Health Effects of Air Pollution Foundation

21865 Copley Drive 🗞 Diamond Bar CA 91765

Ben Benoit, Chair

Annual Meeting of the Board of Directors

January 17, 2020 ♦ 11:00 a.m.*, CC8 *or immediately following the 10:00 a.m. South Coast AQMD Administrative Committee

AGENDA

The public may also attend at the Teleconference Locations listed below:

> 11461 West Sunset Boulevard **Brentwood Room 1** Los Angeles, CA 90049

Members of the public may address this body concerning any agenda item before or during consideration of that item (Gov't. Code Section 548543.(a)). Please provide a Request to Address the Committee card to the Foundation Secretary if you wish to address the Foundation on an agenda item. If no cards are available, please notify South Coast AQMD staff or a Board Member of your desire to speak. All agendas for regular meetings are posted at District Headquarters; 21865 Copley Drive, Diamond Bar, California, at least 72 hours in advance of the regular meeting. Speakers may be limited to three (3) minutes each.

		an <u>member of Director</u>
1.	Approve Minutes of the January 12, 2018 and February 8, 2019 Meetings	Denise Whitcher Foundation Secretary
2.	Update on current and recent projects Staff will provide an update on the status of the currently funded and recently concluded research projects.	Jo Kay Ghosh Health Effects Officer
3.	 Consider Awarding Funding for Continuation Projects: A. Consider Research Proposal from Cedars-Sinai Medical Center titled "Development of the Alzheimer's disease under the exposure of air pollutants 2019-2022" (Principal Investigator: Dr. Keith Black, funding requested: \$2,250,000) B. Consider Research Proposal from University of California, Los Angeles titled "Adverse Health Effects of Volatile Organic Compounds" (Principal Investigator: Dr. Arthur Cho, funding requested: \$471,000) 	Jo Kay Ghosh Health Effects Officer

	C. Consider Research Proposal from University of Southern California titled "Impact of ambient air pollution on the risk of breast cancer and survival in Los Angeles County: The Multiethnic Cohort Study" (Principal Investigator: Dr. Anna Wu, funding requested: \$804,189)	
4.	Financial Report: June 30, 2019 Audited Financial Statement Staff will present the current Audited Financial Statement and provide a report on Foundation revenues, expenses, and cash balance. (Receive and file)	Sujata Jain Treasurer
5.	Other Business Any member of the Foundation, or its staff, on his or her own initiative or in response to questions posed by the public, may ask a question for clarification, may make a brief announcement or report on his or her own activities, provide a reference to staff regarding factual information, request staff to report back at a subsequent meeting concerning any matter, or may take action to direct staff to place a matter of business on a future agenda. (Government Code \$54954.2)	
6.	Next Meeting Will be scheduled as needed.	
7.	Public Comment At the end of the regular meeting agenda, an opportunity is provided for the public to speak on any subject within the Foundation's authority that is not on the agenda. Speakers may be limited to three (3) minutes each.	
	Document Availability All documents (i) constituting non-exempt public records, (ii) relating to an item on an agenda for a regular meeting, and (iii) having been distributed to at least a majority of the Committee after the agenda is posted, are available prior to the meeting for public review at the South Coast Air Quality Management District, Public Information Center, 21865 Copley Drive, Diamond Bar, CA 91765.	
	Americans with Disabilities Act The agenda and documents in the agenda packet will be made available, upon request, in appropriate alternative formats to assist persons with a disability (Govt. Code Section 54954.2(a). Disability- related accommodations will also be made available to allow participation in the meeting. Any accommodations must be requested as soon as practicable. Requests will be accommodated to the extent feasible. Please contact Denise Whitcher at 909-396-3407 from 7 a.m. to 5:30 p.m. Tuesday through Friday, or send the request to dwhitcher@aqmd.gov.	

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Health Effects of Air Pollution Foundation

21865 Copley Drive 🛠 Diamond Bar CA 91765

Ben Benoit, Chair

William A. Burke, Vice Chair

Draft Minutes January 12, 2018

Foundation Chair Ben Benoit called the Health Effects of Air Pollution (HEAP) Foundation Annual Meeting to order at 11:02 a.m. The following Directors were present at AQMD or by teleconference (in alphabetical order):

Mayor Ben Benoit, Chair Dr. William A. Burke, Vice Chair Mayor Pro Tem Judith Mitchell Dr. Clark E. Parker, Sr.

Also present were the following individuals (in alphabetical order):

Derrick Alatorre, DEO/Legislative, Public Affairs & Media Barbara Baird, Chief Deputy Counsel Dr. Philip Fine, DEO/Planning, Rule Development & Area Sources Dr. Jo Kay Ghosh, Health Effects Officer Sujata Jain, Treasurer Susanna Leung, Assistant Treasurer Megan Lorenz, Foundation Counsel Wayne Nastri, Executive Officer Denise Whitcher, Foundation Secretary

Kurt Wiese, General Counsel

1.

2.

APPROVE MINUTES OF THE SEPTEMBER 8, 2017 MEETING

Minutes of the September 8, 2017 meeting were recommended for approval without amendment. This item was moved by Mayor Pro Tem Mitchell, seconded by Dr. Burke, and unanimously approved.

