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TITLE:
Using Affinity-Based Proteomics to Identify Diagnostic and Plasma Biomarkers for Endometriosis

PRINCIPAL INVESTIGATOR: **Towia Libermann, PhD**

CONTRACTING ORGANIZATION: **Beth Israel Deaconess Medical Center, Boston, MA**

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14. ABSTRACT

During the past year, we evaluated the association between 1,305 proteins in blood samples from 142 confirmed endometriosis cases and 74 controls participating in the Women's Health Study: From Adolescence to Adulthood (A2A) and identified 63 proteins significantly associated with endometriosis with an absolute fold change of greater than 1.2. Furthermore, we identified biological pathways associated with endometriosis, including cell migration and angiogenesis that were upregulated in endometriosis compared to controls ($p<6.0x10-9$). Furthermore, we observed that few proteins overlapped across lesion colors, suggesting different etiologic pathways. These findings were presented in an oral presentation at the World Congress of Endometriosis in March 2021. Among the cases we also evaluated proteins and pathways associated with persistent pain. These results were accepted for an oral presentation at the annual ASRM meeting to be held in October 2021. Finally, proteomics data was recently received on NHSII samples and quality control analyses are currently under way.

15. SUBJECT TERMS
None listed.

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. INTRODUCTION:

Endometriosis, which is characterized by pain and infertility, is the most frequent reproductive health diagnosis among female veterans along with menstrual disorders. Notoriously difficult to diagnose, the time between symptom onset and endometriosis diagnosis averages seven years, resulting in prolonged pain symptoms leading to decreased activity and poor mental health, greatly impacting women physically, psychologically, and economically over the life-course. Identifying diagnostic and prognostic biomarkers would enable earlier intervention and prevent progression to severe pain and infertility. However, identification of endometriosis biomarkers has been limited by the heterogeneity of the disease, inappropriate control groups, and lack of prospectively collected samples. Furthermore, progression of endometriosis is not well understood. Discovery of non-invasive diagnostic and prognostic biomarkers for endometriosis has the potential to revolutionize current medical practice, leading to earlier diagnosis and interventions as well as better clinical care that could significantly impact improvement in clinical outcomes of endometriosis. We hypothesize that endometriosis development and progression will lead to altered circulating protein profiles related to systemic inflammation and immunity years before emergence of symptoms and the clinical diagnosis of endometriosis that will be detectable through the novel proteomics technology, SOMAscan, enabling early diagnosis of endometriosis. In addition, alteration of inflammation and immune proteins in systemic environments will be greater among women who do not experience pain remediation after surgical treatment. We will utilize data and specimens from the two population-based cohort studies, the Nurses' Health Study II (NHSII), a prospective cohort study with blood samples collected months to years before endometriosis diagnosis, and the Women's Health Study: Adolescent to Adulthood (A2A), a deeply phenotyped longitudinal cohort of endometriosis patients, to identify non-invasive diagnostic and prognostic protein biomarkers for endometriosis. We urgently need endometriosis biomarkers to reduce the delay to treatment and reveal new potential therapeutic targets to improve treatment outcomes and quality of life in these patients. Our unique resources will enable us to identify novel diagnostic and prognostic blood protein biomarkers for endometriosis. In the **short-term**, the proteomic data generated in our study will provide clinically applicable non-invasive diagnostic and prognostic biomarkers for endometriosis and improve treatment outcomes. **Long-term**, our study will provide biological insight to the heterogeneity and different pathogenesis by types of endometriosis and progression from the aspect of inflammation, immune dysregulation, and angiogenesis, which could lead to potential prevention strategies and development of novel therapeutic targets including immunotherapies.

2. KEYWORDS:

Endometriosis, proteomics, biomarkers, plasma, SOMAscan, diagnosis, predictor, risk model, pain

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Major Task 1. Generating proteomics data

a. Local IRB Approval: IRB Approved 11/14/19 and 12/23/19
b. Milestone #1: HRPO Approval obtained 4/3/20

Specific Aim 1: In prospectively collected samples from 200 NHSII participants with laparoscopically confirmed endometriosis and 200 without, identify proteins that differentiate women who will be diagnosed with laparoscopically confirmed endometriosis from controls.

