BOARD MEETING DATE: March 3, 2017 AGENDA NO. 13

PROPOSAL: Annual Meeting of the Brain & Lung Tumor and Air Pollution

Foundation

SYNOPSIS: This item is to conduct the annual meeting of the Brain & Lung

Tumor and Air Pollution Foundation. The Foundation staff will present an annual report detailing the research supported by the Foundation over the past year, the Foundation's plans for the future, and a financial report. In addition, the Foundation's Board of Directors recommends approval of the proposed amendments to the Foundation's Articles of Incorporation. The amendments will expand the type of research the Foundation can fund from brain and lung tumors to all health conditions that may be caused or aggravated by air pollution. The amendments will also change the Foundation's name to reflect the Foundation's broadened purpose.

COMMITTEE: No Committee Review

RECOMMENDED ACTIONS:

- 1. Receive and file the annual report and ratify the Foundation's disbursements described in the annual report.
- 2. Amend the Foundation's Articles of Incorporation to (1) expand the type of research the Foundation can fund to include all health conditions that may be caused or aggravated by air pollution and (2) change the Foundation's name to the Health Effects of Air Pollution Foundation.

Wayne Nastri Executive Officer

KRW:ML

2017 Annual Report

1. Background

In February 2003, the Board established the Brain Tumor and Air Pollution Foundation. In March 2004 the Foundation amended its Articles of Incorporation to change its name to Brain & Lung Tumor and Air Pollution Foundation (Foundation) and to specify that

its purpose is related to the effects of air pollution on brain tumors and lung cancer. The mission of the Foundation is to support research studies on the association between air pollution and brain and lung tumors, as well as research for the development of novel therapeutics for such tumors. To date, the amount of funding received is \$8,222,568. The current projects being funded by the Foundation are described in Section 3 below.

2. Directors and Officers

The Directors of the Foundation are: Ben Benoit, Vice Chairman

Dr. William A. Burke Dr. Clark E. Parker, Sr.

Judith Mitchell

The Board of Directors will select a Chairperson at an upcoming Board of Directors meeting.

The Foundation's staff is: Wayne Nastri, Chief Executive Officer

Denise Whitcher, Secretary Michael O'Kelly, Treasurer

3. Report on the Foundation's Activities

Recently Completed Research Projects

The following research projects concluded during the past 12 months:

"Chronic Exposure (1 Year) of Mice to Ambient Particles to Study Cancer-Related Stem Cell Activation in the Brain" (BTAP008)

Principal Investigator: Dr. Keith Black (Cedars-Sinai Medical Center)

Summary: This toxicological study investigated the effects of long-term exposure to PM on molecular changes in the brain, focusing on genes and proteins related to tumor development and neurodegenerative diseases. The study also analyzed human brain tumor tissues to identify proteins that may contribute to tumor growth. In the mouse study, the investigators found that long-term exposure to PM increased the expression of several genes associated with increased inflammation and immune response, which indicate possible injury to the brain. Tumor markers and markers of neurological disease were also overexpressed. The study also identified several changes in protein expression in the PM-exposed mice, compared to the mice breathing fresh air. The PMexposed mice, and especially the mice exposed to ultrafine particles, expressed higher levels of proteins linked to inflammation, oxidative stress, protein degradation, and nitrogen oxide signaling. The PM-exposed mice also had lower levels of proteins linked to nerve cell growth and differentiation, tubulin synthesis, calcium metabolism and mitochondrial function. Based on the data on protein expression in mice, long-term exposure to PM was associated with changes that are linked to a number of neurodegenerative diseases and conditions, as well as brain tumor development (glioblastoma multiforme). In the study of human brain tumor tissues, the investigators

found increased expression of a specific protein (laminin) and its receptor integrin, as well as cancer stem cell markers, compared to non-tumor brain samples. These proteins play important roles in tumor growth and development, and inflammation in the brain can contribute to tumor growth by stimulating cancer stem cells.

"Childhood Brain Tumors and Air Pollution" (BTAP009) Principal Investigator: Dr. Roberta McKean-Cowdin (University of Southern California)

Summary: This epidemiological study investigated the potential links between PM2.5 and NO2 exposures and childhood brain tumors among children living in Los Angeles, San Bernardino, Riverside and Orange Counties. The study used data from birth registries and two existing brain tumor studies (the West Coast Childhood Brain Tumor Study and the Southern California Childhood Brain Tumor Study). An air pollution exposure model was developed to estimate PM2.5 and NO2 exposures to each child from birth until diagnosis (for cancer cases) or reference age (for controls), and also for *in utero* exposures. Among the Los Angeles County children, the investigators found being exposed to high PM2.5 levels *in utero* or soon after birth was associated with a higher risk of being diagnosed with childhood brain tumors. Exposure to high levels of NO2 in early childhood was also associated with increased risk of childhood brain tumors. The study evaluated concurrent exposure to PM2.5 and NO2 and concluded that PM2.5 may serve as a better marker of regional traffic-related air pollution exposures in the Los Angeles area, while NO2 may be a better indicator of local traffic sources.

