SLC13A5 Epileptic Encephalopathy

Synonyms:

SLC13A5 Deficiency
Citrate Transporter Disorder
Early Infantile Epileptic Encephalopathy 25
Kohlschütter-Tönz syndrome (non-ROGDI)
GARD: 12901
OMIM: 608305

Inheritance: Autosomal Recessive
Age of Onset: Neonatal
Gene Location: 17p13.1
mRNA size: 3.4 kilobases
Prevalence: Rare

Epidemiology
SLC13A5 Epileptic Encephalopathy is a rare disease. First described in 2014, incidence and prevalence is still unknown. The full extent of contributing alleles remains unknown. 1% of the Icelandic population are heterozygous carriers of the SLC13A5 G219R disease allele.

Disease Background and Progression
SLC13A5 Deficiency is an autosomal recessive disorder. It affects both boys and girls of all races and ethnicities. It is a newly diagnosed form of infantile epilepsy and developmental delays with seizures beginning within the first days of life. This rare form of epileptic encephalopathy is due to mutations in SLC13A5 gene.

Affected children present with seizures beginning within a few days of birth which persist throughout life. They show difficulty with speech production, limited and slow motor progress with problems standing or walking independently. Problems with tone are also reported with episodes of body stiffening and weakening. Almost all the affected children have abnormalities in their tooth enamel. Brain MRIs appear normal or have subtle changes in the white matter (Weeke et al, 2017). This disorder is caused by mutations in both copies of the gene SLC13A5 which codes for a sodium dependent citrate transporter. To date all tested mutations result in no or a very reduced amount of the citrate transporter in the cells (Thevenon et al, 2014; Hardies et al, 2015; Klotz et al, 2016; Weeke et al, 2016).

Children can succumb to complications of the seizures. The oldest known child with this disease is now 28 years old, fairly stable, but dependent on caregivers.

Citrate
Citrate is a key metabolite and is known to play an important role in the energy generation pathways in the cells. It may also be involved in regulating the concentration of other ions inside and outside of the cells due to its chelating properties (Bhutia et al., 2017). Children have elevated citrate levels in their blood, urine, and CSF.

Management and Treatment
There is no cure for SLC13A5 Deficiency and patients require constant supervision and care. Antiepileptic drugs such as phenobarbital, valproate, and acetazolamide have shown varying success in controlling seizures.