The Supportive Oncology Research Group

Resistant starch-rich diet attenuates chemotherapy-related neuroinflammation in mice

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** Denotes shared senior authorship

Introduction

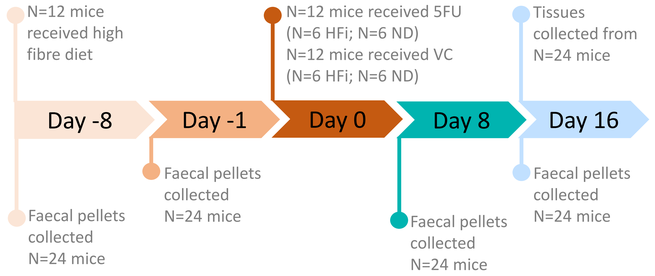
- Chemotherapy-induced neuroinflammation is thought to underlie the neuropsychological symptoms associated with chemotherapy[1]
- These symptoms often cluster with gastrointestinal side effects, which are known to result from the damaging impact of chemotherapy on the gut microbiota[2]
- The gut microbiota is a critical driver of neuroinflammation in other disease states[3]
- Despite this, there has been no attempt to ameliorate chemotherapy-induced neuroinflammation using microbiota targeted therapies

? **Does a high fibre diet promote microbial metabolite production and reduce neuroinflammation in mice treated with 5-FU?**

- We hypothesise that a high fibre diet may minimise neuroinflammation associated with the chemotherapeutic 5-fluorouracil (5-FU)

Methods

- 24 female mice (n=6 / group) were treated with 5-FU or vehicle control, with or without a high fibre diet. Tissues were collected as outlined below:



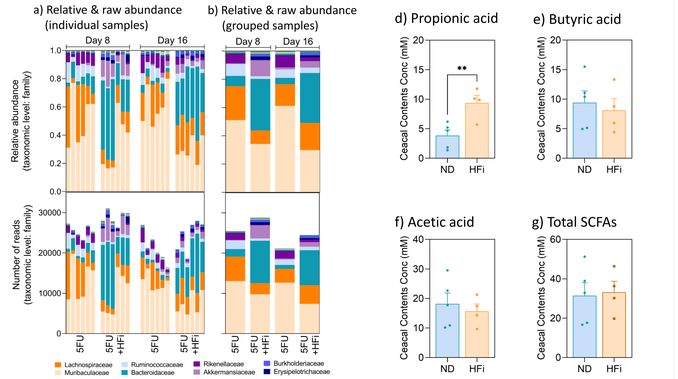
- SCFAs quantified using GC-MS and microbiota composition analysed using 16S
- Immunofluorescence staining for glial fibrillary acidic protein (GFAP) was used to assess astrocyte abundance in the brain, as a marker of neuroinflammation

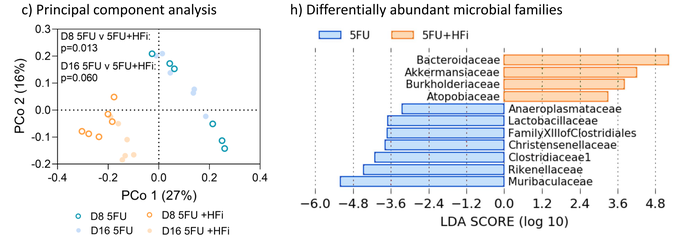
References

1. Santos & Pyter (2018). *Front Immunol*, vol.9
2. Cryan et al. (2019). *Physiol Rev*, vol.99(4)
3. Subramaniam et al. (2020). *Neurosci Biobehav Rev*, vol.116

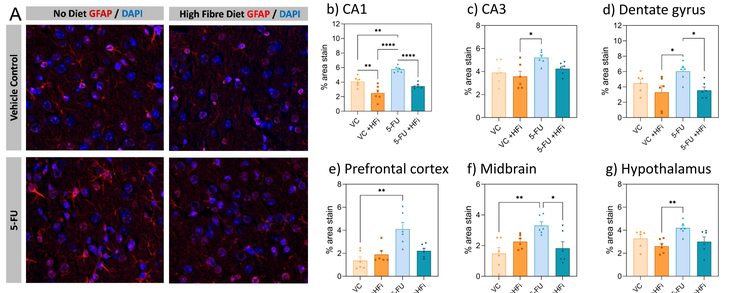
Results

High fibre diet altered faecal microbiota composition and increased caecal propionic acid concentrations

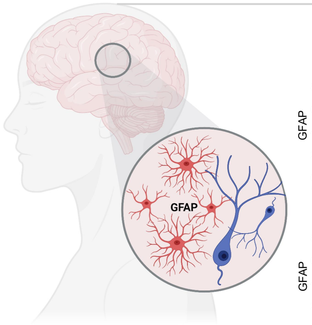


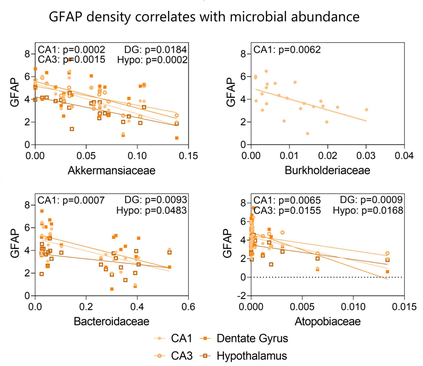


High fibre diet mitigates the increases to astrocyte staining density induced by 5-FU treatment

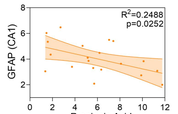


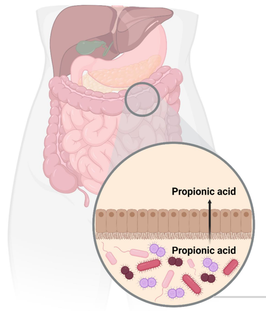
Propionic acid and microbes differentially abundant with high fibre diet both significantly correlate with astrocyte abundance

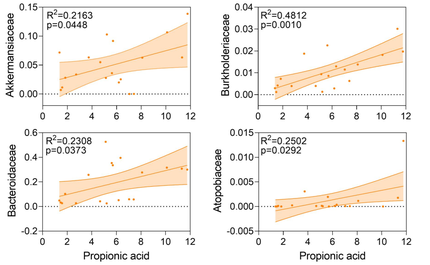




GFAP density correlates with propionic acid concentrations







Microbial abundance correlates with propionic acid concentrations

Conclusions

- Fibre supplementation, and resulting microbial changes, mitigate 5-FU-induced neuroinflammation via propionic acid, warranting further investigation to reveal how these findings can be optimally translated for therapeutic intervention

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