Diabetic Complications Consortium

Application Title: "Does fecal transplantation alleviate indices of peripheral neuropathy and impact nerve system inflammation in mouse models of diabetes?"

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1. Project Accomplishments:

We generated cohort of diabetic mice HFD/low STZ and spent the past 6 months performing fecal transplantation. For rigor, we generated 3 cohorts. We observed that, FMT tend to improve glucose metabolism (one cohort is still ongoing) and data related to pain and neuropathy are still being analyzed. We evaluated the change in immune cells in the DRG and we did not observe any changes after FMT. We did not observe differences using db/db mice. We used this funding to characterize a novel model to better define inflammation in vivo.

2. Specific Aims:

Aim 1. Determine if fecal transplantation improves neuropathy in mouse models of type II diabetes

FMT from lean to db/db or HFD/low STZ mice were performed, and indices of peripheral neuropathy measured. We also comprehensively evaluate glucose homeostasis. FMT improved glucose homeostasis in HFD/STZ mice only. We are still analyzing neuropathy and pain data.

Samples were sent to specific cores and we are waiting on the data that evaluate the gut species using 16S sequencing, fecal and circulating butyrate using lipidomics.

Aim 2. Determine if fecal transplantation modifies PNS immune cell profiling in mouse models of type II diabetic neuropathy.

We used specific immune cell panels and a flux cytometry approach to quantitatively evaluate the change in immune cell population in the spinal cord, DRG and sciatic nerve of control and diabetic mice ± FMT. Using this method, we did not observe difference in listed tissues. However, we used a novel biosensor mouse that we characterized (metabolism and sensory functions) to monitor caspase activation in live animal and we observed that change in gut microbes was altering the caspase 1 activation in many tissue of type II diabetic mice. These experiments are still on-going, and the mice model we characterized is detailed in the Biorxiv publication listed below.

3. Publications:

Live Monitoring of Inflammation Reveals Tissue and Sex-specific Responses to Western Diet

Raiza Bonomo, Sarah Talley, Jomana Hatahet, Chaitanya Gavini, Tyler Cook, Ben Chu n, Pete Kekenes-Huskey, Gregory Aubert, Edward Campbell, Virginie Mansuy-Aubert

doi: https://doi.org/10.1101/2021.09.22.461384

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