

## **Past-A is a Novel Sugar Transporter that is Expressed in Response to Change of Extracellular pH Environment**

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The ventral medullary surface (VMS) of medulla oblongata is known as the site of the central chemosensitive neurons in mammals. These neurons sense excess  $H^+/CO_2$  dissolved in the cerebrospinal fluid and induce hyperventilation. To elucidate the mechanism of neuronal cell adaptation to changes of  $H^+/CO_2$ , we screened for hypercapnia-induced genes in the VMS. Here we report cloning and characterization of a novel gene called proton-associated sugar transporter-A (Past-A), which is induced in the brain after hypercapnia and mediates glucose uptake along the pH gradient. Past-A comprises 751 amino acid residues containing 12 membrane-spanning helices, several conserved sugar transport motifs, three proline-rich regions, and leucine repeats. Past-A transcript was predominantly expressed in the brain. Moreover, the Past-A-immunoreactive neural cells were found in the VMS of the medulla oblongata, and the number of immunoreactive cells was increased by hypercapnic stimulation. Transient transfection of Past-A cDNA in COS-7 cells leads to the expression of a membrane-associated 82 kDa protein, which possesses a glucose transport activity. The acidification of extracellular medium facilitated glucose uptake, while the addition of carbonyl cyanide *m*-chlorophenylhydrazone, a protonophore, inhibited glucose import. Taken together, our results indicate that Past-A is a brain-specific glucose transporter to represent an adaptation mechanism regulating sugar homeostasis in neuronal cells following hypercapnia. Furthermore, analysis of Past-A should provide new insights into the molecular mechanisms of endocrine disrupters.