Through the gut, and into the brain – dietary tryptophan targeting the brain-gut-axis to modulate enteritis

Summary:

Tryptophan (TRP) is an essential amino acid with key functions in immune and neuroendocrine regulation of fish, having shown these properties when added to diets. This project explores whether TRP supplementation can alleviate intestinal inflammation, focusing on its two main metabolic pathways: the kynurenine and the serotonin pathways. The site of the nutraceutical absorption is the target tissue (intestine), which is replenished of both enterochromaffin (serotonin producers) and immune cells (kynurenine producers). The project aims at i) uncover the complex dynamics of diet-induced enteritis in fish; ii) determining the extension of enteritis to the brain-gut axis; iii) assessing the modulatory effect of TRP supplementation on enteritis and on the brain-gut axis. Rainbow trout (RT, Oncorhynchus mykiss) will serve as the model species. The sequences of two TRP metabolic enzymes and that of one immune cell receptor will be cloned and transformed into bacteria for recombinant protein production and respective antibodies. An in vivo trial targeting a gut inflammation model will be conducted, where TRP will be added to a plant-based, enteritis-inducing diet which will be provided to RT for four weeks. Samplings will be undertaken to obtain blood, brain and different gut portions. Collected samples will enable: (i) assessment of systemic immune and neuroendocrine responses using blood markers such as leukocyte counts, lysozyme activity, and cortisol; (ii) characterization of local intestinal responses through gene expression (RNA-seq) and immunohistochemistry analysis; (iii) quantification of brain TRP metabolites by LC-MS/MS, and iv) enteritis and/or TRP-induced microbiome changes. The project expects to explore the role played by the brain-gut axis during enteritis (unveiling its potential as a target for future therapeutic strategies) and to demonstrate TRP's immunomodulatory and intestinal protective effects, potentially presenting itself as a non-deleterious therapeutic strategy that enables the use of new, alternative ingredients in aquaculture without compromising fish welfare.

Main Metodologies:

To achieve the proposed goals, the student will undertake different methodology approaches: cloning, transformation and recombinant protein expression; gene expression (rtPCR); western blot analysis; microbiome and transcriptome analyses; LC-MS/MS; classical histology and immunohistochemistry; humoral immune parameters.

References:

(1) Zhang et al 2022: 10.3389/fnut.2022.1014502; **(2)** O'Mahony et al 2015: 10.1016/j.bbr.2014.07.027; **(3)** Seibel 2022: 10.3390/fishes7010022; **(4)** Azeredo et al. 2024: 10.3390/biology13050309; **(5)** Peixoto et al. 2025: 10.1038/s41598-025-01079-y

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Place of Work

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Will the Proposal research idea be funded by a specific project?

Yes, by COMPETE2030-FEDER-00824200

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