State of California
AIR RESOURCES BOARD

RESEARCH PROPOSAL

Resolution 10-13

February 25, 2010

Agenda Item No.: 10-2-1

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 2699-266, entitled "Peripheral Blood Gene Expression in Subjects with Coronary Artery Disease and Exposure to Particulate Air Pollutant Components and Size Fractions," has been submitted by the University of California, Irvine (UC Irvine);

WHEREAS, the Research Division staff has reviewed and recommended this proposal for approval; and

WHEREAS, the Research Screening Committee (RSC) has reviewed and recommends for funding:

Proposal Number 2699-266 entitled "Peripheral Blood Gene Expression in Subjects with Coronary Artery Disease and Exposure to Particulate Air Pollutant Components and Size Fractions," submitted by UC Irvine, for a total amount not to exceed $274,931.

NOW, THEREFORE, BE IT RESOLVED that ARB, pursuant to the authority granted by Health and Safety Code section 39703, hereby accepts the recommendation of RSC and approves the following:

> Proposal Number 2699-266 entitled "Peripheral Blood Gene Expression in Subjects with Coronary Artery Disease and Exposure to Particulate Air Pollutant Components and Size Fractions," submitted by UC Irvine, for a total amount not to exceed $274,931.

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 $274,931.

I hereby certify that the above is a true and correct copy of Resolution 10-13, as adopted by the Air Resources Board.

Sandra Bannerman, Clerk of the Board

ATTACHMENT A

Peripheral Blood Gene Expression in Subjects with Coronary Artery Disease and Exposure to Particulate Air Pollutant Components and Size Fraction

Background

There is a gap in information on whether gene expression in biological pathways relevant to particulate matter (PM) exposure effects is associated with urban PM exposure in humans at potentially increased cardiac risk. There are two important classes of particles for which little is known regarding health effects in human populations: 1) Primary organic aerosols (POA) from combustion sources, which are primarily traffic-related in Los Angeles; 2) Secondary organic aerosols (SOA), which are photochemically produced from combustion-related, industrial, and biogenic volatile or semi-volatile precursors. Transition metals, such as those found in coarse particles, may have cardiovascular effects and examining these metals in coarse particles will be helpful in determining their toxicity in humans. The size, composition and sources of particles will likely determine their toxicity, their ability to enter the circulation, and pathophysiological mechanisms of effect. However, there is limited toxicity data in human populations. To address these research gaps, the proposed study will analyze the possible relationship between gene expression and particle composition and sources. The present study will leverage the data from a study funded by the National Institute of Environmental Health Sciences (NIEHS), referred to as the Cardiovascular Health and Air Pollution Study (CHAPS) as well as a genetic analysis of 42 specific genes in the same cohort funded by NIEHS.

Objective

The main objectives of this proposed research are to determine the organic composition of the accumulation mode PM2.5 in both indoor and outdoor environments throughout the study years; to conduct an extensive source apportionment study, which will include quasi-ultrafine PM exposures (already measured); and to analyze relationships of the various characterized exposures, including data from coarse particle mass and metals, to gene expression in the study subjects.

Methods

This study will make use of information from CHAPS and a genetic study of the same cohort funded by NIEHS. Subjects in CHAPS included 60 nonsmokers with a history of coronary artery disease (CAD) living in four retirement communities in the Los Angeles air basin. Each subject was followed intensively over 7-month periods with a number of health endpoints measured. An intensive exposure assessment at the retirement communities has been included to characterize exposures to indoor and outdoor criteria pollutant gases; PM gravimetric mass of quasi-ultrafine (PM0.25), accumulation (PM0.25-2.5), and (PM2.5-10) coarse modes; elemental and organic carbon; black carbon; and particle number concentration. Gene expression data for 42 selected genes will be available from the ongoing NIEHS funded work. This includes genes involved in oxidative stress, antioxidant defense, xenobiotic metabolism, inflammation, coagulation, and endoplasmic reticulum stress.

The proposed study will produce new particle composition data from archived accumulation mode filter samples, and then conduct an analysis of available gene expression data from CHAPS. The chemical speciation of quasi-ultrafine particles has been completed. Composition and source tracers will be used to detect differences in associations between POA and SOA. The investigation will compare gene expression in exposures to quasi ultrafine and accumulation mode particles carrying these organic aerosol types as well as transition metals and mass in coarse particles.

Expected Results
The study should demonstrate the value of gene expression analysis in circulating whole blood as a biomarker of response to air pollution exposure. This work has the potential to advance the knowledge of air pollution health effects in a susceptible population by using gene expression in peripheral blood and employing detailed pollutant measurements on particle sources, size and composition.

