

HOFFMAN PROGRAM 2015-2016 REPORT

MARYLIN B. HOFFMAN PROGRAM ON CHEMICALS AND HEALTH
HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
[HTTP://SITES.SPH.HARVARD.EDU/HOFFMAN-PROGRAM/](http://sites.sph.harvard.edu/hoffman-program/)



HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH



PROGRAM STAFF

To coordinate collaborative events and facilitate successful research activities, we have built a strong team with great leadership, diverse research background, and experienced administrative skills.

Leadership



JOSEPH BRAIN
Professor



JOHN SPENGLER
Professor

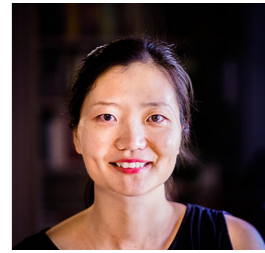
Research



DIANA CEBALLOS
Visiting Scholar



MEMO CEDEÑO LAURENT
Research Fellow



ZHAO DONG*
Research Associate
(*author of this report)

Administrative



JOAN ARNOLD
Program
Coordinator



LISA BOEHM
Program
Coordinator (alumni)



JULIE GOODMAN
Pilot Program
Manager



From right: John Spengler, Joan Arnold, Joseph Brain, Memo Cedeño Laurent, Lisa Boehm, Zhao Dong.

PROGRAM REPORT 2015-2016

HOFFMAN PROGRAM ON CHEMICALS AND HEALTH

The mission of the Hoffman Program on Chemicals and Health is to advance the understanding of environmental and chemical intolerance in people and to reduce the risk of contaminant exposures.

The Hoffman Program was founded in 2014 with a generous bequest from Ms. Marilyn B. Hoffman. It is dedicated to the study of chemical and particle exposures and their subsequent human health effects. We focus on environmental and chemical intolerance, commonly known as multiple chemical sensitivities (MCS), also known as toxic-induced loss of tolerance (TILT), or DELTA. This last term, DELTA, emphasizes the ways in which earlier exposures alter responses to subsequent exposures.

*John Spengler & Joseph Brain
Program Directors*



P.06

Program website

We have created a program website to provide relevant scientific information and program updates to the public.

P.08

Seminar Series

We host a seminar series, featuring leading scientists on various topics related to chemical exposures and MCS/TILT/DELTA.

P.10

Pilot Grant Program

The Hoffman Program offers a Pilot Grant Program to promote scientific understanding and public awareness of chemical exposures.

P.16

Research Activities

We conduct research to advance understanding of MCS/TILT/DELTA and the health consequences of chemical exposures

PROGRAM WEBSITE

<http://sites.sph.harvard.edu/hoffman-program/>

We have developed a program website under the Harvard domain to archive and disseminate scientific information relevant to MCS/TILT/DELTA.



Opening Video for the Hoffman Website featuring program directors Spengler and Brain



A tribute page dedicated to Ms. Marilyn B. Hoffman

For the convenience of our website visitors who could not join the seminar series in person, lectures were filmed and posted on the website.



Dr. Richard Doty's talk on Neurological Diseases and Olfactory Function



Research Projects

The website features ongoing research projects funded by the Hoffman Program, and publications resulting from these projects.



Chemical & Health Blog

We share our own research stories and ideas, and provide updates on our events and activities through our Chemicals & Health Blog.



Pilot Grant Announcement and Application

Opening of the pilot grant is announced yearly on the website, and applications can be submitted online. Grantees are also featured on the website.



Other Related Resources

The website hosts a library of scientific articles and information relevant to chemical sensitivities, including related publications, useful tools and links.

SEMINAR SERIES

2015 SPEAKERS



Dr. Halûk Özkaynak

February 26, 2015

Modeling Human Exposures to Chemicals of Concern for Rapid Prioritization and Screening

Formerly a Sr. Scientist with the U.S. Environmental Protection Agency, Office of Research and Development/National Exposure Research Laboratory.