APPOINT TREASURER OF THE FOUNDATION TO REPLACE MICHAEL O'KELLY

Executive Officer Wayne Nastri recommended that SCAQMD Assistant DEO/Finance Sujata Jain be appointed as Foundation Treasurer, due to the recent departure of Michael O'Kelly in December 2017. This item was moved by Mayor Pro Tem Mitchell, seconded by Dr. Burke, and unanimously approved.

3. APPOINT AN ASSISTANT TREASURER

Mr. Nastri recommended that the SCAQMD Controller be appointed as Assistant Treasurer to Treasurer Sujata Jain to increase operational efficiency and serve as back-up to sign checks and make transfers between bank accounts to ensure grant payments are made in a timely manner. The current SCAQMD Controller is Susanna Leung. The adoption of the resolution appointing the Assistant Treasurer was moved by Dr. Burke, seconded by Mayor Pro Tem Mitchell, and unanimously approved.

4. <u>REPORT ON CURRENT RESEARCH PROJECTS FUNDED BY THE FOUNDATION</u>

Health Effects Officer Dr. Jo Kay Ghosh reported there are four active research grants currently underway and that none are completed: two with Cedars Sinai, and one each with USC and UCLA. Mayor Pro Tem Mitchell inquired whether it would be helpful to have grant recipients provide a report to the Governing Board. Dr. Ghosh responded that last year USC previewed its research during a Governing Board Meeting; however, she recommended it would be more informative to report on the research after its completion in late 2018 or potentially 2019. Dr. Ghosh further recommended staff keep the Executive Officer well informed, and report to the Governing Board at the appropriate time. Mayor Pro Tem Mitchell concurred. This being a receive and file item, there was no further action on this matter.

5. FINANCIAL REPORT: JUNE 30, 2017 AUDITED FINANCIAL STATEMENT

Treasurer Sujata Jain reported on 2016-17 audit results, advising the firm of BCA Watson Rice had provided an unmodified, clean audit of the Foundation's finances. Ms. Jain further indicated that of the approximately \$9 million received since the Foundation's inception, there had been \$5.8 million in grants distribution, leaving a balance of \$3.3 million of which \$3.1 remains obligated for current research grants. Upon inquiry from Dr. Burke, Ms. Jain advised the non-obligated fund balance is approximately \$100,000. This being a receive and file item, there was no further action on this matter.

6. OTHER BUSINESS

There was no other business to discuss.

7. <u>NEXT MEETING</u>

The next scheduled meeting will be calendared at the convenience of the Foundation Board Members.

8. PUBLIC COMMENT

There was no public comment.

There being no further business, the meeting was adjourned at 11:11 a.m.

Dated:

Denise Whitcher, Foundation Secretary

APPROVAL OF MINUTES:

Date:

Health Effects of Air Pollution Foundation

21865 Copley Drive * Diamond Bar CA 91765

Ben Benoit, Chair

2.

William A. Burke, Vice Chair

Draft Minutes February 8, 2019

Foundation Vice Chair Dr. William Burke called the Health Effects of Air Pollution (HEAP) Foundation Annual Meeting to order at 11:10 a.m. The following Directors were present at AQMD or by teleconference (in alphabetical order):

Dr. William A. Burke, Vice Chair Mayor Pro Tem Judith Mitchell

The following Directors were absent:

Mayor Ben Benoit, Foundation Chair Dr. Clark E. Parker, Sr.

Also present were the following individuals (in alphabetical order):

Dr. Jo Kay Ghosh, Health Effects Officer Sujata Jain, Treasurer Susanna Leung, Assistant Treasurer Megan Lorenz, Foundation Counsel Wayne Nastri, Executive Officer Nancy Velasquez, Executive Secretary

APPROVE MINUTES OF THE JANUARY 12, 2018 MEETING

Minutes of the January 12, 2018 meeting were recommended for approval without amendment. This item was moved by Mayor Pro Tem Mitchell, and seconded by Dr. Burke; however, a quorum was not present, therefore the minutes were held over for approval at the next meeting.

REPORT ON CURRENT RESEARCH PROJECTS FUNDED BY THE FOUNDATION

Health Effects Officer Dr. Jo Kay Ghosh reported there are four active research grants currently funded through the Foundation and which are still in process, two with Cedars Sinai, and one each with USC and UCLA. Dr. Ghosh advised several of the grants had recently received no-cost extensions, after staff verified the research is progressing and grant funds were appropriately expended. Each of the projects have made significant progress, two are expected to be completed by mid-year, and two are expected to be completed by year-end or next year. The extensions will allow validation studies and preparation of abstracts for publication. This being a receive and file item, there was no further action on this matter.

3. FINANCIAL REPORT: JUNE 30, 2018 AUDITED FINANCIAL STATEMENT

Treasurer Sujata Jain reported on 2017-18 audit results, advising the firm of BCA Watson Rice had provided an unmodified, clean audit of the Foundation's finances. Ms. Jain further indicated that of the approximately \$9 million received since the Foundation's inception, there had been \$7.5 million in grants distribution, leaving a balance of \$1.5 million of which \$1.4 million remains obligated for current research grants. Upon inquiry from Dr. Burke, Ms. Jain advised that in 2008 the South Coast AQMD Governing Board adopted the policy directing 20% of penalty monies over \$4 million would be transferred to the Health Effects Research Fund (HERF); and, as a result \$2 million was transferred to the HERF in 2018. However, in recent years past, the HERF transfer from penalty money had not been made. Staff further advised, however, that said fund transfer may be made up with additional penalty funds rather than an adjustment from the general fund, and that appropriate Board action would be taken to recognize the HERF transfer to the Foundation. Dr. Burke requested staff to provide him with a briefing and recommendations in a subsequent meeting.

