A. COVER PAGE

Project Title: World Trade Center Tissue Biobank	
Grant Number: 5U01OH011704	**Project/Grant Period**: 07/01/2018 - 06/30/2023
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Program Director/ Principal Investigator EMANUELA TAIOLI , MD MS PHD Phone number: 212 659 9590 Email: Emanuela.taioli@mountsinai.org	**Administrative Official Information** AMANDA AMESCUA One Gustave L. Levy Place, Box 1075 New York, NY 100296574 Phone number: 646-605-8659 Email: amanda.amescua@mssm.edu
Change of Contact PD/PI: No	
Human Subjects: Yes	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** : No

B. ACCOMPLISHMENTS

B.1. What are the major goals of the project?

The overarching goal of this research study is to investigate the relatedness of WTC exposure to cancer and if present, how it may have caused the cancer. We propose to update the existing biobank of human solid organ tissues from each cancer diagnosed among the WTC rescue and recovery workers from 2010 onward, and to include a central repository of organs tissue samples from all the rodent experiments involving exposure to WTC dust at Mount Sinai and NYU, in order to facilitate and promote future clinical research and translational studies on cancer etiology, biology and cancer outcome. The repository may be used for future research addressing specific hypotheses. The specific aims of the project are: 1) To update the current WTCHP participants' biobank of solid organ tissues with the newly diagnosed cancers (after 2010). Relevant information from pathology and cytology reports from each cancer will also be centrally stored. This repository will have the capability to be linked with the main WTCHP data set containing clinical, epidemiological and exposure information, both at the time of inclusion in the WTCHP and during the regularly performed follow up, and to the blood sample collected at baseline. 2) To initiate, standardize and manage a central repository of tissue samples from various organs from rodents exposed to WTC dust. Relevant information from pathology reports will also be centrally stored, along with details of the exposure amount and duration, and of the experimental design. 3) To establish the bank as a resource for the scientific community. The human and animal tissue banks will be managed in conjunction, and will follow the same process for receiving requests of samples from qualified applicants for research purposes, and for ongoing evaluation of the bank utilization. Objective: We propose to continue the tissue bank system for the WTC newly diagnosed cancers, focused on advancing the understanding of the biology of the tumors that occurred after the WTC disaster. We will also initiate, standardize and manage a central repository of tissue samples from various organs from rodents exposed to WTC dust IRB approval has been received for this project and cancer patient information has been received from the WTC data center. Standardized methods for both human and animal sample storage have been established. Requesting consent from cancer patients was started late, due to IRB approval covering Q1 and Q2.

B.2. What did you accomplish under these goals?

No

B.3. Competitive Revisions/Administrative Supplements

No

B.4. What opportunities for training and professional development did the project provide?

NOTHING TO REPORT

B.5. How did you disseminate the results to communities of interest?

The availability of the WTC Biobank as a resource has been disseminated throughout Mount Sinai health system to various departments and institutes, resulting in inquiries into the capabilities and details of the resource. This has resulted in a linkage with the BioMe repository at Mount Sinai, a connection that was published in the BioMe winter newsletter and sent to addresses to over the 60,000 participants present in the BioMe repository. An image of the WTC Biobank in the BioMe newsletter is included below. Speakers brought by ITE to Mount Sinai have also been informed on the WTC Biorepository. This has resulted in an interest to sequence thyroid samples of WTC participants in order to compare them to other populations who have developed thyroid cancer. These connections have begun offering the biobank as a resource for the scientific community. Additionally, the biorepository is advertised via the Institute for Translational Epidemiology's website with a link to request more information and collaborate (http://icahn.mssm.edu/research/epidemiology/capabilities/biorepository-wtc) . A new brochures describing the

biobank is also disseminated at professional conferences and during workshops that ITE holds multiple times per year. Publication of the descriptive paper of the biorepository of WTC cancer tissue in humans has continued to result in inquiries to utilize cancer tissue as well as general notoriety of the resource. The publication of the descriptive paper of the rodent tissue bank as a complementary resource to the human tissue bank has also resulted in inquires about the capabilities of the resource and possible collaborations and research questions.

