Detection of novel endocrine-disrupting chemicals in the water

The health risk to humans, aquatic life and fauna, posed by endocrine-disrupting chemicals (EDCs) in our environment, water, food, and consumer products has been underestimated and difficult to measure with currently existing technologies. EDCs interfere with normal function of the endocrine system and have been associated with developmental defects, metabolic disorders, immune dysfunction, and cancer. Detection and monitoring of water sources for steroidal EDCs frequently relies on a laborious analysis of chemical structures using HPLC, MS/GS and related technologies. These are very costly, time consuming and frequently do not lead to identification of a chemical structure due to a natural biodiversity of modifications. Steroid hormones, such as estrogens, have been detected in water sources, and their deleterious effects are well documented. Considering that many natural sterols are rapidly metabolized, their derivatives cannot be easily identified and are not present in the currently existing libraries. Thus, their levels are not monitored or regulated. In addition, it is unclear whether the EDCs detected by chemical methods elicit specific biological responses in mammalian systems. The testing for biological activity of glucocorticoids and many other steroid EDCs had not been previously performed. To overcome these obstacles, we developed a high-throughput assay for biological testing of EDCs using mammalian cell lines that express GFP-tagged nuclear steroid receptor constructs. This assay is based on translocation of a fluorescent marker from the cytoplasm to the nucleus in the presence of the hormone or the contaminant(s). Using this assay, combined with studies on transcriptional activation, we screened water samples collected from 14 states in the US. We found androgen activity in 35% of samples, and a previously unrecognized glucocorticoid (GC) activity in 27% of the samples. Androgen receptor (AR)-dependent transcriptional activation was detected for AR-responsive genes. Glucocorticoid receptor (GR)-dependent transcriptional activation was also detected using several targets. Induction of a circadian rhythm gene, Per1, was detected at concentrations equal to those present in a water sample. This site was positive from both, a sample from extraction of a filter (POCIS membranes) as well as a grab sample obtained several years later. A previous report from China indicated that environmentally relevant concentrations of synthetic GCs have deleterious effects on fish. The anti-inflammatory properties of GCs make them highly prescribed pharmaceuticals and these could readily enter water sources. Moreover, waste water treatment plants (WWTP) are not capable of efficiently removing steroids and it is well documented that anti-inflammatory chemicals are among the most resistant to treatment (30-40% of removal rate). A growing body of epidemiological and animal studies suggests that prenatal and early life conditions contribute to health later in life. Exposures to stress hormones, including glucocorticoids, during the prenatal period have programming effects on the hypothalamic-pituitary-adrenal axis, brain neurotransmitter systems, and cognitive abilities of the offspring.

We conclude that wide-spread contamination with steroids is a possible health hazard not only for the aquatic ecosystems, but may also negatively impact the human population. Our automated, inexpensive and highly reproducible assay for detection of biologically active steroidal EDCs is suitable for a wide application on water and other environmental samples. We are seeking to establish a global screening of water samples and develop standards for safety and monitoring of water contamination with EDCs.

Biography

Varticovski is a Hematologist/Oncologist with over 20 years of clinical and laboratory experience who joined NCI in 2003 where she directed the Preclinical Models Strategy Team, Molecular Targeting Unit, Lung Cancer Stem Cell Core, and participated in clinical trials at the NCI for patients with drug-resistant tumors. She is a member of ASH, ASCO and AACR. Her research made long-standing contributions to cancer drug development, mechanisms of drug resistance, and cancer stem cells. Her current research is in mapping global chromatin landscape by DNaseI hypersensitivity using nuclear receptors as a model.

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