Mayor Mitchell inquired about the use of Foundation funds, and Ms. Lorenz confirmed the strict use of the Foundation funds for research-related activities and to research institutions. Upon Mayor Mitchell's further inquiry, staff responded that the HERF contained \$3 million which could potentially be transferred to the Foundation on the Board's direction, adding that when current research is completed additional funds may be designated. Mayor Mitchell recalled that the Foundation name and mission had been expanded to broaden study beyond the previous emphasis on brain tumors. Dr. Burke lamented on the lack of recent interest and inquiries as a way to gage interest in the Foundation and its work. Mr. Nastri responded staff could develop a request for research proposals similar to an RFP, which would be sent to current research partners and other institutions. Mayor Mitchell asked that such request be provided to asthma research entities, since the Board receives so many complaints related to asthma; she mentioned Loma Linda as a possible research partner. At Mr. Nastri's suggestion, Dr. Ghosh will also inquire of the current research partners on possible follow-on projects.

With no quorum available, the members present communicated a concurrence of staff's position above.

4. OTHER BUSINESS

There was no other business to discuss.

5. <u>NEXT MEETING</u>

The next scheduled meeting will be calendared at the convenience of the Foundation Board Members.

6. PUBLIC COMMENT

Harvey Eder commented on behalf of the Solar Power Coalition, encouraged total immediate conversion to solar power, and commented on destruction due to climate change.

There being no further business, the meeting was adjourned at 11:32 a.m.

Dated:

APPROVAL OF MINUTES: Date: Denise Whitcher, Foundation Secretary

HEAPF Funding Proposal to study development of Alzheimer's disease under the exposure of air pollutants 2019-2022

Synopsis

Air pollution reduces global life expectancy by nearly 2 years and poses the single greatest threat to human health (<u>https://aqli.epic.uchicago.edu/</u>). Surprisingly little is known about air pollution-induced pathology, especially its influence on nervous system health. We studied the effects of airborne particulate matter (PM) collected from the Los Angeles basin on gene expression in brains of normal, tumor-bearing and Alzheimer's mice. Our aim was to establish an understanding of PM contribution to the development and progression of brain cancer and Alzheimer's disease (AD).

Summary of previous findings

In each separate experiment we exposed normal mice, tumor-bearing mice and triple transgenic AD mice to airborne PM. We used state-of-the-art quantitative RNA-seq transcriptome sequencing to analyze gene expression changes that occur in the brains of PM-exposed mice. <u>Our overarching initial hypothesis stated that PM will trigger inflammatory gene and oncogene expression</u>. We confirmed this hypothesis but unexpectedly discovered (1) massive gene dysregulation in the brains of mice with tumors and AD, and (2) significant gene activity in novel and unexpected molecular pathways with unknown roles in disease. In normal mice, PM exposure triggered only a modest change in the nervous system transcriptome with predominant activity in genes related to endocrine system and inflammation. In contrast, we found a brain-wide upregulation of inflammatory genes in tumor-bearing mice. This effect was specifically linked to ultrafine PM-25 and indicates a PM-triggered inflammatory response in the brains of tumor-bearing mice. PM exposure of AD mice triggered a brain-wide downregulation of genes related to extracellular matrix proteins, collagens and laminins. <u>These data collectively show</u> <u>distinct biological responses to PM dependent on the normal or pathological condition of our mice (Fig.1).</u>

Novelty. 1. Pathological brain is much more susceptible/reactive to injury (air pollutant exposure) resulting in massive gene dysregulation; 2. As a result of exposure to air pollutants, molecular changes were discovered in triple transgenic AD mice. These include pronounced downregulation of the extracellular matrix genes important as a structural basis of the vascular system and of brain cells. Moreover, we discovered for the first time hitherto unknown changes in protein synthesis apparatus throughout ribosomal genes. Also, pre-selection for specific environmental conditions to live is required based on individual genetic profile for the future occupational and/or living planning.



Figure 1: Tumor-bearing and AD mice show highly altered gene expression when compared to normal Biological pathways mice. that are linked to dysregulated genes arè unique for each animal model. Tumor-bearing mice inflammatory gene show activity whereas AD mice show downregulation of genes that encode extracellular matrix proteins.

Proposed specific aims: Based on our findings above, we propose to conduct experiments that will uncover the contributions of novel inflammatory and extracellular matrix-related protein synthesis pathways to the understanding of the etiology of AD with possible prevention and/or treatment approaches. Our strategy will consist of the following projects:

Project 1: Validation of RNA-seq data and biological pathways in mouse AD models. We will conduct state-of-the-art genomic, proteomic and bioinformatic validation of genes that are affected by PM exposure. We will focus on genes that contribute to inflammation, and extracellular matrix protein synthesis in AD mouse models. Overall, we aim to validate multiple genes / proteins within single molecular pathways and to study the roles of these genes via experimental or drug-mediated (see below) modifications.

Project 2: We will conduct additional PM exposure experiments using transgenic mouse AD models mimicking human pathology. We will extend PM exposure duration from 6 to 18 months total. We will introduce new metrics to examine the effects of exposure including behavioral testing of mice to assess their cognitive abilities before, during and after air pollution exposure.

