High-Fat Diet Induced Mitochondrial Dysfunction Links Intestinal Dysbiosis and Colorectal Cancer

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Introduction

In CRC patients, levels of colibactin-producing Enterobacteriaceae (e.g., E. coli) are observed in the feces. In individuals on a high-fat diet, a bloom of facultative anaerobes is also observed in the feces. Enterobacteriaceae expansion of facultative anaerobic bacteria (e.g., a Western-style high-fat) consumption, smoking, obesity, and dietary patterns promoting tumorigenesis and include alcohol consumption, obesity, and dietary patterns promoting tumorigenesis.

Environmental risk factors play an important role in colorectal cancer and diet-induced obesity are also observed in the feces.

• CRC is the 2nd most common cancer and the 2nd leading cause of cancer-related deaths.
• Most CRC cases and deaths occur after age 50. Rising incidence of CRC at younger ages (before age 50).
• 35-40% of CRC cases are attributed to family history of CRC or to inherited genetic mutations. 60-65% of CRC cases arise sporadically.
• Both colorectal cancer and diet-induced obesity are associated with gut dysbiosis, specifically the expansion of facultative anaerobic Enterobacteriaceae.
• Dysbiosis of the gut is characterized by a change in the microbial composition (dysbiosis).
• Dysbiosis is associated with a range of gastrointestinal diseases, including colorectal cancer.

In CRC patients, levels of colibactin-producing E. coli and colibactin-producing gene expression are elevated.

Dysbiosis is associated with changes in colonic tissue. Ongoing and future experiments will involve longer time points and infection with E. coli SP15 deficient in the production of colibactin.

Future experiments will assess mitochondrial function of colonocytes isolated from LFD and HFD mice.

Conclusions and Future Directions

• Our preliminary in vivo results suggest that the combination of high-fat diet and exposure to colibactin-producing E. coli SP15 may promote colorectal carcinogenesis in adult C57BL/6J mice. Ongoing and future experiments will involve longer time points and infection with E. coli SP15 deficient in the production of colibactin.

• Our preliminary in vivo results suggest that saturated fatty acids, like palmitate, perturb mitochondrial function and metabolism and may promote colorectal carcinogenesis in vivo that may promote the bloom of facultative anaerobic bacteria in the colonic lumen. Future experiments will assess mitochondrial function of colonocytes isolated from LFD and HFD mice.

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