Bench to Bayou: Environmental Analysis of Endocrine Disrupting Effects from Hydrocarbon Contaminants in the Ecosystem

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Overview

Abstract

Chaired by President Clinton, the National Science and Technology Council (NSTC) is the principal means for the President to establish national goals and coordinate science, space, and technology policies across the federal government. The NSTC, in identifying its national research needs, recognized the growing body of evidence suggesting that chemicals in the environment can disrupt the endocrine system of animals (i.e., wildlife and humans) and adversely impact the development of these species.

In response, the NSTC formed the Endocrine Disruptors Working Group (EDWG) to ensure timely scientific advances in the field of environmental endocrine disruptors (environmental hormones) and guide national policy on the issue through collaborations between the federal government, academia, and the private sector. Research areas identified by the EDWG include human health, ecological effects, and exposure assessment for determination of the likely risk resulting from endocrine-disrupting chemicals.

In order to address these research needs, the Department of Energy (DOE), is collaborating with the Environmental Protection Agency, Department of the Interior, Department of Health and Human Services (National Institute of Environmental Health Sciences), Department of Commerce (National Oceanic and Atmospheric Administration), Department of Agriculture, Department of Defense, Centers for Disease Control and Prevention, Food and Drug Administration, and the Office of Science and Technology Policy on an innovative, multi-disciplinary research effort to address the remaining scientific uncertainties in the field of environmental endocrine disruptors. The DOE, in particular, funds research on endocrine disrupting chemicals as part of its effort to characterize and reduce the environmental and public health threats from its facilities. This study reports the progress of 1.5 years of a three-year grant awarded to the Tulane/Xavier Center for Bioenvironmental Research (CBR) and represents the DOE Environmental Management Science Program's only research on the impacts of endocrine-disrupting chemicals.

The objective of this project is to determine how environmental contaminants of concern to DOE, namely hydrocarbons, can act as hormones or anti-hormones in different species present in aquatic ecosystems. The CBR has over five years of expertise in developing model aquatic ecosystems for evaluation of environmental problems relevant to DOE activities. In addition, the CBR's director has been recognized for decades as the international pioneer in the field of environmental endocrinology. Species of particular focus in this study are those which can serve as sentinel species (e.g., amphibians) and, thus, provide early warning signals for more widespread impacts on an ecosystem and its wildlife and human inhabitants.

The activities employed by this project to determine these impacts include development of biotechnology screens (in vitro), animal screens (in vivo), and other analyses of aquatic ecosystem biomarkers of exposure. The results from this study can elucidate how chemicals in the environment, including those from DOE activities, can signal (and alter) the development of a number of species in aquatic ecosystems. These signals can have detrimental impacts not only on an organismal level, but also on community, population, and entire ecosystem levels, including humans.

PUBLICATIONS AND PRESENTATIONS

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Jin, L., D.Q. Tran, C.F. Ide, J.A. McLachlan, and S.F. Arnold. 1997. Several synthetic chemicals inhibit progesterone receptor-mediated transactivation in yeast. *Biochemical and Biophysical Research Communications* 233:139-146.

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Oberdörster , E. 1998. Panelist for Discussion Session on Endocrine Disruptor Detection and Risk Assessment. 37th Annual Society of Toxicology meeting, Seattle, WA. March 1998

Oberdörster, E. 1997. Decline of Macro- and Meio-faunal Communities in Bayou Trepagnier, LA University of New Orleans, Mississippi River Water Quality Conference: Clean Enough? New Orleans, LA. September 21, 1997.

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Oberdörster E and J.A. McLachlan. Interaction of PAHs and phytochemicals with Ecdysone receptor using a multi-tiered approach. Submitted to *Toxicology and Applied Pharmacology* 1998 (submitted).

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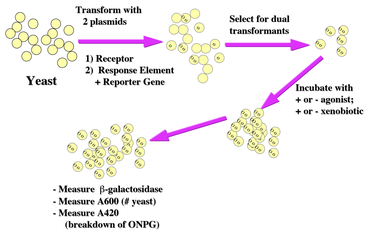
Oberdörster, E., J.A. McLachlan. 1998. Interaction of PAHs, PCBs and phytoestrogens with the Drosophila Ecdysone Receptor in vitro. *Toxicologist*. 37(1):239.

Tran, D.Q., C.F. Ide, J.A. McLachlan, and S.F. Arnold. 1997. The anti-estrogenic activity of selected polynuclear aromatic hydrocarbons in yeast expressing human estrogen receptor. *Biochemical and Biophysical Research Communications* 229:102-108.

Molecular Toxicology



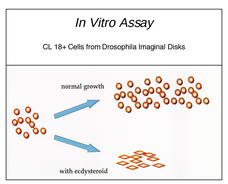
Hormone Receptor	ACTIVITY	
	Mimic	Block
Estrogen Receptor		2,3 benzofluorene benxo[a]pyrene 6-hydroxychrysene dibenz[a,h]anthracene
Progesterone Receptor		6-hydroxychrysene 1-hydroxypyrene
Glucocorticoid Receptor		2,3 benzofluorene 6,8 dimethylbenzanthracene
Thyroid Receptor	naphthalene	

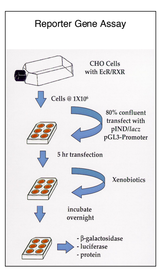
Receptors Involved with Differentiation

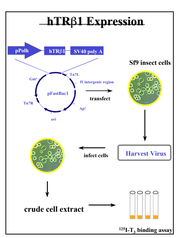
Thyroid hormone (in vertebrates) and the molting hormone, ecdysone (in invertebrates), regulate the differentiation processes that occur in the transformation of larvae into juvenile and adult animals. These two hormone systems were the focus of study for 1997-98.

