Marine-derived bioactives and nutraceuticals: sustainable use of marine products for health and wellbeing

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Date of activities: February 28, 2022 to March 1, 2023

Abstract

Intestinal barrier dysfunction plays an important role in varying disease-development risks and gut microbiota-derived metabolites are an attractive target to influence intestinal homeostasis and barrier function, which has also been linked with dementia risk. Dietary intake of marine-derived macroalgae (seaweed) has been shown to modulate gut microbiota and metabolite production attributed to a range of diverse constituents. This project screened a range of algal extracts for protective effects in a novel neuronal coculture and gut epithelial barrier system in vitro.

The protective effects of polysaccharide-enriched extracts from red seaweed *Gracillaria fisheri* (PG) and green seaweed *Ulva rigida* (PU) and pigment-enriched extract from *U. rigida* (PM) on gut barrier function and the expression of tight junctions in functional intestinal epithelial Caco-2 cell monolayers were investigated. PG and PU prevented gut metabolite sodium deoxycholate (SDC) and microbial metabolite *p*-cresol-induced alterations in barrier function by significantly increasing transepithelial electrical resistance (TEER) and decreasing fluorescein isothiocyanate-dextran 40 kDa (FITC-D40) flux. Seaweed extracts increased protein tight junction (TJ) claudin 1 and occludin expression compared to control and SDC with *p*-cresol-treated samples. Additionally, these protective effects were investigated in an *in vitro* coculture system between epithelial Caco-2 and neuronal PC12 cells. There were no significant interaction effects of neuronal coculture on Caco-2 intestinal permeability, cell viability or TJ expression, however alterations induced by SDC and *p*-cresol were prevented by seaweed extracts and increased PC12 cell viability. Treatment with PM also partly restored the expression of claudin 1 and occludin from SDC and *p*-cresol-treated cells. Subsequent metabolomic analysis revealed a complex set of interactions in co-coculture and variable effects on analyte profiles arising from incubation with bacterial metabolites, with notable changes in phenylalanine and pyrimidine metabolism..

Activities/reports (agenda/itinerary)

1. We established monthly Zoom meetings from March 2022 through February 2023 to set the objectives and implement the experimental plans of the project.
2. PI-B Charoensiddhi was hosted by PI-A Smid in Adelaide from Feb-Nov 2022 to conduct cell culture experiments.
3. All PIs established experimental plans to commence the project from March 2022. The majority of experimental cell culture work was conducted between Feb to Nov 2022 in

PI-As lab, with further metabolomic analyses conducted at The University of Adelaide and Kasetsart University from Nov 2022 to Jan 2023.

4. PI-C conducted complementary high throughput content imaging studies of epithelial monolayers in latter half of 2022..
5. All PIs held a joint online meeting/workshop in September as a milestone research meeting to discuss findings and additional studies required.
6. A joint meeting was held at Kasetsart University in January 25-27, 2023 with PI-A, B & C in attendance to discuss the major findings, approaches to further data analysis and to commence discussions around outputs such as publications. This was hosted by PI-B Charoensiddhi.
7. February 2023 – consolidation of findings; final Zoom meeting for discussion of metabolomic analysis and write-up.

Achievements of activities

1. We established a suite of bacterial and intestinal metabolites that consistently inhibit intestinal epithelial barrier function, producing increased permeability (so-called leaky gut").
2. This reduction in barrier function is associated with a selective decrease in tight junction protein expression, providing a molecular correlate/basis to the functional changes observed.
3. Seaweed and other freshwater acquatic-derived extracts offset these functional deficits to bacterial metabolites, protecting barrier function and associated reductions in tight junction protein expression.
4. The integration of a neuronal and intestinal epithelial line created a successful coculture system. We revealed an interaction of these two cell populations through functional, metabolomic and principal component analysis that may act to mitigate the damaging effects of bacterial and intestinal metabolite stressors on gut barrier function and thus permeability.

Conclusions

These results demonstrate that a diverse range of macroalgal and other extracts have a potential to protect gut barrier integrity and function and improve neuronal cell viability from bacterial and intestinal metabolite stressors linked to dysbiosis, with integrative gut and neuronal benefits associated with positively impacting neurodegenerative diseases. Such extracts may therefore provide potential health benefits in a myriad of disorders potentially linked to the gut-brain axis.

Achievements made within SPF collaboration

The demonstration of a positive influence of marine seaweed and aquatic-derived plant extracts on gut barrier function in this model reinforced the potential of inexpensive, natural and readily sustainable plan and seaweed biomass to be used in the diet as functional foods or supplements for improving gut and brain health. Further studies are required to optimize the coculture model and to consider approaches that will incorporate living commensal gut bacteria in vitro to better replicate this model relative to the gut-brain-microbiome axis.

Outcomes in-progress involve the compiling of two original research papers for publication in suitable peer-reviewed journals to enable further dissemination of research outcomes. Additionally, consideration will be given to the presentation of this research to suitable conferences in marine science and biotechnology such as ISS (International Seaweed Symposium) or ANZMBS (Australia-NZ Marine Biotechnology Society Symposium).

-Budget summary (please use Template 4)

Separate template provided

-Photos & link(s)

AC21 Investigators: Left to Right, PI-B Charoensiddhi, PI-C Kato and PI-A Smid at AC21 meeting, Kasetsart University, Bangkok Jan 25-27, 2023.

Guest Seminar session at FST, Kasetsart University, Jan 26

PI-A Smid talk on Gut & Brain Health at FST, Kasetsart University, Jan 26