## Accepted Manuscript

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PII: S0145-305X(18)30294-5

DOI: 10.1016/j.dci.2018.08.001

Reference: DCI 3229

To appear in: Developmental and Comparative Immunology

Received Date: 6 June 2018

Revised Date: 3 August 2018

Accepted Date: 3 August 2018

Please cite this article as: Cabas, I., Chaves-Pozo, E., Mulero, V., García-Ayala, A., Role of estrogens in fish immunity with special emphasis on GPER1, *Developmental and Comparative Immunology* (2018), doi: 10.1016/j.dci.2018.08.001.

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## Role of estrogens in fish immunity with special emphasis on GPER1

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Abstract: It is well accepted that estrogens, the primary female sex hormones, play a 9 key role in modulating different aspects of the immune response. Moreover, estrogens 10 11 have been linked with the sexual dimorphism observed in some immune disorders, such 12 as chronic inflammatory and autoimmune diseases. Nevertheless, their effects are often controversial and depend on several factors, such as the pool of estrogen receptors 13 (ERs) involved in the response. Their classical mode of action is through nuclear ERs, 14 which act as transcription factors, promoting the regulation of target genes. However, it 15 has long been noted that some of the estrogen-mediated effects cannot be explained by 16 these classical receptors, since they are rapid and mediated by non-genomic signaling 17 pathways. Hence, the interest in membrane ERs, especially in G protein-coupled 18 19 estrogen receptor 1 (GPER1), has grown in recent years. Although the presence of nuclear ERs, and ER signaling, in immune cells in mammals and fish has been well 20 documented, information on membrane ERs is much scarcer. In this context, the present 21 22 manuscript aims to review our knowledge concerning the effect of estrogens on fish immunity, with special emphasis on GPER1. For example, the numerous tools 23

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