University of Prince Edward Island

Faculty of Veterinary Medicine
Summary of Dissertation

Submitted in Partial Fulfilment
of the Requirements for the

DEGREE OF DOCTOR OF PHILOSOPHY

Dr. Eyesun Fajei
Department of Pathology and Microbiology at AVC

Supervisory Committee

Dr. David Groman (Chair)
Dr. Mark Fast
Dr, Wenlong Cai
Bradley Haltli
Dr. Fred Kibenge

Examination Committee

Dr. Chelsea Martin (Chair)
Dr. Mark Fast
Mr. Bradley Haltli
Dr. Lisanework Ayalew
Dr. Mike Duffy (UNB) (External examiner)

Immunomodulatory Effects of PACAP in Fish: Administration Route-Dependent Protection Against Bacteria and the Impacts of Stress and Co-exposure

This thesis investigates the immunomodulatory and protective effects of Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP-38) in teleost fish, particularly Nile tilapia (Oreochromis niloticus) and Atlantic salmon (Salmo salar), under pathogenic and environmental stress conditions. PACAP-38, a multifunctional neuropeptide, is known for its antimicrobial, anti-inflammatory, and stress-mitigating properties.

A series of experimental trials evaluated the efficacy of PACAP-38, in both native and modified forms, delivered via various routes including intraperitoneal injection, nasal/gill flushing, and dietary supplementation. In Nile tilapia, intraperitoneal PACAP-38 significantly reduced mortality from Flavobacterium columnare infection and cold stress, while also downregulating inflammatory markers such as il1β. Transcriptomic analysis of gill tissues under cold stress further revealed that PACAP-38 induced dynamic gene expression changes, particularly in pathways related to metabolism, immune regulation, and cellular repair. Systemic administration was found to be more effective than localized delivery.

In Atlantic salmon, feeding with amidated and non-amidated PACAP-38 enhanced survival against Yersinia ruckeri infection. Both forms of PACAP-38 formulated feed influenced expression of key immune genes (e.g., il10, hepcidin, mmp9) and immunoglobulin levels, suggesting modulation of both innate and adaptive responses.

Additionally, the role of environmental stressors, such as harmful algal blooms (Chaetoceros spp.), was assessed in salmon. Exposure led to mild gill damage and increased cortisol levels, particularly when followed by Tenacibaculum maritimum infection, though immune gene expression changes were limited.

Overall, the findings highlight PACAP-38's potential as an immunotherapeutic agent to enhance disease resistance and stress resilience in aquaculture species. Its route-dependent efficacy and pleiotropic effects warrant further investigation to optimize its application in fish health management under intensive farming conditions.

Publications

1.Fajei E, Cai WC, Whyte SK, Despres B, Dixon B, Carpio Y, Estrada M, Fast MD. Assessing the impact of two forms of PACAP-38 (pituitary adenylate cyclase-activating polypeptide) on Nile tilapia (Oreochromis niloticus) immune response following challenge with Flavobacterium columnare. Comparative Immunology Reports. 2024 Dec 1;7:200155.

2. Fajei E, Méndez LR, Whyte SK, Velazquez J, Dantagnan P, Soto-Davila M, Rodríguez-Ramos T, Proskos E, Dixon B, Carpio Y, Estrada M. Investigation of two different PACAP-38 (pituitary adenylate cyclase activating polypeptide) formulated feeds on Atlantic salmon (Salmo salar) immune responses with enteric red mouth disease (Yersinia ruckeri). Comparative Immunology Reports. 2025 Jun 1;8:200221.

3. Fajei E, Whyte SK, Soto-Davila M, Eslamloo K, Groves L, Storey K and Ghanei-Motlagh R, Groman D, Purcell SL, Fast MD. Impact of Co-Exposure to Chaetoceros Spp. And Tenacibaculum Maritimum on Atlantic Salmon (Salmo Salar) Gills. Available at SSRN: https://ssrn.com/abstract=5346055 or http://dx.doi.org/10.2139/ssrn.5346055

4.Whyte SK, Kaur K, Colombo SM, Tibbetts SM, Brocca G, Ghanei-Motlagh R, Fajei E, Soto-Davila M, Fast MD. Effects of dietary inclusion of Antarctic krill (Euphausia superba) meal in low fishmeal diets on Atlantic salmon (Salmo salar L.) growth, nutrient utilization, fillet quality, and wound healing capacity. Aquaculture Reports. 2025 Sep 15;43:102853.

5. Cai W, Zhong L, Parrish K, Kumar S, Eslamloo K, Fajei E, Whyte SK, Purcell SL, Jahangiri L, Li R, Solares AC. Synergies of co-infecting pathogens, sea lice (Lepeophetheirus salmonis) and Moritella viscosa, are impacted by exposure order, and host response to initial infection. Aquaculture. 2024 Oct 15;591:741115.

Presentations

Presentation about" Investigation of two different PACAP-38 formulated feeds on Atlantic salmon (Salmo salar) with Enteric red mouth disease." At the Canadian Society of Zoologists conference, May 7th, 2024, in Moncton, Canada.

Poster Presentation about" Examining two feeds supplemented with PACAP-38 on Atlantic salmon (Salmo salar) responses to Enteric red mouth disease." At the Aquaculture Association of Canada conference, June 2024, in Charlottetown, Canada.

Presentation about" Implication of PACAP-38 (Pituitary Adenylate Cyclase-Activating Polypeptide) administration on Nile tilapia (Oreochromis niloticus) immunophysiology." At Veterinary Vaccine conference, November 30th , 2022, Varadero, Cuba.

Presentation about" Implication of PACAP-38 (Pituitary Adenylate Cyclase-Activating Polypeptide) administration on Nile tilapia (Oreochromis niloticus) immunophysiology." On November 24th , 2022, Havana, Cuba.

Presentation about "Assessing impacts of two forms of PACAP-38 (Pituitary Adenylate Cyclase-Activating Polypeptide) on infectious Nile tilapia (Oreochromis niloticus) immunophysiology". On November 4th, 2022, at Canadian Emerging Scholars Summits (CEVSS), Calgary, Canada.

Presentation about "Possible impacts of PACAP (Pituitary Adenylate Cyclase-Activating Polypeptide) on Nile tilapia (Oreochromis niloticus) immunophysiology." On October 13th, 2022, at the UPEI annual graduate students conference in Charlottetown, PE, Canada.

Presentation about " Immune responses of Flavobacterium columnare-infected Nile tilapia (Oreochromis niloticus) to two forms of PACAP-38 (Pituitary Adenylate Cyclase-Activating Polypeptide) on June 7th, 2022, in NACI workshop, Banff, Alberta, Canada.

Presenting research project (Boosting Nile tilapia immune system using PACAP) at the Annual UPEI Graduate Students Conference on October 13th,2021

Virtual presentation about "Boosting tilapia (Oreochromis niloticus) immune responses using PACAP (Pituitary Adenylate Cyclase Activating polypeptide)." At NACI 2021 workshop

Awards

2023 G. Murray and Hazel Hageman Scholarship, AVC

2022 James E. Bateman Memorial Scholarship in Aquatic Health Research, AVC

2022 nominated for Canadian Emerging Scholars Summits (CEVSS), Calgary, Canada.

Biographical Data

Born in Tehran, Iran.