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TITLE: Defining Endometriosis Physiologic Subphenotypes and Subsequent Cancer and Comorbidities Risk Through Discovery of Novel Genetic Variants

PRINCIPAL INVESTIGATOR: Stacey A. Missmer, ScD

CONTRACTING ORGANIZATION: Michigan State University, Grand Rapids, MI

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Michigan State University
15 Michigan St. NE
Grand Rapids, MI 49503

Brigham and Women's Hospital
221 Longwood Ave
Boston, MA 02115

Boston Children's Hospital
1 Autumn Street, 5th floor
Boston, MA 02215

8. PERFORMING ORGANIZATION REPORT NUMBER

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

SPECIFIC AIMS AND OBJECTIVES: The main objectives of this study are: 1) To identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation. These novel sub-phenotype-specific variants will suggest distinct physiologic pathways that underlie the poorly understood endometriosis heterogeneity, potentially catalyzing discovery of precision medicine treatment and prevention targets. 2) To determine the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis. To address these objectives, we will capitalize upon our ongoing International Endometriosis Genome Consortium (IEGC) investigations and deploy our existing genetic analysis pipeline on a wider scale. The IEGC is a consortium of well-established case:control and cohort studies all of which have completed genome-wide genotyping of their participants. Within the IEGC, nine studies have harmonized clinical data compliant with the Endometriosis Phenome and Biobanking Harmonization Project (WERF-EPHect) tools to facilitate deeply phenotyped definitions of potentially informative endometriosis sub-phenotypes. Also, in the exploratory analyses, we will delve more deeply into one consortium cohort, the Women's Health Study: from Adolescence to Adulthood (A2A), which in addition to the genotyped and deeply-phenotyped EPHect compliant data, has measured an array of blood chemokine and cytokine markers. Operationalizing these time- and cost-efficient unique resources available in-hand, we will evaluate the following specific aims:
Aim 1. Using data from the IEGC, we will identify novel germline genetic risk variants associated with individual endometriosis surgical sub-phenotypes, symptomatic sub-phenotypes, and gynecologic comorbidities.
Aim 2. Using data from the IEGC, we will identify shared germline genetic risk variants between endometriosis sub-phenotypes and subsequent risk of cancer, cardiovascular disease (CVD) or autoimmune diseases.
Aim 3. In an exploratory analysis, using data from the A2A cohort, we will evaluate the interaction between genetic risk variants and the inflammatory milieu with endometriosis symptoms sub-phenotypes.

PROGRESS: In this period, we have focused on process, updating the publicly available and consortium-specific summary data (datasets that include at least 300 endometriosis cases) that have become available across the globe to address these aims and planning the analysis plans for aims 1 and 2. For aim 1, we have requested that those with summary data confirm the in-hand surgical and symptom-based sub-phenotype variables for their cases and controls to finalize which sub-phenotypes have adequate power to explore. We conducted a pilot analysis comparing two analysis methods for understanding the shared genetic basis between endometriosis and other common complex conditions for aim 2. For the pilot analysis, we utilized data to which our core investigators had existing access (European GWAS summary results for endometriosis (21,779 cases: 449,090 controls; Rahmioglu et al., 2023) and uterine fibroids (38,466 cases: 329,437 controls; Sliz et al., 2023)); we focused on uterine fibroids as this condition showed very strong genetic correlation with endometriosis (rg=0.48 (SE=0.046), p=2x27x10-25). We tested: (1) multi-trait association analysis (MTAG), and (2) three stratified GWAS approaches: (i) Endometriosis cases with uterine fibroids vs. healthy controls, (ii) Endometriosis cases without uterine fibroids vs. healthy controls, iii) Uterine fibroid cases without endometriosis vs. healthy controls. We meta-analyzed these GWAS summary results using fixed-effects models in METAL. The identified lead variants for each condition and those that are identified as shared and unique to each condition were compared between the two approaches.

15. SUBJECT TERMS
None listed.

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRDC
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Unclassified	Unclassified	Unclassified			

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1. **INTRODUCTION:**

Endometriosis is a chronic inflammatory gynecologic disease, marked by the presence of endometrial-like tissue outside the uterus, that impacts approximately 10% of women worldwide during their reproductive years. Endometriosis impacts active duty service members in the US Armed Forces, including 6% of the female U.S. Army population, causing approximately 200,000 days of lost duty time per year. However, so far genetic and pathophysiologic discovery has largely treated endometriosis as a single entity. Further, the current major treatment options are limited to hormonal therapy and surgical removal of lesions, with no systematic guidance for tailoring treatment according to informative sub-phenotypes. As subtype discovery has revolutionized cancer pathophysiologic understanding and catalyzed targeted treatment research that has had a direct impact on prognosis and long-term survival, there is a pressing need to understand the heterogeneity of endometriosis. Uncovering the underpinnings of biologically and clinically informative sub-phenotypes will leap knowledge of endometriosis forward. Enhanced understanding of the pathways between genetic risk variants and sub-phenotypes, including modifying factors such as inflammation, will provide biologic targets driving differences among women with endometriosis in progression of the disease and subsequent risk for cancer and other morbidities for which women with endometriosis are at higher risk. We hypothesize that sub-phenotypes of endometriosis are associated with unique genetic variants above and beyond those identified in our prior studies of endometriosis as a homogenous entity. We further hypothesize that some variants may be shared between specific sub-phenotypes and the subsequent risk of morbidities including cancers, autoimmune and cardiovascular diseases – suggesting either a common etiology or a life course risk attributable to endometriosis through genetically indicated physiologic pathways upon which we may be able to intervene. Finally, we hypothesize in an exploratory analysis that the sub-phenotype-specific genetic variant associations may be modified via interaction with the endogenous inflammatory environment such that hyper-inflammatory pathways are more prominent in some endometriosis sub-phenotypes. To address these objectives, we will capitalize upon our ongoing International Endometriosis Genome Consortium (IEGC) investigations and deploy our existing genetic analysis pipeline on a wider scale. The IEGC is a consortium of well-established case:control and cohort studies all of which have completed genome-wide genotyping of their participants. Within the IEGC, nine studies have harmonized clinical data compliant with the Endometriosis Phenome and Biobanking Harmonization Project (WERF-EPHect) tools to facilitate deeply phenotyped definitions of potentially informative endometriosis sub-phenotypes. Also, in the exploratory analyses, we will delve more deeply into one consortium cohort, the Women's Health Study: from Adolescence to Adulthood (A2A), which in addition to the genotyped and deeply-phenotyped EPHect compliant data, has measured an array of blood chemokine and cytokine markers. Operationalizing these time- and cost-efficient unique resources available in-hand. In the short-term, the results from the study will (1) identify the genetic underpinning of endometriosis sub-phenotypes, (2) define the shared risk variants and determine the genomic drivers of women with endometriosis at highest risk for subsequent development of cancer, autoimmune diseases, and CVD, and (3) evaluate interactions between genes and the inflammatory environment, clarifying the pathways from genes to specific endometriosis sub-phenotypes. In the long-term, our study will provide biologic insight that could transform the current one-size-fits all approach to endometriosis treatment and pave the way for more precise diagnostics and treatments targeted to clinically informative subgroups.

2. **KEYWORDS:**

Endometriosis, endometrioma, deep endometriosis, superficial peritoneal endometriosis, genes, SNPs, sub-phenotypes, genetic variants, risk variants, biomarkers, plasma, inflammatory markers, inflammation, pain, infertility, co-morbidities, cancer, autoimmune diseases, cardiovascular disease

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

The major goals of the project are as follows:

Aim 1: Using data from the International Endometriosis Genome Consortium (IEGC) (Nine contributing studies: N=18,867 endometriosis cases with sub-phenotype defining information, N=301,088 controls), we will identify germline genetic variants associated with individual endometriosis sub-phenotypes.