B.6 - What do you plan to do during the next reporting period to accomplish the goals?
Not applicable

C. PRODUCTS

C.1. Publications, conference papers, and presentations

Lieberman-Cribbin W, Tuminello S, Gillezeau C, van Gerwen M, Brody R, Donovan M, Taioli E. The development of a Biobank of cancer tissue samples from World Trade Center responders. J Transl Med. 2018 Oct 11;16(1):280. doi: 10.1186/s12967-018-1661-x. PMID: 30309352; PMCID: PMC6182816.

van Gerwen MAG, Tuminello S, Riggins GJ, Mendes TB, Donovan M, Benn EKT, Genden E, Cerutti JM, Taioli E. Molecular Study of Thyroid Cancer in World Trade Center Responders. Int J Environ Res Public Health. 2019 May 7;16(9):1600. doi: 10.3390/ijerph16091600. PMID: 31067756; PMCID: PMC6539993.

Tuminello S, van Gerwen MAG, Genden E, Crane M, Lieberman-Cribbin W, Taioli E. Increased Incidence of Thyroid Cancer among World Trade Center First Responders: A Descriptive Epidemiological Assessment. Int J Environ Res Public Health. 2019 Apr 9;16(7):1258. doi: 10.3390/ijerph16071258. PMID: 30970543; PMCID: PMC6479621.

Gong Y, Wang L, Yu H, Alpert N, Cohen MD, Prophete C, Horton L, Sisco M, Park SH, Lee HW, Zelikoff J, Chen LC, Hashim D, Suarez-Farinas M, Donovan MJ, Aaronson SA, Galsky M, Zhu J, Taioli E, Oh WK. Prostate Cancer in World Trade Center Responders Demonstrates Evidence of an Inflammatory Cascade. Mol Cancer Res. 2019 Aug;17(8):1605-1612. doi: 10.1158/1541-7786.MCR-19-0115. Epub 2019 Jun 20. Erratum in: Mol Cancer Res. 2019 Aug;17(8):1774. PMID: 31221798; PMCID: PMC6684261.

Yu H, Tuminello S, Alpert N, van Gerwen M, Yoo S, Mulholland DJ, Aaronson SA, Donovan M, Oh WK, Gong Y, Wang L, Zhu J, Taioli E. Global DNA methylation of WTC prostate cancer tissues show signature differences compared to non-exposed cases. Carcinogenesis. 2022 Jun 27;43(6):528-537. doi: 10.1093/carcin/bgac025. PMID: 35239955; PMCID: PMC9234756.

van Gerwen M, Cerutti JM, Mendes TB, Brody R, Genden E, Riggins GJ, Taioli E. TERT and BRAF V600E mutations in thyroid cancer of World Trade Center Responders. Carcinogenesis. 2023 Jun 24;44(4):350-355. doi: 10.1093/carcin/bgad029. PMID: 37144982; PMCID: PMC10290513.

C.2. Website(s) or other Internet site(s) – include URL(s)
https://icahn.mssm.edu/research/epidemiology/capabilities/biorepository-wtc

C.3. Technologies or techniques
Not applicable

C.4. Inventions, patent applications, and/or licenses

Not applicable

C.5. Other products and resource sharing
Not applicable

D. PARTICIPANTS

D.1. What individuals have worked on the project? Please include calendar, academic, and summer months.

Commons ID	S/K	Name	Degrees(s)	Role	Cal	Aca	Sum	Foreign	Country	SS
TAIOLI		Emanuela Taioli		PI	1.83					
		Rebecca Schwartz		Co-I	1.20					
		Christina Gillezeau		Coordinator	4.26					
		Joseph Rapp		Coordinator	9.04					
		Ashley Moreland		Coordinator	7.34					

D.2 Personnel updates

a. Level of Effort:
b. New Senior/Key Personnel:
c. Changes in Other Support:
d. New Other Significant Contributors:

E. IMPACT

E.1 - What is the impact on the development of human resources, if applicable?
Not Applicable

E.2 - What is the impact the Public Health Relevance and Impact? The investigator should address how the findings of the project relate beyond the immediate study to improved practices, prevention or intervention techniques, legislation, policy, or use of technology in public health.

