Searching for blood biomarkers to improve the diagnosis and the management of patients with epilepsy

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Introduction and Hypothesis: The diagnosis of epilepsy it is still challenging. It is estimated that misdiagnosis of epilepsy occurs in about 25% of cases [1]; therefore, the development of innovative biomarkers to assist in the diagnosis of epilepsy is a priority. In addition, one third of patients with epilepsy do not have seizure remission despite appropriate therapy with anti-epileptic-drugs (AED). Major causes of drug resistant epilepsy (DRE) are mesial temporal lobe epilepsy (MTLE) and focal cortical dysplasia (FCD). Therefore, the identification of biomarkers for AED response could potentially speed-up the diagnosis of medically refractory seizures, which in turn would lead to an earlier indication of an effective alternative treatment [2,3]. One potential candidate for biomarkers are circulating microRNAs; these are small noncoding RNAs present in extracellular human body fluids including plasma or serum. It is well known that induced changes of microRNAs levels are stable in plasma and can be strongly associated with specific disease states and it is noninvasively and easily quantifiable technique [4].

Objective: The aims of this study are: i) to determine whether robust and non-invasive molecular signatures of circulating microRNAs could help to improve diagnosis and or management of patients with epilepsy, including MTLE, FCD and genetic generalized epilepsies (GGE) and ii) to identify and validate whether these molecular signatures could be also associated with response to AEDs.

Methods: Next-generation sequencing technology (RNA-seq) will be used to measure plasma levels of microRNAs in two phases of the study: an initial discovery phase with 10 patients with MTLE who are responsive to AED treatment, 10 patients with MTLE who are AED pharmacoresistant, 10 patients with FCD type II, 10 patients with GGE and 10 control individuals. In the subsequent validation phase, we will enroll an additional independent cohort of at least 100 patients with MTLE using the same diagnostic criteria as previously described and assay the most significant microRNAs found in phase 1 using RT-qPCR. We will also recruit an additional 200 healthy individuals without epilepsy as a control group.

Results/Discussion and Conclusion: To date, we have successfully completed the recruitment of patients and have performed experiments in order to improve mRNA isolation and RNA-seq experiments in order to improve the protocols.

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