Major Task 1: Obtain relevant ethical and legal agreements

a. Subtask 1: Ethical approvals
    i. Submit IRB applications or amendments at MSU, BWH, and BCH
    ii. Coordinate site-specific HRPO review
    iii. Submit amendments, adverse events and protocol deviations as needed
    iv. Coordinate with Sites for annual IRB report for continuing review
        1. Milestone: Local IRB Approval:
            a) Mass General Brigham IRB approved 06/08/2021
            b) Mass General Brigham IRB Amendment #1 approved 04/28/2022 – study personnel updated

c) SMART IRB determination obtained 04/28/2022 – Mass General Brigham IRB accepts review for Brigham and Women's Hospital and Michigan State University
d) Mass General Brigham IRB Amendment #2 approved 05/23/2022 – Michigan State University added as study site
e) Mass General Brigham IRB continuing review 03/22/2023, MSU IRB and OHRO notified of continued approval

2. Milestone: OHRO / HRPO Approval obtained 07/15/2022

b. Subtask 2: Material/Data agreements
   i. Coordinate data transfer / use agreements
      1. Milestone: DUA approval at MSU, BWH, BCH – Given establishment of MGB IRB as the primary IRB site with MSU ceding review to MGB, the BWH site is overseeing data sharing agreements. In October 2022, the terms subaward agreement were determined to cover data sharing and no separate DUAs were executed.

Major Task 2: Data cleaning and harmonization – these milestones were delayed given the protracted solidification of consultation by Dr. Rahmioglu approved by USAMRMC, and also, very positively, identification of additional sources of publicly available genomic data that can increase the sample size of summary statistic data that will be meta-analyzed in years 3 and 4. We are actively progressing with a firm IEGC execution plan with expanded data sources and will complete the Major Task 2 milestones in the first quarter of Year 3.

a. Subtask 1: Participating IEGC sites confirm understanding and adoption of common analytic plan
b. Subtask 2: Each site conduct any additional cleaning/harmonizing of sub-phenotype variables and covariates
   i. Review distributions of all variables, investigate unrealistic answers
      1. Milestone: Analysis plan finalized, data confirmed and harmonized

Major Task 3: Data analysis for Aim 1 – as noted in the year 1 report, these milestones have been restructured to be completed by the middle of year 3 rather than the end of year 2.

a. Subtask 1: IEGC sites confirm previous QC (quality control) metrics
   i. Calculate % of samples that fail for each SNP and % SNPs that fail for each participant; exclude outliers
   ii. Check for sex discrepancies
   iii. Check for minor allele frequency (MAF) and include SNPs above the threshold
   iv. Calculate Hardy Weinberg Equilibrium and exclude markers that deviate
   v. Evaluate heterozygosity, relatedness and population stratification; exclude based on preset thresholds
b. Subtask 2: Site-specific application of analysis plan for single SNP analysis to identify novel variants associated with endometriosis subphenotype (e.g. clinical, surgical), gynecologic co-morbidity
   i. Run regressions for association to identify de novo coding variants
   ii. Upload summary statistics to the IEGC cloud server
c. Subtask 3: Meta-analyses
   i. Confirm valid upload of site-specific summary statistics and upload of modeling variables
   ii. Meta-level quality control of GWAS summary results
   iii. Run meta-analysis regression for each subphenotype and comorbidity
   iv. Run QC for meta-analysis output
   v. Select SNPs for top hit identification and follow-up
   vi. Run colocalization analysis for SNPs
      1. Run pathway analysis evaluating for SNP-enrichment to predict significant pathways
      Milestone: Analyses completed

Aim 2. Using data from the International Endometriosis Genome Consortium (IEGC) (Twelve contributing studies with data on subsequent cancer/CVD/autoimmune diseases: N=22,349 endometriosis cases, N=359,348 controls), we will identify shared germline genetic risk variants between endometriosis and subsequent risk of cancer, CVD or autoimmune diseases.

Major Task 4: Data analysis for Aim 2 – as noted in the year 1 report, to make up delays caused by the lengthy IRB / ORHO approval process, we are combining Aim 1 and Aim 2 tasks to run most simultaneously rather than consecutively as originally planned ensuring completion by end of year 3 of both aims 1 and 2 milestones.

a. Subtask 1: Identify candidate subsequent cancer/morbidity SNPs
   i. Comprehensive literature review to identify candidate SNPs
   ii. Evaluation by LD to eliminate linked SNPs
b. Subtask 2: Run regression for each candidate subsequent cancer/morbidity SNP and endometriosis sub-phenotypes
c. Subtask 3: Run regression for each candidate subsequent cancer/morbidity SNP and endometriosis sub-phenotypes restricted to NHSII and WGHS temporality imposed cohort data
   1. Milestone: Data analysis for Aim 2 complete

Aim 3. In an exploratory analysis, using data from the Adolescence to Adulthood (A2A) cohort, including N=1,005 participants with deeply phenotyped clinical and biomarker data, we will evaluate the interaction between genetic risk variants and the inflammatory milieu with endometriosis symptoms sub-phenotypes.

Major Task 5: Data analysis for Aim 3

a. Subtask 1: Assemble A2A dataset with inflammatory markers, genetic data, and sub-phenotypes
b. Subtask 2: Quantify effect modification by inflammatory markers on association between SNPs and sub-phenotypes
    1. Milestone: Data analysis for Aim 3 complete

Major Task 6: Prepare manuscripts and publish papers

a. Subtask 1: Summarize and interpret results
    ii. Create tables and figures to summarize results
    iii. Review results with colleagues
b. Subtask 2: Draft manuscripts
    i. Create working groups with regular meeting times to develop manuscripts
    ii. Literature search
    iii. Draft text, revise, circulated to coauthors
    iv. Add references and format for appropriate journal
        1. Milestone achieved: Submit final papers to journals for publication

What was accomplished under these goals?

In addition to obtaining all regulatory approvals as noted in year 1, we have identified and contacted all past and potential (with newly existing GWAS data since our Nature Genetics 2023 publication) consortium members with datasets including at least 300 endometriosis cases for aims 1 and 2 discovery. Sites with these existing data are in the process of reporting surgical and symptom-based sub-phenotype data to include in the aim 1 summary statistics. For aim 2, this year we conducted a pilot analysis comparing two analysis methods for understanding the shared genetic basis between endometriosis and other common complex conditions such as cancer, CVD and autoimmune conditions. Both of these steps are contributing to the analysis plans for both aims 1 and 2 that will be finalized in the first quarter of year 3. PI, Dr. Missmer, and the key personnel meet bi-weekly with frequent digital communication in between. These meetings will be shifted to weekly as needed.

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

Nothing to Report in Year 2.

How were the results disseminated to communities of interest?

Nothing to Report.

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

During the next reporting period we will work with the participating IEGC sites to revise as needed the analysis plans, with data confirmed and harmonized. We will begin data analysis for Aim 1 with IEGC sites confirming previous quality control metrics including:

- Calculate % of samples that fail for each SNP and % SNPs that fail for each participant; exclude outliers
- Check for sex discrepancies
- Check for minor allele frequency (MAF) and include SNPs above the threshold
- Calculate Hardy Weinberg Equilibrium and exclude markers that deviate
- Evaluate heterozygosity, relatedness and population stratification; exclude based on preset thresholds
- Site-specific application of analysis plan for single SNP analysis to identify novel variants associated with endometriosis subphenotypes (e.g. clinical, surgical), gynecologic co-morbidity
- Run regressions for association to identify de novo coding variants
- Upload summary statistics to the IEGC cloud server
- Meta-analyses
- Confirm valid upload of site-specific summary statistics and upload of modeling variables
- Meta-level quality control of GWAS summary results
- We will also begin data analysis for Aim 2 by identifying candidate subsequent complex condition SNPs
- Comprehensive literature review to identify candidate SNPs
- Evaluation by LD to eliminate linked SNPs

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:

We do not have any significant changes to report. The project is following the approved SOW but with delays documented above. We have moved forward creatively approaching elements of the timeline concurrently rather than consecutively, to get back on track for Aim 1 and Aim 2 milestones completion.