Dr. Arlene Blum

April 10, 2015

Flame Retardants and "Six Classes" of Harmful Chemicals: How Science Can Impact Policy

Visiting Scholar in Chemistry, University of California, Berkeley Executive Director, Green Science Policy Institute



Dr. Richard Doty

October 8, 2015

Neurological Diseases and Olfactory Function

Professor of Otorhinolaryngology, School of Medicine, University of Pennsylvania



Dr. Christopher Lowry

November 4, 2015

Environmental Microbial Exposure and Mental Health

Associate Professor, Department of Integrative Physiology and Center for Neuroscience, University of Colorado Boulder



Dr. Torben Sigsgaard

December 17, 2015

Studies of Environmental Exposures in a Human Exposure Chamber

Professor, Department of Public Health, Section of Environment, Occupation & Health, University of Aarhus, Denmark



HOFFMAN PILOT GRANTEES 2015



EILEEN MCNEELY

Dr. Eileen McNeely currently conducts research and teaches at Harvard. She is co-director of the SHINE program at Harvard Center for Health and the Global Environment.



RAMON MOLINA

A research scientist at Harvard, Dr. Molina's interest and expertise is pulmonary toxicology and pharmacokinetics of inhaled and ingested particles and other toxins in the environment.



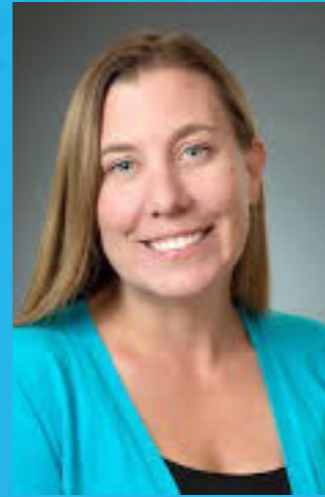
DIDDIER PRADA

Dr. Prada is currently a research associate at Harvard. He is interested in environmental toxicology, epigenetics, and their relationship with human diseases, especially those age-related.



MARC WEISSKOPF

Dr. Weisskopf is an associate professor at Harvard. His research interests focus on how environmental factors affect the nervous system, as well as the epidemiology of neurologic disorders.



ROBIN DODSON

Dr. Dodson graduated from Harvard and is currently a research scientist at the Silent Spring Institute, with expertise in exposure assessment and indoor air pollution.

HOFFMAN PILOT PROJECTS

- 1 Investigation of Airline Crew Health Complaints Before and After New Uniforms (Eileen McNeely)
- 2 DELTA: Do Repeated Pulmonary Exposures to Zinc Induce Sensitization or Adaptation? (Ramon Molina)
- 3 Breast Milk Exosomes and Mechanisms of Immunotoxicity from PFCs and PCBs (Didier Prada)
- 4 Environmental Risk Factors for Autism in Israel (Marc Weisskopf)
- 5 Healthy Green Campus Project (Robin Dodson)

DEPARTMENT OF ENVIRONMENTAL HEALTH

ABOUT THE HOFFMAN PILOT GRANT PROGRAM

The Hoffman Program offers a Pilot Grant Program to promote scientific understanding and public awareness of chemical exposures, with a focus on multiple chemical sensitivities (MCS), also known as toxicant-induced loss of tolerance (TILT) or DELTA.

The Pilot Grant Program aims to: stimulate research on MCS/TILT/DELTA; advance understanding of health consequences of chemicals and other toxins in the environment; identify and promote actions to protect vulnerable populations.

Ordinarily, grants of up to \$25,000 are offered once a year. Funds are typically used for feasibility studies and to produce preliminary data to compete for independent funding.

// We live in a chemical soup.

-- Linda Burnbaum
Director, National Institute of Environmental Health Sciences

Project 04: Environmental Risk Factors for Autism in Israel (PI: Marc Weisskopf)



This study capitalizes on a unique international setting—Israel—where we have total population data on ASD from the Israeli National Insurance Institute and advanced models of exposure to PM and NO₂ (a marker of traffic-related pollution), to contrast different pollutants, explore specific exposure windows, and consider susceptible groups (e.g. male fetuses) to an extent not previously done.