Current Research Projects

The following research projects were approved for funding by the Foundation Board in November 2016:

"A Cohort Study of Air Pollution, Malignant and Benign Brain Tumors in Los Angeles County" (BTAP010)

Principal Investigator: Dr. Anna Wu (University of Southern California)

Approved Funding: \$758,978

Summary: The proposed study will leverage the Multiethnic Cohort (MEC) study to examine whether air pollution is associated with primary malignant and benign brain tumors. The investigators leverage previous air pollution exposure work and propose adding new components (e.g. ultra-fine particle exposure, air toxics) to comprehensively assess air pollution exposures in the MEC cohort. The study proposes to examine associations between traffic air pollution and malignant primary brain cancer and meningiomas (non-cancerous brain tumors).

"Role of particle-induced inflammation in progression of brain tumors and neurodegenerative brain diseases" (BTAP011)

Principal Investigator: Dr. Keith Black (Cedars-Sinai Medical Center)

Approved Funding: \$733,461

Summary: The investigators propose to study whether exposure to ambient air pollution-derived particulate matter (PM) alters the progression of brain tumors in mice. The mice proposed to be used in the experiments have brain tumors initiated from human glioblastoma cell lines. The PM will be concentrated for experimental use from Irvine, CA ambient air. As part of this study, changes in tumor progression and inflammatory markers (measured by changes in gene expression) and stem cell activation will also be evaluated.

"Do Changes in Amount and Composition of Ambient PM Influence Induction or Exacerbation of Brain and Lung Tumors?" (BTAP012)

Principal Investigator: Dr. Arthur Cho (University of California, Los Angeles)

Approved Funding: \$979,182

Summary: This study proposes to use cellular and mouse models to investigate whether exposure to air pollution (PM and vapor phase) increases the expression of biological markers that are associated with the development or progression of lung or brain cancers. The investigators propose to collect ambient air samples at several locations and in different seasons in the Los Angeles Air Basin. The samples will be characterized for their potential biological actions, and then used in studying the potential effects in human lung cancer cells and brain cancer cells. Biological markers relevant to cancer development or progression (oxidative stress, inflammation, tumor cell growth stimulators, and invasive behavior of cells) will be evaluated in these experiments. The air samples will also be used in an exposure study of mice induced with brain cancer cells, to monitor and quantify tumor growth. Additionally, the study will separate the PM from the air samples into "fractions" with different chemical properties, and these PM fractions will be tested for toxicity using human lung and brain cancer cells, using the same biological markers for inflammation and tumor cell growth.

4. Financial Report

The Foundation's fiscal year ended June 30, 2016. Financial statements were prepared by staff and audited by Simpson and Simpson, CPA (Auditor). Total expenses for the fiscal year were \$1,369 and included audit fees (\$1,209) and other fees/taxes (\$160). The Auditor issued an unmodified opinion, indicating that the financial statements were presented fairly, in all material respects, and in accordance with generally accepted accounting principles.

As of January 31, 2017, the Foundation had a cash balance of \$2,585,671. Following is an accounting of the Foundation's operations since its inception (7/23/03):

| Revenue from Operations | |
|--------------------------------|-------------|
| Contributions | \$8,222,568 |
| Interest Income | 41,420 |
| Total Revenue from Operations | \$8,263,988 |
| Operating Expenses | |
| Grants | |
| -Cedars-Sinai | \$5,309,250 |
| -USC | 351,328 |
| Corporation Filing Costs | 1,550 |
| Bank charges | 589 |
| Professional fees-audit | 15,600 |
| Total Operating Expenses | \$5,678,317 |
| Cash Balance | \$2,585,671 |

5. Amendment of the Foundation's Articles of Incorporation

At the Foundation's Board of Directors meeting on February 10, 2017, the Board voted to amend the Foundation's Articles of Incorporation to expand the type of research the Foundation can fund. Currently, the Articles of Incorporation specify that the purpose of the Foundation is (i) to aid, assist, and support research on the incidence, detection and causes and cures of brain and lung tumors, especially those caused or aggravated by air pollution; and (ii) to receive and utilize funds acquired through the solicitation of donations, gifts, and bequests for the purposes for which the Foundation was formed. The amendments approved by the Board of Directors expand the Foundation's purpose from supporting brain and lung tumor research to supporting research of all health conditions that may be caused or aggravated by air pollution. In addition, the amendments change the Foundation's name to the "Health Effects of Air Pollution Foundation" to reflect the Foundation's broadened purpose. It is proposed that the Governing Board approve the proposed amendments. If approved by the Governing Board, a certificate of amendment will be filed with the Secretary of State.

6. Plans for the Upcoming Year

The Foundation will continue monitoring the progress of the existing research projects.

