XDS Inc.

(Xenobiotic Detection Systems, Inc.)

is proud to present the:

LUMI-CELL® ER assay

for Estrogenic Endocrine Disrupters
High Through-Put Reporter Gene Assay

A Message from Our President...

We at Xenobiotic Detection Systems, Inc. would like to take this opportunity to thank you for expressing interest in our company and our products. Our primary goal is to use the latest advances in biotechnology to develop accurate and cost-effective assays for environmental testing. This is becoming increasingly important as both government and industry realize that frequent biologically active testing is necessary to safeguard the environment and human health.

XDS is proud to offer you the **LUMI-CELL® ER** assay. The LUMI-CELL® ER assay is the culmination of over 30 years of collaborative research in biotechnology and environmental testing. The result is a test for estrogenic endocrine disruptor compounds that offers fast results and superior accuracy at only a fraction of the cost of standard animal testing and high resolution mass spectrometry analysis.

XDS is committed to providing quality analysis and developing biological assays to their fullest potential. I am confident that our testing methods will meet your expectations. We look forward to fulfilling your testing needs.

Sincerely,

George Clark, Dr. P.H.
President

George Clark brings over 30 years of experience to XDS. His education includes a Ph.D. in toxicology from the University of North Carolina at Chapel Hill and Masters degrees in immunology from the University of California at Berkeley and biochemistry from North Carolina State University. He has previously worked for GlaxoSmithKline, and the National Institute of Health.

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Mission Statement:

XDS exists to develop and advance the commercial acceptance of biological methods that will facilitate assessment of environmental and human health risks.

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I. Why are we concerned with estrogenic endocrine disruptor chemicals?

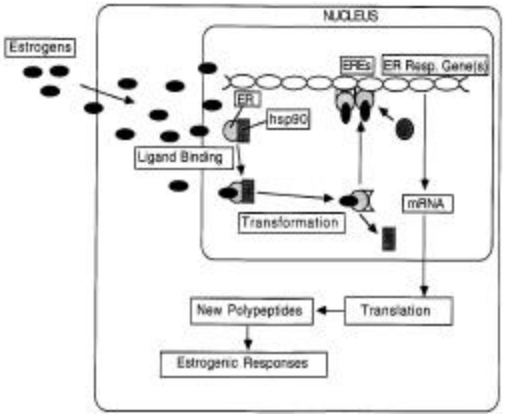
Estrogenic compounds can have a significant detrimental effect on the endocrine and reproductive systems of both human and other animal populations. Studies by Jefferson et al, (2002) have shown a strong association between several EDCs (17ß-Estradiol, DES, Zeralanol, Zeralenone, Coumestrol, Genistein, Biochanin A, Diadzein, Naringenin, Tamoxifin) and estrogenic activity via uterotropic assay, cell height, gland number, increased lactoferrin, and a transcriptional activity assay using BG1Luc4E2 cells (provided by Xenobiotic Detection Systems International Inc. (XDS), Durham, NC). Some other examples of the effects of these endocrine (hormone) disruptor chemicals (EDCs) are: decreased reproductive success and feminization of males in several wildlife species; increased hypospadias along with reductions in sperm counts in men; increase in the incidence of human breast and prostate cancers; and endometriosis. Because these chemicals are ubiquitous, highly lipophilic, and often chlorinated, it ensures their persistent presence in the environment (i.e. water supply, soil, river sediment) resulting in their bioaccumulation in the food chain. Taken together, these data show a pattern of food chain contamination and the detrimental effects of EDCs, therefore understanding the estrogenic potency of these and other potential EDCs, is extremely important.

II. U.S. Government Involvement:

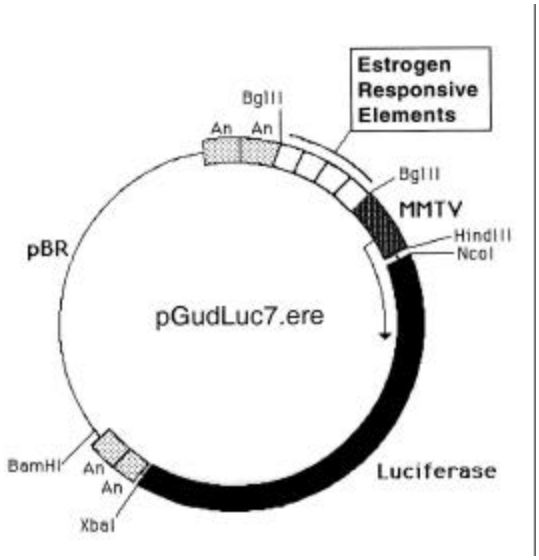
The association between the exposure and bioaccumulation of EDCs and their adverse effects on human and wild life populations has raised worldwide concern. These concerns over the effects of environmental EDCs, led to the passage of U.S. Congressional legislation (Food Quality Act of 1996 and Safe Water Reauthorization Act Amendments of 1996), which mandated the EPA to investigate the exposure to environmental EDCs. Based on this mandate, the EPA established the Endocrine Disruptor Steering and Testing Advisory Committee (EDSTAC), a committee charged with defining the course of action to accomplish this goal. EDSTAC submitted their report to the U.S. Congress in August of 2000. Subsequent to this report, the EPA established the Endocrine Disruptor Screening Program (EDSP) within the agency. This EDSTAC report proposed that the EPA pursue the standardization and validation of Tier I (screening) and Tier II (testing) assays specific and sensitive for EDCs, which may act as agonists and/or antagonists. Therefore, there is a growing need for a fast, reliable high-throughput system for the screening of known and potential environmental contaminants, which act to disrupt normal endocrine homeostasis.

