PROPOSED

State of California
AIR RESOURCES BOARD

Are Adverse Health Effects from Air Pollution Exposure Passed on from Mother to Child?

RESEARCH PROPOSAL

Resolution 15-14

May 21, 2015

Agenda Item No.: 15-4-1

WHEREAS, the Air Resources Board (ARB or Board) has been directed to carry out an effective research program in conjunction with its efforts to combat air pollution, pursuant to Health and Safety Code sections 39700 through 39705;

WHEREAS, a research proposal, number 2785-282, titled "Are Adverse Health Effects from Air Pollution Exposure Passed on from Mother to Child?" has been submitted by the University of California, Davis, for a total amount not to exceed $330,483;

WHEREAS, the Research Division staff has reviewed Proposal Number 2785-282 and finds that in accordance with Health and Safety Code section 39701, the results of the study will contribute to the development of health-protective air quality standards by providing insight into whether epigenetic changes, and changes in lung function and immune response, that result from air pollution exposure can be transmitted to offspring who have not undergone the exposure; and

WHEREAS, in accordance with Health and Safety Code section 39705, the Research Screening Committee has reviewed and recommends funding the Research Proposal.

NOW, THEREFORE BE IT RESOLVED that the Air Resources Board, pursuant to the authority granted by Health and Safety Code section 39700 through 39705, hereby accepts the recommendations of the Research Screening Committee and staff and approves the Research Proposal.

BE IT FURTHER RESOLVED that the Executive Officer is hereby authorized to initiate administrative procedures and execute all necessary documents and contracts for the Research Proposal as further described in Attachment A, in an amount not to exceed $330,483.

ATTACHMENT A

"Are Adverse Health Effects from Air Pollution Exposure Passed on from Mother to Child?"

Background

There is suggestive evidence from epidemiologic and animal studies that air pollution exposure during early life could lead to health impacts later in life. While environmental exposures do not alter an individual's genetic code, recent evidence suggests that environmental exposures can induce changes in how genes function. These epigenetic changes can be passed on to offspring, who then have the same change in responses as their parent, without having experienced the exposures. A previously funded Board study of nonhuman primates exposed to high PM2.5 enriched with wildfire smoke during infancy found persistent changes in lung function and reduced production of markers of immune response to microbial challenge compared to animals of the same age which had not been exposed. The finding of a persistent change in both lung and immune function long after exposure returned to typical levels suggests that epigenetic changes occurred in the study animals that led to a less robust response to microbial challenge. These results have public health significance, in that animals, and by extension humans, who have reduced responses to microbial challenge are at increased risk of contracting infectious diseases. If this risk can be transmitted to offspring who have not undergone the exposure, the implication is that disease burden can be maintained long after exposures have significantly declined in unexposed individuals.

Objective

The project will determine whether: 1) the modulated peripheral blood immune function response previously observed in the 2008 animals remains, and whether the same response is evident in the animals' unexposed offspring; 2) parameters of lung health (volume, density, obstruction) that were compromised in the 2008 animals continue to be compromised and whether the same response is evident in the animals' unexposed offspring; and 3) peripheral blood epigenetic changes in the form of histone modifications are evident in the 2008 animals and their unexposed offspring.

Methods

Animals will be brought from their colony into the laboratory one time. There will be the following animal groups, all exclusively raised and housed in outdoor colonies:

1. Female animals born between April 1-June 15 2008 (2008 females; n=30)
2. Female offspring of 2008 females (n=15)
3. Male offspring of 2008 females 8 (n=15)
4. Female animals born between April 1-June 15 2009 (2009 females; n=30)
5. Female offspring of 2009 females (n=15)
6. Male offspring of 2009 females (n=15)

While in the laboratory, the animals will be sedated and undergo lung imaging studies to assess lung volumes and structure, and blood will be drawn for assessment of immune responses of red blood cells to microbial challenge, using biochemical assays, and for epigenetic assays. The epigenetic assays will be performed using comprehensive nano-liquid chromatography tandem mass spectrometry. The investigator will evaluate the medical histories of the animals that also participated in the earlier study to determine whether there is a relationship between the changes in lung and immune function observed in the previous study and subsequent health. All tests proposed are minimally invasive. The research involves only blood samples and lung function tests.

Expected Results
The investigator anticipates that the offspring animals will have lung and immune function values that mirror their mother's. This would indicate that air pollution-induced changes in lung and immune function can persist in the population, even in individuals that did not experience sufficient exposure to induce these effects.

Significance to the Board
A previously funded Board study of nonhuman primates exposed to high PM2.5 enriched with wildfire smoke during infancy found persistent changes in lung function and reduced production of markers of immune response to microbial challenge compared to animals of the same age which had not been exposed. This research will provide insight into whether epigenetic changes and changes in lung function and immune response that result from air pollution exposure can be transmitted to offspring who have not undergone the exposure. The results will contribute to development of health-protective ambient air quality standards.

Contractor:
University of California, Davis

Contract Period:
24 months

Principal Investigator (PI):
Lisa A. Miller, Ph.D.

Contract Amount:
$330,483

Basis for Indirect Cost Rate:
The State and the UC system have agreed to a ten percent indirect cost rate.

Past Experience with this Principal Investigator:
Dr. Lisa Miller has worked at the UC Davis Primate Center for many years where she has performed and published a number of studies related to lung and immune function. She was the PI for the study on which this study is based. The prior study was well

conducted, and the PI was responsive and timely in her interactions with ARB staff. She has all of the requisite skills needed to successfully complete this project.

Prior Research Division Funding to the University of California, Davis:

Year	2014	2013	2012
Funding	$ 2,249,136	$ 1,131,716	$ 4,949,363

BUDGET SUMMARY

Contractor: University of California, Davis

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DIRECT COSTS AND BENEFITS				
1.	Labor and Employee Fringe Benefits	$	126,252	
2.	Subcontractors	$	0	
3.	Equipment	$	0	
4.	Travel and Subsistence	$	0	
5.	Electronic Data Processing	$	0	
6.	Reproduction/Publication	$	0	
7.	Mail and Phone	$	0	
8.	Supplies	$	103,837[1]	
9.	Analyses	$	70,350[2]	
10.	Miscellaneous	$	0	
	Total Direct Costs			$ 300,439
INDIRECT COSTS				
1.	Overhead	$	30,044	
2.	General and Administrative Expenses	$	0	
3.	Other Indirect Costs	$	0	
4.	Fee or Profit	$	0	
	Total Indirect Costs			$ 30,044
TOTAL PROJECT COSTS				**$ 330,483**

[1] Supplies and materials for cell culture studies ($26,400); ELISA analyses ($9,000); DNA analysis supplies and reagents ($4,600); costs for use of animals, veterinary care, lung imaging studies, and animal anesthesia ($63,837).

[2] Quantitative image analysis of the lung imaging data ($15,000); analysis of gene activation pathways ($37,350; and epigenetic changes in blood cells ($18,000).