

We have a logo!

## Superfund Research Program University of California Davis

**Dr. Bruce D. Hammock, Director**

### Research Update No. 5

Dec 2012

#### Introduction

The primary purpose of this Research Update is to inform staff in State and Federal government involved in legislation and regulation of toxic substances in the environment about research results emanating from the UC Davis Superfund Program. Additionally, others involved in the mitigation and assessment of toxic substances in the environment may find some value in these updates. The goal of these updates is to provide information about the National Institutes Environmental Health Sciences (NIEHS) funded Superfund Research Program (SRP)<sup>1</sup> that has been at UC Davis for the past 26 years. This national program was initiated to address human and environmental problems such as Love Canal, NY where improper disposal of chemical wastes occurred or Times Beach where oil containing chlorinated dioxins was sprayed as a dust suppressant. The mission of the SRP is stated below<sup>2</sup>

*"Since its inception in 1987, the SRP has applied a multidisciplinary approach to basic research focused to provide a solid foundation which environmental managers and risk assessors can draw upon to make sound decisions related to Superfund and other hazardous waste sites. We believe that basic research plays a crucial role in addressing challenges posed by environmental contamination such as health risks, toxicity, exposure predictions, fate and transport, and the need for cost-effective treatments for hazardous waste sites found throughout the United States"*

The Superfund Program at UC Davis<sup>3</sup> has provided basic research information to address these needs. We continue to develop innovative, novel technology to investigate human exposures, environmental fate and transport of toxic substances, as well as cost-effective methods for the treatment and remediation these chemicals. The success of our program is due to the breadth of the multidisciplinary approach to these complex scientific issues of chemical exposure that continue to pose hazards to human and environmental health.

This program exports its findings beyond academic journals and publications to other venues and audiences. As required by the NIEHS, we have concerted efforts to effectively partner with government, transfer technology to commercial ventures, or communicate with broader public audiences for the purpose of improving human and environmental health. Research Translation of scientific results is important for society to understand the goals of the SRP in the mitigation of toxic substances in the environment.

#### This newsletter highlights three relevant areas of research from the program:

- 1) Alternative testing methods: protecting health, one cell line at a time
- 2) Minute materials can have a large impact on health -- young respond differently than their elders
- 3) Antimicrobial agent, triclosan, does more than kill bacteria; it impairs heart and skeletal muscle function

<sup>1</sup> Name changed from Superfund Basic Research Program to Superfund Research Program in 2008

<sup>2</sup> [www.niehs.nih.gov/research/supported/srp/about/index.cfm](http://www.niehs.nih.gov/research/supported/srp/about/index.cfm)

<sup>3</sup> [www-sf.ucdavis.edu/](http://www-sf.ucdavis.edu/)

## 1) Alternative testing methods: protecting health, one cell line at a time

### *Background*

We might be familiar with food alternatives such as milk/dairy alternatives and peanut/tree nut alternatives, but science also offers an alternative to animal testing: cell lines. Instead of using whole animals as a proxy for understanding how humans *might* react to a specific insult, cell lines can provide highly useful information, while also being cost-effective, practical, and expedient. A particular cell line, developed by UCD-SRP scientist Dr. Michael Denison, has been internationally accepted to identify substances with *in vitro* estrogen activity. Chemical substances that interact with hormone receptors mimic or block normal hormone function, causing adverse health effects, such as reproductive and developmental problems in humans and wildlife. Identifying these chemicals in the environment is the first step in preventing these human health problems.

The recombinant cell line and its accompanying protocol is referred to as BG1Luc Estrogen Receptor (ER) Transactivation (TA) bioassay. The US Federal Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) evaluated the scientific validity of the BG1Luc ER TA bioassay and recommended it could be used to identify substances that activate or inhibit human ER activity *in vitro*. In developing the recommendations, ICCVAM considered comments from its scientific advisory committee, an independent scientific peer review panel, and members of the public. ICCVAM promotes the scientific validation and regulatory acceptance of safety testing methods and strategies that more accurately assess the safety and health hazards of chemicals and products and that reduce, refine, or replace animal use. This November, the BG1Luc-ER-TA bioassay was officially adopted as an accepted method for detection of estrogenic chemicals by the OECD (Organization for Economic Cooperation and Development) in OECD test guidelines TG455 and TG457 and the assay may now be used for regulatory purposes in 34 member countries. The bioassay has now been included in the USEPA Endocrine Disruptor Screening Program and the NIEHS/NTP Tox21 test method panel.