Major Task 2. Generating proteomics data on NHSII samples

a. Subtask 1. Identify appropriate cases and controls in NHSII. Retrieve and aliquot plasma samples: Due to the Covid-19 pandemic all labs were shut down for 4 months which delayed the identification and retrieval of samples from NHSII. Nevertheless, the samples were identified, retrieved from storage, aliquoted, and delivered to the Libermann lab by 8/31/20.
b. Subtask 2. Create quality control (QC) samples and plan how to align the blinded QCs and samples for proteomics assay: Samples with integrated QCs were delivered to the Libermann lab on 08/31/20.
c. Subtask 3. Measure 1,305 proteins and check quality control for variation within and between plates on NHSII samples: Assays are complete as of 9/10/21 and quality controls metrics have been calculated as of 9/17/21.
d. Milestone #2: Generating proteomics NHSII data. Completed as of 9/10/21.

Major Task 3. Identify proteins that differentiate endometriosis cases from controls using proteomics data from 200 cases and 200 controls in the NHSII

a. Subtask 1. Identify proteins that differentiate endometriosis cases from controls using the prospective samples in NHS: Planned completion by 06/01/22
b. Subtask 2. Manuscript preparation: Planned completion by 8/31/22
c. Milestone #3: Publish proteomics data predictive of endometriosis

Specific Aim 2: In plasma from 150 deeply phenotyped cases and 50 matched controls from the A2A study, determine whether proteins differ between subtypes.

Major Task 4. Identify proteins that differentiate endometriosis subtypes using proteomics data from 150 cases and 50 controls in the A2A

a. Subtask 1. Identify proteins that differentiate endometriosis cases from controls in A2A: Completed SOMAscan run on 7/20/20. Data analysis is complete, results were presented as oral presentation at the World Congress of Endometriosis on 03/07/21, and manuscript has been drafted. The manuscript is currently under review by coauthors, and we expect to have it submitted by 10/31/21.
b. Subtask 2. Evaluate whether proteins identified perform better than CA125 to discriminate cases from controls: Planned completion by 3/31/22
c. Subtask 3. Manuscript preparation: We expect this task to yield two manuscripts. The first has been drafted and will be submitted this calendar year (2021). We have completed data analyses for the second and we expect to have that manuscript drafted by the next progress report (September 2022).
d. Milestone #4: Publish protein performance compared to CA125 and by endometriosis subtype

Specific Aim 3: In preoperative samples from 100 women with endometriosis from the A2A study, identify proteins and pathways that discriminate between those who have progressive disease, characterized by chronic pain and poor quality of life, and those who improve after surgery.

Major Task 5. Identify proteins associated with progression of endometriosis

a. Subtask 1. Identify proteins associated with persistent pain and/or poor quality of life after surgical treatment of endometriosis in the A2A progression study: Completed SOMAscan run on 7/20/20. Data analyses were completed in August 2021.
b. Subtask 2. Use systems biology to identify pathways relevant to progression of endometriosis: Pathway analyses have been completed and an abstract was submitted to the American Society for Reproductive Medicine (ASRM) conference and invited for an oral presentation on 10/20/21

c. Subtask 3. Manuscript preparation: Planned completion by 10/31/22
d. Milestone #5: Publish proteins associated with endometriosis progression

What was accomplished under these goals?