HOFFMAN PILOT PROJECTS 2015

Project 01: Investigation of Airline Crew Health Complaints Before and After New Uniforms (PI: Eileen McNeely)



Alaska Airlines (AA) Flight Crew reported health complaints such as skin rash, eyes, ears, nose and throat irritation, hair loss, fatigue, chemical sensitivity, and thyroid disease, after the introduction of new crew uniforms in 2011. We have collected ~700 health surveys from Alaska crew on each of three occasions in 2007, 2013, and 2015, and plan to conduct a multivariate analysis of health changes from the uniform switch.

Project 02: DELTA: Do Repeated Pulmonary Exposures to Zinc Induce Sensitization or Adaptation? (PI: Ramon Molina)



Zinc, an important component of air pollution particulate matter as well as of a variety of nano-enabled products, will be used to develop a reproducible animal model will be developed to demonstrate either adaptation or sensitization phenomenon and explore the mechanisms responsible. Differences between single and multiple exposures and then to characterize the metabolic and cellular changes will be explored.

Project 03: Breast Milk Exosomes and Mechanisms of Immunotoxicity from PFCs and PCBs (PI: Diddier Prada)



Exosomes, tiny endosome-derived membrane vesicles containing proteins, bioactive lipids and nucleic acids, have been recently identified in breast milk, and may represent a novel signaling system for immune communication between the mother and the child. We will characterize exosomes in the Faroe Islands birth cohort and determine if their changes may reflect maternal exposures and predict immune development in children.

PROJECT 05: HEALTHY GREEN CAMPUS PROJECT

PI: Robin Dodson (in collaboration with John Spengler's research group)

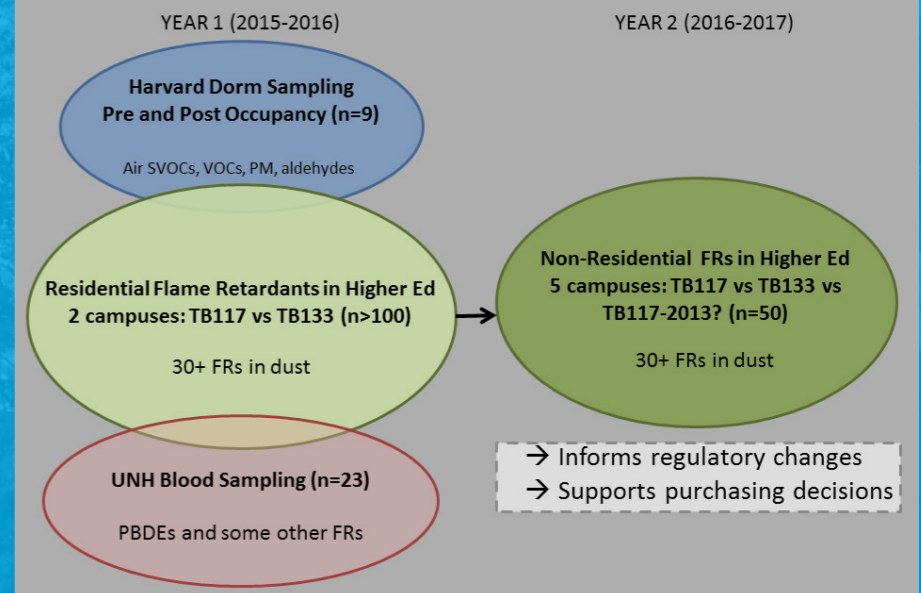
The Healthy Green Campus project is a collaborative project with Silent Spring Institute, Harvard Center for Health and the Global Environment, and Harvard Office for Sustainability. The goal is to integrate human health and chemicals into sustainability programs in higher education. With support from the Hoffman Program, we are studying flame retardant exposures on college campuses as our first chemical case-study since strategies to reduce exposure to these chemicals are emerging and research suggests that levels indoors are influenced by local flammability standards and manufacturing processes. We continue to engage with the Boston Fire Department and the Boston City Council, among others, to evaluate the impact of Boston's current fire safety standards. A project website was created in spring 2015: www.healthygreencampus.org

PRELIMINARY FINDINGS

In our first year, we collected over 100 dust samples (targeting 54 flame retardant chemicals and 7 legacy organic chemicals) from residential spaces on 2 New England college campuses adhering to different furniture flammability standards. One campus adheres to California TB133 (higher FR quantities) and the other to TB117 (lower FR). Data analysis is currently being done. For year two the sampling efforts have expanded to five campuses in the New England area, and now include non-residential spaces. This second phase will look at the changes in flame retardant concentrations after some of the sampled spaces go through an interior renovation process in the next 12 months.

