A. OVERALL COVER PAGE

Project Title: Evolution of risk factors for lung function decline in WTC exposed firefighters	
Grant Number: 5U01OH011302-03	**Project/Grant Period:** 09/01/2016 - 08/31/2019
Reporting Period: 09/01/2018 - 08/31/2019	**Requested Budget Period:** 09/01/2018 - 08/31/2019
Report Term Frequency: Annual	**Date Submitted:** 11/24/2020
Program Director/Principal Investigator Information: MICHAEL D WEIDEN , MD BS MS **Phone Number:** 212 263 6479 **Email:** michael.weiden@med.nyu.edu	**Recipient Organization:** NEW YORK UNIVERSITY SCHOOL OF MEDICINE One Park Avenue 6th Floor NEW YORK, NY 10016 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: KHULANGOO RIZAJ One Park Ave New York, NY 100165800 **Phone number:** 6467544679 **Email:** Khulangoo.Rizaj@nyumc.org	**Signing Official:** ANTHONY CARNA 360 Park Avenue South 10th Floor New York, NY 10010 **Phone number:** (212) 263-8822 **Email:** grants.office@med.nyu.edu
Human Subjects: NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Specific AIM 2 will test the hypothesis that the IgE and cytokines measured in the 6 months post-9/11 will be associated incident airway reactivity.
We have published our analysis of serum cytokines and IgE.

We have made significant progress on specific AIM number one. Since the initiation of funding we have published a report demonstrating that IFN-□, IL-21 and IgE are predictors of airway reactivity. We have published the following abstract: Association of Th-2 Biomarkers with FEV1 Decline: A 17-Year Longitudinal Study of World Trade Center Exposed Firefighters

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

B.2 (B2.pdf)

Final Progress report

Grant Award#: OH011302 - Project Title: Evolution of risk factors for lung function decline in WTC exposed firefighters

B2
Narrative

Specific AIM 1 will test the hypothesis that Eos, PMN, IgE and inflammatory cytokines measured in the 6 months post-9/11 are risk factors for enhanced-FEV_1-decline.

We have made significant progress on specific AIM number one. Since the initiation of funding we have published 4 reports about risk factors for accelerated FEV_1 decline. Including IgE (Zeig-Owens et al., 2016) eosinophils (Zeig-Owens et al., 2018) and CT abnormalities (Liu et al., 2019). We have also confirmed that eosinophils predict upper airway injury producing Chronic Sinusitis (Putman et al., 2018). In the process of analyzing the IgE data we also observed significant association of another immune-globulin IgA with lung function. The no cost extension supported the following work

Low serum IgA and airway injury in World Trade Center-exposed firefighters: a 17-year longitudinal study.
Putman B, Lahousse L, Zeig-Owens R, Singh A, Hall CB, Liu Y, Schwartz T, Goldfarb D, Webber MP, Prezant DJ, Weiden MD.
Thorax. 2019 Dec;74(12):1182-1184. doi: 10.1136/thoraxjnl-2019-213715. Epub 2019 Oct 14.
PMID: 31611340

Abstract
Serum IgA ≤70 mg/dL (low IgA) is associated with exacerbations of chronic obstructive pulmonary disease. The association of low IgA with longitudinal lung function is poorly defined. This study included 917 World Trade Center (WTC)-exposed firefighters with longitudinal spirometry measured between September 2001 and September 2018 and IgA measured between October 2001 and March 2002. Low IgA, compared with IgA >70 mg/dL, was associated with lower forced expiratory volume in 1 s (FEV_1) % predicted in the year following 11 September 2001 (94.1% vs 98.6%, p<0.001), increased risk of FEV_1/FVC <0.70 (HR 3.8, 95% CI 1.6 to 8.8) and increased antibiotic treatment (22.5/100 vs 11.6/100 person-years, p=0.002). Following WTC exposure, early IgA ≤70 mg/dL was associated with worse lung function and increased antibiotic treatment.

Specific AIM 2 will test the hypothesis that the IgE and cytokines measured in the 6 months post-9/11 will be associated incident airway reactivity.
We have published our analysis of serum cytokines and IgE.

We have made significant progress on specific AIM number one. Since the initiation of funding we have published a report demonstrating that IFN-□, IL-21 and IgE are predictors of airway reactivity. We have published the following abstract:

Association of Th-2 Biomarkers with FEV1 Decline: A 17-Year Longitudinal Study of World Trade Center Exposed Firefighters

Putman, B (Putman, B.)[1] ; Singh, A (Singh, A.)[2] ; Zeig-Owens, R (Zeig-Owens, R.)[2] ; Lahousse, L (Lahousse, L.)[3] ; Prezant, DJ (Prezant, D. J.)[2] ; Weiden, MD (Weiden, M. D.)[1] AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE Volume: 201 Meeting Abstract: A5970 Published: 2020

Introduction. Accelerated FEV1 decline, defined as a FEV1 slope (rate of change in FEV1) <-64 ml/year, occurs in 12.7% of World Trade Center (WTC)-exposed firefighters. Accelerated-FEV1 decline and elevation of T-helper 2 (Th-2) biomarkers within 6 months of WTC exposure are both risk factors for asthma/COPD overlap. Conversely, IFN, a T-helper 1 (Th-1) biomarker, is protective. The longitudinal association between Th-1/Th-2 biomarkers and FEV1 decline has not been thoroughly investigated. We hypothesized a persistent longitudinal association between Th-1/Th-2 biomarkers and FEV1 decline.
Methods. Serum was drawn from Fire Department of the City of New York (FDNY) firefighters 1-6 months