1) Major activities

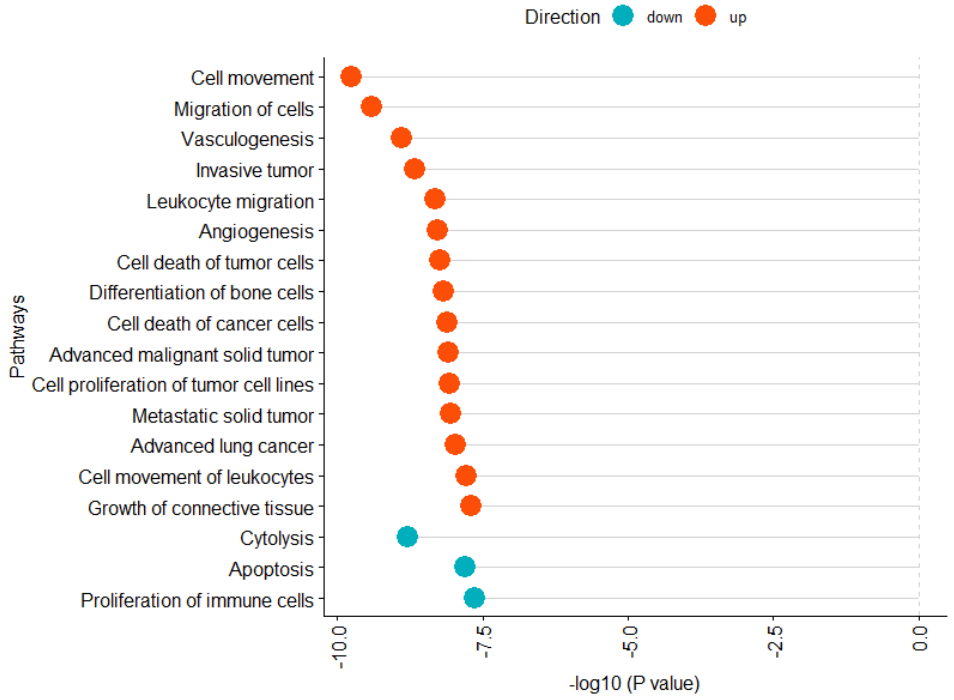
Over the past year, we accomplished the following major activities. For Aim 1, we successfully generated proteomics data on 1,305 proteins using the SOMAscan platform on 200 cases and 200 control samples from the Nurses' Health Study II cohort. Data analyses to evaluate the reproducibility of blinded quality control samples demonstrated high quality and reproducibility of the SOMAscan data. For Aim 2, we completed our data analyses evaluating individual proteins and proteomic pathways that differentiate cases and controls and the manuscript draft is currently under review by coauthors. In addition, we completed analyses on proteins and pathways associated with different endometriosis subtypes. For Aim 3, we have successfully completed data analyses and submitted an abstract to the ASRM conference which was selected for an oral presentation which will be delivered by Dr. Naoko Sasamoto on 10/20/21 in Baltimore, Maryland.

2) Specific Objectives

a. Identify proteins that differentiate endometriosis cases from controls in prospectively collected samples from the Nurses' Health Study II.
b. Identify proteins that differentiate cases and controls in A2A.
c. Evaluate whether proteins identified perform better than CA125 to discriminate cases from controls.
d. Identify proteins associated with persistent pain and/or poor quality of life after surgical treatment of endometriosis in the A2A progression study.

3) Significant results or key outcomes, including major findings, developments, or conclusions

Figure 1. Top pathways associated with endometriosis based on 63 proteins with p<0.05 and absolute fold change >1.2



This year we were able to move our research to discover diagnostic and prognostic biomarkers for endometriosis forward on several fronts. First, in the discovery of diagnostic biomarkers, we successfully measured 1,305 protein levels on 200 endometriosis cases and 200 matched controls from the Nurses' Health Study II (Aim 1). Although we have not had a chance to analyze these results yet (the stated goal in our original grant was to complete this by the end of year 2), the proteins levels have been measured and the quality control metrics with regard to normalization and calibration are good, suggesting the results are valid and reliable. Analyses of the blinded quality control samples demonstrated that 90% (1182/1305) of the proteins have a CV<25% and an ICC>0.4, adding strong evidence that the SOMAscan data for these NHS II samples are highly reproducible. Given delays due to the pandemic, leading to a late receipt of the samples by the lab, we are pleased with our progress on this front.

In Aim 2, we sought to evaluate case control differences in proteins by analyzing baseline data cross sectionally from the A2A. Using proteomics data generated from the A2A specimens in year 1, we analyzed data with Dr. Long Ngo performing the statistical analyses and all investigators contributing in real time to the analysis plan and interpretation of results through weekly Zoom meetings. Through these analyses we identified 63 proteins associated with endometriosis with a nominal p-value <0.05 and absolute fold change >1.2. Furthermore, we identified biological pathways that were associated with endometriosis. As illustrated in **Figure 1**, pathways related to cell migration and angiogenesis were upregulated in endometriosis compared to controls (p-value<$6.0x10^{-9}$). Furthermore, when we examined proteins associated with lesion colors, there were few proteins that overlapped across lesion colors, suggesting different pathways of pathogenesis as illustrated by the Venn diagram in **Figure 2**. A manuscript has been drafted by Dr. Sasamoto and is currently being reviewed by coauthors.

