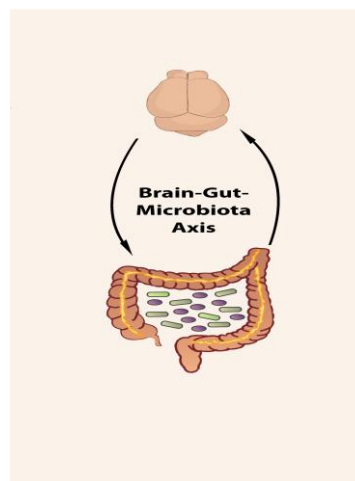


Project number: 6590
Funding source: DAFM/FIRM

Date: Sept 2018
Project dates: 2013 -2018

SMART FOOD– Science Based ‘Intelligent’/Functional and Medical Foods for Optimum Brain Health, Targeting Depression



Key external stakeholders:

DAFM, dairy and other functional and medical foods companies, medical profession.

Practical implications for stakeholders:

- Methodology was developed and species identified, for production of microalgal biomass rich in omega-3 fatty acids. Protocols were designed to produce sufficient volume of low molecular weight phorotannin extract from Irish seaweed (*Fucus vesiculosus*), and bioactivity assessed and supplied by NUI Galway to Teagasc/UCC for testing on animal models of depression.
- The effects of microalgae-derived omega-3 fatty acids and polyphenols on primary neuronal culture from the cortices of P1 pups and established human cell lines (SH-SY5Y neuronal cell line) were assessed. This work confirmed the impact of omega-3 marine lipids and neuroprotective effect of 10 polyphenols on neuronal cell lines.
- Studies were conducted that demonstrated the impact of dietary intervention with marine omega-3 fatty acids and sea polyphenols as functional foods for prevention of depression in maternally separated animals.

Main results:

Microalgae-derived omega 3 fatty acids and macro-algae-derived polyphenols have potential as medical food ingredients to be used in combination with conventional antidepressants for treatment of depression.

Opportunity / Benefit:

PUFA rich fish oil and marine polyphenols have potential as nutraceuticals for alleviation of depression.

Collaborating Institutions:

Teagasc, UCC, NUIG

Teagasc project team: Prof. Catherine Stanton (Project Leader)

External collaborators: Prof. John Cryan, UCC
Prof. Dagmar Stengel, NUIG

1. Project background:

Worldwide incidence of depression is increasing substantially and is predicted to be the second leading cause of disability by 2020 (WHO). Novel strategies, both social and biological, to prevent depression are urgently needed. Recent preclinical and some clinical data suggest that nutrition may reduce depressive symptoms and alleviate cognitive decline, but scientific substantiation of efficacious dietary components is

required. The overall aim of this project is to investigate the potential of a combination of omega-3 PUFA and sea polyphenols with known antioxidant activity as nutritional supplement strategies with efficacy to enhance mental health and cognition. Given the high level of predicted growth for cognitive health foods, this project will generate necessary scientific information on the health benefits of marine Ingredients for brain health and their stable incorporation into functional/medical foods. Indeed, cognitive health foods are a major opportunity for the food industry, predicted to grow at a compound annual growth rate (CAGR) of 11.8% between 2009 and 2014 (to \$2.095bn, DATAMONITOR, 2013). The information generated in this project will provide Ingredient suppliers and the Health Professionals with essential knowledge relating to the impact of nutrition on depression.

2. Questions addressed by the project:

1. This proposal aims to investigate the potential of marine-algal-derived omega-3 polyunsaturated fatty acids (PUFA) and marine polyphenols as dietary ingredients with efficacy to enhance mental health and cognition.

3. The experimental studies:

This project involved *in vitro* and *in vivo* preclinical studies to determine the role of omega-3 PUFA and phytochemicals of marine origin in mood regulation. We used a combination of omega-3 PUFA and sea polyphenols exhibiting antioxidant activity, as a nutritional supplement strategy in an animal model of depression, and did studies to unravel the biological mechanisms. The results of this project provide data for development of functional food ingredients for prevention of depression, and medical foods to increase the potency of conventional antidepressants drugs.