Significance to the Board
This study will provide information on the genetic effects of air pollution in a sensitive population under real life conditions and will also add new information on the effect of impacts by particle source, size, and composition. The exposure assessment data is a major strength of this proposal. Previous studies have largely relied on air monitoring data from central sites located far from subjects with little or no information about particle composition or sources. The data on detailed exposure assessment will be important for developing effective pollution control strategies for ARB in the future, since it could link biological outcomes to pollutant sources that have a major contribution to personal and indoor particle levels. It may also lay the groundwork for future studies of the mechanisms of air pollution impacts in vulnerable populations.

Contractor:
University of California, Irvine

Contract Period:
24 months

Principal Investigator (PI):
Dr. Ralph Delfino

Contract Amount:
$274,931

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:
ARB has established a strong working relationship with the principal investigator, Dr. Ralph Delfino, which has resulted in successful completion of several studies to illuminate health effects of air pollution.

Prior Research Division Funding to UC Irvine:

Year	2008	2007	2006
Funding	$685,203	$1,457,755	$340,905

BUDGET SUMMARY

Contractor: University of California, Irvine

Peripheral Blood Gene Expression in Subjects with Coronary Artery Disease and Exposure to Particulate Air Pollutant Components and Size Fractions

DIRECT COSTS AND BENEFITS			
1.	Labor and Employee Fringe Benefits	$ 87,998	
2.	Subcontractors	$ 170,163[1]	
3.	Equipment	$ 0	
4.	Travel and Subsistence	$ 600	
5.	Electronic Data Processing	$ 0	
6.	Reproduction/Publication	$ 200	
7.	Mail and Phone	$ 400	
8.	Supplies	$ 200	
9.	Analyses	$ 0	
10.	Miscellaneous	$ 1,300	
	Total Direct Costs		$260,861
INDIRECT COSTS			
1.	Overhead	$ 14,070	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$14,070
TOTAL PROJECT COSTS			**$274,931**

[1] Subcontractors will carry out sample preparation, conduct analyses, perform quality assurance and control checks, and serve to direct portions of the research.

SUBCONTRACTORS' BUDGET SUMMARY

Subcontractor: University of Southern California

Description of subcontractor's responsibility: Sample preparation and chemical and gravimetric analysis of air pollutants will be conducted here.

DIRECT COSTS AND BENEFITS				
1.	Labor and Employee Fringe Benefits	$	81,678	
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	$	0	
9.	Analyses	$	0	
10.	Miscellaneous	$	8,640	
	Total Direct Costs			$90,318
INDIRECT COSTS				
1.	Overhead	$	24,504	
2.	General and Administrative Expenses	$	0	
3.	Other Indirect Costs	$	0	
4.	Fee or Profit	$	0	
	Total Indirect Costs			$24,504
TOTAL PROJECT COSTS				**$114,822**

SUBCONTRACTORS' BUDGET SUMMARY

Subcontractor: University of Wisconsin-Madison

Description of subcontractor's responsibility: Dr. Schauer will serve as co-PI and overall project director. A post-doctoral scholar will review all data, perform level 2 quality assurance / quality control (QA/QC) checks, generate the data base for the project and will work on source attribution analysis. The subcontractor will also perform all of the chromatography / mass spectrometry analysis including the extraction, sample concentration, instrumental analysis, and quantification as well as all of the required QA/QC.

DIRECT COSTS AND BENEFITS			
11.	Labor and Employee Fringe Benefits	$ 43,310	
12.	Subcontractors	$	
13.	Equipment	$	
14.	Travel and Subsistence	$	
15.	Electronic Data Processing	$	
16.	Reproduction/Publication	$ 50	
17.	Mail and Phone	$ 15	
18.	Supplies	$ 6,935[2]	
19.	Analyses	$	
20.	Miscellaneous	$	
	Total Direct Costs		$50,310
INDIRECT COSTS			
5.	Overhead	$ 5,031	
6.	General and Administrative Expenses	$	
7.	Other Indirect Costs	$	
8.	Fee or Profit	$	
	Total Indirect Costs		$5,031
TOTAL PROJECT COSTS			**$55,341**

[2] Essential supplies include substrates (sample collection filters, QA/QC support); chemicals (solvents for extraction, standards for GCMS analysis, chemicals for sample derivatization, GCMS gases); analytical supplies (instrumental consumables including GC columns, liners, and injectors parts) and office supplies (e.g., paper, data storage disks).