Project 3: We will conduct a combinatorial study to examine not only the effects of single PM but also their combinations on gene expression in the brain. All of our work thus far has examined the contributions of individual PM, without mixing these. We propose that PM mixtures and step-wise addition of other common air pollution compounds (carbon monoxide, ozone) will reveal the full spectrum of pathological effects triggered by the Los Angeles air pollution.

Project 4: Using our knowledge obtained from genetic, molecular and protein level studies, we will design drug delivery systems that are aimed at enhancing or suppressing the activity of certain cellular pathways. The group of Dr. Ljubimova is expertly familiar with novel drug design and brain delivery of new drugs. This know-how will allow us to readily produce vehicles that effectively target and interfere with molecular and cellular pathways that are identified as part of **Project 1**.

Project 5: We will validate gene expression findings from **Projects 1-4** in a follow-up study using human brain tissue collections. Our scientific experience and access to Cedars-Sinai Biobank allow us to rapidly acquire diverse types of human brain tissue, and thus to validate and relativize our findings to the human population of the South Coast basin.

Project 6: Our data demonstrate that heavy metals (e.g. Ni, Co, Zn), as a significant component of air pollutants, induced changes in the brain of experimental animals, which leads to inflammatory response. Chronic exposure of double and triple transgenic AD mice will be used to understand the specific role of heavy metals in AD development through increase in the inflammation processes in the brain. These studies may help to create the special equipment for industry and even for commercial space missions to prevent brain pathology development for short- and long-term PM exposure.



Relevance/Summary

This project will advance our understanding of brain tumor and Alzheimer's disease etiology and progression, and will establish definitive links between air pollution exposure and increased prevalence of these diseases in our urban population and even long-term commercial space missions. The identification of relevant biomarkers is a key goal of our research and it will not only further our understanding but will provide us with novel drug targets for future treatments of brain diseases. Finally, with our results, we hope to better educate the public and governing bodies about the need for better regulation of energy, industry and transportation expansion, all of which result in enhanced emissions of PM that impact air quality and human health.

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Adverse Health Effects of Volatile Organic Compounds

Arthur K. Cho

Introduction

I and my colleagues wish to extend our current findings regarding the role of particulate matter on the exacerbation of cancer to the effects of ambient volatile organic compounds (VOCs) on three toxicologically important proteins, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), Kelch-like ECH-associated protein-1 (Keap1) and paraoxonase-1 (PON-1) to be used as markers for toxicological events.

The currently funded South Coast Air Quality Management District (SCAQMD) funded project, HEAP FO12, examines the biological and chemical properties of particulates and vapors from ambient air samples collected at multiple sites in the Los Angeles Basin. In our biological assays we determined the effects of these samples on non small cell lung cancer cells using changes in hemeoxygenase-1 (HO-1) as the marker for low level or early response to oxidative or electrophilic challenge. The results thus far indicate that although the particulate fraction (PM2.5) only marginally affected HO-1 expression, the vapor phase or volatile organic compounds (VOCs) were highly effective in increasing this cellular response. Additionally, the VOCs suppressed the expression of caveolin-1 (CAV-1), a tumor suppressive protein. This VOC effect correlated with the electrophile and prooxidant content of the samples, measured by our GAPDH and dithiothreitol (DTT) assays, respectively. We interpret these results to indicate that ambient volatile organic prooxidants and/or electrophiles are capable of exacerbating the progression of cancer in at least one cell line. We attribute the cellular responses to the actions of these reactive chemical species on, the Nrf2/Keap1 system, which regulates HO-1 expression (Li, Alam et al. 2004, Pierce, Piyankarage et al. 2016, Dinkova-Kostova, Kostov et al. 2017). The correlation of HO-1 expression with both DTT and GAPDH assay activities indicates that redox based reactive oxygen and or covalent modification of regulatory proteins can be involved. Of these interactions, covalent modification of proteins can be more worrisome because of its cumulative possibility. Recovery from covalent modification of proteins will require resynthesis of the affected protein. Then, even though the electrophile exposure is low, its continuous nature results in a gradual accumulation of modified protein such that the resulting cellular effects can become significant.

The HEAP FO12 project will have generated acute toxicological data of ambient samples from the Los Angeles Basin relevant to cancer progression in lung and brain. Furthermore, quantitative data on the chemical properties of the samples relevant to toxicity will also be collected. This data base of the multiple samples from the 5 locations and 2 seasons will provide the background for the examination of the VOCs in the study described below.

The proposed project will examine the interaction of the VOCs with specific proteins that could be used as markers for assessment of potential adverse health effects, specifically Keap1, the regulator of the Nrf2/antioxidant response element that controls anti-inflammatory responses to environmental challenges and PON-1, a plasma protein whose loss of activity is correlated with coronary artery disease. Dr. Jesus Araujo of the Department of Medicine has examined this protein in human subjects (Ramanathan, Yin et al. 2016) following exposure to concentrated particulates but not following exposure to ambient air or VOCs. He will participate in the project in developing protocols for subsequent human subject studies. Activities of these two proteins have been shown to be reduced by exposure to ambient air components.

Attachment 3(B)

Adverse health effects of volatile organics

The objectives of the study we propose are:

- 1. To determine the inhibitory potencies of ambient VOCs from our current study on these two proteins in addition to GAPDH. We will determine the role of prooxidants and electrophiles using the protocols developed for our GAPDH assay.
- 2. To identify the electrophiles in the ambient VOCs that affect the three proteins by liquid chromatograpy/ mass spectral analyses (HPLC/MS).

