Docosahexaenoic Acid May Reduce Risk factors of Cancer Development in a Mouse Model of Colitis-Associated Colorectal Cancer

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Colorectal Cancer

- Colorectal cancer (CRC) has increased prevalence in more developed countries
- Risk factors include lifestyle, family history, and diet
- Colon inflammation (colitis) is a key predictor of CRC
- Diet distinctly alters colitis outcomes

Docosahexaenoic acid (DHA)

- DHA is an omega-3 fatty acid in some fish, algae oil, and some seeds and nuts
- DHA has been studied for its effects in brain development, but not as widely studied in inflammation models
- DHA is a precursor to several inflammation resolving compounds
- DHA restores key ratio of microbiota to a healthy level in mice
- DHA effectively inhibits autoimmune inflammation in mice

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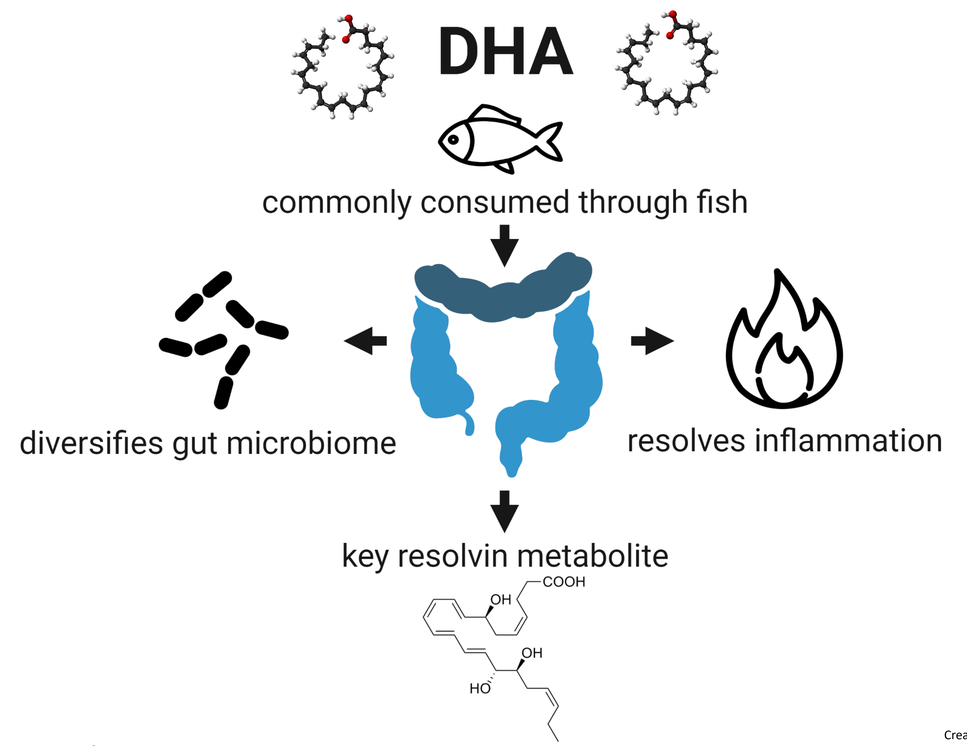

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Microbiome

- DHA increases abundance of beneficial taxa, such as *Bifidobacteria*
- DHA balances a key ratio of taxa, *Firmicutes/Bacteroidetes*, which is linked to positive health outcomes in mice
- Supplementation of DHA-rich foods improved gut microbiome disorder in rats fed a high-fat diet

Inflammation

- DHA supplementation decreases production of proinflammatory molecules, including cytokines and omega-6 derived eicosanoids.
- DHA-derived metabolites exhibit anti-inflammatory effects. Two such metabolites are resolvin and short-chain fatty acids.
- DHA has been shown to have a protective effect against intestinal barrier dysfunction, which contributes to inflammation.

Planned Study Design

Objective

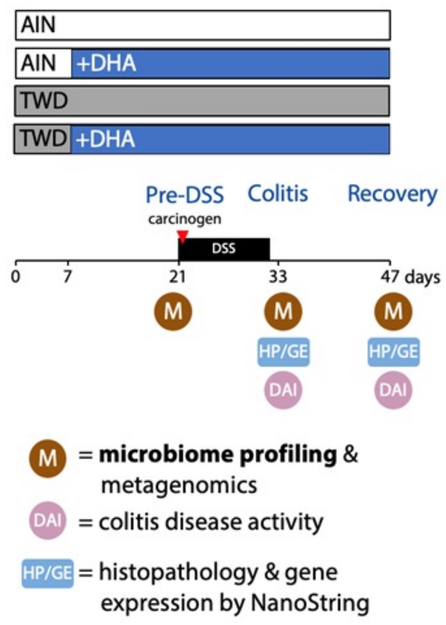
- The objective of this study is to determine the effect of basal diet and DHA supplementation on colon inflammation, mucosal injury, and microbiome profile before, during, and after colitis.

Diets

- AIN93G – a healthy rodent diet
- Total Western Diet (TWD) – mimics a Western-type diet, previously shown to promote CRC

Cancer Model

- Mice will be given the carcinogen azoxymethane on day 21, followed by 1% DSS dissolved in drinking water for 12 days to promote colitis



Expected Results

We expect measures of disease index and mucosal damage to be increased in animals fed a Western-type diet, and for these measures to be decreased when the diet is supplemented with DHA. Additionally, We expect microbiota profiles to be differentiated between the AIN and Western-diets, with DHA restoring the microbiota profile to be comparable with that of the AIN control diet.

Key References

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