

Summary

We live in constant symbiosis with complex microbial communities in our gut and on our skin. Collectively these communities are known as the human microbiome. The human microbiome, consisting of bacteria, fungi, protozoa, and parasitic worms, is thought to play a beneficial role for the human host. The gut microbiome has a significant impact on metabolism and the endocrine system, and it has been suggested that it may also directly influence the brain. The gut and brain are engaged in constant bi-directional communication that is referred to as the gut-brain axis. The brain gut axis plays an important role in maintaining homeostasis and its dysfunction has been linked to various psychiatric and nonpsychiatric disorders. There is a need for future trials focusing on the best combinations of probiotic strains, especially in the aspect of the appropriate supplementation with prebiotics, which stimulate the normal growth of probiotic bacteria.

Research Project Objectives

The aim of the proposal is to evaluate the impact of preventive diet using a natural prebiotic in the form of powdered topinambur (TPB) on chronic stress, cognitive functions and the process of neurogenesis in the chronic unpredictable mild stress model (CUMS) in mice. Based on preliminary results from our studies, I set the hypothesis that preventive diet using prebiotic in the form of natural supplements such as TPB stimulates the development of probiotic bacteria, necessary for proper functioning of the gut-brain axis, and thus acts preventively on stress, cognitive functions and normal neurogenesis in animals exposed to chronic unpredictable mild stress.

Research Project Methodology

All experiments will be performed on 6 weeks old male C57/BL mice. The animals will be randomly assigned to experimental groups consisting of 10 mice. Both CUMS and healthy animals will participate in the experiment, in order to evaluate the impact of diet on cognitive functions and the process of neurogenesis in a healthy brain..

The experiments will be conducted in two series:

SERIES I-healthy mice: control, topinambur (TPB), fluoxetine (FLU)

SERIES II - CUMS mice: control, topinambur (TPB), fluoxetine (FLU)

The diet will last for 14 weeks. Animals from the TPB CUMS group will start a prebiotic diet 8 weeks before starting the CUMS induction (prevention). Stress will be induced for 6 weeks, with TPB administration at the same time. During the 14-week diet, all animals will be weighted at three time points: 1 - before starting the diet, 2- after eight weeks of diet (before starting CUMS), 3 - after 14 weeks of diet to assess changes in body weight after CUMS. In addition, on the twelfth week of the diet, the animals will receive a BrDU (cell proliferation marker) as an intraperitoneal injection once daily at dose 50 mg/kg for 5 days. After the end of the diet and CUMS, the animals will be subjected to behavioral tests assessing anxiety (EPM Elevated Plus Maze), spatial learning and memory (Morris water Maze test). Before the last stage of research fecal samples will be collected for determine the composition of the microbiome, then animals will be perfused and their brains will be extracted for quantitative analysis of neurogenesis.

Research Project Impact

The main and fundamental aspect of the proposed studies is to search for new natural prebiotic which can be used as is a preventic diet against developing chronic stress and as protection of cognitive functions and neurogenesis. In addition, a preventive diet using a prebiotic can stimulate the development of probiotic bacteria, necessary for the proper functioning of the gut-brain axis. Our investigations is going to be performed on 6 weeks old mice under chronic unpredictable mild stress reflecting patients with chronic stress. Disturbed proliferation of neural cells includes a risk of learning and memory dysfunction, which for patients is very important. Achieving positive results (preventive action of TPB on chronic stress, protection of cognitive functions and a proper neurogenesis) will certainly be qualified for more advanced pre-clinical investigations, especially in the group of patients suffering from chronic stress. Results from the studies will be published in journals from the Philadelphia List as well as presented on international and national conferences and will constitute the basis for the author's PhD thesis.