The procedures to be used for (1) will be based on our GAPDH paradigm which determines inhibitory potency and the role of prooxidants and electrophiles. The procedures for (2) will involve the HPLC/MS analysis of samples prepared using conditions established in objective (1) and collaboration with Dr.Julian Whitelegge of the UCLA Mass Spectrometry Facility. Dr. Whitelegge has performed preliminary studies on GAPDH exposed to VOCs and demonstrated adduct formation and has indicated that the specific peptide affected and the nature of the adduct can be identified. If so, this extension will, for the first time identify toxicologically relevant VOCs in terms of their biological targets and their potencies. While extensive studies have been performed on particulate fractions of air pollution, VOCs have received relatively little attention. However, their presence in the atmosphere, especially in regions of high non-diesel vehicular traffic is substantial and our current results indicate further studies are clearly needed.

The deliverables we would provide are:

- 1. Potencies of the inhibition of three toxicologically relevant proteins by VOCs from 5 sites in the Los Angeles Basin.
- 2. The role of electrophiles and prooxidants in the inhibition/
- 3. The identity of electrophilic VOCs that form covalent bonds with the 3 proteins.
- 4. The relationship between the inhibitory actions on the target proteins with the toxicities determined with lung and brain cancer cells.

We anticipate the work to require 2 years. In year 1 we will perform the work for objective 1 and in year 2 we will perform the work for object 2 and complete a report of the findings.

We estimate the total direct costs to be approximately \$300,000.

Indirect costs at 57% are \$171,000.

Total Direct cost	\$ 300,000.00
Indirect @57%	\$ 171,000.00
Total	\$ 471.000.00

Adverse health effects of volatile organics

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Impact of ambient air pollution on the risk of breast cancer and survival in Los Angeles County: The Multiethnic Cohort Study

MPI: Anna H. Wu, PhD and Iona Cheng, PhD

Submitted to: Dr. Jo Kay Ghosh Health Effects of Air Pollution Foundation

Specific Aims

In 2014, the International Agency for Cancer (IARC) classified outdoor air pollution and particulate matter (PM) as carcinogenic to humans (Goup1). In a study of 2,729 incident breast cancers identified from 57,589 women in the Multiethnic Cohort Study (MEC), largely residing in Los Angeles County, we found both gaseous and PM pollutants were positively associated with breast cancer risk. Specifically, women who lived within 500 meters of major roads displayed statistically significant increased risk of breast cancer with exposure to NO2 and NOx (HRs ranged from 1.21 to 1.44) and PM10 and PM2.5 (HRs ranged from 1.29 to 1.85)¹. Stronger associations of NO_x and NO₂ were observed among African American (HR 1.26. 95% CI 1.01-1.58) and Japanese American (HR 1.42, 95% CI 1.05-1.91) women, who were largely concentrated in communities along the 405 freeway with exposures not only to vehicle emissions, but also to refineries, ports, and the Los Angeles International Airport. In subgroup analyses by hormone receptor status, risk of estrogen/progesterone receptor negative (ER-/PR-) breast cancer increased 25% per 10 µg/m³ increase in krigged PM for all women. New results from the nationwide Nurses' Health Study showed that higher ambient PM exposure may adversely impact breast cancer survival, particularly among patients with Stage 1 breast cancer², providing evidence in support of a prior registry-based study that reported county-based PM levels at breast cancer diagnosis were associated with higher breast cancer-specific mortality rates³. In addition, two provocative European studies suggested that chronic noise pollution 4.5 may increase the risk of breast cancer although it is unclear if these findings were independent of the effects of air pollution. To our knowledge, noise pollution and breast cancer risk has not been investigated in US studies.

These recent results on PM exposure and breast cancer survival ^{2,3} and our findings of air pollution and breast cancer risk¹, add to the accumulating evidence that breast cancer is adversely impacted by ambient air pollution exposure⁶. Yet, confirmatory studies are still needed to provide the necessary scientific evidence to inform public policy and action. This proposal aims to expand our investigation of the air pollution and breast cancer by increasing the sample size to approximately 4,000 incident breast cancers with 8 additional years of follow-up, refining the spatiotemporal resolution of our assessment of gaseous and PM pollutants, and adding measures on air toxics and airport-related ultrafine particulates. We expect these efforts to improve our understanding of the associations between air pollution and breast cancer, in particular the risk patterns for African Americans and Japanese Americans residing near the 405 freeway that would likely be applicable to other residents in these areas. Furthermore, with ~3 million US women living with breast cancer, it is important to determine whether reductions in air pollution have the potential to improve breast cancer survival. Thus, we propose the following three primary aims and an exploratory aim:

Aim 1. To generate new estimates of NO_x, NO₂, and PM_{2.5} at a high spatiotemporal resolution using the state-of-the art machine learning techniques and to include air toxics and airportrelated ultrafine particulates for 57,589 female CA MEC participants using residential geocodes. Weekly NO₂ and NO_x concentrations at a high spatial resolution will be estimated based on our newlydeveloped and extensively evaluated spatiotemporal models using both long-term monitoring station data and rich short-term field campaign data⁷. Weekly PM_{2.5} will be estimated at a 1-km resolution using autoencoder-based residual deep network as well as satellite aerosol optical depth, local spatial variables, and meteorological data. These top-notch spatiotemporal models will improve exposure assessment of NO₂, NO_x, and PM_{2.5} in temporal resolution (from monthly to weekly), spatial resolution (e.g. from sparse monitoring-based measurements to 1-km resolution for PM_{2.5}), and accuracy of estimates (e.g. R² of 0.87-0.90 for independent tests of NO₂ and NO_x models). Air toxics will be derived from measured and modeled data from U.S. EPA as well as the MATES measurements from SCAQMD. We will focus on air toxics with a high potential to increase cancer risk and with less missing data. Ultrafine particle impacts from airport emissions will be estimated based on field measurements and dispersion model outputs.