In July 2015, the Foundation Board authorized the release of RFP# BLTAPF-1 to solicit research proposals related to the incidence, detection, and causes and cures of brain and lung tumors that are caused or aggravated by air pollution. In November 2016, the Foundation Board authorized funding for the three proposals noted above. The contract awarded to Cedars-Sinai funds a study of the effects of air pollution on brain tumors (\$733,461 for a 1-year study). The proposal from Cedars-Sinai also included a second phase of the study, which is a study of air pollution and Alzheimer's disease. This

second phase of the study was not funded through the RFP. The approximate total cost for this second phase is \$750,000, for a 1-year project period. The proposed study is a toxicological study of mice that are genetically pre-disposed to develop Alzheimer's disease. The study would look at specific genes that may be activated when mice are exposed to PM air pollution (coarse/fine/ultrafine). In February 2017, the Foundation Board approved funding the proposal for the second phase of the study, contingent on the transfer of funds from the Health Effects Fund and the Governing Board's approval of the amendments to the Articles of Incorporation and their subsequent filing with the Secretary of State.

Resource Impacts

None.

Attachment

Articles of Incorporation

CERTIFICATE OF AMENDMENT RESTATED ARTICLES OF INCORPORATION

OF

BRAIN AND LUNG TUMOR AND AIR POLLUTION FOUNDATION

a California nonprofit public benefit corporation

Wayne Nastri and Denise Whitcher certify that:

- 1. They are the Chief Executive Officer and Secretary, respectively, of the Brain and Lung Tumor and Air Pollution Foundation, a California nonprofit public benefit corporation.
- 2. The Articles of Incorporation of this Corporation are hereby amended and restated in their entirety to read as follows:

"I.

NAME

BRAIN AND LUNG TUMOR AND HEALTH EFFECTS OF AIR POLLUTION FOUNDATION

The name of this Corporation is Brain and Lung Tumor and Health Effects of Air Pollution Foundation.

I.

PURPOSES

This corporation is a nonprofit public benefit corporation and is not organized for the private gain of any person. It is organized under Nonprofit Public Benefit Corporation Law for public and charitable purposes.

The specific purposes of this corporation are: (i) to aid, assist, and support research on the incidence, detection and causes and cures of brain and lung tumors various health conditions that may be, especially those caused or aggravated by air pollution; and (ii) to receive and utilize funds acquired through the solicitation of donations, gifts, and bequests for the purposes for which this corporation was formed.

Notwithstanding any other provision of these Articles of Incorporation, this corporation shall not carry on any other activities not permitted to be carried on by a corporation exempt from Federal income tax under section 501(c)(3) of the Internal Revenue Code of 1986 (or the corresponding provision of any future United States Internal Revenue Law), or by a corporation, contributions to

which are deductible under section 170(c)(2) of the Internal Revenue Code of 1986 (or the corresponding provision of any future United States Internal Revenue Law).

III.

MEMBER

This corporation shall have only one member within the meaning of Section 5056 of the California Corporations Code ("CCC"), and it is the South Coast Air Quality Management District, a district formed under statutes.

IV.

DEDICATION AND DISSOLUTION

- (a) The property of this corporation is irrevocably dedicated to public and charitable purposes, and no part of the net income or assets of this corporation shall ever inure to the benefit of any director, officer, or member thereof, or to the benefit of any private person.
- (b) On the dissolution or winding up of the corporation, its assets remaining after payment of, or provision for payment of, all debts and liabilities of this corporation shall be distributed to a nonprofit fund, foundation, or corporation which is organized and operated exclusively for public or charitable purposes and which has established its tax-exempt status under section 501(c)(3) of the Internal Revenue Code of 1986 (or the corresponding provision of any future United States Internal Revenue Law), and whose sole member is the South Coast Air Quality Management District.
- (c) If this corporation holds any assets in trust, or if the corporation is formed for charitable purposes, then such assets shall be disposed of in such manner as may be directed by decree of the superior court of the county in which the corporation has its principal office, on petition therefore by the Attorney General or by any person concerned in the liquidation, in a proceeding to which the Attorney General is a party.

V.

LIMITATION ON CORPORATE ACTIVITES

No substantial part of the activities of this corporation shall consist of the carrying on of propaganda, or otherwise attempting to influence legislation, nor shall this corporation participate or intervene in any political campaign (including publishing or distribution of statements) on behalf of or in opposition to any candidate for public office.

VI.

AMENDMENT

These Articles of Incorporation may not be amended, restated, or modified without the consent of its sole member and without the consent of more than two-thirds (2/3) majority of the Board of Directors of this corporation."

- 3. The foregoing amended and restated Articles of Incorporation have been duly approved by the Board of Directors of this Corporation.
- 4. The foregoing amended and restated Articles of Incorporation have been duly approved by the member of this Corporation. This Corporation has one member.

We further declare under penalty of perjury under the laws of the State of California that the matters set forth in this certificate are true and correct of our own knowledge.

| Dated: | | |
|--------|-------------------------|--|
| | Wayne Nastri | |
| | Chief Executive Officer | |
| | | |
| | Denise Whitcher | |
| | | |
| | Secretary | |