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Madeira, Portugal
October 4-7, 2021

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ABSTRACTS

VACCINATION OF GILTHEAD SEABREAM (*Sparus aurata*) AFTER ESTROGENIC ORAL MODULATION ALTERS THE GUT ENDOBOLOME AND IMMUNE STATUS VIA GPER1

Isabel Cabas^{1,†,*}, P. Castejón^{1,†}, Victoria Gómez¹, Elena Chaves Pozo², Isabel Cerezo-Ortega³, Miguel Ángel Moriñigo³, Eduardo Martínez Manzanares³, Alfonsa García-Ayala^{1,‡}, Jorge Galindo-Villegas^{4,‡}

¹ Department of Cell Biology and Histology, Regional Campus of International Excellence “Campus Mare Nostrum,” University of Murcia, IMIB, CIBERER, 30100 Murcia, Spain

² Oceanographic Center of Murcia (IEO), Mazarrón, 30860 Murcia, Spain

³ Department of Microbiology, Faculty of Sciences, University of Malaga, Spain

⁴ Faculty of Biosciences and Aquaculture, Nord University, 8049 Bodø, Norway

^{†,‡} These authors contributed equally to this work.

* Email: icabas@um.es

Introduction

In fish culture setting grounds, exogenous steroids input is a matter of concern. Recently, we unveiled that in the gilthead seabream (*Sparus aurata*), the G-protein-coupled estrogen receptor agonist G-1 (G1) and the endocrine disruptor 17 α -ethinylestradiol (EE₂) are potent modulators in polyreactive natural antibodies production. However, the integral role of the microbiota upon antibody production under the effect of EE₂ remains largely unexplored.

Material and Methods

Here, 240 juvenile seabreams continuously exposed for 84 days to oral G1 or EE₂ at a fixed dose (5 μ g/g food) were i.p. vaccinated on day 42 with the model antigen keyhole limpet hemocyanin (KLH). A critical panel of systemic and mucosal immune markers, serum vitellogenin, humoral enzymatic, and bacteriolytic activities were recorded and correlated with the gut bacterial microbiome 16S rRNA status one day post priming (dpp). Besides, 15 dpp animals received a boost to explore the systemic- and mucosal-specific anti-KLH titers production by the end of the trial.

Results and Conclusion

EE₂ but not G1 induced a significant shift in the serum vitellogenin level one dpp. Simultaneously, in the serum and gut mucus of the EE₂ treated group, we recorded significant changes in some immune enzymatic activities. While we only inferred an attenuated profile in the immunized groups. The gut genes qPCR analysis exhibited a related pattern only emphasized by the significant shift on the EE₂ group *illb* expression. The gut bacterial microbiome undergoes dynamic changes in alpha diversity indices, but only with exposure to dietary G1, supporting functional alterations on cellular processes, signaling, and lipid metabolism. By the same token, the immunization in both treated groups decreased the relative abundance of Fusobacteria and remarkably promoted changes in the estrogen-associated bacterial genera. Besides, systemic and mucosal KLH-specific IgM/T titers observed significant changes after 84 days of estrogenic oral administration.

In summary, these are the first results highlighting the intrinsic relationship between estrogens and their associated receptors in the ubiquitous fish immune regulation and the subtle but significant crosstalk with the gut endobolome.

Acknowledgements

This study was funded by Fundación Séneca, Coordination Center for Research, CARM (04538/GERM/06). The Spanish Ministry of Science and Innovation (AGL2008-04575-C02-01 co-funded with Fondos Europeos de Desarrollo Regional/European Regional Development Funds). Ministerio de Ciencia e Innovación and FEDER (AGL2017-85978-C2-1-R). The Fundación Séneca (CARM) (19883/GERM/15).