Figure 2. Venn diagram of overlapping proteins by lesion colors among endometriosis cases

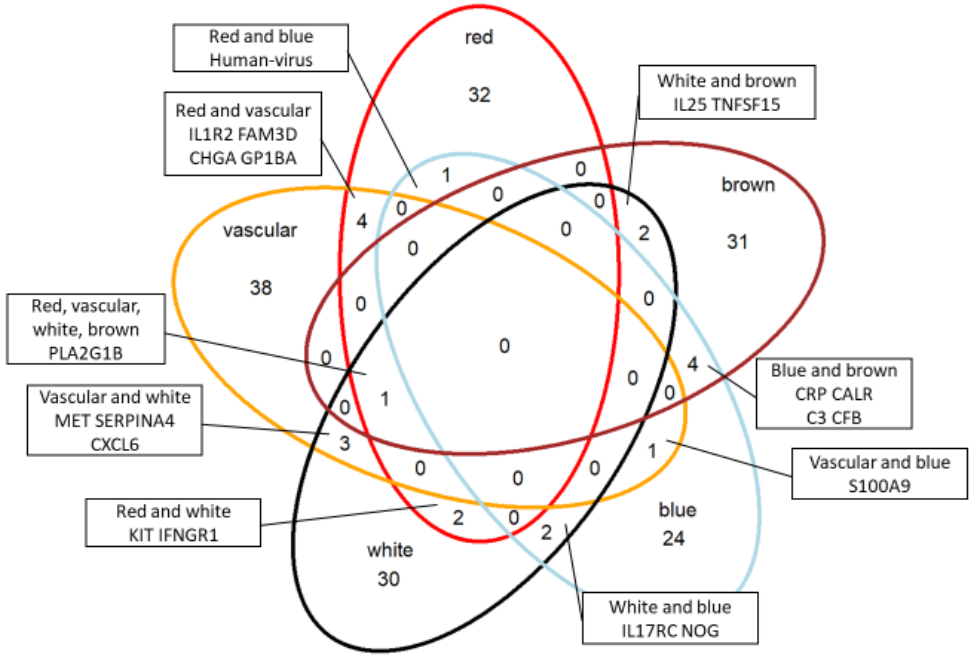
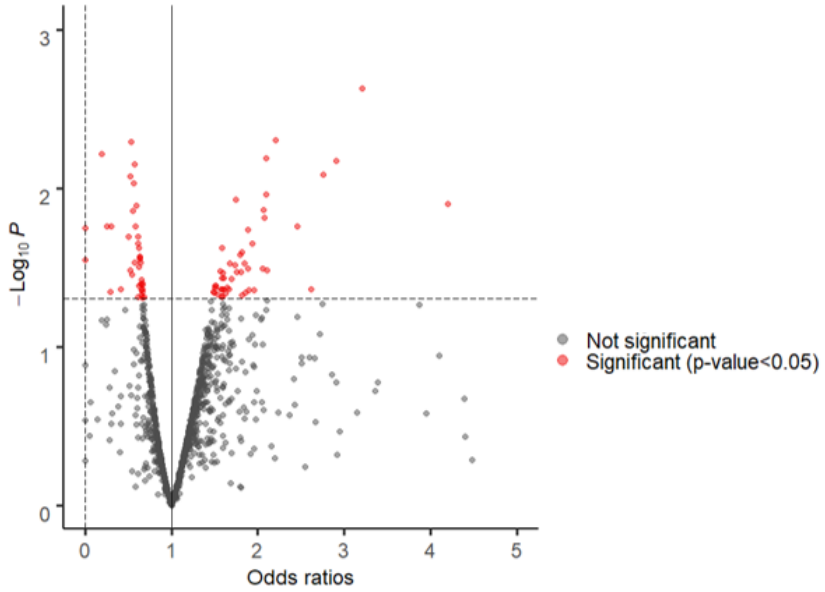


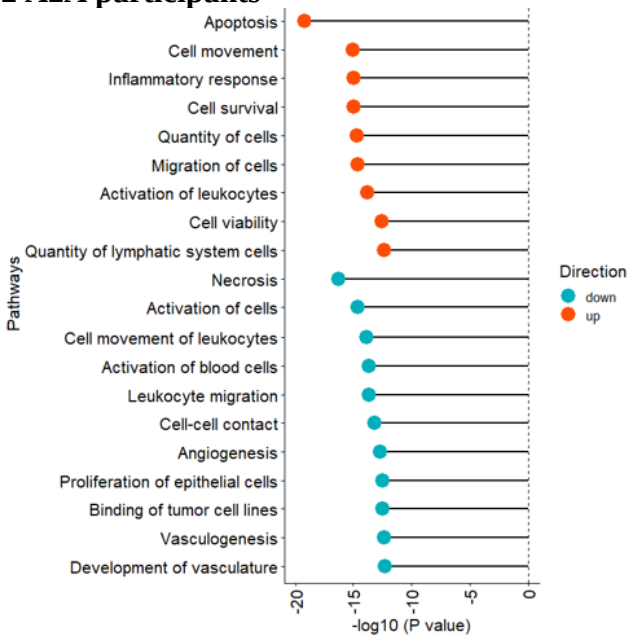
Figure 3. 94 proteins measured at baseline are associated with persistent pain after endometriosis surgery among 142 A2A participants (p<0.05)