The work of Silent Spring has transcended beyond campuses. Their work with the Boston City council has reflected in the change of Boston's fire code. Boston was the only major city in the U.S. enforcing flammability standard TB133, which required the use of chemicals in furniture even for buildings with automatic sprinklers. Thanks to their tireless efforts, Boston City Councilors passed a bill to amend the code, allowing hospitals, schools, colleges and other public buildings with sprinkler systems to use furniture free of toxic flame retardant chemicals.

Healthy Green Campus Workflow



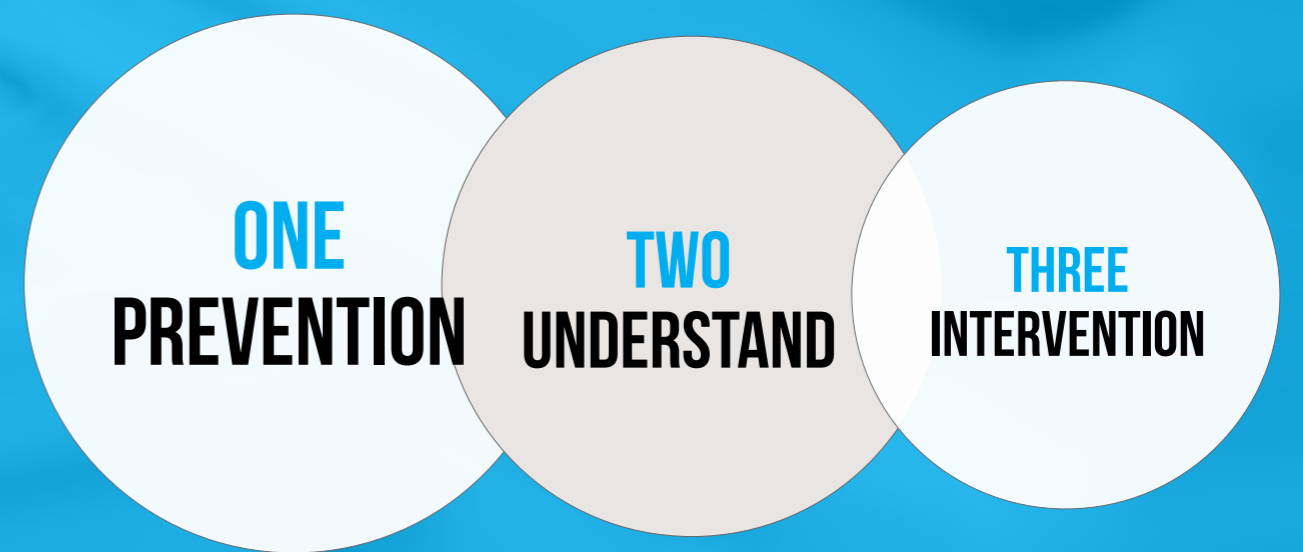


We are developing a three phase research approach to study environmental sensitivities. First, we are studying environmental conditions and mechanisms that may increase the risk of developing environmental sensitivities in healthy individuals. Second, we will study patients with environmental sensitivities to understand underlying mechanisms that may help us with developing interventions and treatments. What we learn from our studies with healthy individuals and patients will help us develop and assess the effectiveness of interventions to prevent or mitigate environmental sensitivity symptoms.

FOUR-YEAR RESEARCH PLAN



THREE-PHASE RESEARCH APPROACH



01 HEALTHY INDIVIDUALS

Studying environmental conditions and mechanisms affecting the development of environmental sensitivity.

02 MCS PATIENTS

Studying mechanisms affecting the triggering of environmental sensitivity symptoms.

03 IMPROVING SYMPTOMS

Studying the development and effectiveness of interventions to prevent or reduce environmental sensitivity symptoms.

