

ANTINEOPLASTIC AGENTS: ENVIRONMENTAL PREVALENCE AND ADVERSE OUTCOMES IN AQUATIC ORGANISMS

Alexis M. Wormington^{1,2}, Maite De María^{1,3}, Hajime G. Kurita^{1,3}, Joseph H. Bisesi Jr^{1,2}, Nancy D. Denslow^{1,3,4}, Christopher J. Martyniuk^{1,3,4,5}

¹Center for Environmental and Human Toxicology, University of Florida, Gainesville, FL, USA

²Department of Environmental and Global Health, College of Public Health and Health Professions, University of Florida, FL, USA

³Department of Physiological Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

⁴University of Florida Genetics Institute, Gainesville, FL, USA

⁵Interdisciplinary Program in Biomedical Sciences Neuroscience, Gainesville, FL, USA

Cancer is the second leading cause of death worldwide, with 9.6 million cancer-related deaths in 2018. The global health burden attributable to cancer has increased over time, rising the prescription of chemotherapeutic drugs. These drugs, known as antineoplastic agents, are designed to disrupt specific cell cycle processes and there is a narrow window of safety between therapeutic and toxic doses. Similar to other pharmaceuticals, antineoplastic agents enter the aquatic environment primarily through human excretion into waste streams. Since many antineoplastics are not adequately removed during wastewater treatment, these compounds can pose a risk to aquatic life. The objectives of this critical review were to investigate the risk of antineoplastics to aquatic species and to summarize the current state of knowledge regarding their levels in the environment. We conducted two separate literature reviews to synthesize global information on environmental prevalence and toxicity of antineoplastics. Based on our review, the antineoplastics most frequently detected in the environment included cyclophosphamide, ifosfamide, tamoxifen, methotrexate and 5-fluorouracil; all are detectable in multiple water sources, including effluent and surface waters. These antineoplastics span three different mechanistic classes, with cyclophosphamide and ifosfamide classified as alkylating agents, tamoxifen as a hormonal agent, and methotrexate and 5-fluorouracil as antimetabolites. Studies that characterize the risk of antineoplastic agents released into aquatic environments are scarce. In this review, we summarize the biological impacts of the most environmentally prevalent antineoplastics on aquatic organisms and propose an adverse outcome pathway for cyclophosphamide and ifosfamide, two highly prescribed alkylating agents with a similar immunotoxic mode of action. Acute and chronic ecotoxicity studies using aquatic models are necessary for risk characterization.

PRESENTER BIO: Hajime Kurita is a PhD candidate in the Department of Physiological Sciences at the College of Veterinary Medicine-UF under the supervision of Dr. Nancy Denslow. Kurita is a Paraguayan Government's scholarship holder from the first cohort of this kind, which was awarded to six people nation-wide.