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PROJECT TITLE: Exploring the effects of gut microbiota perturbation on DNA methylation program to control intestinal homeostasis and inflammation

Project description:

Although considerable research has been conducted on the diversity of the gut microbiome, little is known about how it influences intestinal homeostasis under normal and pathogenic conditions. Emerging evidence suggests that epigenetic mechanisms may function at the interface between the microbiota and the intestinal epithelium. This project aims to investigate the effects of gut microbiota alterations in a mouse model of dysbiosis induced by antibiotic treatment and subsequent probiotic intervention with *Lactobacillus reuteri* on host intestinal homeostasis and inflammation, with a particular focus on changes in DNA methylation profiles.

To further elucidate host-microbe interactions and move toward a mechanistic understanding, we will examine the immunomodulatory properties of molecules released by the microbiota of mice treated with antibiotics and *L. reuteri* using in vitro epithelial and immune cell models. Specifically, we will assess the potential of both supernatants and purified lipopolysaccharides from fecal samples to trigger inflammatory responses, modulate immune functions, and reshape cellular DNA methylation landscapes.

This project seeks to determine whether microbiota-driven epigenetic programming is essential for the maintenance of intestinal homeostasis and immune regulation.

REFERENCES:

- 1)Pepke ML, Hansen SB, Limborg MT. Unraveling host regulation of gut microbiota through the epigenome-microbiome axis. Trends Microbiol. 2024 Dec;32(12):1229-1240. doi: 10.1016/j.tim.2024.05.006. Epub 2024 Jun 4. PMID: 38839511.
- 2) Wang L, Zhang W, Wu X, Liang X, Cao L, Zhai J, Yang Y, Chen Q, Liu H, Zhang J, Ding Y, Zhu F, Tang J. MIAOME: Human microbiome affect the host epigenome. Comput Struct Biotechnol J. 2022 May 17;20:2455-2463. doi: 10.1016/j.csbj.2022.05.024. PMID: 35664224; PMCID: PMC9136154.
- 3) Ansari I, Raddatz G, Gutekunst J, Ridnik M, Cohen D, Abu-Remaileh M, Tuganbaev T, Shapiro H, Pikarsky E, Elinav E, Lyko F, Bergman Y. The microbiota programs DNA methylation to control intestinal homeostasis and inflammation. Nat Microbiol. 2020 Apr;5(4):610-619. doi: 10.1038/s41564-019-0659-3. Epub 2020 Feb 3. PMID: 32015497.

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Project title: A multiscale integrated approach to the study of the nervous system in health and disease (MNESYS)