Aim 2. To quantify and characterize the associations of air pollution with breast cancer incidence among 57,589 female CA MEC participants. In a prospective study with over 20 years of follow-up of MEC women, we will examine the impact of air pollutants derived in Aim 1 on breast cancer incidence (~4000 cases: 1520 African Americans, 1275 Latinos, 475 Japanese Americans, 730 Whites). In addition, we will evaluate differences in associations by race/ethnicity, social environment (racial/ethnic residential segregation, neighborhood socioeconomic status (nSES), and tumor characteristics (ER/PR status, stage, grade). We will also evaluate differences in associations by proximity to major roads and moving status.

Aim 3. To quantify and characterize the associations of air pollution with <u>breast cancer survival</u> <u>among 3,691</u> CA female MEC breast cancer cases. In a case-only study of MEC women, we will prospectively evaluate the impact of air pollution exposure on all-cause mortality, breast cancer specific mortality, cardiovascular (CVD) mortality, and other non-breast and non-CVD mortality. In addition, we will examine differences in associations by race/ethnicity, social environment (racial/ethnic residential segregation, neighborhood socioeconomic status (nSES), tumor characteristics (stage, ER/PR status grade), and history of comorbidities, to improve our understanding of whether specific subgroups of breast cancer patients are particularly vulnerable to the effects of pollution.

Exploratory Aim. As heavily polluted areas are often near noisy, busy roadways, an exploratory aim will derive spatiotemporal estimates for noise pollution from roadway, airport, and rail sources for 57,589 female CA MEC participants. We will explore breast cancer risk patterns by sources of noise (roadway, airport, rail), and investigate distinct and synergistic impact of air pollution and noise pollution on risk of breast cancer.

Impact. Breast cancer is a public health priority. A growing body of evidence supports the premise that air pollution and noise pollution influences breast cancer risk and survival. This will represent one of the few prospective studies with long-term data on these two highly prevalent environmental exposures that may disproportionally impact minority populations and groups of lower socioeconomic status. The impact of this research will be not only improvement of our understanding of breast cancer development and outcome but also may provide evidence for policy makers and strategies for intervention.

References

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Year		University of Southern	University of California,	University of California,
		California (USC)	San Francisco (UCSF)	Irvine (UCI)
· · · · · · · · · · · · · · · · · · ·	· · · · ·	(Anna Wu)	(Iona Cheng)	(Jun Wu)
1 (direct)	\$255,000	\$72,000	\$85,658	\$98,000
2 (direct)	\$245,000	\$96,000	\$94,986	\$54,000
Total direct	\$500,644	\$168,000	\$180,644	\$152,000
Indirect*	\$303,545	\$106,243	\$110,662	\$ 86,640
Total	\$804,189	\$274,243	\$291,306	\$238,640

Estimated draft budget (direct cost +indirect cost) for a two-year study

*Indirect cost rate at 63.24% at USC, 61.26% at UCSF, and 57.0% at UCI

<u>Scope of Work at USC (Yrs 1 and 2)</u>: Dr. Anna Wu (10%, 12%) will serve as the contact-PI and will assume fiscal and administrative management of study. Drs. Wu and Cheng led the recently completed study of air pollution and breast cancer in the Southern California Multiethnic Cohort (MEC).¹ With their the multidisciplinary team and the geospatial research infrastructure they have established for the air pollution studies within the MEC; Dr. Wu will co-lead the proposed study activities with Dr. Cheng including the implementation of all procedures and processes and preparing study reports and manuscripts. Responsibilities for the large amount of data analysis for Aims 2 and 3 will be shared between the study teams at USC and UCSF. Dr. Dan Stram is a senior statistical oversight (5%, 5%). Ms. Chiuchen Tseng (25%, 45%) has experience in air pollution analyses; she will work closely with the UCSF team to conduct data analyses. Dr. Tim Larsen and Dr. Scott Fruin will serve as consultants and will oversee the updating of ultrafine measures for MEC participants. Dr. Beate Ritz is an experienced environmental epidemiologist and will serve as consultant to provide advice in air pollution exposure estimates and analyses.

<u>Scope of Work at UCSF (Yrs 1 and 2)</u>: Dr. Iona Cheng (10%, 12%) is an experienced investigator of the Multiethnic Cohort (MEC) and her team has developed extensive multilevel neighborhood measures on the MEC. Dr. Cheng will be assisted by Dr. Salma Shariff-Marco (5%, 5%) who has expertise in studies of geospatial contextual factors. Dr. Shannon Conroy (10%, 10%) will work closely with University of Hawaii to obtain updated address files, follow-up information, and covariate data for MEC study participants for analyses. She will provide the necessary MEC analytic datafiles to the USC team to conduct data analyses. Dr. Juan Yang (20%, 20%) is an experienced biostatistical analyst with expertise in multilevel and longitudinal models and will work closely with Ms. Tseng at USC on air pollution analyses. Dr. Pushkar (5%, 5%) is a geospatial data scientist and will generate maps of air pollutant exposures and estimate distance to major roads for new addresses.