ABOUT THE STUDY

This research study will explore how stress caused by social and environmental factors can interact with chemical exposures and affect our body. Chemical exposures will include those encountered at work and the use of personal care products. We will document stresses in early life as well as work, school, and life stress. Recent studies have shown that exposure to stress early in life may increase the risk of chronic illness later in life and there has been documentation that many environmentally sensitive individuals relate to traumatic experiences early in childhood. We are particularly interested in understanding how the interactions of stress and chemicals make us more susceptible to inflammation, and how inflammation may accelerate the development of environmental sensitivity symptoms.

WHY NURSES?

Nurses provide an ideal study population to assess environmental sensitivities as they often encounter chemical exposures during their work activities along with high levels of stress.

PHASE I: THE NEWS STUDY EL PASO, TX

The Hoffman team has embarked on a 5 year longitudinal epidemiological cohort (Nurse Engagement and Wellness Study, or NEWS) of student nurses in collaboration with the University of Texas El Paso (UTEP), School Of Nursing, titled "Environmental Sensitivities Student Nurses Study: Assessing Chemical and Stress Exposures and Environmental Sensitivities in Student Nurses." Approximately, 1000 students will be enrolling in this study at UTEP. Student nurses will be followed for two years during the student nursing program and one year as professional nurses. Student nurses are starting to be enrolled in the study Spring 2016.

PHASE II:

COLLABORATION IN DENMARK

We started a collaboration with the researchers at the Danish Research Center for Prevention and Health, Aarhus University and the University of Copenhagen.



Denmark is one of the few countries in the world that has established a research center dedicated to the study of chemical sensitivities. Moreover, their universities and research centers have established a multidisciplinary team of experts in areas such as environmental health, neuroscience, and biostatistics.



The wide range of their areas of expertise reflects on the hypotheses they are currently investigating in already finalized cohort studies. For the Hoffman program, the opportunity to participate in the analysis of existing data represents a unique chance to catalyze our research objectives.



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- Environment and Society
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- Topics in Environmental Central and Eastern Europe

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OUR PROPOSED STUDY OBJECTIVES

Aim 1: Elaborate a summary of epidemiology measures for MCS: Create a definition of MCS by combining the reporting of trigger groups, organ system reactions, and the level of impact in daily activities, and use the definition to estimate the incidence by age category and gender

Aim 2: Explore the association between triggers and symptoms, and identify mediation effects by characteristics of social dynamics performance: Estimate the association between triggers grouped by material classes and index of symptoms grouped by organ systems, compare associations with non-MCS patients, and identify which behavioral mechanisms influence the associations

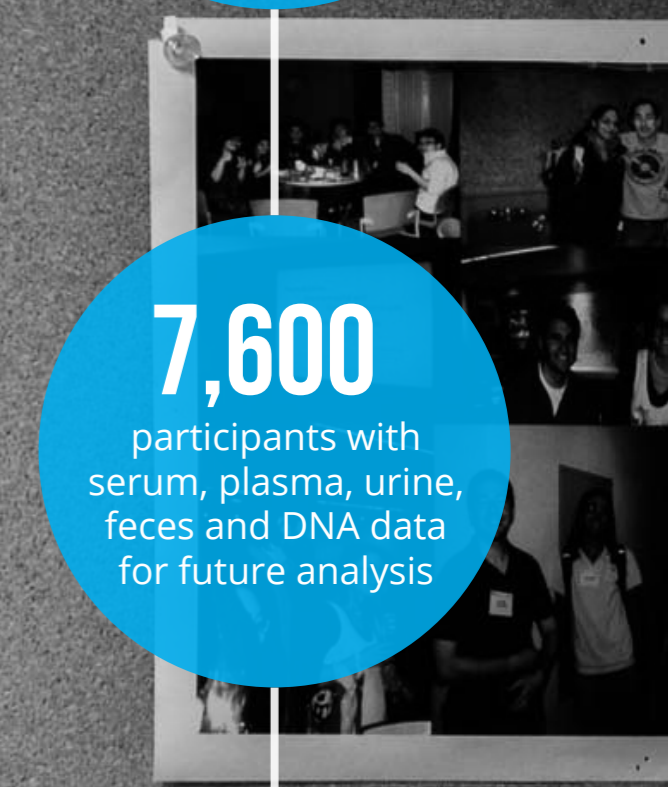
Aim 3: Quantify changes in MCS status through time and compare the effectiveness to improve quality of life of different adaptation strategies: Estimate changes in MCS status over time, and evaluate if improvement of quality of life is differentially associated with life-limiting measures versus active coping measures

