**Transcriptome profile of dorsal and ventral dentate gyrus of the pilocarpine model of temporal lobe epilepsy**

Matos AHB1, Vieira AS1, Canto AM1, Rocha SC1, Carvalho B1, Pascoal VDB1,2, Glioli R3, Lopes-Cendes I1

1Department of Medical Genetics, School of Medical Sciences, University of Campinas - UNICAMP, SP, BRAZIL and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN).

2Department of Basics Sciences, Fluminense Federal University - UFF, Nova Friburgo, RJ, BRAZIL.

3Laboratory of Animal Quality Control (CEMIB), University of Campinas – UNICAMP, Campinas, SP, BRAZIL.

**Introduction:** Mesial temporal lobe epilepsy (TLE) is the most frequent type, representing 40% of the patients and these are often refractory to medical treatment. One of the most used tools to study the mechanisms involved in TLE are animal models. Despite several animal models currently available and widely studied, the majority of these present lesions which are not commonly identified in patients such as: ischemia, trauma and status epilepticus (SE). The gene expression profile of specific tissue region provides relevant biological information on the molecular mechanisms potentially involved in complex biological phenomena. RNAseq-based transcriptome analyzes offers the possibility of accurate profiling global gene expression. The aim of this study was to analyze and correlate gene expression profile using next generation sequencing technology in different sub-regions of the dentate gyrus.

**Materials and Methods:** Male Wistar rats were injected with methyl-scopolamine (1 mg/kg) thirty minutes before of the systemic injection of pilocarpine hydrochloride (320 mg/kg) to reduce peripheral cholinergic side effects. Four hours after the administration of pilocarpine diazepam was administrated (4 mg/kg) in order to stop seizures. Control rats were injected with saline after the methyl-scopolamine injection. Fifteen days following induction rats were euthanized (n=4) and the brains were processed for laser microdissection using Zeiss PALM LCM. Dorsal and ventral dentate gyrus (DG) were collected from each rat, total RNA was extracted, and libraries were prepared from total RNA and RNA sequencing was performed in an Illumina Hiseq platform. Sequences were aligned and quantified with the TopHat/DESeq2 pipeline for total RNA. Gene Onthologies, molecular networks and gene interactions were analyzed with the MetaCore® software.

**Results and Discussion:** We found a total of 969 and 308 genes differentially expressed (p<0.05) when comparing control and pilocarpine rats dDG and vDG respectively. Gene ontology analysis indicates a predominance of inflammation related molecules in up-regulated genes and synaptic transmission in genes down-regulated in both dDG and vDG. Exclusively in the dDG there was a significant down-regulation of calcium transport network. We found various differentially regulated genes involved in neuropeptides signaling, potassium and sodium transport. The transcriptome data suggest an interaction among several molecular components leading to epileptogenesis in this animal model that displays hippocampal damage.

**Conclusion:** The present data indicates that even though similar mechanisms may be found in different regions of the dentate gyrus, the molecular components involved in processes such as, ion transportation, seem to be region specific.

**References:**

- Fanselow, M.S., Dong H.W. Are the dorsal and ventral hippocampus functionally distinct structures? Neuron. 14; 65(1):7-19. doi: 10.1016/j.neuron.2009.11.031 (2010).

- Wang, Z., Gerstein, M. & Snyder, M. RNA-Seq: a revolutionary tool for transcriptomics. Nat

Rev Genet 10, 57-63, doi:10.1038/nrg2484 (2009).