The gut microbiome influences the gene expression profile of neuroendocrine and enteroendocrine systems

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Objective/Hypothesis: The gut microbiome influences metabolism, but the underlying mechanisms are not completely understood. We hypothesized that the gut microbiome modulates metabolism by regulating the expression of key neuroendocrine and enteroendocrine genes such as neuropeptide Y (*Npy)* which is a potent brain orexigenic peptide and G-protein-coupled receptor-17 (*Gpr17)* which decreases incretin secretion in the gut.

Approach: The gene expression profiles in mouse hypothalamus and gastrointestinal tract segments (duodenum, jejunum, ileum, and colon) were compared from germ-free (GF) mice (n=9 females, n=9 males) and conventional mice (n=9 females, n=9 males). Gene transcription was determined through total RNA yield extracted from the various tissues using qRT-qPCR. The data was analyzed using two-way ANOVA and unpaired t-test.

Results: We found that RNA yield in brain and gut tissues differed in a sex and microbiome dependent manner. The medial basal hypothalamus of the female germ-free mice had lower RNA yield compared with conventional female mice (p=0.0082). In the intestine, the RNA concentrations of the germ-free mice showed a decrease from the proximal to distal gut, however, an opposite trend was observed in the conventional mice with an overall increase of concentration from the proximal to distal gut. This trend may reflect the high concentration of the microbiota in the distal gut. Regarding gene expression of the neuroendocrine and enteroendocrine systems, *Npy* had lower expression in the medial basal hypothalamus (MBH) of conventional males (p=0.004), *Gpr17* showed moderate duodenal expression in conventional mice (p=0.029), and *Gpr17* showed increased duodenal expression in germ-free females (p=0.044).

Summary/Conclusions: With enriched microbiota in the ileum and colon, our results indicate that gut microbiota increase host gene transcription in the distal gut segments. Future studies will aim at investigating the mechanistic link between the microbiome and regulation of gene expression in neuroendocrine and enteroendocrine tissues.