Characterization of gut microbiome in patients with different forms of epilepsy and autoimmune encephalitis through metagenomic analysis

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Introduction and Hypothesis:
Over time, man and microorganisms have co-evolved simultaneously to integrate a complex ecosystem. This symbiotic relationship is responsible for the regulation of physiological processes related to nutrition and metabolism and are essential for the correct function and development of immune system [1]. The intestine is considered the largest reservoir of these microorganisms, and the colon reaches the maximum density of germs [2]. Studies have shown that enteric microbiota may play a key role not only in proper digestion of food and maintenance of homeostasis, but also in the progression of diseases mediated by autoimmune mechanisms [3]. Such bidirectional communication is achieved through different pathways that includes neuroanatomic, circulatory, endocrine and immune system pathways [4]. In this context, the main objective of this work is to apply next-generation sequencing techniques of faecal samples to characterize the intestinal microbiome composition in individuals with different forms of epilepsy, autoimmune encephalitis as well as healthy controls [5]. Results obtained could reveal the potential impact in the onset, phenotypic variability and activity of different types of neurological diseases. It could also contribute to the development of new therapeutic targets [6].

Objective:
To determine if there are differences in gut microbiota composition between patients with different forms of epilepsy and autoimmune encephalitis in regard to healthy controls.

Methods:
Total faecal human DNA will be extract and purified using the QIAmp DNA stool Mini Kit (Quiagen) from a cohort of 90 individuals classified as follows: 30 patients diagnosed with mesial temporal lobe epilepsy; 30 patients with genetic generalized epilepsy and 30 patients affected with autoimmune encephalitis. All of them will be sex and age matched. DNA libraries will be sequenced via Illumina HiSeq 2500 platform. The reads of individual libraries will be paired and assembled into contigs using different algorithms (IDBA-UD, MIRA and MetaVelvet). Taxonomic classification, phylogenetic and functional analysis will be done applying tools like MEGAN and MG-RAST. Prediction gene will be perform using MetaGene approach. Final results will be statistically validated and shared.

Relevance:
The identification of new microbial communities capable of modulating and regulating different physiological processes related to the gut-brain axis will allow the development of alternative therapeutic strategies for the treatment of specific neurological conditions such as managing difficult epilepsies and autoimmune encephalitis. The data generated in our study will constitute the first gene catalogue of normal gut microbiota in Brazilian population. This data will be also banked/stored in a public database (www.bipmed.org) and therefore, used by any national or international research group interested in studying the intestinal microbiota and Brazilian individuals.

References: [1] doi:10.1016/j.chom.2015.04.011; [2] doi: 10.4103/0366-6999.190667; [3] doi: 10.1038/nn.4476; [4] doi: 10.1002/ana.24901; [5] doi: 10.4137/BBI.S12462 [6] doi: 10.1038/nature11209