Although the objectives in Aim 3 are scheduled for year 3 we were able to get started on these analyses this year while we were waiting for the NHSII data needed for Aim 1. Specifically, we evaluated proteins measured at baseline and persistent pelvic pain after surgery. Again, statistical analyses were led by Dr. Ngo with discussion among the investigators at our weekly meetings. Our analyses included 142 laparoscopically confirmed endometriosis cases from the A2A study. All endometriosis cases had superficial peritoneal lesions only and underwent excision and ablation of all visible disease. One-year post-surgery, pelvic pain worsened for 51 (36%) endometriosis

cases, while pelvic pain stayed the same for 25 (18%) and improved for 66 (46%). We identified 94 proteins (**Figure 3**) associated with worsening pelvic pain one-year post-surgery (nominal p<0.05). Compared to those with improved pelvic pain one year post-surgery, those with worsening pelvic pain had higher plasma levels of CD63 antigen (OR=3.21, 95% CI:1.52-6.81), N-acetyl-D-glucosamine kinase (OR=2.21, 95% CI:1.27-3.84) and lower levels of parathyroid hormone (OR=0.54, 95% CI: 0.35-0.83), soluble angiopoietin-1 receptor (OR=0.20, 95% CI: 0.06-0.63). Pathways related to cell movement and inflammatory response were upregulated and pathways related to angiogenesis were downregulated in endometriosis cases with worsening post-surgical pelvic pain compared to those with improved pain (**Figure 4**). Dr. Sasamoto submitted an abstract on this work and was invited to give an oral presentation at the ASRM annual meeting in Baltimore on October 20, 2021.

Figure 4. Top 20 pathways associated with worsening pain at 12 months after endometriosis surgery among 142 A2A participants



What opportunities for training and professional development has the project provided?

A high school summer student, Alexa Poremba, shadowed our group for the summer and submitted an abstract on a related pilot project using the same proteomic platform used in our project to measure 1,305 proteins in peritoneal fluid samples to the Discover Brigham meeting which is a local meeting at Brigham and Women's Hospital that allows trainees and junior faculty to present ongoing work to the local academic and public community. Alexa will be preparing a poster presentation of this work on November 3, 2021.

How were the results disseminated to communities of interest?

Results of the cross-sectional analysis was selected as oral presentation at the 14th World Congress of Endometriosis on March 07, 2021 and will be submitted for publication in a scientific journal in the next few months and results of the persistent pain analyses will be presented at the ASRM annual meeting in October 2021.

What do you plan to do during the next reporting period to accomplish the goals?

In the next reporting period, we will analyze the proteomics data from the prospectively collected Nurses Health Study II to identify proteins associated with endometriosis risk and we will continue our analyses of proteomics data in the A2A participants, including the evaluation of how change in protein levels over time relate to prognosis and persistent pain. Finally, in the next funding period we will prepare and submit a manuscript related to proteins measured in the A2A study and persistent pain.

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

We continue to feel the impact of lab closures and delays on the lab queues which resulted in delayed retrieval and aliquoting of the NHSII samples. We expected to have analyzed these results over the past year, but we just received the data this month. Consequently, we will analyze the results in the upcoming year.

Actual or anticipated problems or delays and actions or plans to resolve them

Since we have all our proteomics data in hand, we do not anticipate and further delays.

Changes that had a significant impact on expenditures

No changes were made that impacted expenditures.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

No changes in human subjects.

Significant changes in use or care of vertebrate animals

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

We do not have any publications so far. We anticipate one or two publications in the next grant year.

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations.

Results on proteomic profiles associated with endometriosis compared to controls were presented as selected oral presentation at the international World Congress of Endometriosis on 03/07/21. Results on proteomics profiles by endometriosis lesion color was presented at the local Connors Brigham Research Institute Symposium on 05/24/21.