(early n=846) and 12-13 years (late n=809) after WTC exposure; 120 individuals had serum drawn at both time intervals. IFN-□, IL-4, IL-13, IL-5 and IgE were assayed by multiplex Luminex. Individual FEV1 slopes for 1,535 WTC-exposed firefighters were calculated using spirometric measurements taken between 9/11 and September 10, 2018. Effect of early and late biomarkers on FEV1 slope after biomarker measurement were analyzed by multivariable linear regression.
Results. In both early and late time intervals, higher levels of IFN were associated with a slower rate of FEV1 decline (Table 1). Alternatively, IL-4 and IL-13 measured 1-6 months and 12-13 years after WTC exposure both predicted greater rate of FEV1 decline. A different pattern emerged with IL-5 and IgE. Higher levels of IL-5 and IgE measured 1-6 months after WTC exposure were associated with increased rate of FEV1 decline, but IL-5 and IgE measured 12-13 years after WTC exposure were no longer significantly related to subsequent rate of FEV1 decline.
Conclusions. In WTC-exposed firefighters, elevated serum IL-4 and IL-13, but not elevated IgE or IL-5, are associated with greater FEV1 decline throughout longitudinal follow-up. Drugs targeting IL-4 and IL-13 are candidates to treat accelerated-FEV1-decline persisting years after an irritant exposure.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Girvin F, Zeig-Owens R, Gupta D, Schwartz T, Liu Y, Weiden MD, Prezant DJ, Naidich DP. Radiologic Features of World Trade Center-related Sarcoidosis in Exposed NYC Fire Department Rescue Workers. Journal of thoracic imaging. 2016 September;31(5):296-303. PubMed PMID: 27442523; DOI: 10.1097/RTI.0000000000000230.
N/A: Not NIH Funded	Putman B, Zeig-Owens R, Singh A, Hall CB, Schwartz T, Webber MP, Cohen HW, Prezant DJ, Bachert C, Weiden MD. Risk factors for post-9/11 chronic rhinosinusitis in Fire Department of the City of New York workers. Occupational and environmental medicine. 2018 December;75(12):884-889. PubMed PMID: 30337339; DOI: 10.1136/oemed-2018-105297.
N/A: Not NIH Funded	Singh A, Liu C, Putman B, Zeig-Owens R, Hall CB, Schwartz T, Webber MP, Cohen HW, Berger KI, Nolan A, Prezant DJ, Weiden MD. Predictors of Asthma/COPD Overlap in FDNY Firefighters With World Trade Center Dust Exposure: A Longitudinal Study. Chest. 2018 December;154(6):1301-1310. PubMed PMID: 30028968; PubMed Central PMCID: PMC6289858; DOI: 10.1016/j.chest.2018.07.002.
N/A: Not NIH Funded	Liu C, Putman B, Singh A, Zeig-Owens R, Hall CB, Schwartz T, Webber MP, Cohen HW, Fazzari MJ, Prezant DJ, Weiden MD. Abnormalities on Chest Computed Tomography and Lung Function Following an Intense Dust Exposure: A 17-Year Longitudinal Study. International journal of environmental research and public health. 2019 May 13;16(9). PubMed PMID: 31085989; PubMed Central PMCID: PMC6540073; DOI: 10.3390/ijerph16091655.
N/A: Not NIH Funded	Cleven KL, Ye K, Zeig-Owens R, Hena KM, Montagna C, Shan J, Hosgood HD 3rd, Jaber N, Weiden MD, Colbeth HL, Goldfarb DG, Spivack SD, Prezant DJ. Genetic Variants Associated with FDNY WTC-Related Sarcoidosis. International journal of environmental research and public health. 2019 May 23;16(10). PubMed PMID: 31126090; PubMed Central PMCID: PMC6572061; DOI: 10.3390/ijerph16101830.
N/A: Not NIH Funded	Putman B, Lahousse L, Zeig-Owens R, Singh A, Hall CB, Liu Y, Schwartz T, Goldfarb D, Webber MP, Prezant DJ, Weiden MD. Low serum IgA and airway injury in World Trade Center-exposed firefighters: a 17-year longitudinal study. Thorax. 2019 December;74(12):1182-1184. PubMed PMID: 31611340; DOI: 10.1136/thoraxjnl-2019-213715.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
WEIDEM01	Y	Weiden, Michael D.	BS,MS,MD	PD/PI	4.0	0.0	0.0			NA

Glossary of acronyms:

S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS 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 REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

Not Applicable

G.4.b Inclusion Enrollment Data

File(s) uploaded:
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G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

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

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

Planned Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title: Evolution of risk factors for lung function decline in WTC exposed firefighters

Domestic/Foreign: Domestic

Comments: Demographics of subjects in data base for study.

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	**0**
Asian	9	61	6	16	**92**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	79	450	25	233	**787**
White	165	9882	51	395	**10,493**
More Than One Race	0	0	0	0	**0**
Total	**253**	**10,393**	**82**	**644**	**11,372**

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

Results. In both early and late time intervals, higher levels of IFN were associated with a slower rate of FEV1 decline (Table 1). Alternatively, IL-4 and IL-13 measured 1-6 months and 12-13 years after WTC exposure both predicted greater rate of FEV1 decline. A different pattern emerged with IL-5 and IgE. Higher levels of IL-5 and IgE measured 1-6 months after WTC exposure were associated with increased rate of FEV1 decline, but IL-5 and IgE measured 12-13 years after WTC exposure were no longer significantly related to subsequent rate of FEV1 decline.
Conclusions. In WTC-exposed firefighters, elevated serum IL-4 and IL-13, but not elevated IgE or IL-5, are associated with greater FEV1 decline throughout longitudinal follow-up. Drugs targeting IL-4 and IL-13 are candidates to treat accelerated-FEV1-decline persisting years after an irritant exposure.