6. PRODUCTS:

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Stacey Missmer, ScD
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0003-3147-6768
Nearest person month worked: 0.9 Academic, 0.3 Summer
Contribution to Project: Dr. Missmer oversees all aspects of the study including budget management, study design, statistical analyses, coordination with Brigham-based study staff, interpretation of results, writing manuscripts for publication in peer-reviewed journals, and scientific communication with DoD as well as the scientific and clinical communities.
Funding Support:

Name: Ana Vazquez, PhD
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.27 Academic, 0.09 Summer
Contribution to Project: Dr. Vazquez provides biostatistical expertise.
Funding Support:

Name: Kathryn Terry, ScD
Project Role: Subcontract Principal Investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-8540-7066
Nearest person month worked: 0.94 Calendar
Contribution to Project: Dr. Terry is responsible for scientific direction of the BCE at both Boston Children's and Brigham and Women's Hospitals, as well as overseeing all collaboration between the biorepository and external laboratories.
She will continue her close working relationship with Dr. Missmer, ensuring access to A2A data and samples pertinent to the proposed aims and contribute expertise regarding study design, statistical analyses, coordination with Children's and Brigham-based study staff, interpretation of results, writing manuscripts for publication in peer-reviewed journals, and scientific communication with the DOD as well as the scientific, clinical, and patient education communities.
Funding Support:

Name: Naoko Sasamoto, MD
Project Role: Co-investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-4526-2181
Nearest person month worked: 0 Calendar
Contribution to Project: Dr. Sasamoto is contributing to the development and implementation of the study protocol, analysis plans, statistical programming, data interpretation and manuscript preparation.
Funding Support:

Name: Amy Shafrir, ScD
Project Role: Consultant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0 Calendar
Contribution to Project:
Funding Support:

Name: Madhavi Kulkarni, PhD
Project Role: Postdoctoral Fellow
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 5.5 Calendar
Contribution to Project: Dr. Kulkarni is a postdoctoral fellow in the Department of Obstetrics, Gynecology, and Reproductive Biology at Michigan State University. She received her degree in epidemiology with a concentration in perinatal epidemiology in 2017 from Michigan State University. Her dissertation involved conceptualizing and designing a study utilizing medical and pharmacy claims linked with Michigan birth certificate data to investigate the associations of psychological conditions, related medications, and pregnancy complications in reproductive age women. Supervised by Dr. Missmer, and meeting at least weekly with the data management team and Dr. Terry, Dr. Kulkarni will advance hypotheses, develop analysis plans, conduct statistical analyses in collaboration with Ms. Ghiasi, interpret results, and contribute to manuscript drafting.

Funding Support:

Name: Mary Paiz
Project Role: Project Administrator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 5.5 Calendar
Contribution to Project: Ms. Paiz provides oversite for communication and coordination among the study sites, as well as adherence to conflict of interest documentation and MSU IRB reliance compliance and communication, maintaining the administrative calendar and meeting scheduling, and preparing required DoD and MSU forms and reports.
Funding Support:

Name: Laurie Fitzpatrick
Project Role: Project Administrator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.48 Calendar
Contribution to Project: Ms. Fitzpatrick contributes to communication and coordination among the study sites and the IEGC, supplies ordering, ensuring project action queues are ordered and executed to ensure meeting of milestones, providing editorial assistance for reports and correspondence, preparing manuscript submissions and necessary documentation, conducting library searches and maintenance of publication/reference libraries where needed, and preparing required DoD and University forms and reports.
Funding Support:

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

Changes in other support are noted in the attached OS documents.

What other organizations were involved as partners?

Nothing to Report.

8. **SPECIAL REPORTING REQUIREMENTS**

9. **APPENDICES:**

Note: changes from previous Other Support are in red.

SUPPORT
MISSMER, STACEY A.

POSITIONS/SCIENTIFIC APPOINTMENTS

2016-Present	Professor	Obstetrics, Gynecology, and Reproductive Biology	Michigan State University
2016-Present	Lecturer	Pediatrics	Harvard Medical School
2016-Present	Adjunct Professor	Epidemiology	Harvard T.H. Chan School of Public Health

PREVIOUS

Title: Integrative Analysis of Genomic, Epigenomic and Phenotypic Data for Disease Stratification of Endometriosis
Project Goals: This global project that includes collaborative sites the US, UK, and Australia proposes to perform genome-wide DNA methylation analyses and genotyping of nearly 1000 existing, phenotypically well-annotated eutopic endometrium tissue samples of women with endometriosis and controls, collected by standard operating procedures, to test the hypothesis that environmental and genetic influences contribute to endometriosis and leave long-term signatures in the DNA methylome in the uterine endometrium contributing to disease pathogenesis and pathophysiology, with promise for translational diagnostics and therapeutic target development.
Specific Aims: To Source of Support Address the hypotheses that 1) environmental and genetic influences contribute to endometriosis and leave long-term signatures in the DNA methylome in the eutopic endometrium that contribute to disease pathogenesis and pathophysiology; and 2) these can serve to stratify disease risk and inform new avenues for drug target discoveries and diagnostic development.
Project Number: NIH R01 HD089511
Role: MPI (Overall PI: Linda Giudice)
Source of Support: University of California San Francisco
Source of Support Source of Support Address:
UCSF
Box 0850
3333 California Street 485R
San Francisco, CA 94143
Contracting/Grants Officer: Nicole Gaisbauer
Performance Period: 09/26/2016 - 04/30/2021
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2016	0.9 Academic 0.3 Summer
2. 2017	0.9 Academic 0.3 Summer
3. 2018	1.8 Academic 0.6 Summer
4. 2019	1.08 Academic 0.36 Summer

Years	Person Months
5. 2020	1.08 Academic 0.36 Summer
6. 2021	1.08 Academic 0.36 Summer

Overlap: None

Title: Subfertility and Assisted Conception Study of Parent and Child Health Outcomes
Project Goals: The project will provide expertise in developing an understanding of the subfertility-related diagnoses by performing analyses of women's and children's health outcomes as part of the project team.
Specific Aims: Aim 1: To evaluate the effect of maternal subfertility diagnoses on long-term health; Hypothesis: Women with a history of subfertility diagnoses, independent of treatment, have higher risks of compromised health outcomes compared to women without indicators or treatment of subfertility; Aim 2: To evaluate the health of children born to women and men with subfertility diagnoses; Hypothesis: Children born to women and/or men with subfertility diagnoses, independent of treatment, have a higher risk of compromised health outcomes compared to children born to women without indicators of subfertility; and Aim 3: To develop a cost-of-subfertility measure for women and their children; Hypothesis: Women with a history of subfertility-related diagnoses and their children have higher healthcare costs compared to their counterparts without indicators or treatment of subfertility.
Project Number: NIH R01 HD067270
Role: MSU **s**ubcontract PI (Overall PI: Judy Stern)
Source of Support: Dartmouth College
Source of Support Address:
Dartmouth College
Office of Sponsored Projects
11 Rope Ferry Road #6210
Hanover, NH 03755
Contracting/Grants Officer: Aarron Clough
Performance Period: 06/23/2016-09/30/2021
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2016	0.9 Academic 0.3 Summer
2. 2017	0.9 Academic 0.3 Summer
3. 2018	0.9 Academic 0.3 Summer
4. 2019	1.35 Academic 0.45 Summer
5. 2020	1.12 Academic 0.37 Summer
6. 2021	0.45 Academic 0.15 Summer

Overlap: None

Title: Inflammation and the Malignant Transformation of Endometriosis
Project Goal / Specific Aims: The overall goal of this project is to better understand how inflammatory

exposures, both local and systemic, influence cancer driver mutations in endometriosis lesions, allowing us to gain better insight into the natural history of endometriosis and its potential for malignant transformation.
Project Number: DoD W81XWH18PRMRPDA
Role: MSU subcontract PI (Overall PI: Holly Harris)
Source of Support: Fred Hutchinson Cancer Research Center
Source of Support Address:
1100 Fairview Ave N.
Seattle, WA 98109
Contracting/Grants Officer: Alexandria Nagel
Performance Period: 04/01/2019-09/30/2021
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2018	0.45 Academic 0.15 Summer
2. 2019	0.45 Academic 0.15 Summer
3. 2020	0.45 Academic 0.15 Summer