Aim 4: Evaluate and use key questions from the Danish study in a chemical exposure assessment module of the Nurses Health Study III, a longitudinal cohort study with more than 40,000 nurses enrolled



10,000

survey participants on chemical sensitivities, comorbidities, and life adversity measures



7,600

participants with serum, plasma, urine, feces and DNA data for future analysis

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ANNOUNCEMENT

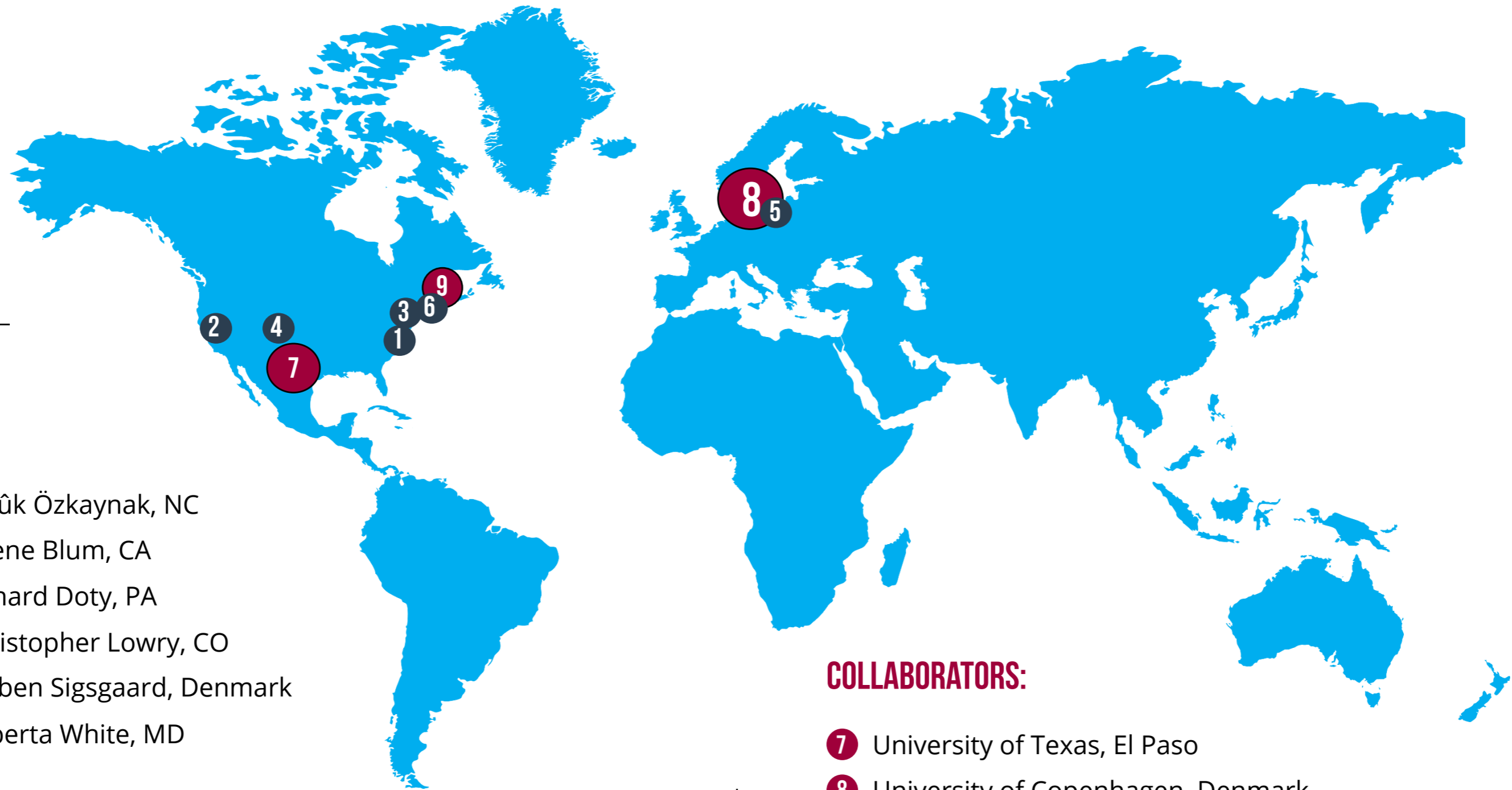
...PH students and faculty are invited to attend the seminar of ... Wagner
Ph.D. Program in Biological Sciences in Public Health