- **Website(s) or other Internet site(s)**

Nothing to report

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name: Towia Libermann, PhD
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-4006-8179
Nearest person month worked: 2
Contribution to Project: Dr. Libermann oversees the study protocol, SOMAscan proteomics work, data analysis, interpretation of the data and manuscript writing.
Funding Support: Next section

Name: Long Ngo, PhD
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-8903-9352
Nearest person month worked: 1
Contribution to Project: Dr. Ngo is leading the data analysis and statistical analysis of the study, data interpretation and manuscript preparation.
Funding Support: Next Section

Name: Simon Dillon, PhD
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0002-4417-178X
Nearest person month worked: 4
Contribution to Project: Dr. Dillon oversees and performs all the proteomics experiments of the study. He is also contributing to data interpretation and manuscript writing.
Funding Support: NA

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Other Support Changes for Key Personnel is attached

What other organizations were involved as partners?

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES:

OTHER SUPPORT
Libermann, Towia

ACTIVE

P30 CA 006516 (Glimcher) 12/01/2019-11/30/2021 **.24 CM**
NIH/NCI (Subcontract only)
Cancer Center Support Grant
The primary goal of the Center is to promote collaborative interactions that will lead to new approaches to cancer prevention, diagnosis and treatment.
Role: Core Director

R01 AG 051658 (Marcantonio/Libermann MPI) 01/15/2016-12/31/2021 **0.36 CM**
NIH/NIA (Total Cost for Libermann Budget)
Advancing the Understanding of Postoperative Delirium Mechanisms via Multi-Omics
Our goal is to identify and validate protein, metabolite and lipid biomarkers in plasma and CSF for predicting postoperative delirium and for understanding the pathophysiological mechanisms underlying the development of delirium.

R01 AG 051658 Supplement (Marcantonio/Libermann MPI) 01/15/2016-12/31/2021 **0.36 CM**
NIH/NIA (Total Cost for Libermann Budget)
Advancing the Understanding of Postoperative Delirium Mechanisms via Multi-Omics
Our goal is to identify and validate protein, metabolite and lipid biomarkers in plasma and CSF for predicting postoperative delirium and for understanding the pathophysiological mechanisms underlying the development of delirium.

P01 AG 031720 (Inouye) 06/01/2018-05/31/2023 **1.80 CM**
NIH/NIA (Subcontract Only)
Delirium, Dementia and the Vulnerable Brain: An Integrative Approach
The goal is to identify the role of inflammation in the pathophysiology of delirium and its associated long term cognitive decline.
Role: Co-I

R03 AG 61582 (Vasunilashorn) 02/15/2019-11/30/2021 **0.36 CM**
NIH/NIA (Total Cost for Total Budget)
Genetic and Neuroinflammatory Mechanisms of Delirium and Alzheimer's Disease and Related Dementias
Objectives: To examine older patients undergoing major elective surgery to advance an understanding of the potential shared pathophysiology underlying the delirium-ADRD relationship.
Role: Co-I

W81XWH18PRMRPIIRA (Libermann, Terry) 09/01/2019-08/31/2022 **3.92 CM**
Department of Defense (Total Costs for Libermann Budget)
Using affinity based proteomics to identify diagnostic and prognostic plasma biomarkers for endometriosis
The goal is improve dietary management in patients with IBD through new diagnostic tools.

R21 CA 238651 (Zhang) 12/12/2019-11/30/2021 **0.36 CM**
NIH/NCI (Subcontract Only)
Proteomic Study of Non-virus Related Hepatocellular Carcinoma Risk
Currently, there are no accurate non-invasive biomarkers that can be used for effective screening tests for HCC in clinical practice. The aim of this proposal is to identify new protein biomarkers to contribute to early detection and diagnosis of liver cancer.
Role: Consortium PI

Pilot Proteomics Study (Lai) 01/01/2010-12/31/2021 **0.24 CM**
Harvard University (Budget Only)
Early Detection of non-viral Hepatocellular Carcinoma: A Pilot Proteomics Study

Role: Co-I

P30 CA 006516 (Balk) 12/22/2016-11/30/2021 **1.20 CM**
DF/HCC Cancer Center Grant (Total Costs for Total Budget)
The primary goal of the Center is to promote collaborative interactions that will lead to new approaches to cancer prevention, diagnosis, and treatment.
Role: Co-I

Departmental Genomics Core (Libermann) 10/01/2018-09/30/2021 **1.80 CM**
BIDMC Internal Funding n/a
BIDMC departmental core facility
Role: Core Director

