State of California

AIR RESOURCES BOARD

Effects of Ultrafine Particulate Matter Exposure in an Animal Model of Neurodegenerative Disease

RESEARCH PROPOSAL

Resolution 14-20

July 24, 2014

Agenda Item No.: 14-6-1

WHEREAS, the Air Resources Board (ARB) 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 2776-279, titled "Effects of Ultrafine Particulate Matter Exposure in an Animal Model of Neurodegenerative Disease," has been submitted by the University of California, Los Angeles; and

WHEREAS, the Research Division staff has reviewed Proposal Number 2776-279 and finds that in accordance with Health and Safety Code section 39701, research is needed to explore how ultrafine particles could contribute to Parkinson's disease in a mouse model;

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

> Proposal Number 2776-279 titled "Effects of Ultrafine Particulate Matter Exposure in an Animal Model of Neurodegenerative Disease," submitted by the University of California, Los Angeles, for a total amount not to exceed $497,821.

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 Research Division staff and approves the following:

> Proposal Number 2776-279 titled "Effects of Ultrafine Particulate Matter Exposure in an Animal Model of Neurodegenerative Disease," submitted by the University of California, Los Angeles, for a total amount not to exceed $497,821.

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 effort proposed herein, and as described in Attachment A, in an amount not to exceed $497,821.

I hereby certify that the above is a true and correct copy of Resolution 14-20 as adopted by the Air Resources Board.

Tracy Jensen, Clerk of the Board

"Effects of Ultrafine Particulate Matter Exposure in an Animal Model of Neurodegenerative Disease"

Background

Numerous epidemiological and toxicological studies have demonstrated that exposure to ambient particulate matter (PM) is associated with increased cardiopulmonary morbidity and mortality; much less is known about the effects of PM exposure on the brain. Recent research findings from human epidemiology, animal exposure, and in vitro studies suggest that air pollutant exposures may be associated with adverse central nervous system effects. Additionally, numerous animal models of neurodegenerative disease have been developed that demonstrate various pathological, immune, and cognitive or behavioral facets of neurodegenerative disease. However, the role of ultrafine PM exposure on central nervous system pathology and cognition in these animal models has been largely unexplored. The proposed research will begin to address this gap.

Objective

The objectives of this study are to determine: 1) whether long-term exposure to ultrafine particulate matter (UFPM) is associated with the development of neurodegenerative processes in a mouse model of Parkinson's disease; 2) whether UFPM exposure accelerates progression of innate immune responses in the brain; and 3) whether cognitive or behavioral deficits develop as a result of UFPM exposures.

Methods

This project will utilize a well-characterized transgenic mouse model of Parkinson's disease. Transgenic and wild-type (control) mice will be exposed to concentrated ambient UFPM for assessment of its potential to induce behavioral and brain deficits that are associated with the development and progression of Parkinson's disease and related neurodegenerative diseases. Concurrently, matched transgenic and wild-type mice will be exposed simultaneously to filtered, purified air as a control exposure. As the transgenic mice age, they develop motor and cognitive deficits, together with other brain deficits that are characteristic of progressive Parkinson's disease. Mice will be exposed to air containing concentrated UFPM for a 5-month term, with concurrent assessment of motor and cognitive behaviors at the beginning and end of their exposures. Brain tissue will then be analyzed for pro-inflammatory, oxidative stress, and other cellular defense responses resulting from exposure to UFPM.

Expected Results

The results of this study are expected to show whether ambient UFPM exposure in a mouse model of Parkinson's disease helps to initiate or exacerbate innate immune responses in the brain, changes in brain pathology, and changes in cognition or behavior.

Significance to the Board
The results of this study will provide to the ARB a quantitative assessment of UFPM exposure that models human exposures in Southern California and may endanger public health. These findings will assist ARB in its mission of protecting public health, particularly in the elderly.

Contractor:
University of California, Los Angeles

Contract Period:
36 months

Principal Investigator (PI):
Arthur K. Cho, Ph.D.

Contract Amount:
$497,821

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. Cho's main research interest is the chemical basis for the actions of foreign compounds on biological systems, which has included the study of dopamine neurochemistry. Dr. Cho also has examined the cellular effects of quinones and relevant ambient air samples and addressed the role of oxidative and electrophilic stress in adverse health effects due to air pollutants. This experience will play an important role in the current project, which addresses the actions of air pollutants on the dopamine system in the brain as a target in the exacerbation of Parkinson's disease development.

Prior Research Division Funding to UCLA:
UCLA has successfully completed numerous projects with the Air Resources Board over the years.

Year	2013	2012	2011
Funding	$819,131	$400,000	$630,264

BUDGET SUMMARY

Contractor: University of California, Los Angeles

"Effects of Ultrafine Particulate Matter Exposure in an Animal Model of Neurodegenerative Disease"

DIRECT COSTS AND BENEFITS			
1.	Labor and Employee Fringe Benefits	$ 258,050	
2.	Subcontractors	$ 156,456	
3.	Equipment	$ 0	
4.	Travel and Subsistence	$ 2,915	
5.	Electronic Data Processing	$ 380	
6.	Reproduction/Publication	$ 0	
7.	Mail and Phone	$ 400	
8.	Supplies	$ 44,423	
9.	Analyses	$ 0	
10.	Miscellaneous	$ 4,164	
	Total Direct Costs		$ 466,787
INDIRECT COSTS			
1.	Overhead	$ 31,033	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$ 31,033
TOTAL PROJECT COSTS			**$ 497,821**

ATTACHMENT 1

SUBCONTRACTORS' BUDGET SUMMARY

Subcontractor: University of California, Irvine

Description of subcontractor's responsibility: Dr. Michael Kleinman and his associates at UCI will conduct the exposure component upon which the project is based. Dr. Kleinman has established a protocol for animal exposure to concentrated air pollution from the Irvine area which neighbors two major freeways. As a major contributor to the project, Dr. Kleinman will also participate in the discussions of the results obtained and in the documents associated with the project.

DIRECT COSTS AND BENEFITS			
1.	Labor and Employee Fringe Benefits	$ 135,075	
2.	Subcontractors	$ 0	
3.	Equipment	$ 0	
4.	Travel and Subsistence	$ 0	
5.	Electronic Data Processing	$ 0	
6.	Reproduction/Publication	$ 0	
7.	Mail and Phone	$ 200	
8.	Supplies	$ 1,850	
9.	Analyses	$ 0	
10.	Miscellaneous	$ 5,108	
	Total Direct Costs		$142,233
INDIRECT COSTS			
1.	Overhead	$ 14,223	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$ 14,223
TOTAL PROJECT COSTS			**$ 156,456**