4. Main results:

Conditions were optimised and species identified, for production of microalgal biomass rich in omega-3 fatty acids. Protocols were designed to produce sufficient volume of low molecular weight phlorotannin extract from Irish seaweed (*Fucus vesiculosus*), and bioactivity assessed and supplied by NUI Galway to Teagasc/UCC for testing for product development and on animal models of depression.

Protocols for production of stable omega-3/polyphenol rich food ingredients from microalga/macroalgae sources for incorporation into food products are available. Fortified yoghurt and spray dried ingredients were successfully developed enriched in omega-3 fatty acids and extracts from Irish seaweed.

We assessed the effects of microalgae-derived omega-3 fatty acids and polyphenols on primary neuronal culture from the cortices of P1 pups and established human cell lines (SH-SY5Y neuronal cell line).

Studies were conducted that demonstrated the impact of dietary intervention with marine omega-3 fatty acids and sea polyphenols as functional foods for prevention of depression in maternally separated rodent animals. Animal studies (rodents) also revealed the impact of microalgae-derived omega 3 fatty acids and macro-algae-derived polyphenols as medical foods in combination with conventional antidepressants for treatment of depression. While fish oil and fluoxetine treatment resulted in significant manipulation of important neurobiological markers, only the changes in the fluoxetine treated animals translated to significant behavioural differences, representing a reduction in a depressive or anxious state.

The findings from this study demonstrated the potential of a combination of omega-3 PUFA and sea polyphenols with known antioxidant activity as nutritional supplement strategies with efficacy to enhance mental health and avoid depression.

5. Opportunity/Benefit:

Cognitive health foods are identified as a major opportunity for the food industry, and this project has generated novel scientific information on the health benefits of marine Ingredients for brain health and their stable incorporation into functional/medical foods. The information generated in this project will provide Ingredient suppliers and the Health Professionals with essential knowledge relating to the impact of nutrition on depression.

This work is relevant to the food industry for development of functional and medical foods enriched in omega-3/polyphenols.

6. Dissemination:

Main publications:

Moroney, NC, O'Grady, M.N., Robertson, R.C., Stanton, C., O'Doherty, J.V. and Kerry, J.P. (2015). Influence of level and duration of feeding polysaccharide (laminarin and fucoidan) extracts from brown seaweed (*Laminaria digitata*) on quality indices of fresh pork, *Meat Science* (2015), pp. 132-141 DOI information: 10.1016/j.meatsci.2014.08.016.

Ruairi C. Robertson, Freddy Guihéneuf, Bojlul Bahar, Matthias Schmid, Dagmar B. Stengel, Gerald F. Fitzgerald, R. Paul Ross and Catherine Stanton. (2015). The Anti-Inflammatory Effect of Algae-Derived Lipid Extracts on Lipopolysaccharide (LPS)-Stimulated Human THP-1 Macrophages. *Mar. Drugs*, 13, 5402-5424; doi: 10.3390/md13085402.

Pusceddu MM, Nolan YM, Green HF, Robertson RC, Stanton C, Kelly P, Cryan JF, Dinan TG. (2015). The Omega-3 Polyunsaturated Fatty Acid Docosahexaenoic Acid (DHA) Reverses Corticosterone-Induced Changes in Cortical Neurons. *Int J Neuropsychopharmacol*. 2015 Dec 12. pii: pyv130. doi: 10.1093/ijnp/pyv130. [Epub ahead of print].

Pusceddu MM, El Aidy S, Crispie F, O'Sullivan O, Cotter P, Stanton C, Kelly P, Cryan JF, Dinan TG. (2015). N-3 Polyunsaturated Fatty Acids (PUFAs) Reverse the Impact of Early-Life Stress on the Gut Microbiota. *PLoS One*. 2015 Oct 1; 10 (10):e0139721. doi: 10.1371/journal.pone.0139721. eCollection 2015. Erratum in: *PLoS One*. 2015;10 (10):e0142228.

Ruairi C. Robertson, Clara Seira Oriach, Kiera Murphy, Gerard M. Moloney, John F. Cryan, Timothy G. Dinan, R. Paul Ross and Catherine Stanton. Omega-3 polyunsaturated fatty acids critically regulate behaviour and gut microbiota development in adolescence and adulthood. *Brain, Behavior, and Immunity*. June-2016.

