Title of presentation

SLC2A1 gene induction to treat Glut1 deficiency.

Abstract

Glut1 deficiency syndrome (Glut1 DS) results from low Glucose Transporter-1 protein owing to haploinsufficiency of the *SLC2A1* (Glut1 gene). The nature of the disease is such that most patients retain one intact copy of the gene. Induction of this copy to compensate for mutations in the other allele is therefore an intuitively appealing means of raising Glut1 levels for therapeutic purposes. Such induction may be accomplished using small molecules. Alternatively, Glut1 levels may also be raised by modulating the levels of regulatory elements. We and others have identified a novel regulatory non-coding RNA that concordantly regulates Glut1. Expressing the RNA in transgenic mice raises Glut1 expression and mitigates disease in a model of Glut1 deficiency. Yet, the increase in Glut1 does not trigger supraphysiological levels of the protein, which can result in adverse effects and constitute a risk factor for cancers. To extend the transgenic studies and develop a practical way of delivering the non-coding RNA to the Glut1 DS model, AAV vectors are being tested as delivery vehicles. Initial data suggests that the administering the RNA in such vectors prevents onset of disease in a mouse model of Glut1 DS. These results and investigations of an optimal AAV serotype for delivery will be discussed in the presentation.