and potential function of its novel members. Molecular Membrane Biology 18 247–256.


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