### *Impact*

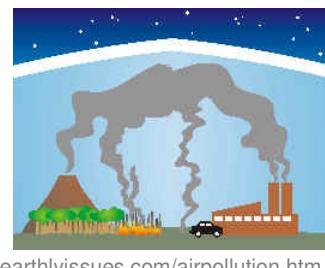
The need for alternatives to the traditional use of animals in toxicity testing was officially recognized by the U.S. government in 1993. Cell lines offer the advantages of being more reliable, economical and efficient in screening for estrogen activity when compared to animal models used to accomplish the same result. In addition, cell lines serve as a preliminary screening mechanism to determine if animal testing is needed and which animal model should be used to gain the most insights. NIEHS/NTP Director Dr. Linda Birnbaum, wrote "These alternative test methods should be routinely considered and used where appropriate, in order to avoid or minimize animal use." "NIEHS and the NTP will ... promote and encourage the consideration and use of the BG1Luc ER TA for research and testing where determined appropriate." This is a considerable highlighted achievement from the UCD-SRP, which included years of work to develop the assay, and many more years of work to validate the test for international and governmental agencies acceptability.

## 2) Minute materials can have a large impact on health -- young respond differently than their elders

### *Background*

Airborne particulate matter (PM) pollution is all around us and it may be harmful to our health. PM can consist of soot, metals, allergens, and liquid particles and when breathed in can exacerbate asthma and other respiratory ailments.

Superfund Researchers from UC Davis have developed a laboratory based PM devoid of metals and allergens that can be replicated to study health effects of specific PM components in animal models. The researchers, led by Dr. Laura Van Winkle, exposed rats - young and grown - to a dose comparable to the levels of PM found in downtown Fresno, California. The young neonatal rats were more susceptible to the pollution than the adult rats, based on biological changes exhibited, such as significant increases in markers of cellular toxicity in the conducting airways.



[earthlyissues.com/airpollution.htm](http://earthlyissues.com/airpollution.htm)

### *Impact*

An increase in the severity of many airway diseases, such as bronchitis and asthma, has been linked to either acute or chronic exposures to PM in young children. "This study adds to the evidence that young children may

be uniquely susceptible to PM," said Dr. Ian Kennedy. Their unique susceptibility emanates from the fact that they are more aerobically active outdoors and consume more oxygen per body weight than adults. This study provides strong evidence that adult animals would generate misleading results if trying to identify PM exposures in susceptible populations, such as young children.



### 3) Antimicrobial agent, triclosan, does more than kill bacteria, it impairs heart and skeletal muscle function

#### Background

Triclosan (TCS) was first used in hospitals as an antibacterial surgical scrub. Since then, its use has spread quickly to schools, households, and businesses. According to Dr. Isaac Pessah, the principal investigator for the study of TCS effects on heart and skeletal muscles, "Triclosan is found in virtually everyone's home and is pervasive in the environment." TCS is problematic because of its tendency to accumulate in the environment and subsequently our bodies. The diagram below illustrates the 'life-cycle' of TCS.

Investigators tested the effects of TCS *in vivo* (in live mice and fish) and *in vitro* (in test tubes and live cells from heart and skeletal muscle). The results (published in the Aug 2012 issue of the *Proceedings of the National Academy of Sciences of the USA*) showed impaired muscle contractions of isolated skeletal muscle fibers and heart muscle cells. Mice had a reduction in grip strength for up to an hour after exposure and a reduction in cardiac function; and larval fathead minnows exhibited significantly reduced swimming activity.

#### Impact

The studies have helped define a mechanism by which TCS weakens cardiac and skeletal muscle contractility. They demonstrated the idea in cardiac and skeletal muscle cells and then recreated the same effect - reduced functionality - in live animals. Overall, this means that by using TCS, you are potentially impacting muscular health, especially if you already have a preexisting muscle disorder.

Environmentally speaking, most of the products that contain TCS are used in a way that results in them being washed down the drain.... with every shower, every hand wash, every dish cleaning. Wastewater treatment does not remove all of the chemical. Triclosan then enters our waterways and is transported widely throughout the environment, where it is toxic to aquatic wildlife.

Victory! It is studies like this that we hope agencies and manufacturers take notice of. Johnson & Johnson has recently decided to remove triclosan along with other potentially harmful chemicals from all of their products.

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This newsletter continues to evolve to improve its intended purpose. Therefore, we value critique so that in the future it will improve and therefore better meet the needs of the recipients. Some areas on which we would like comment are content, effectiveness of communication and how it can build interactions and relationships with others outside the UC Davis Superfund Research Program. Please share this Research Update with your colleagues who may have an interest in the results of our research.

For more information about the UC Davis SRP, please contact:

Candace Spier, Research Translation Coordinator, [crspier@ucdavis.edu](mailto:crspier@ucdavis.edu) or (530) 752-8465