NOTHING TO REPORT

F. CHANGES

F.1 – Changes in approach and reasons for change, including changes that have a significant impact on expenditures
Not Applicable

F.2 - Actual or anticipated challenges or delays and actions or plans to resolve them
Not applicable

F.3 - Significant changes to human subjects, vertebrate animals, biohazards, and/or select agents
Not applicable

G. Special Reporting Requirements

G.1 Special Notice of Award Terms and Funding Opportunities Announcement Reporting Requirements
NOTHING TO REPORT

G.2 Responsible Conduct of Research

Not Applicable

G.3 Mentor's Research Report or Sponsor Comments

Not Applicable

G.4 Human Subjects

G.4.a Does the project involve human subjects?

Yes
G.4.b Inclusion Enrollment Data

No
G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?
No

G.5 Human Subject Education Requirement

Are there personnel on this project who are newly involved in the design or conduct of human subject's research?

No

G.6 Human Embryonic Stem Cells (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?
No

G.7 Vertebrate Animals

Does this project involve vertebrate animals?
Yes

G.8 Project/Performance Sites

Primary: MOUNT SINAI SCHOOL OF MEDICINE 078861598 ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI
1 GUSTAVE L. LEVY PL NEW YORK NY 100296574

New York University School of Medicine.. 121911077 NY-012 57 Old Forge Road Tuxedo NY 109875007

G.9 Foreign Component

No foreign component

G.10 Estimated Unobligated Balance

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

G.11 Program Income

Is program income anticipated during the next budget period?

G.12 F&A Costs

Is there a change in performance sites that will affect F&A costs?
Not applicable

I. OUTCOMES

I. Provide a concise summary of the outcomes or findings of the award, written for the general public in clear and comprehensible language, without including any proprietary, confidential information or trade secrets

Note: project outcome information will be made public in NIH RePORTER

Biospecimen resources and their clinical annotations are among some of the most powerful resources fueling translational research. The tissue bank represents the necessary infrastructure for addressing questions such as the link between specific carcinogens exposures and cancer developed in certain sites such as prostate and thyroid, molecular signatures of exposure, which could be linked to cancer, and specific markers of tumor aggressiveness among WTC responders.

This project has several important innovative aspects, including the comparison of human and animal response to exposure to WTC carcinogens. This project gives the opportunity for the first time to compare systemic and

local changes observed in rodents exposed in a controlled fashion to WTC dust to what is observed in human peripheral blood, normal and cancer tissues of WTC responders

Comparative research between animal and human studies is highly translational and may play a central role in understanding if there is an association between WTC exposure and tumor biology and aggressiveness. Thus, the proposed inclusion of both human and animal tissue banking will provide a new platform to facilitate examination of the underlying mechanisms of cancer development associated with WTC exposure. The WTCHP runs separate data sets containing comprehensive clinical information and details on environmental exposures that occurred at the WTC site. These data sets can be conveniently linked with the biobank, thus providing future investigators endless possibilities for studies on cancer etiology, biology and outcome in the WTC population. A bank of peripheral blood collected at the time of enrollment in the WTCHP is also available and can be linked to each cancer case. This will facilitate studies of the systemic inflammatory and immuno-response in the immediate aftermath of the disaster, along with analyses of WTC toxicants and carcinogens in the blood that could be linked to the subsequent cancer development. Another key element is that these rodents are exposed to different doses of WTC dust and for different time spans, thus available tissues will reflect and mimic both the intensity and the duration of exposure that occurred in WTC responders.

The tissue bank offers both human and animal biological specimens for comparison; the results are analyzed in conjunction with the exposure, epidemiologic and clinical information available from the WTCHP. The biobank will facilitate translational studies that for the first time will give a comprehensive view of the effect of WTC exposure on cancer etiology, occurrence and aggressiveness. Examples of various multicentric, collaborative biomarkers studies which have used tissues tissues are: DNA methylation as a consequence of environmental exposure to carcinogens and prostate cancer, comparison of local tissue markers of inflammation in prostate tumors from WTC responders and in cancer patients not related to the WTC event, staining of thyroid cancer tissues to assess false positive diagnoses, HPV study on head and neck cancer tissues. All these studies are using the WTC tissue bank and would benefit from confirming their findings in corresponding tissues from organs of animals experimentally exposed to WTC dust.