Clara Seira Oriach, Ruairi C. Robertson, Catherine Stanton, John F. Cryan, Timothy G. Dinan. Food for thought: The role of nutrition in the microbiota-gut-brain axis. *Clinical Nutrition Experimental*. 6 (2016) 25-38.

Ruairi C. Robertson, Maria Rosa Gracia Mateo, Michael N. O'Grady, Freddy Guihéneuf, Dagmar B. Stengel, R. Paul Ross, Gerald F. Fitzgerald, Joseph P. Kerry, Catherine Stanton. An assessment of the techno-functional and sensory properties of yoghurt fortified with a lipid extract from the microalga *Pavlova lutheri*. *Innovative Food Science and Emerging Technologies* (2016) DOI: 10.1016/j.ifset.2016.03.017.

D.A. Kirke, T.J. Smyth, D.K. Rai, O. Kenny and D.B. Stengel (2016) 'The chemical and antioxidant stability of isolated low molecular weight phlorotannins'. *Food Chemistry*. <http://dx.doi.org/10.1016/j.foodchem.2016.11.050>

Snehal Gite, R. Paul Ross, Dara Kirke, Freddy Guihéneuf, Justine Aussant, Dagmar B. Stengel, Timothy G. Dinan, John F. Cryan and Catherine Stanton. Nutraceuticals to Promote Neuronal Plasticity in Response to Corticosterone-induced Stress in Human Neuroblastoma cells. *Manuscript Nutritional Neuroscience*. (Manuscript accepted for publication Nov. 2017).

Gite, S, Ross, RP, Kirke, D, Guihéneuf, F, Aussant, J, Stengel, DB, Dinan, TG, Cryan, JF, Stanton, C. (2018). Nutraceuticals to promote neuronal plasticity in response to corticosterone-induced stress in human neuroblastoma cells. *Nutritional Neuroscience* Jan 29:1-18. doi: 10.1080/1028415X.2017.1418728. [Epub ahead of print].

Codagnone MG, Spichak S, O'Mahony SM, O'Leary OF, Clarke G, Stanton C, Dinan TG, Cryan JF. (2018). Programming Bugs: Microbiota and the Developmental Origins of Brain Health and Disease. *Biol Psychiatry*. 2018 Jun 27. pii: S0006-3223(18)31605-6. doi: 10.1016/j.biopsych.2018.06.014. [Epub ahead of print].

van de Wouw M, Boehme M, Lyte JM, Wiley N, Strain C, O'Sullivan O, Clarke G, Stanton C, Dinan TG, Cryan JF. (2018). Short-chain fatty acids: microbial metabolites that alleviate stress-induced brain-gut axis alterations. *J Physiol*. 2018 Oct;596(20):4923-4944. doi: 10.1113/JP276431. Epub 2018 Aug 28.

Cussotto S, Strain CR, Fouhy F, Strain RG, Peterson VL, Clarke G, Stanton C, Dinan TG, Cryan JF.

(2018). Differential effects of psychotropic drugs on microbiome composition and gastrointestinal function. *Psychopharmacology (Berl)*. 2018 Aug 28. doi: 10.1007/s00213-018-5006-5. [Epub ahead of print].

Popular publications:

APC Microbiome Institute Symposium, Cork, 2016.

22nd International Seaweed Symposium (ISS). 19th – 24th June, 2016. Copenhagen, Denmark.

Young Neuroscience Ireland Symposium, 2018.

8th World Congress on Polyphenol Applications, Lisbon, Portugal (June 2014).

Natural Product Biotechnology 2014, 18-20 November 2014, Inverness, Scotland.

ESAI's Environ 25: Sustainability and Opportunities for Change. IT Sligo, Sligo. 8-10th April 2015.

NutraMara Conference 2015: Harnessing Marine Bioresources for Innovations in the Food Industry. Royal Dublin Society, Dublin, Ireland. 29-30th June 2015.

6th European Phycological Congress (EPC6) London, England. 23-28th August 2015.

Neuroscience Ireland Conference, Sept-2015. Dublin, Ireland.

6th ISAP Congress of International Society for Applied Phycology, La cite, Nantes, France, 18-23th June 2017.

ISAP Congress of International Society for Applied Phycology, Nantes, France, 18-23th June 2017.

7. Compiled by: Catherine Stanton