III. Detection Mechanism Development:

In order to detect the endocrine disrupting potency of samples and compounds using a bioassay system, XDS has developed the LUMI-CELL® ER bioassay. BG-1 (human ovarian carcinoma) cells were stably transfected with an estrogen-responsive luciferase reporter gene plasmid (pGudLuc7ere) containing the estrogen responsive element (ERE) and luciferase reporter gene. The resulting cell line (BG1Luc4E2), used in the LUMI-CELL® ER estrogenic cell bioassay system, responds in a time, dose-dependent and chemical-specific manner with the induction of luciferase gene expression in response to exposure to estrogen and estrogenic chemicals in a high-throughput screening (HTPS) format.



Molecular mechanism for estrogen hormone action



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IV. Uses

The LUMI-CELL® ER bioassay has been shown to be effective on many matrices: food, feed stuffs, biologicals, water, pharmaceuticals, cosmetics, and many more. This assay is able to detect total estrogenic activity for a sample. The LUMI-CELL® ER bioassay can be used for detection of agonist or antagonist estrogenic activity or both. The assay has a detection limit of ~ 0.04 pg/g.

V. Pricing

The cost of the LUMI-CELL® ER bioassay analyses are far lower than HR GC/MS fees and substantially reducing the need and cost of any animal study. There is also a considerable savings in time as well with other assays taking weeks, months and even years for some animal studies. These substantial savings make the LUMI-CELL® ER bioassay an excellent screening tool and allow researchers, laboratories, and government agencies the option to screen many samples or compounds in a very short time. This assay should ultimately be able to reduce, refine and in many instances replace the use of animals in testing.

V.I Selected References

1. Rogers, J. M. and M. S. Denison (2000). "Recombinant cell bioassays for endocrine disruptors: development of a stably transfected human ovarian cell line for the detection of estrogenic and anti-estrogenic chemicals." In Vitr Mol Toxicol 13(1): 67-82.
2. Jefferson, W. N., E. Padilla-Banks, et al. (2002). "Assessing estrogenic activity of phytochemicals using transcriptional activation and immature mouse uterotrophic responses." J Chromatogr B Analyt Technol Biomed Life Sci 777(1-2): 179-89.
3. John D. Gordon, Andrew C. Chu, Michael D. Chu, Michael S. Denison and George C. Clark. (2004). "Detection of Estrogen Receptor Endocrine Disruptor Potency of Commonly Used Organochlorine Pesticides Using The LUMI-CELL™ ER Bioassay". Organohalogen Compounds, 169:2967-2973.
4. Gordon, J., A. Chu, et al. (2003). "Validation of THE LUMI-CELL™ ER Recombinant Bioassay for Rapid Evaluation of Chemicals for Potential Estrogenic Activity." Organohalogen Compounds 65: 78-81.

Assay	Examples	Advantages	Disadvantages
Chemical	HPLC GC/MS	• Highly specific • Allows for Quantification	• Multiple assays requited to test for known estrogenic compounds. • Can not test for compounds not previously shown to posess estrogenic activity. • Does not give total estrogenic activity of sample. • May result in high percentage false negative results.
In Vivo	Uterotrophic assay, Immature mouse/rat, Ovariectomized mouse/rat, Vaginal opening endpoint	• Detectes agonist and antagonist activity • Measures several endpoints • Highly sensitive.	• Expensive • Uses many animals • Time consuming, • Cannot identify individual estrogenic compounds.
In Vitro	MCF-7 YES (yeast E screen) assay	• No animals required • Easy to use • Economical • Highly sensitive.	• May not detect all estrogenic compounds, which could result in high percentage false negative results. • Cannot identify individual estrogenic compounds.
	LUMI-CELL â ER	**• No animals required • Easy to use • Detects total estrogenic activity • Can be used to detect agonist and/or antagonist activity • Economical • Highly Sensitive.**	**• Cannot identify individual estrogenic compounds.**

* Thigpen, J.E. et. al. (2004). Selecting the Appropriate Rodent Diet for Endocrine Disruptor Research and Testing Studies. ILAR Journal 45(4): 401-416.