PENDING

UC2 (Lederer) 11/01/2021-10/31/2026
NIH (Proposed; Subcontract only)
Cellular and Proteomic Discovery of Blood Biomarkers Across Autoimmune Diseases
The goal is to identify new plasma protein biomarkers for multiple autoimmune diseases using SOMAscan proteomics and single cell immunophenotyping.
Role: Consortium PI

P30 (Balk) 12/01/2021-11/30/2026
NIH (Proposed; Subcontract only)
Cancer Center Support Grant
The primary goal of the Center is to promote collaborative interactions that will lead to new approaches to cancer prevention, diagnosis, and treatment.
Role: Co-I

R01 (Libermann) 04/01/2022-03/31/2027
NIH (Proposed)
Identifying prediagnostic plasma proteomic biomarkers for early detection of hepatocellular cancer
The goal is to identify and validate new plasma protein biomarkers for early detection of hepatocellular cancer in multiple epidemiological cohorts prior to diagnosis.

U19 (Felson/Neogi MPI) 04/01/2022-03/31/2027
NIH (Proposed; Subcontract only)
Novel Insights into Osteoarthritis, Pain and Function: MOST4
The goal is to identify and validate new plasma protein biomarkers in knee osteoarthritis (OA) synovial fluid and plasma associated cross-sectionally with knee OA features, longitudinal worsening of knee OA features, and with multi-site OA.
Role: Consortium PI

R01 (Shadyab/McEvoy MPI) 07/01/2022-06/30/2027
NIH (Proposed; Subcontract only)
Plasma Proteomic Biomarkers and Signatures for Alzheimer's Disease and Related Dementias
The goal is to determine associations of validated proteomic clocks of aging and 7,000 protein SomaScan with incident MCI and ADRD, cognitively healthy longevity, and ADRD endophenotypes.
Role: Co-I

R01 (Hartman) 09/01/2022-08/31/2027
NIH (Proposed; Subcontract only)
Reducing prolonged sitting time to improve healthy aging in breast cancer survivors
The goal is to test that sitting less improves healthy aging and the biological age evaluated by the proteomic clocks of aging in breast cancer survivors.
Role: Consortium PI

OVERLAP
None

OTHER RESOURCES
None

OTHER SUPPORT – LONG NGO

ACTIVE

R01 AG051568-01 (Marcantonio/Libermann MPI) 1/01/16 - 12/31/21 1.20 CM
NIH *28716*
Advancing the Understanding of Postoperative Delirium Mechanisms via Multi-Omics
The major goals of this project are to identify and validate protein, metabolite and lipid biomarkers in plasma and CSF for predicting postoperative delirium and for understanding the pathophysiological mechanisms underlying the development of delirium.
Role: Co-investigator

R01 AG030618-07 A1 (Marcantonio) 04/01/16 – 03/31/22 0.60 CM
NIH *28856*
READI: Researching Efficient Approaches to Delirium Identification
The major goals of this project are to develop a practical, effective, and cost-efficient protocol for detection and monitoring of delirium in high risk hospitalized older adults, and to generate the evidence base needed to facilitate its widespread implementation
Role: Co-investigator

1 R01 DK 112886-01 (Donnino) 9/1/18-6/30/2023 0.36 CM
NIH/NIDDK *60995*
Thiamine in Septic Shock Patients with Alcohol Abuse
The major goal of this project is to investigate thiamine in septic shock patients with alcohol abuse
Role: Co-investigator

R21 CA 218960-01 (Libermann) 07/15/18 – 06/30/21 0.60 CM
NIH *61142*
Identification of Plasma and Exosome Based Protein Biomarkers for Early Detection of Pancreatic Cancer
The major goal of this project is to examine the role of plasma and exosome based proteins to define biomarkers for pancreatic ductal adenocarcinoma using SOMA scan
Role: Co-investigator

R03AG61582 (Vasunilashorn) 2/15/2019-11/30/2021 0.24 CM
NIH/NIA *61336*
Genetic and Neuroinflammatory Mechanisms of Delirium and Alzheimer's Disease and Related Dementias
Objectives: To examine older patients undergoing major elective surgery to advance an understanding of the potential shared pathophysiology underlying the delirium-ADRD relationship.
Role: Co-investigator