Overlap: None

Title: Harnessing biomarker and phenotypic diversity among adolescents and women with endometriosis to advance personalized medicine for diagnosis and pain remediation.
Project Goal / Specific Aims: Within the Women's Health Study: from Adolescence to Adulthood (A2A; a prospective cohort of >1200 adolescents and young women, oversampled for those with surgically-confirmed endometriosis, followed for >4 years), we will combine WERF EPHect compliant data from participant surveys, electronic medical records, and stored blood samples collected annually. These data will capture informative changes in pain experience, inflammatory and oxidative stress milieu, and central sensitization to advance our understanding of phenotypic diversity among adolescents and women with endometriosis – the foundation for successful personalized, precision medicine to shorten diagnostic delay and maximize successful pain remediation.
Project Number: NIH R21 HD096358
Role: PI
Source of Support: NICHD
Source of Support Address:
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 05/01/2019-04/30/2022
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2019	0.9 Academic 0.3 Summer
2. 2020	0.9 Academic 0.3 Summer
3. 2021	0.9 Academic

Years	Person Months
	0.3 Summer
4. 2022	0.09 Academic 0.03 Summer

Overlap: None

Title: Translation in Pelvic Pain (TriPP)
Project Goal / Specific Aims: The ultimate aims of this multi-center international project are to develop: • Tools that allow the stratification of chronic pelvic pain patients on the basis of the underpinning pathophysiological mechanisms. • Refined preclinical models of endometriosis-associated pain and bladder pain symptoms to allow rapid, efficient and relevant screening of novel therapeutic compounds with a high chance of clinical success.
Project Number: IMI2-2016-10-03C
Role: MSU subcontract PI
Source of Support: University of Oxford (European Union)
Source of Support Address:
University of Oxford
Women's Centre, John Radcliffe Hospital
Oxford, OX3 9DU England
Contracting/Grants Officer: Tom Ibbotson
Performance Period: 1/01/2018-3/31/2023
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2018	0.18 Academic 0.06 Summer
2. 2019	0.18 Academic 0.06 Summer
3. 2020	0.09 Academic 0.03 Summer
4. 2021	0.09 Academic 0.03 Summer
5. 2022	0.09 Academic 0.03 Summer No Cost Extension
6. 2023	0.09 Academic 0.03 Summer No Cost Extension

Overlap: None

Title: An AHEI Dietary Intervention to Reduce Pain in Women with Endometriosis
Project Goal / Specific Aims: The overall goal of this study is to evaluate the effects of a 12-week dietary intervention among premenopausal women aged 18-45 years, with laparoscopically-confirmed endometriosis, recruited from the Seattle area, who had a pain score of at least 5 out of 10 on the Visual Analog Scale (VAS) in the month prior to baseline. 100 women will be randomized to a 3-month dietary intervention (n=50) or a wait-list control group (n=50). The intervention will consist of a diet based on the AHEI-2010 guidelines.

Project Number: NIH R01 NR017951
Role: MSU subcontract PI (Overall PI: Holly Harris)
Source of Support: Fred Hutchinson Cancer Research Center
Source of Support Address:
1100 Fairview Ave N.
Seattle, WA 98109
Contracting/Grants Officer: Alexandria Nagel
Performance Period: 02/11/2019-12/31/2022
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2019	0.45 Academic 0.15 Summer
2. 2020	0.36 Academic 0.12 Summer
3. 2021	0.36 Academic 0.12 Summer
4. 2022	0.9 Academic 0.3 Summer

Overlap: None

Title: Endometriosis, Infertility, and Risk of Stroke
Project Goal / Specific Aims: Leveraging existing data from the Nurses' Health Study II, this proposal will fill important gaps in knowledge of the association between incidence of stroke and endometriosis and infertility. This proposal is well powered to evaluate three categories of exposure: women with endometriosis but not infertility, women with infertility but not endometriosis, and women with both endometriosis and infertility.
Project Number: NIH R21 HD099623
Role: MSU subcontract PI (Overall PI: Leslie Farland)
Source of Support: University of Arizona
Source of Support Address:
Arizona Board of Regents, University of Arizona
888 North Euclid Avenue, Room 510
Tucson, AZ 85719-4824
Contracting/Grants Officer: Melissa Kramer
Performance Period: 07/01/2020-06/30/2023 (No cost extension started 7/1/2022)
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2020	0.45 Academic 0.15 Summer
2. 2021	0.72 Academic 0.24 Summer
3. 2022	0.72 Academic 0.24 Summer
4. 2023	0.09 Academic 0.03 Summer

Overlap: None

CURRENT

Title: The Boston Center for Endometriosis
Project Goals: Design and conduct for study enrollment and data and biologic sample collection within Mass General Brigham Hospital and Boston Children's Hospital
Specific Aims: Establish a longitudinal cohort of girls and women with endometriosis and appropriate comparison girls/women with detailed life course data and extensive biologic samples storage.
Project Number: N/A
Role: MSU subcontract PI (Overall PI: Marc Laufer)
Source of Support: J.Willard and Alice S. Marriott Foundation
Source of Support Address:
J. Willard and Alice S. Marriott Foundation
10400 Fernwood Road, Department 925
Bethesda, MD 20817
Contracting/Grants Officer: Margaret Buckley
Performance Period: 07/01/2012-12/31/2024
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2016	4.5 Academic 1.5 Summer
2. 2017	4.5 Academic 1.5 Summer
3. 2018	4.05 Academic 1.35 Summer
4. 2019	0.09 Academic 0.03 Summer
5. 2020	0.09 Academic 0.03 Summer
6. 2021	0.09 Academic 0.03 Summer
7. 2022	1.35 Academic 0.45 Summer
8. 2023	1.35 Academic 0.45 Summer
9. 2024	1.35 Academic 0.45 Summer

Overlap: None

Title: MSU Women's Outcomes Research and Knowledge (WORK) Cohort
Project Goals / Specific Aims: This observational longitudinal cohort study will evaluate the clinical, medical and surgical journey from pelvic pain onset and identify diagnostic paths that lead to a shorter time to diagnosis and initiation of successful pain remediating treatment. Adolescent and young women, ages 12-30, who have ever reported chronic pelvic pain will be invited to enroll.
Project Number: 4201018531
Role: PI

Source of Support: AbbVie Inc.
Source of Support Address:
AbbVie
1 N Waukegan Road
North Chicago, IL 60064
Contracting/Grants Officer: Michelle Parks
Performance Period: 04/01/2018 – 12/31/2024 (No Cost Extension started 6/1/2021)
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2018	0.45 Academic 0.15 Summer
2. 2019	0.45 Academic 0.15 Summer
3. 2020	0.72 Academic 0.24 Summer
4. 2021	0.72 Academic 0.24 Summer
5. 2022	0.09 Academic 0.03 Summer No Cost Extension
6. 2023	0.09 Academic 0.03 Summer No Cost Extension
7. 2024	0.09 Academic 0.03 Summer No Cost Extension

Overlap: None

Title: What is Endometriosis? Deep Phenotyping to Advance Diagnosis and Treatment
Project Goals: We will utilize three existing diverse studies of adolescents and women for whom surgical, clinical and participant data as well as blood and tissue samples have been harmonized via the WERF EPHect tools. The goal of our study will be to identify unique classifications of endometriosis patients that inform non-invasive diagnostics, response to current treatments, and novel treatment pathways - stratifying discoveries by participant symptom presentation, and for the cases, by surgical and imaging visualized disease characteristics to capture the full heterogeneity of endometriosis.
Specific Aims: Aim 1: Identify plasma markers of endometriosis across independent and synergistic pathways; Aim 2: Quantify informative heterogeneity in associated transcriptomic and milieu-related plasma markers by disease phenotype; Aim 3: Further identify informative disease phenotypes by symptom presentation; Aim 4: Evaluate heterogeneity in plasma markers, disease phenotype, and symptom presentation by participant characteristics.
Project Number: NIH R01 HD094842
Role: PI
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004

Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 08/01/2018 - 04/30/2024 (No Cost Extension started 5/1/2023)
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2018	1.12 Academic 0.37 Summer
2. 2019	2.25 Academic 0.75 Summer
3. 2020	1.26 Academic 0.42 Summer
4. 2021	0.67 Academic 0.23 Summer
5. 2022	0.67 Academic 0.23 Summer
6. 2023	0.67 Academic 0.23 Summer
7. 2024	0.09 Academic 0.03 Summer No Cost Extension

Overlap: None

Title: Menstrual health during the Covid-19 pandemic: A longitudinal study among young people with and without endometriosis (Supplement to project listed above)
Project Goal / Specific Aims: The impact of SARS-CoV-2 infection or vaccination on menstrual health is unknown, despite anecdotal reports of post-vaccination change in menstruation. We will utilize an ongoing prospective study (A2A cohort; N=1569) comprised primarily of adolescents and young adults who have already answered the first in a planned series of COVID-19 focused questionnaires and have in-hand pre- and peri-pandemic menstrual characteristics data. Accounting for change in menstruation impacting medications, medical conditions, or pandemic-related psychosocial upheaval, we will determine if infection or vaccination affect menstrual characteristics compared to pre-pandemic characteristics or to those neither infected nor vaccinated.
Project Number: NIH R01 HD094842-04S1
Role: PI
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 08/27/2021-04/30/2024 (No Cost Extension started 5/1/2022)
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2022	0.45 Academic

Years	Person Months
	0.15 Summer
2. 2023	0.09 Academic 0.03 Summer
3. 2024	0.09 Academic 0.03 Summer No Cost Extension

Overlap: None

Title: What is Endometriosis? Deep Phenotyping to Advance Diagnosis and Treatment (Supplement to project listed above)
Project Goal / Specific Aims: To further develop the research capabilities of Claire Lunde, a predoctoral student at the University of Oxford, and to ensure completion of her Ph.D., and continued progress and mentoring toward obtaining a postdoctoral fellowship.
Project Number: NIH R01 HD096033-05S1
Role: PI
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 08/27/2022-04/30/2024 (No Cost Extension aligned with close of parent R01) **Total Award Amount:**
Person Months per budget period:

Year	Person Months
1. 2022	Mentor
2. 2023	Mentor
3. 2024	Mentor

Overlap: None

Title: Infertility History and Chronic Disease Profile
Project Goal / Specific Aims: In response to PA-17-091, within the Nurses' Health Study II (a prospective cohort of 116,430 women followed for >30 years), we will combine data from women's infertility and infertility treatment history, stored blood samples collected at two time points during follow-up (1st and 2nd collection, 10 years apart), and genome wide data to evaluate the relationship between infertility and the risk of cardiovascular diseases (myocardial infarction and stroke), type 2 diabetes, and breast cancer, including inflammatory, cardiometabolic, hormonal, and genetic profiles.
Project Number: NIH R01 HD096033
Role: PI
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 05/15/2019-04/30/2024

Total Award Amount: Person
Months per budget period:

Years	Person Months
1. 2019	0.9 Academic 0.3 Summer
2. 2020	1.8 Academic 0.6 Summer
3. 2021	1.35 Academic 0.45 Summer
4. 2022	1.35 Academic 0.45 Summer
5. 2023	1.8 Academic 0.6 Summer
6. 2024	1.8 Academic 0.6 Summer

Overlap: None

Title: COVID-19 vaccination and menstrual health (Supplement to project listed above)
Project Goal / Specific Aims: The impact of SARS-CoV-2 infection or vaccination on menstrual health is unknown, despite anecdotal reports of post-vaccination change in menstruation. We will utilize two ongoing prospective cohorts (NHS3 and GUTS) with combined 17,000 female participants who have already answered a year-long series of COVID-19 focused questionnaires and have in-hand pre- and peri-pandemic gynecologic characteristics data. Accounting for change in menstruation impacting medications, medical conditions, or pandemic-related psychosocial upheaval, we will determine if infection or vaccination affect menstrual characteristics compared to pre-pandemic characteristics or to those neither infected nor vaccinated.
Project Number: NIH R01 HD096033-03S1
Role: PI
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 08/27/2022-04/30/2024 (No Cost Extension started 5/1/2022)
Total Award Amount:
Person Months per budget period:

Year	Person Months
1. 2022	0.18 Academic 0.06 Summer
2. 2023	0.09 Academic 0.03 Summer
3. 2024	0.09 Academic 0.03 Summer No Cost Extension

Overlap: None

Title: Using affinity based proteomics to identify diagnostic and prognostic plasma biomarkers for

endometriosis
Project Goal / Specific Aims: The major goals of this project are to identify proteomic markers associated with early detection and progression of endometriosis using data and specimens from the Nurses' Health Study II cohort and Women's Health Study: Adolescence to Adulthood (A2A). Elucidating the proteome with critical consideration for reliable measurement, advanced statistical analyses, and population sampling that embraces rather than ignores endometriosis heterogeneity - may solve this critical issue of non-invasive diagnosis for girls and women with endometriosis.
Project Number: DoD W81XWH1910318
Role: MSU subcontract PI (Overall PI: Kathryn Terry)
Source of Support: Mass General Brigham Hospital
Source of Support Address:
399 Revolution Drive, Suite 745
Somerville, MA 02145
Contracting/Grants Officer: Kevin Moore
Performance Period: 09/01/2019-08/31/2023 (No Cost Extension started 9/1/2022)
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2019	0.67 Academic 0.23 Summer
2. 2020	0.9 Academic 0.3 Summer
3. 2021	0.9 Academic 0.3 Summer
4. 2022	0.9 Academic 0.3 Summer
5. 2023	0.09 Academic 0.03 Summer

Overlap: None

Title: Defining the role for descending pain modulation and reward-aversion processes towards the development of chronic pain in endometriosis
Project Goal / Specific Aims: A neuroimaging study that examines changes in brain structure and function and correlates these findings with psychological functioning, and pain sensitivity across three aims: (1) Age-Related Changes: Examining differences across 3 age cohorts of women with surgically confirmed endometriosis (12-17; 18-25; 26-44) compared to healthy controls. (2) Surgical Treatment Responsivity: Comparing the same brain and psychological and pain sensitivity tests in adolescent and young adult women presenting for surgery for endometriosis; comparing those that have and those that do not have pain at 3 months post-surgery. (3) Comparison with Existing Data: Comparing data from Aim 1 to existing databases of matched patients across the same age groups with migraines who have undergone the same type of testing.
Project Number: DoD W81XWH18PRMRPIIRA
Source of Support: Boston Children's Hospital
Source of Support Address:
300 Longwood Avenue
Boston, MA 02115
Contracting/Grants Officer: Jamie Chan
Performance Period: 08/15/2019-08/14/2023 (No Cost Extension started 8/15/2022)

Total Award Amount: Person
Months per budget period:

Years	Person Months
1. 2019	0.45 Academic 015 Summer
2. 2020	0.45 Academic 0.15 Summer
3. 2021	0.72 Academic 0.24 Summer
4. 2022	0.72 Academic 0.24 Summer
5. 2023	0.09 Academic 0.03 Summer No Cost Extension

Overlap: None

Title: Epigenetic regulatory mechanisms and therapeutic opportunities in endometriosis
Project Goal / Specific Aims: This proposal will advance research relevant to the health of women by expanding the genomic and phenotypic characterization of endometriosis, a disease that affects 10% of women. The primary objectives of this proposal are to identify the genetic and epigenetic regulatory mechanisms that contribute to endometriosis etiology and pathogenesis in efforts to find new ways to therapeutically target abnormal endometrial cells.
Project Number: NIH R01 HD103617
Role: Co-I (Overall PI: Ronald Chandler)
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Olamide Adeniyi
Performance Period: 08/15/2021-06/30/2026
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2021	0.18 Academic 0.06 Summer
2. 2022	0.18 Academic 0.06 Summer
3. 2023	0.18 Academic 0.06 Summer
4. 2024	0.18 Academic 0.06 Summer
5. 2025	0.18 Academic 0.06 Summer
6. 2026	0.18 Academic