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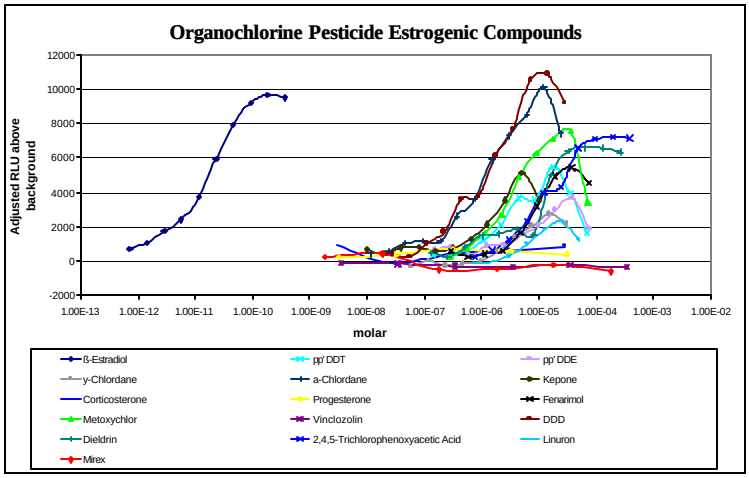
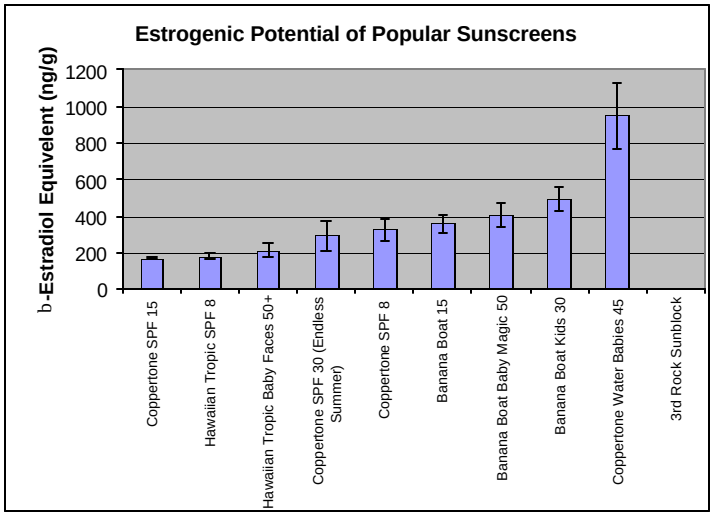
The LUMI-CELL® ER assay

An effective tool for testing:

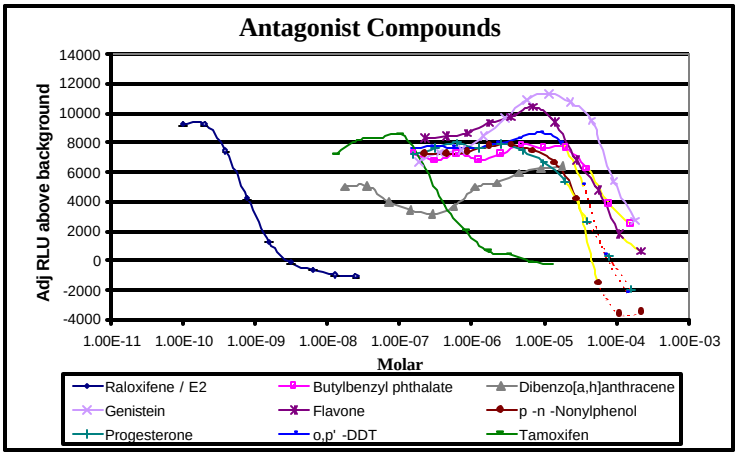
Pesticides



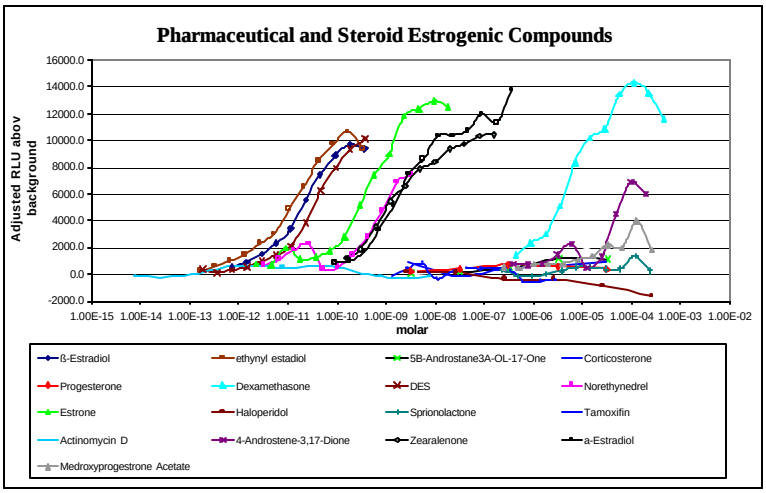
Sunscreens and Cosmetics



Antagonist Dose Response



Pharmaceutical and Steroid Products



and much more!!!

For additional information and research abstracts please contact Xenobiotic Detection Systems, Inc. at www.dioxins.com or

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