Environmental Chemicals as Transcriptional Modulators: Understanding Health Effects as a Function of

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V(A). Planned Program (Summary)

1. Name of the Planned Program

Environmental Chemicals as Transcriptional Modulators: Understanding Health Effects as a Function of

V(B). Program Knowledge Area(s)

1. Program Knowledge Areas and Percentage

KA Code	Knowledge Area	%1862 Extension	%1890 Extension	%1862 Research	%1890 Research
723	Hazards to Human Health and Safety			100%	
	Total			100%	

V(C). Planned Program (Inputs)

1. Actual amount of professional FTE/SYs expended this Program

Year: 2007	Extension		Research	
	1862	1890	1862	1890
Plan	0.0	0.0	2.5	0.0
Actual	0.0	0.0	1.0	0.0

2. Actual dollars expended in this Program (includes Carryover Funds from previous years)

Extension		Research	
Smith-Lever 3b & 3c 0	1890 Extension 0	Hatch 69626	Evans-Allen 0
1862 Matching 0	1890 Matching 0	1862 Matching 560000	1890 Matching 0
1862 All Other 0	1890 All Other 0	1862 All Other 974470	1890 All Other 0

V(D). Planned Program (Activity)

1. Brief description of the Activity

The research will utilize several model systems and several disease endpoints to understand the changes cell signaling induced in different target tissues by chemicals. Investigators worked to identify biomarkers that are expressed in response to a set of relevant model toxicants, to generate stable reporter animals using gene regulatory elements. In this research subprogram, the investigator has demonstrated that the zebrafish is an outstanding model to unravel interactions between Aryl Hydrocarbon Receptor (AHR) activation and other signal transduction pathways. The investigator is also working to screen a wide range of commonly manufactured nanomaterials to determine their potential interactions with biological systems. Ultimately, many relationships between nanomaterial composition and effects will be defined; a first step in being able to predict nanomaterial-biological interactions. In the immune supression subprogram, the researcher has investigated the underlying mechanisms of immune suppression by which natural bioactive chemicals in food protect against human diseases such as cancer, inflammation and microbial infection, specifically focusing on the ability of three phytochemical groups: chlorophyll and its derivatives, indole-3-carbinol, and tea polyphenols. Investigators in the maternal diet subprogram have examined the potential for three of the major phytochemicals known to prevent cancer in the fetus by maternal exposure to chemical carcinogens. They are using a mouse model to study the potency and efficacy of the phytochemicals groups, I3C, green tea and chlorophyllin, as transplacental chemoprotective agents. Results in this program have been disseminated through publications, presentations at local, regional, national and international meetings, and integrated into the toxicology curriculum.

2. Brief description of the target audience

Scientists, Medical organizations

V(E). Planned Program (Outputs)

1. Standard output measures

Target for the number of persons (contacts) reached through direct and indirect contact methods

	Direct Contacts Adults	Indirect Contacts Adults	Direct Contacts Youth	Indirect Contacts Youth
Year	**Target**	**Target**	**Target**	**Target**
Plan	100	0	0	0
2007	15	0	0	0

2. Number of Patent Applications Submitted (Standard Research Output)

Patent Applications Submitted

Year	**Target**
Plan:	0
2007:	0

Patents listed

3. Publications (Standard General Output Measure)

Number of Peer Reviewed Publications

	Extension	**Research**	**Total**
Plan			
2007	0	6	6

V(F). State Defined Outputs

Output Target
Output #1

Output Measure

SCHOLARLY excellence in referred articles, book chapters, and books; participation on professional boards and panels, as well as science panels.

Year	Target	Actual
2007	8	10

Output #2

Output Measure

EFFECTS ON AND PROTECTION OF HUMAN HEALTH For a diverse set of developmental toxicants, identify, validate, localize and characterize specific responsive genes, which have the potential to serve as biomarkers Develop a number of transgenic lines that show changes in reporter gene expression in response to toxicants Assessed risk of dioxins to humans Understand downstream pathways and novel antagonists for Ah receptor Understand immunosuppressive effects of Ahr activation Explore potential role of Ahr in thymocytes and T cells as a factor in the development of T cell lymphomas Examine chlorophylls/chlorophyllin absorption and transport across biological barriers and explore mechanism(s) of action in a mouse transplacental carcinogenesis model. Examine pathology and possible mechanisms of absorption action, primarily by employing a genomics approach. Examine dose response with DBP and I3C, examination of additional PAHs including some environmental mixtures such as diesel exhaust, coal tar and urban dust.

Year	Target	Actual
2007	7	10

V(G). State Defined Outcomes

O No.	Outcome Name
1	Characterize and model • Characterization of specific responsive genes to toxicants • Model system to evaluate dioxin toxicity to humans • Role of human AhR polymorphisms and role of Arnt in mediating dioxin toxicity • Understand downstream effectors of and Ahr antagonists to relieve dioxin toxicity • Examine mechanisms that underlie the immune suppression induced by TCDD • Novel role for Ahr in the induction of Treg cells • Identify agents, mechanisms of action, and dose response for reducing fetal risk from toxic chemicals
2	Develop transgenic lines of zebrafish for response to toxicants
3	Advance scientific knowledge Evaluate gene expression changes in control and toxicant exposed animals over time Ability to conduct genetic or small molecule screens for modifiers of the toxic response Risk assessment of various hydrocarbons to humans Development of agents to treat accidental human dioxin exposure or deliverate poisoning Modulate maternal diet to reduce the risk to the fetus from toxic chemicals

Outcome #1

1. Outcome Measures

Not reporting on this Outcome for this Annual Report

2. Associated Institution Types

3a. Outcome Type:

3b. Quantitative Outcome

Year	Quantitative Target	Actual

3c. Qualitative Outcome or Impact Statement

Issue (Who cares and Why)

What has been done

Results

4. Associated Knowledge Areas

KA Code	Knowledge Area

V(H). Planned Program (External Factors)

External factors which affected outcomes

Appropriations changes
Public Policy changes
Competing Public priorities

Brief Explanation

V(I). Planned Program (Evaluation Studies and Data Collection)

1. Evaluation Studies Planned

Other ()

Evaluation Results

{No Data Entered}

Key Items of Evaluation

{No Data Entered}