Years	Person Months
	0.06 Summer

Overlap: None

Title: Defining Endometriosis Physiologic Sub-Phenotypes and Subsequent Cancer and Comorbidities
Project Goal / Specific Aims: This study will: 1) identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation; 2) determine the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis. We will capitalize upon our ongoing International Endometriosis Genome Consortium (IEGC) investigations and 3) in exploratory analyses, delve more deeply into the Women's Health Study: from Adolescence to Adulthood (A2A), which has measured an array of blood chemokine and cytokine markers.
Project Number: DoD W81XWH2110744
Role: PI
Risk Through Discovery of Novel Genetic Variants
Source of Support: Department of Defense USAMRAA
Source of Support Address:
820 Chandler Street
Fort Detrick, MD 21702-5014
Contracting/Grants Office: Brittany Hebb
Performance Period: 08/15/2021-08/14/2025
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2021	0.9 Academic 0.3 Summer
2. 2022	0.9 Academic 0.3 Summer
3. 2023	0.9 Academic 0.3 Summer
4. 2024	0.9 Academic 0.3 Summer
5. 2025	0.9 Academic 0.3 Summer

Overlap: None

Title: Research Gift: Advancing endometriosis discovery
Project Goal / Specific Aims: Research support from the Worldwide Endometriosis March from the Nezhat Family Foundation.
Project Number: N/A
Role: PI
Source of Support: Nezhat Family Foundation
Source of Support Address:
PO Box 720374
Atlanta, GA 30358
Contracting/Grants Officer: Camran Nezhat
Performance Period: 01/11/2022-12/31/2024

Total Award Amount:
Person Months per budget period: N/A
Overlap: None

Title: The role of neurotrophins in chronic pelvic pain and central sensitization among adolescents and women with endometriosis
Project Goal / Specific Aims: The goal of this project is to explore how neurotrophins and inflammatory cytokines are associated with chronic pelvic pain and central sensitization among adolescents and women with endometriosis. This research will explore how molecules within the peritoneal cavity may contribute to prolonged pain symptoms among women with endometriosis, even after surgery to remove the endometriotic lesion providing insights into the role of nerve growth factors and inflammation on the chronicity of endometriosis-related pain.
Project Number: NIH R21 HD107075-01A1
Role: MSU subcontract PI (Overall PI: Amy Shafrir)
Source of Support: Boston Children's Hospital
Source of Support Address:
300 Longwood Avenue
Boston, MA 02115
Contracting/Grants Officer: Jamie Chan
Performance Period: 09/01/2022-08/31/2024
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2022	0.45 Academic 0.15 Summer
2. 2023	0.45 Academic 0.15 Summer
3. 2024	0.45 Academic 0.15 Summer

Overlap: None

Title: Novel biomarkers and pathways of persistent endometriosis-associated pain across the life course.
Project Goal / Specific Aims: Endometriosis-associated pelvic pain (EAPP), which often originates during adolescence, evolves into chronic pelvic pain in some women, leading to decreased quality of life and altered life trajectory impacting well into adulthood. The proposed research will leverage unique data from two longitudinal cohorts to identify proteins and pathways that confer increased risk of persistent pain in patients with endometriosis despite receiving current standard treatments. Results from this study will advance our understanding of the underlying mechanisms that contribute to pain and inform strategic selection of treatments and interventions in vulnerable patients before pain becomes entrenched.
Project Number: NIH R01 HD111242-01
Role: MSU subcontract PI (Overall PI: Sawsan As-Sanie)
Source of Support: University of Michigan
Source of Support Address:
1540 E Hospital Dr, Floor 9
Ann Arbor, MI 48109
Contracting/Grants Officer: Not Assigned
Performance Period: 03/23/2023-02/29/2028
Total Award Amount:

Person Months per budget period:

Years	Person Months
1. 2023	0.9 Academic 0.3 Summer
2. 2024	0.9 Academic 0.3 Summer
3. 2025	0.9 Academic 0.3 Summer
4. 2026	0.9 Academic 0.3 Summer
5. 2027	0.9 Academic 0.3 Summer
6. 2028	0.9 Academic 0.3 Summer

Overlap: None

PENDING

Title: MOSART (Massachusetts Outcomes Study of Assisted Reproductive Technology) EQUITY
Project Goal/Specific Aims: MOSART EQUITY is a sequential mixed-methods study and will employ both quantitative and qualitative methodology to investigate the prevalence and factors associated with racial/ethnic disparities in perinatal health outcomes after fertility treatment among those who have experienced a live birth. Aim 1 will utilize the MOSART data system approach with more recent data from SART CORS linked with PELL to study the ART population. Aim 2 will propose a new linkage of PRAMS with PELL in MA to provide population estimates of perinatal experiences of bias and discrimination and social determinants of health and their association with adverse maternal and infant health outcomes following receipt of any type of fertility treatment. In Aim 3, we will employ qualitative methodology to investigate the lived experiences of NHB and Hispanic women who have received fertility treatment.
Project Number: PA-20-185
Role: MSU subcontract PI (Overall PI: Sunah Hwang)
Source of Support: NIH
Source of Support Address:
Contracting/Grants Officer: TBD
Performance Period: 04/01/2024-03/31/2029
Total Award Amount:
Person Months per budget period:

Year	Person Months
1. 2024	0.9 Academic 0.3 Summer
2. 2025	0.9 Academic 0.3 Summer
3. 2026	0.9 Academic 0.3 Summer
4. 2027	0.9 Academic 0.3 Summer
5. 2028	0.9 Academic 0.3 Summer

Title: Endometriosis and Lifelong Health

Project Goal / Specific Aims: We will utilize two existing longitudinal cohort studies: the Nurses' Health Study II (NHSII) and the Women's Health Study: from Adolescence to Adulthood (A2A). Among 7,376 NHSII endometriosis participants, we will: Aim 1) Identify dynamic, modifiable, and static predictors of future chronic conditions known to have a higher incidence among those with endometriosis; Aim 2) Investigate dynamic, modifiable, and static mediators and modifiers of mental health disorders and QoL; Aim 3) Identify inflammatory, hormonal, and adipokine markers that are mediators and modifiers of chronic conditions including changes in these markers over a 10-year period. Exploratory analyses: For Aims 1 and 2, we will assess how behaviors and characteristics identified in the NHSII are similarly associated with indicators of endometriosis-associated conditions and QoL among 793 surgically-confirmed A2A endometriosis participants (72%, <26 years at enrollment). For Aim 3, we will investigate biological pathways that are informative of underlying risk of endometriosis-associated conditions among a younger population including change over 3 years of follow-up among 188 A2A endometriosis participants.

Project Number: DoD TBD

Role: PI

Source of Support: Department of Defense USAMRAA

Source of Support Address:

820 Chandler Street

Fort Detrick, MD 21702-5014

Contracting/Grants Officer: TBD

Performance Period: 09/01/2024-08/31/208

Total Award Amount:

Person Months per budget period:

Year	Person Months
1. 2024	1.8 Academic 0.6 Summer
2. 2025	1.8 Academic 0.6 Summer
3. 2026	1.8 Academic 0.6 Summer
4. 2027	1.8 Academic 0.6 Summer
5. 2028	1.8 Academic 0.6 Summer