Friday, May 7, 2015
2:30-5:30PM
FXB 301

"From Neural Stem Cells to Children: Secreted Phosphoprotein 1 in Lead Neurotoxicity"

Dissertation Advisors:
Quan Lu, Ph.D.
Associate Professor of Environmental Genetics and Pathophysiology

OUR ACTIVITIES AND CONNECTIONS



SPEAKERS:

- 1 Dr. Halûk Özkaynak, NC
- 2 Dr. Arlene Blum, CA
- 3 Dr. Richard Doty, PA
- 4 Dr. Christopher Lowry, CO
- 5 Dr. Torben Sigsgaard, Denmark
- 6 Dr. Roberta White, MD

COLLABORATORS:

- 7 University of Texas, El Paso
- 8 University of Copenhagen, Denmark
- 9 Silent Spring Institute, MA

2014

2015

2016

2017

2018

As an overview, in the year 2015 we have invited leading scientists from different parts of the country and of the world to speak on various topics related to chemical exposures and MCS/TILT/DELTA, and have made plans to collaborate with researchers and physicians in future events and projects at various regions. We hope to expand our connections, leverage national and international collaborations, and enlarge our impacts in this research field in the years to come.

FUTURE DIRECTIONS:

- Phase II:**
1. Collaborate with MCS patient groups and organize events
 2. Analysis of clinical datasets on MCS patients
- Phase III:**
1. Studies on possible interventions (mindfulness, diet, etc.)
 2. Citizen science approaches to effectively cope with MCS

LABORATORY RESEARCH FROM THE BRAIN LAB

01 ANIMAL MODELS

The Brain Lab is known for developing animal models for studying toxicological and physiological effects of inhaled chemicals, particulates, and microbes.



02 SENSITIZATION OR ADAPTATION

Of particular interest to the group is to understand what determines whether a series of exposures will lead to sensitization or adaptation.

AUTOMATIC GAMMA COUNTER

This machine conducts radiochemical detection and measurement and can be used to measure radiolabeled toxins fed to animals in toxicological studies.



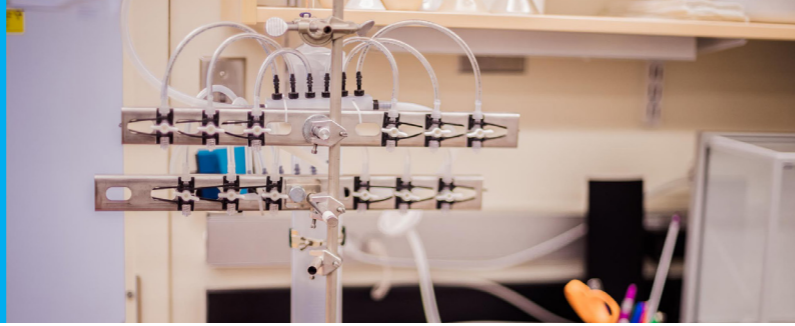
MICE CAGE

This cage can be used to collect urine and feces samples from mice or rats while the animal receives feeds dosed with environmental toxins.



AUTOMATED MICROPLATE READING SYSTEM

This instrument can detect biological, physical, or chemical reactions of multiple samples in microtiter plates, and is very commonly used in toxicological research.