PR 181444P1 (Libermann) 09/01/19 – 08/30/22 0.60 CM
DOD *61484*
Using Affinity-Based Proteomics to Identify Diagnostic and Plasma Biomarkers for Endometriosis
To identify proteins and pathways that discriminate between those who continue to be impacted by the disease and those who improve after surgery in the Progression Study
Role: Co-investigator

R01HS 27367-01 (Bell) 2/01/20 – 01/31/23 1.20 CM
AHRQ *62932*
Answering the call to engage patients and families in the diagnostic process: A new patient-centered approach using health information transparency to identify diagnostic breakdowns in ambulatory care
The major goals of this project are to establish a patient-centered framework for analyzing diagnostic breakdowns and to calculate the incidence of diagnostic breakdowns in ambulatory visits using this framework.
Role: Co-investigator

PO1 AG 031720 (Inouye) 09/15/18 – 05/31/23 1.20 CM
NIH *62477*
Core C: DELIRIUM, DEMENTIA, AND THE VULNERABLE BRAIN: AN INTEGRATIVE APPROACH
The major goal of this project is to examine the role of Inflammation in the pathophysiology of delirium and its associated long term cognitive decline
Role: Co-investigator

R01 HL154744 (Nezafat) 7/1/20 – 6/30/24 0.60 CM
NIH/NHLBI *62552*
Gadolinium Free Cardiac MR Imaging of Scar and Fibrosis
The goal of this project is to reduce utilization of Gadolinium contrast agent in MRI.
Role: Co-investigator

R21 NS 109728-01 A1 (Soman) 7/1/2020-6/30/2022 1.20 CM
NIH *62554*
Improved MRI Detection of Cerebral Microbleeds with Novel Susceptibility Mapping
The goal is to study differences in how neuro-audiologists read images for evaluating CMBs and if those differences would lead to different patient care
Role: Co-investigator

1 RO1 HL 129157 (Nezafat) 5/15/17-4/30/22 0.60 CM
NIH/NIDDK *62611*
Myocardial Tissue Characterization with MR Relaxometry in Heart Failure
The major goal of this project is to assess incremental value of CMR vs. non-CMR markers of HF progression and adverse cardiac events. Role: Co-investigator

R01CA242747 (Schonberg) 5/1/2020-4/30/2024 1.20 CM
NCI/NIH *62660*
A Prediction Model to Simultaneously Estimate Personal Risk of Breast Cancer
The goal is to extend a breast cancer prediction model to predict 10-year risk of death from causes other than breast cancer using competing risk regression (CRR) and Nurses' Health Study data and to examine the effect of adding breast density and genomic data.
Role: Co-investigator

R01HL155717-01 (Tsao) 9/1/2020 – 8/13/2025 0.60CM
NHLBI
Myocardial Radiomics and Mechanics in the Pathology and Prognosis of Cardiovascular Disease
This project will apply novel analyses of cardiovascular magnetic resonance images and integrate these measures with broad existing data including risk factors, genetics, and blood biomarkers to obtain a comprehensive understanding of structure and function of the heart in older adults in the community.
Role: Co-investigator

R01 HL158098 (MPI: Nezafat, Maron) 4/15/21 – 3/31/25 1.20 CM
NIH/NHLBI
Cardiac MR-Based Risk Stratification for Heart Failure and Atrial Fibrillation in HCM
The goal of this project is to develop machine learning approaches to identify HCM patients at risk of developing heart failure and atrial fibrillation
Role: Co-Investigator

PENDING

R01 HL158077 (PI: Nezafat) 4/1/21 – 3/31/26 0.60 CM (JIT)
NIH/NHLBI
Cardiopulmonary Exercise MRI in Heart Failure with Preserved Ejection Fraction
The goal of this project is to assess diagnostic and prognostic value of a cardiopulmonary exercise MRI in heart failure and preserved ejection fraction
Role: Co-Investigator

R01 HL129185 (PI: Nezafat) 7/1/21 – 6/30/26 0.60 CM (JIT)
NIH/NHLBI
Cardiovascular MRI Characterization of the Arrhythmogenic Heart in Nonischemic Cardiomyopathy
The goal of this project is to develop novel risk markers of arrhythmia in patients with nonischemic cardiomyopathy
Role: Co-Investigator

OVERLAP:
There is no financial or scientific overlap

If or when pending grants are funded, then financial support will be adjusted on current and awarded grants without reducing the scientific impact. Total NIH effort will remain <95%.

OTHER RESOURCES / FOREIGN RESOURCES

N/A