

Evaluation of Effects of Environmental Pharmaceuticals on Fish Reproduction

Principal Investigator: Kiyoshi SOYANO

Institution: Organization for Marine Science and Technology, Nagasaki University, 1551-7 Taira-machi, Nagasaki City, 851-2213, JAPAN

Tel: +81-95-850-7701 / Fax: +81-95-840-1881

E-mail: soyano@nagasaki-u.ac.jp

Cooperated by: Kochi University, Kyoto University, Tokyo University of Science

[Abstract]

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The environmental pharmaceuticals that are prescribed in Japan and expected to be detected at high concentrations in environmental water are G-protein coupled receptor inhibitors (GPCR inhibitors) and antidepressants. Since these pharmaceuticals act on nerve cells, it is highly likely that they will affect the central nervous system and neuroendocrine system, especially the brain, thereby interfering with normal behavior and physiological functions of fish. Therefore, a study was conducted to understand the dynamics of environmental pharmaceuticals in bodies of water and relate these chemicals to cellular, molecular, and individual responses, as well as to evaluate their effects on the ecosystem. This research was conducted from the perspectives of sub-theme 1, "Analysis of the effects of environmental pharmaceuticals on fish behavior and reproduction," sub-theme 2, "Understanding the actual presence of environmental pharmaceuticals in aquatic environments," and sub-theme 3, "Identification and evaluation of fish biomolecules that are targets of environmental pharmaceuticals.

As a result, 1) an in vitro assay for quantifying the concentration of environmental pharmaceuticals in bodies of water (equivalent quantity) was made possible by using a cell line expressing fish receptors that are a target of pharmaceuticals, and 2) the development of simultaneous analysis using a mass spectrometer, which made it possible to measure the concentrations of environmental pharmaceuticals and some metabolites in bodies of water. This enables efficient analysis of the actual state of environmental pharmaceuticals present in bodies of water. In addition, as a result of analyzing the effects of environmental pharmaceuticals on fish behavior and reproduction, it became clear that 3) swimming and spawning behavior were inhibited by pharmaceuticals targeting monoamine transporters, and 4) reproduction (next-generation production) was affected through a reduction in the number of spawned eggs. In addition, a comprehensive analysis of response genes using pharmaceutical-exposed individuals revealed that 5) some genes increased or decreased by exposure to pharmaceuticals, and that circadian rhythm-related genes, including central clock molecules, in particular may be affected. These results are indispensable for understanding the extent of contamination of environmental pharmaceuticals in rivers, treated wastewater, etc. and the biological effects caused by them, including their mechanisms of action, and have completed the foundation for establishing an Adverse Outcome Pathway (AOP) that includes effects on the ecosystem.

[References]

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