

# Functional and histological characterization of glutamine like transporter in the central nervous system of mice

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SLCs are on the largest classes of integral membrane proteins mediating physiological functions, and by far the largest class of transporters in animals, with about 384 members in human. However, the heterogeneity among their functions and difficulty to clone and express these very large proteins has hampered their characterization. There are currently over 120 orphan SLCs and 51 of these are most closely related to amino acid transporters. About 25% of SLC genes transport amino acids as their primary substrate. Until now there are eleven known families that code for amino acid transporters, seven of them are expressed in the plasma membrane and account for transport from the extracellular medium into the cytosol, while four of them are intracellular and found in either lysosomes, mitochondria or synaptic vesicles. Amino acid transporters are important in neurons as neurotransmitter transporters, as nutrient sensors (to monitor extracellular amino acid concentrations) and as transporters for precursors for neurotransmitter (hence regulating the neurotransmitter contents in the cells). Many amino acid transporters have a promiscuous substrate profile while others are very specific. Also, the specific repertoire of transporters expressed by certain cell types varies. It is important to, in a systematic way, sort out the cell type specificity as well as tissue localization to identify the functional role of these transporters.

In this project, we provide new insights regarding the biological significance of glutamine like an orphan transporter TMEM104 by investigating its expression pattern, tissue distribution and cellular specificity at the mRNA and protein levels by performing *in situ* hybridization and immunohistochemistry on mouse brain and peripheral tissues. Glutamine is a non-essential amino acid and primary precursor for the glutamate neurotransmitter in brain. Glutamate is synthesized from glutamine in presynaptic glutamatergic neurons and released into synaptic cleft during action potentials. Neuronal glutamine transporters play an important role in regulating the glutamate/glutamine cycle in brain to avoid excitotoxicity. We show that TMEM104 is expressed in all neurons including excitatory and inhibitory neurons but not in astrocytes and axons. Our results suggest that TMEM104 might play a role in glutamine transport.

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