Abstract

The GLUT9 transporter, coded by the *SLC2A9* gene, is one of the key proteins enabling the trasnfer of uric acid across the membrane in epithelial cells of the proximal tubule. In humans, this protein is naturally expressed in two variants: long (GLUT9L) and short (GLUT9S), which differ from one another by their N-terminus sequence. Each of these isoforms is localized on a different pole of the epithelial cell. The signal sequence/motif responsible for this difference is presumed to be located in the aforementioned N-terminus domain. Numerous allelic variants influencing the transport properties of the protein have also been described. The first aim of this thesis is to verify the influence of a newly discovered variant, characterized by substituting of valine for leucine in the 114th position (V114L, in the short form its corresponding variant V85L) on the ability to transport uric acid. Second aim is to verify the influence of mutations in selected motifs, which could be responsible for the localization of the protein, thus also changing its transport properties. Two dileucine motifs 12LGL14 and 33LL34 and one tyrosine motif 84YIKA87 were tested. Functional studies using ^{14}C radiolabeled urate demonstrated significant decrease of transport ability for the V114L/V85L allelic variant in both isoforms of the protein in the efflux direction. The selected localization motifs LL, LGL and YIKA have also been examined. When compared to wild-type variants, all three have shown weaker membrane signals and greater clustering in the cell cytoplasm. They also influenced the urate transport ability. Lastly, influence of the presence of glucose in the incubation buffer has been tested. The preliminary results indicate possible importance of extracellular glucose for the urate efflux transport.

Key words

Uric acid, urate transporters, GLUT9, *in vitro* transport assay, HEK293A