Overlap: None

Title: Macrophage phenotypes and endometriosis: Understanding their role in etiology and progression.
Project Goal/Specific Aims: In this application, we propose to evaluate endometriosis- specific gene expression profiles of circulating blood monocytes with upregulated phagocytosis pathways in endometriosis cases and controls from the A2A and examine the peritoneal environment of adolescents and young women with endometriosis, using a state-of-the-art proteomics platform to measure 7000 proteins, including both inflammatory and immune markers, in peritoneal fluid. Aim 1. Evaluate an endometriosis-specific gene expression signature in peripheral blood monocytes from newly collected blood samples from 100 endometriosis cases and 100 controls currently enrolled in the A2A study. Aim 2. Evaluate the macrophage-related cytokine profiles in peritoneal fluid of 352 adolescents and young women with laparoscopically-confirmed endometriosis in the A2A in relation to endometriosis associated symptom progression over time.
Project Number: NIH TBD
Role: MSU subcontract PI (Overall PI: Kathryn Terry)
Source of Support: Mass General Brigham Hospital
Source of Support Address:
399 Revolution Drive, Suite 745
Somerville, MA 02145
Contracting/Grants Officer: TBD
Performance Period: 06/01/2024-05/31/2029
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2024	0.9 Academic 0.3 Summer
2. 2025	0.9 Academic 0.3 Summer
3. 2026	0.9 Academic 0.3 Summer
4. 2027	0.9 Academic 0.3 Summer
5. 2028	0.9 Academic 0.3 Summer
6. 2029	0.9 Academic 0.3 Summer

Overlap: None

Title: Identifying plasma proteomic profiles of chronic pain development in endometriosis from adolescence to adulthood.
Project Goal / Specific Aims: 1. Predictors of chronic pain development in adolescent endometriosis. We will identify predictors of chronic pain development using baseline questionnaire and plasma proteomic data collected in adolescents with endometriosis. We will conduct a detailed pain assessment in adulthood using validated self-report measures on neuropathic pain, leveraging our Name of Individual: Stacey A. Missmer, ScD Commons ID: SAM123 Page 13 Other Support – S. Missmer existing observational longitudinal cohort of adolescents with endometriosis which will enable evaluation of biomarkers and pain metrics 10 years after enrollment. 2. Biological pathways involved in chronic pain development from adolescence to adulthood. We will identify change in protein levels and biological pathways from adolescence to adulthood, which will also

inform the dysregulated biological pathways involved in development of chronic pain. We will measure 7,000 plasma proteins in the paired blood samples collected in adolescence and adulthood using the SomaScan proteomics platform, which allows comprehensive assessment of the human proteome for novel discovery in the relevant biological pathways involved in chronic pain development from adolescence to adulthood.
Project Number: NIH DP2 HD112176-01
Role: MSU subcontract PI (Overall PI: Naoko Sasamoto)
Source of Support: Mass General Brigham Hospital
Source of Support Address:
399 Revolution Drive, Suite 745
Somerville, MA 02145
Contracting/Grants Officer: TBD
Performance Period: 01/01/2023-12/31/2025
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2023	0.45 Academic 0.15 Summer
2. 2024	0.45 Academic 0.15 Summer
3. 2025	0.45 Academic 0.15 Summer

Overlap: None

Title: The impact of hormonal modulation on systemic inflammation and central sensitization.
Project Goal / Specific Aims: Treating pelvic pain remains a significant challenge as current treatment strategies are dependent on our limited understanding of the underlying mechanisms that promote pain. Findings from the proposed clinical trial will help clinicians and researchers better understand the impact of pelvic and systemic inflammation on central nervous system sensitization, and how these pathways are affected by hormonal suppression. These results will have broad implications for understanding the neurobiological mechanisms through which hormonal suppression produces pain relief in many women with pelvic pain.
Project Number: 1R01HD108253-01A1
Role: MSU subcontract PI (Overall PI: Sawsan As-Sanie)
Person Months per budget period:

Years	Person Months
1. 2022	0.45 Academic 0.15 Summer
2. 2023	0.45 Academic 0.15 Summer
3. 2024	0.45 Academic 0.15 Summer
4. 2025	0.45 Academic 0.15 Summer
5. 2026	0.45 Academic 0.15 Summer
6. 2027	0.45 Academic 0.15 Summer

Source of Support: University of Michigan
Source of Support Address:
1540 E Hospital Dr, Floor 9
Ann Arbor, MI 48109
Contracting/Grants Officer: Not Assigned
Performance Period: 09/01/2022-08/31/2027
Total Award Amount:
Overlap: None

Title: Examination of factors influencing the racial disparity in fibroid incidence
Project Goal / Specific Aims: A major barrier to understanding the relative contributions of established and yet-to-be identified risk factors that may contribute to the fibroid disparity is that no single study has adequate numbers of both Black and White women to apply advanced epidemiologic methods (e.g., mediation analyses, population attribute risks) to evaluate these differences. Further, while an association between perceived interpersonal racism and fibroids has been shown, no studies have examined the role of structural racism in fibroid incidence. We propose to study women from two prospective U.S. cohorts — Black women from the Black Women's Health Study (BWHS) and White women from the Nurses' Health Study II (NHSII) — to identify factors that explain the differences in fibroid incidence between Black and White women. Importantly, the racial disparity in fibroid incidence undoubtedly involves an interplay of reproductive, lifestyle, psychosocial (e.g., stress), and environmental (e.g., air pollution) factors, and structural racism which our prospective cohorts with over 25 years of follow-up are uniquely positioned to examine.
Project Number: NIH PA-20-195
Role: MSU subcontract PI (Overall PI: Holly Harris)
Source of Support: Fred Hutchinson Cancer Research Center
Source of Support Address:
1100 Fairview Ave N.
Seattle, WA 98109
Contracting/Grants Officer: Trisha Brinton
Performance Period: 10/01/2023-09/30/2028
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2023	0.45 Academic 0.15 Summer
2. 2024	0.45 Academic 0.15 Summer
3. 2025	0.45 Academic 0.15 Summer
4. 2026	0.45 Academic 0.15 Summer
5. 2027	0.45 Academic 0.15 Summer
6. 2028	0.45 Academic 0.15 Summer

Overlap: None

Title: Proteomics-based biological aging signature and long-term health outcomes of endometriosis
Project Goal / Specific Aims: Our long-term goal is to identify novel blood-based biomarkers that predict increased risk of long-term comorbidities among women with endometriosis and modifiable factors that will alter acceleration of biological aging. Aim 1. Determine the association between accelerated biological aging and endometriosis in the A2A longitudinal cohort. Aim 2. Among endometriosis cases, determine the association between accelerated biological aging and long-term comorbidities in the NHSII prospective cohort. Aim 3. Identify behavioral factors (e.g., physical activity, healthy diet, aspirin use?) that alter biological aging in the NHSII prospective cohort.
Project Number: DoD TBD
Role: MSU subcontract PI (Overall PI: Naoko Sasamoto)
Source of Support: Mass General Brigham Hospital
Source of Support Address:
399 Revolution Drive, Suite 745
Somerville, MA 02145
Contracting/Grants Officer: TBD
Performance Period: 06/01/2024-05/31/2028
Total Award Amount:
Person Months per budget period:

Years	Person Months
1. 2024	0.45 Academic 0.15 Summer
2. 2025	0.45 Academic 0.15 Summer
3. 2026	0.45 Academic 0.15 Summer
4. 2027	0.45 Academic 0.15 Summer
5. 2028	0.45 Academic 0.15 Summer

Overlap: None

Title: A Longitudinal study of the epidemiology of endometriosis after menopause
Project Goal / Specific Aims: The **overall** goal of the proposed study is to identify predictive time-varying exposure-window-specific risk factors for PME, including inflammatory markers, to better understand the pathways of endometriosis among postmenopausal women. In addition, we propose to investigate the variation of risk factors by endometriosis diagnosis timing (pre vs postmenopausal), hypothesizing that the pathogenesis may differ between premenopausal and postmenopausal endometriosis. Ultimately this would establish risk groups who could be identified for pre- and perimenopausal surveillance and preventive care.
Project Number: DoD TBD
Role: Co-I (Overall PI: Madhavi Kulkarni)
Source of Support: Department of Defense USAMRAA
Source of Support Address:
820 Chandler Street
Fort Detrick, MD 21702-5014
Contracting/Grants Officer: TBD
Performance Period: 01/01/2024-12/31/2025
Total Award Amount:

Person Months per budget period:

Year	Person Months
1. 2024	0.7 Academic 0.2 Summer
2. 2025	0.7 Academic 0.2 Summer

Overlap: None

Title: A Community-Clinical Integrated Prenatal Care Model to Advance Maternal Health Equity.
Project Goal / Specific Aims: This study will test a scalable clinical-community integrated model of maternity care centered on community health workers (CHWs), specifically designed for reducing PRMM and disparities among Black and Hispanic birthing persons. This study aims to improve maternal health outcomes for Medicaid eligible birthing individuals, and especially for Black and Hispanic, therefore reducing the disparities in pregnancy-related morbidity and mortality.
Project Number: U54 HD113291
Role: Co-I (Overall PI: Cristian Meghea)
Source of Support: NIH
Source of Support Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: TBD
Performance Period: 03/01/2024-02/31/2031
Total Award Amount:
Person Months per budget period:

Year	Person Months
1. 2024	0.18 Academic 0.06 Summer
2. 2025	0.18 Academic 0.06 Summer
3. 2026	0.18 Academic 0.06 Summer
4. 2027	0.18 Academic 0.06 Summer
5. 2028	0.18 Academic 0.06 Summer
6. 2029	0.18 Academic 0.06 Summer
7. 2030	0.18 Academic 0.06 Summer
8. 2031	0.18 Academic 0.06 Summer

Overlap: None

IN-KIND SUPPORT

None.