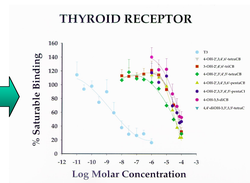
Disruption of thyroid hormone binding to it's receptor (TR) by chlorinated compounds was investigated using a recombinant human TR and purified human serum transport proteins.

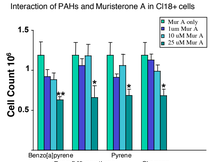
Interaction of PAHs with ecdysone-dependent reporter gene expression was investigated using a stably transfected CHO cell line, and ecdysone-dependent cell differentiation was investigated in a *Drosophila* imaginal disk cell line.

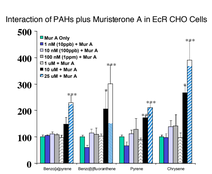


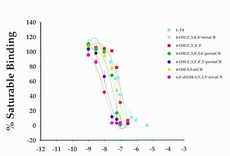




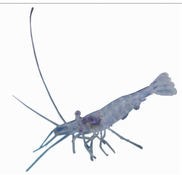




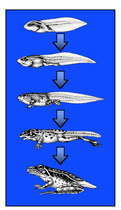




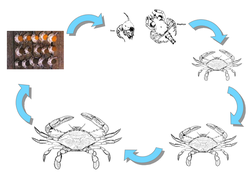
Organismal Toxicology



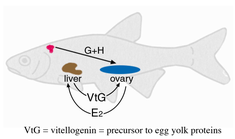
Development in Invertebrates and Vertebrates as a Model for Endocrine Disruption



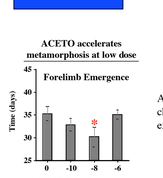
Thyroid hormone mediates the process of tadpole metamorphosis. Environmental cues, including temperature and chemicals can interact with internal thyroid hormone levels to delay or accelerate metamorphosis. Forelimb emergence is used as an indicator of metamorphic climax.



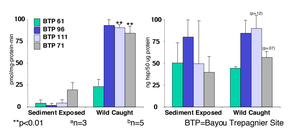
Control of Reproduction in Fish



VtG = vitellogenin = precursor to egg yolk proteins

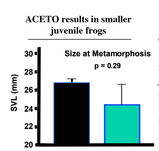


Acetochlor (ACETO) is a chlorinated herbicide used extensively on corn.

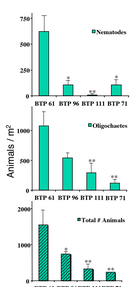


VtG Induction: Environmental Estrogen Exposure

Treatment of male or juvenile fish with estrogen or an environmental estrogen induces the egg yolk precursor protein vitellogenin.



Chronic exposure to 10 nM ACETO accelerates metamorphosis and juvenile frogs are smaller. Smaller frogs generally have decreased survivorship and performance.

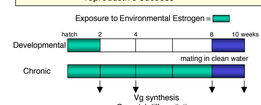


The impact of polycyclic aromatic hydrocarbon (PAH) and lead contamination on benthic community structure and grass shrimp (*Palaeomonetes* spp.) biochemical markers were investigated in a Bayou which has been heavily contaminated since the 1920s. The benthic invertebrate community has long been used as an indicator of pollution, and we found that the benthic community had decreased species richness as well as decreased numbers of individuals along a contamination gradient.

Grass shrimp caught in the wild showed a contaminant-gradient increase in heat shock protein 63 and cytochrome P450 1A (as measured by ECOD metabolism). Grass shrimp exposed to contaminated sediment in the laboratory showed a trend for elevated ECOD metabolism, however individual variation was too large for statistical significance. Heat shock proteins were also not significantly elevated in laboratory exposed shrimp. This lack of significant increase in these two biomarkers could be due to the short exposure regime. A long-term chronic sediment exposure is currently underway and will be finished 8/5/98. Heat shock proteins and CYP1A will be measured in these shrimp.

Ongoing Research

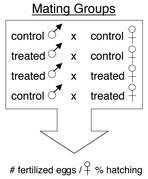
Hypothesis: Vg concentration and changes in sex differentiation are correlated with decreased reproductive success



Critical period for sex differentiation occurs during the first two weeks after hatch

Measurement of reproductive success

Mating Groups



- President Clinton's National Science and Technology Council has determined federal agency evaluation of ecological and human impacts of endocrine disrupting chemicals (environmental hormones) as a priority.
- Chemicals in the environment can disrupt the endocrine system of wildlife and humans and adversely impact the development of these species.
- DOE funds research on endocrine disrupting chemicals as part of its effort to characterize and reduce the environmental and public health threats from its facilities.
- The Tulane/Xavier Center for Bioenvironmental Research (CBR) represents the DOE Environmental Management Science Program's only research on the impacts of environmental hormones.
- The CBR has over five years of expertise in developing model aquatic ecosystems for evaluation of environmental problems relevant to DOE activities.
- The CBR's director has been recognized for decades as the international pioneer in the field of environmental endocrinology.
- The CBR is utilizing its existing expertise to determine how environmental contaminants of concern to DOE, namely hydrocarbons, can act as hormones or anti-hormones in different species present in aquatic ecosystems.

Chronic Exposure of Shrimp

8 week exposure of shrimp to PAHs
–molting pattern
–lipovitellin levels
–CYP 1A levels
–reproductive success