<u>Scope of Work at UCI (Yrs 1 and 2)</u>: Dr. Jun Wu (8%, 8%) led the air pollution exposure measurements in our completed study on air pollution and breast cancer.¹ She has expertise in developing and applying various models to improve population and individual exposure estimates of air pollution. For this proposed study, she will use state-of-the art machine learning techniques to obtain improved high spatiotemporal resolution measures of NO₂, NO_x, and PM_{2.5} for the MEC participants. Dr. Jun Wu will supervise a postdoc (100%, 50%) to complete the work on air toxics, air and noise pollution estimates. She expects that updated air toxics data will be available by month 3, new spatiotemporal estimates of NO₂ and NO_x by month 7, estimates of PM_{2.5} by month 12, and measures of noise pollution by month 16. This schedule of coordinating and completing the air pollution exposure work will allow the USC and UCSF teams to conduct data analyses during years 1 and 2 and to complete the proposed work in an efficient manner.

HEALTH EFFECTS OF AIR POLLUTION Foundation

(Formerly Brain & Lung Tumor and Air Pollution Foundation)

Financial Statements With Independent Auditor's Report

FOR THE YEAR ENDED JUNE 30, 2019 (WITH COMPARATIVE TOTALS FOR 2018)



2355 Crenshaw Blvd. Suite 150 Torrance, CA 90501 t: (310) 792-4640 f: (310) 792-4140

Attachment 4

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Financial Statements with Independent Auditor's Report For the Year Ended June 30, 2019 (With Comparative Totals for 2018)

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Independent Auditor's Report

To the Board of Directors of Health Effects of Air Pollution Foundation

Report on the Financial Statements

We have audited the accompanying financial statements of the Health Effects of Air Pollution Foundation (Formerly Brain & Lung Tumor and Air Pollution Foundation) (the Foundation), which comprise the statement of financial position as of June 30, 2019, and the related statements of activities and cash flows for the year then ended, and the related notes to the financial statements.

Management's Responsibility for the Financial Statements

Management is responsible for the preparation and fair presentation of these financial statements in accordance with accounting principles generally accepted in the United States of America; this includes the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of the financial statements that are free from material misstatement, whether due to fraud or error.

Auditor's Responsibility

Our responsibility is to express an opinion on these financial statements based on our audit. We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the entity's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. Accordingly, we express no such opinion. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Foundation as of June 30, 2019, and the changes in financial position and cash flows for the year then ended, in accordance with accounting principles generally accepted in the United States of America.

Report on Summarized Comparative Information

We have previously audited the Foundation's June 30, 2018 financial statements, and we expressed an unmodified audit opinion on those audited financial statements in our report dated October 12, 2018. In our opinion, the summarized comparative information presented herein as of and for the year ended June 30, 2019 is consistent, in all material respects, with the audited financial statements from which it has been derived.

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7A Watson Rice, LLP

Torrance, CA August 30, 2019

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Statement of Financial Position June 30, 2019 (With Comparative Totals for 2018)

ASSETS	2019	2018		
Cash and cash equivalents	\$ 1,262,274	\$ 2,300,207		
Total Assets	\$ 1,262,274	\$ 2,300,207		
LIABILITIES				
Liabilities	\$	\$		
NET ASSETS				
With donor restrictions	1,262,274	2,300,207		
Total Net Assets	1,262,274	2,300,207		
Total Liabilities and Net Assets	\$ 1,262,274	\$ 2,300,207		

The accompanying notes are an integral part of these financial statements.

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Statement of Activities June 30, 2019 (With Comparative Totals for 2018)

	With Donor	Tot	als
	Restrictions	2019	2018
Revenue and Support			
Interest	\$ 1,438	\$ 1,438	\$ 1,079
Total Revenue and Support	1,438	1,438	1,079
Expenses			
Program services			
Grants provided to other agencies	1,038,053	1,038,053	1,036,480
Total program services	1,038,053	1,038,053	1,036,480
Management and general			
Professional fees	1,287	1,287	1,203
Taxes and fees	31	31	105
Total management and general	1,318	1,318	1,308
Total Expenses	1,039,371	1,039,371	1,037,788
Change in net assets	(1,037,933)	(1,037,933)	(1,036,709)
Net assets at beginning of year	2,300,207	2,300,207	3,336,916
Net assets at end of year	\$ 1,262,274	\$ 1,262,274	\$ 2,300,207

The accompanying notes are an integral part of these financial statements.

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Statement of Cash Flows For the Year Ended June 30, 2019 (With Comparative Totals for 2018)

	2019	2018
Cash Flows From Operating Activities		
Change in net assets	\$ (1,037,933)	\$ (1,036,709)
Net cash (used) provided by operating activities	(1,037,933)	(1,036,709)
Cash Flows From Investing Activities		
Net cash provided by investing activities	<u>_</u>	
Cash Flows From Financing Activities		
Net cash used by financing activities		
Net (decrease) increase in cash and cash equivalents	(1,037,933)	(1,036,709)
Cash and cash equivalents at beginning of year	2,300,207	3,336,916
Cash and cash equivalents at end of year	\$ 1,262,274	\$ 2,300,207

The accompanying notes are an integral part of these financial statements.

