Mechanisms of neuropsychiatric genetic diseases of the SNARE complex: towards therapeutic intervention (SNAREopathy)

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Epilepsy is a severe and disabling disease affecting about 1% of the world's population. Despite years of intense research about 30% of all epilepsies cannot be treated by available drugs. This poses a substantial economic burden for the EU health systems and individuals and their families. To develop new and better treatment options, a detailed knowledge of the mechanisms leading to epilepsy is urgently required. In this proposal, we will focus on a group of difficult-to-treat, severe epilepsies that is caused by gene mutations which mediate the communication between nerve cells (the so-called synaptic transmission). This communication is essential for a regular function of the brain, and mutations disturb the fine balance between nerve excitation and inhibition which can lead to epileptic seizures. Our consortium unites experts in the genetics of epilepsy and neurobiologists working on synaptic transmission to identify the exact mechanisms leading to epilepsy using several sophisticated mouse and zebrafish models, as well as human cell models which are derived from skin biopsies that will be transformed into human neurons in culture. Based on the identified epileptic mechanisms, we will select some of the models for drug screening in neuronal cells and zebrafish to search for novel medications to better and more specifically treat the severely affected epilepsy patients.