DETECTION OF NOVEL ENDOCRINE-DISRUPTING CHEMICALS IN WATER SUPPLIES

SUMMARY

Testing for biological activity of glucocorticoids and many other steroid endocrine-disrupting chemicals (EDCs) has not been previously performed. An automated, highly reproducible, and low cost assay detects biologically active steroidal EDCs and is suitable for wide application in testing water samples. The National Cancer Institute seeks partners for collaborative co-development research and/or licensing to move this technology into the public domain.

REFERENCE NUMBER

E-269-2011

PRODUCT TYPE

- Devices
- Diagnostics
- Research Materials

KEYWORDS

- Assay
- endocrine-disrupting chemicals
- EDC
- contamination

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

CONTACT

John D. Hewes
NCI - National Cancer Institute
240-276-5515

John.Hewes@nih.gov

DESCRIPTION OF TECHNOLOGY

There is a growing interest in the cancer risk posed by EDCs in our environment. Steroidal EDCs interfere with the normal function of the endocrine system and have been associated with cancer. Currently, detection and monitoring of water sources for steroidal contamination of water relies on a laborious analysis of their chemical structures. Considering that many natural steroids are rapidly metabolized, their derivatives are frequently not present in the currently existing libraries and thus cannot be identified. In addition, it is unclear whether EDCs detected by chemical methods can elicit

specific biological responses in mammalian systems.

Scientists at the National Cancer Institute's Laboratory of Receptor Biology and Gene Expression developed a high-throughput assay for testing biological activity of EDCs using mammalian cells that express GFP-tagged nuclear steroid receptor constructs. This automated assay is based on translocation of a fluorescent marker from the cytoplasm to the nucleus in the presence of a ligand that interacts with a specific receptor. The workflow utilizing for image-based screening of environmental contaminants with glucocorticoid activity using Perkin Elmer Opera Image Screening System is shown below:

Using this assay and studies of transcriptional activation, we screened water samples collected from 14 states in the US and found androgen activity in 35% of samples, and a previously unrecognized glucocorticoid (GC) activity in 27% of the samples. Androst-4-en-3,6-dione was identified in one of the samples. Androgen receptor (AR)-dependent nuclear translocation and transcriptional activation was confirmed for two AR-responsive genes, NKX3.1 and RHOU. NKX3.1 is a homeobox gene frequently deleted in prostate cancers, and RHOU is implicated in epidermal growth factor receptor signaling and cell migration. Glucocorticoid receptor (GR)-dependent transcriptional activation was detected using several targets. Induction of a circadian rhythm gene, Per1, was confirmed at concentrations equal to those present in a water sample. This water site was positive in a sample obtained by extraction of a filter (POCIS membranes), as well as a grab water sample obtained several years later.

POTENTIAL COMMERCIAL APPLICATIONS

- Automated, highly reproducible, and low cost assay detects biologically active steroidal EDCs and is suitable for wide application in testing water samples.
- Testing for biological activity of many other steroid EDCs has not been previously performed

COMPETITIVE ADVANTAGES

- Biological activity is determined more efficiently than chemical analysis
- High Specificity and selectivity

INVENTOR(S)

Gordon Hager (NCI) and Diana Stavreva (NCI)

DEVELOPMENT STAGE

- Discovery (Lead Identification)

PUBLICATIONS

Stavreva DA, George AA, Klausmeyer P, Varticovski L, Sack D, Voss TC, Schiltz RL, Blazer VS, Iwanowicz LR, Hager GL. Sci Rep. 2012;2:937

PATENT STATUS

- **U.S. Issued:** 9,040248 (26 May 2015)

- **Foreign Filed:** Applications filed in Europe and Japan

THERAPEUTIC AREA

- Cancer/Neoplasm
- Hormonal Systems, Endocrine, and Metabolic Diseases