Notes to Financial Statements June 30, 2019

NOTE 1 – SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Organization

The Brain & Lung Tumor and Air Pollution Foundation (the Foundation) is a nonprofit public benefit Foundation that was incorporated under the laws of the State of California on February 24, 2003. On February 10, 2017, the Foundation's Board of Directors approved to amend its articles of incorporation by changing the Foundation's name to Health Effects of Air Pollution Foundation and expanding its mission to include not only brain and lung tumors, but the health effects of air pollution in general. The amended articles of incorporation was filed with the Secretary of State in the State of California on March 24, 2017. The Foundation's amended purpose is to aid, assist, and support research on the incidence, detection and causes and cures of various health conditions that may be caused or aggravated by air pollution. The Foundation is managed by a Board of Directors which consists of five volunteers. Income consists of interest on bank deposits and contribution support from South Coast Air Quality Management District (South Coast AQMD).

Basis of Presentation

The financial statements of the Foundation have been prepared on the accrual basis in accordance with the accounting principles generally accepted in the United States of America. The financial statements are presented in accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) 958 dated August 2016, and the provision of the American Institute of Certified Public Accountants (AICPA) "Audit and Accounting Guide for Not-for-profit Organizations" (the "Guide"). ASC 958-205 was effective January 1, 2018.

Under the provisions of the Guide, net assets and revenues, gains and losses are classified based on the existence or absence of donor-imposed restrictions. Accordingly, the net assets of the Organization and changes therein are classified as follows:

<u>Net assets without donor restrictions</u>: Net assets that are not subject to donor-imposed restrictions and may be expended for any purpose in performing the primary objectives of the Corporation. The Foundation's board may designate assets without restrictions for specific operational purposes from time to time. As of June 30, 2019, the Foundation has no net assets without donor restrictions.

<u>Net assets with donor restrictions</u>: Net assets subject to stipulations imposed by donors and grantors. Some donor restrictions are temporary in nature; those restrictions will be met by actions of the Non-Profit Organization or by passage of time. Other donor restrictions are perpetual in nature, where by the donor has stipulated the funds be maintained in perpetuity. As of June 30, 2019, the Foundation has net assets with donor restrictions of \$1,262,274.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Notes to Financial Statements June 30, 2019

NOTE 1 – SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (continued)

Cash and Cash Equivalents

For financial reporting purposes, cash and cash equivalents include cash and investments that have maturities of less than three months.

Income Taxes

The Foundation is exempt from federal income taxes under Section 501(c)(3) of the Internal Revenue Code and Section 23701(d) of the California Revenue and Taxation Code.

New Accounting Pronouncement

On August 18, 2016, FASB issued ASU 2016-14, Not-for-Profit Entities (Topic 958)-Presentation of Financial Statements of Not-for-Profit Entities. The update addresses the complexity and understandability of net asset classification, deficiencies in information about liquidity and availability of resources, and the lack of consistency in the type of information provided about expenses and investment return. The Corporation has adjusted the presentation of these statements accordingly. The ASU has been applied retrospectively to all periods presented.

NOTE 2 – LIQUIDITY MANAGEMENT

The Foundation's financial assets which is consists only of cash and cash equivalents of \$1,262,274 is available within one year of the balance sheet to pay for general expenditures. The Foundation has a policy to structure its financial assets to be available as its general expenditures, liabilities, and other obligations come due. As part of its liquidity management, the Foundation invests excess cash in money market and checking accounts.

NOTE 3 – CONCENTRATION OF CREDIT RISK

During the fiscal year ended June 30, 2019, the Foundation maintained its cash in a single financial institution totaling in excess of the federal deposit insurance limit of \$250,000 per depository account. The Foundation has not experienced any losses in such accounts.

Notes to Financial Statements June 30, 2019

NOTE 4 - NET ASSETS WITH DONOR RESTRICTIONS

Following is a reconciliation of net assets with donor restrictions as of June 30:

	 2019	 2018
Restricted for the research of health effects of		
air pollution:		
Balance, beginning of the year	\$ 2,300,207	\$ 3,336,916
Decrease in restricted net assets	 (1,037,933)	 (1,036,709)
Balance, end of the year	\$ 1,262,274	\$ 2,300,207

NOTE 5 – RELATED PARTY TRANSACTIONS

In 2004, the Board of Directors of the South Coast Air Quality Management District (South Coast AQMD) established the Foundation to fund research into the potential connections between air pollution and brain tumors and lung cancer. South Coast AQMD's Executive Director and Treasurer hold the same positions at the Foundation as volunteers.

NOTE 6 - RECLASSIFICATIONS

The amounts previously reported have been reclassified to conform with the current year presentation. The reclassifications had no impact on the previously reported net assets.

NOTE 7 – COMPARATIVE FINANCIAL DATA

The amounts shown for 2018 in the accompanying financial statements are included only to provide a basis for comparison with 2019 and are not intended to present all information necessary for a fair presentation in accordance with generally accepted accounting principles.

NOTE 8 – SUBSEQUENT EVENTS

In preparing these financial statements, the Foundation has evaluated events and transactions for potential recognition or disclosure through August 30, 2019, the date the financial statements were issued, and concluded no events have occurred that require disclosure or adjustments to the financial statements.