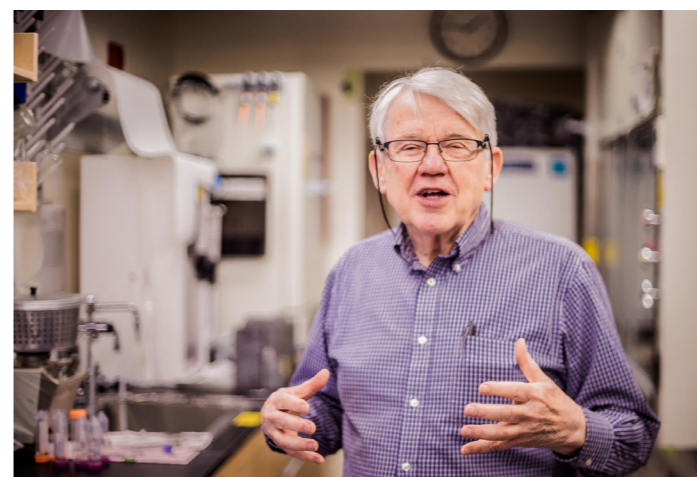


LUNG LAVAGE APPARATUS

This device was designed and created by the Brain Lab to perform lavage and aeration of twelve tiny lungs from mice or rats at a time.

03 MOLD EXPOSURE

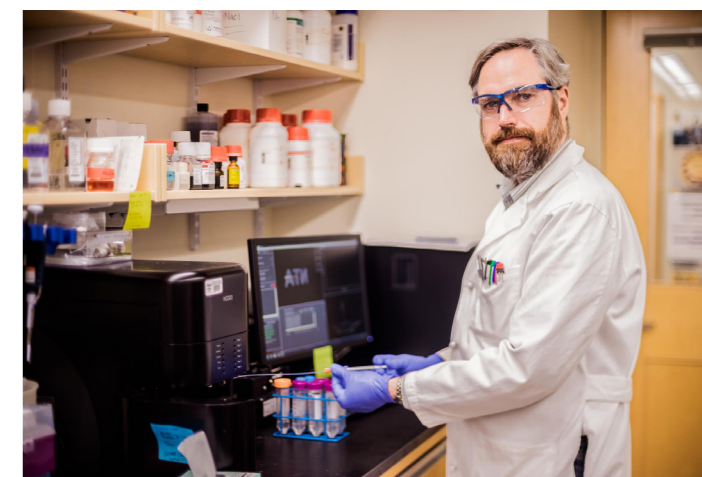
A focus of the research at the Brain Lab is how exposures to mold, especially chronic exposures, can alter immune responses in animals and humans.



Prof. Joseph Brain, introducing his lab for toxicological research using animals.

04 RESPIRATORY RESPONSE

Studies at the Brain Lab extend from the deposition of inhaled particles in the respiratory tract to their clearance by respiratory defense mechanisms.



Thomas Donaghey, Senior Researcher, working in the Brain Lab.

Recent Publication 1:

Environmental Mold and Mycotoxin Exposures Elicit Specific Cytokine and Chemokine Responses

Jamie H. Rosenblum Lichtenstein, Yi-Hsiang Hsu, Igor M. Gavin, Thomas C. Donaghey, Ramon M. Molina, Khristy J. Thompson, Chih-Lin Chi, Bruce S. Gillis, Joseph D. Brain

PLOS ONE 10(5): 2015.

The chemokine and cytokine profiles from patients with a history of mold exposure were significantly different from those of unexposed controls, demonstrating that chronic mold exposures induced changes in inflammatory and immune responses to specific mold and mycotoxin challenges.

Recent Publication 2:

Repeated Mouse Lung Exposures to *Stachybotrys chartarum* Shift Immune Response from Type 1 to Type 2

Jamie H. Rosenblum Lichtenstein, Ramon M. Molina, Thomas C. Donaghey, Yi-Hsiang H. Hsu, Joel A. Mathews, David I. Kasahara, Jin-Ah Park, Andre Bordini, John J. Godleski, Bruce S. Gillis, Joseph D. Brain

American Journal of Respiratory Cell and Molecular Biology 55(4): 2016.

Rats chronically exposed to mold showed profound changes in cytokine production, metabolites, and inflammatory patterns than unexposed controls. This repeated exposure model can more realistically characterize responses to mold.

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