

EPILEPSY AND THE SV2A PROTEIN: new insights about the disease

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Around two million of people worldwide are affected by neurodegenerative diseases, such as Alzheimer, Parkinson or Epilepsy. Despite the social and the economic impact of these diseases, their causes still remain unclear. In the case of the epilepsy, for example, around 25% of the patients suffer drug-resistant epilepsy, for which there is no medicament able to mitigate the epileptic crises or the associated symptomatology, such as cognitive problems and mood disorders. In 1974, UCB Pharma synthesized a new antiepileptic drug with a high therapeutic index: the Levetiracetam. The target of this medicament is the Synaptic Vesicle Protein 2A (SV2A) whose specific role in the pathology is still unknown. The main goal of my thesis is to better understand the relationship between this protein and the epilepsy. On the one hand, the production and phenotyping of conditional knockout mice for the SV2A protein allowed us to discover a possible implication of this protein in the spatial memory and anxiety process, an important part of the epileptic symptomatology. On the other hand, the synthesis of the radiotracer [¹⁸F]UCB-H, with a high affinity for the SV2A protein, enabled the in vivo evaluation (with the mPET technique) of a rat model of the temporal lobe epilepsy through the disease process. Results showed a strong correlation between the severity of the epilepsy (EEG technique) and the SV2A levels in different brain regions, highlighting the importance of this protein in the development of the disease. In summary, although further studies in humans are necessary, this protein emerges as an important key in clinical diagnosis and medical research, being implicated in all the aspects of the epileptic disease.