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

Signature: Stacey A. Missmer

Digitally signed by Stacey A. Missmer
Date: 2023.08.29 19:31:16 -04'00'

SUPPORT
VAZQUEZ, ANA I.

CURRENT

Title: Defining Endometriosis Physiologic Sub-Phenotypes and Subsequent Cancer and Comorbidities Risk Through Discovery of Novel Genetic Variants

Time Commitments:

Year (2021-2025)	Person Months
1. 2021	0.5 academic 0.2 summer
2. 2022	0.5 academic 0.2 summer
3. 2023	0.5 academic 0.2 summer
4. 2024	0.5 academic 0.2 summer
5. 2025	0.5 academic 0.2 summer

Supporting Agency: Department of Defense USMRAA (W81XWH2110744)

Address: 820 Chandler Street Fort Detrick, MD 21702-5014

Contracting/Grants Officer: Brittany Hebb

Performance Period: 08/15/2021 - 08/14/2025

Level of funding:

Project Goals / Specific Aims: This study will: 1) identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation; 2) determine the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis. We will capitalize upon our ongoing International Endometriosis Genome Consortium (IEGC) investigations and 3) in exploratory analyses, delve more deeply into the Women's Health Study: from Adolescence to Adulthood (A2A), which has measured an array of blood chemokine and cytokine markers.

Overlap: None

Title: Using Metabolomics to Define the Behavioral Phenomics of Energy Balance and Exercise Response

Time Commitments:

Year (2019-2023)	Person Months
1. 2019	0.74 academic 0.66 summer
2. 2020	0.74 academic 0.66 summer

Year (2019-2023)	Person Months
3. 2021	0.74 academic 0.66 summer
4. 2022	0.74 academic 0.66 summer
5. 2023	0.74 academic 0.66 summer

Supporting Agency: NIH NIDDK (5R01DK119836-02)

Address: 9000 Rockville Pike Bethesda, MD 20892

Contracting/Grants Officer: Karp, Robert W

Performance Period: 09/18/2019 - 06/31/2023

Level of funding:

Project Goals / Specific Aims: Current treatments for obesity have been largely unsuccessful in maintaining long-term weight loss, demonstrating the tremendous need for new insight into mechanisms that may alter body mass and composition. Public health prevention programs designed to reduce the risk and occurrence of obesity commonly focus on modifiable environments and behaviors such as diet and physical activity, with varied results among individuals. This heterogeneity in response to obesity interventions suggests that there are specific types of individuals who may be responsive to a given intervention while others are not. In this proposal, we will develop statistical methods to jointly examine multiple biological and behavioral factors underlying weight stability and change. Our goal is to reveal new pathways that regulate and influence body mass and fatness before and after exercise training.

Overlap: None

Title: Chemokine-mediated antigen-specific T cell responses and immunotherapies to treat head and neck cancer.

Time Commitments:

Year (2020-2025)	Person Months
1. 2020	0.3 academic 0.3 summer
2. 2021	0.3 academic 0.3 summer
3. 2022	0.3 academic 0.3 summer
4. 2023	0.3 academic 0.3 summer
5. 2024	0.3 academic 0.3 summer
5. 2025	0.3 academic 0.3 summer

Supporting Agency: NIH/NIDCR **(**1R01DE029524-01)

Address: 9000 Rockville Pike Bethesda, MD 20892

Contracting/Grants Officer: Wang, Chiayeng

Performance Period: 07/01/2020 - 04/30/2025

Level of funding:

Project Goals: Human papillomaviruses (HPVs) are causally linked to 5% of all human cancers, including nearly all cervical cancers and ~25% of head and neck squamous cell carcinomas (HNSCCs), largely driving an ongoing epidemic increase of HPV-positive (HPV+) HNSCCs over recent decades. However, little is known about the mechanisms of disease progression driven by HPV, particularly in the context of host immunity. Based on our preliminary findings, we will study the mechanism by which the chemokine CXCL14 suppresses HNSCC growth, and test if CXCL14 serves as a useful immunomodulatory target for novel immunotherapies to treat HPV+ HNSCC. Recently, we have revealed that restoring the suppressed expression of CXCL14 in HPV+ HNSCC cells greatly suppressed tumor growth in immunocompetent syngeneic mice through upregulation of MHC-I antigenpresentation and antigen-specific CD8+ T cells responses. Based on our findings, we hypothesize that CXCL14 induces antitumor immune responses that suppress HPV+ HNSCC by enhancing antigen presentation and eliciting CD8+ T cell responses, and thus CXCL14 is a potential novel immunotherapeutic agent

Specific Aims: To test our hypothesis, we will 1) Define the mechanisms by which CXCL14 upregulates MHC-I antigen presentation to mediate tumor suppression; 2) Define the mechanisms by which CXCL14 induces CD8+ T cell infiltration/activation and tumor suppression; and 3) Test CXCL14-based immunotherapies that induce antitumor immunity and clear HPV+ HNSCC. Our study will provide new mechanistic understanding of antitumor immune defenses in HPV+ HNSCC and may lead to a novel immunotherapy for HNSCC, particularly for the nonresponders in current immunotherapies.

Overlap: None

Title: Functional and Integrative Omics of Recurrent Gout Flares

Time Commitments:

Year (2020-2024)	Person Months
1. 2020	0.9 academic 0.3 summer
2. 2021	0.9 academic 0.3 summer
3. 2022	0.9 academic 0.3 summer
4. 2023	0.9 academic 0.3 summer
5. 2024	0.9 academic 0.3 summer

Supporting Agency: NIH/NIAMS **(**1R01AR077927-01)

Address: 9000 Rockville Pike, Bethesda, MD, 20892

Contracting/Grants Officer: Park, Heiyoung

Performance Period: 9/25/2020 - 7/31/2024

Level of funding:

Project Goals: We hypothesize that differential DNA methylation and gene expression from circulating immune cells of individuals with gout is central to the inflammatory causes of acute gout flares.

Specific Aims: Aim 1. Compare differential expression and methylation of genes associated with the inflammatory component of gout in patients with/without recurrent gout flares.

Aim 2. Determine whether differential DNA methylation and gene transcription is associated with and causes recurrent gout flares in patients on treat-to-target urate lowering therapy.

Overlap: None

PENDING

Title: Shared pathogenic pathways between gout and cardiometabolic co-morbidities.
Time Commitments:

Year (2021-2025)	Person Months
1. 2021	0.3 academic 0.3 summer
2. 2022	0.3 academic 0.3 summer
3. 2023	0.3 academic 0.3 summer
4. 2024	0.3 academic 0.3 summer
5. 2025	0.3 academic 0.3 summer

Supporting Agency: NIH NIAMS **(**R01 Grant#: GRANT13283154)

Address: 1 AMS Circle. Bethesda, MD 20892-3675

Contracting/Grants Officer: Not Assigned

Performance Period: 10/01/2021-09/30/2025

Level of funding:

Project Goals / Specific Aims: In the US gout impacts around 4% of the adult population and its impact is amplified by co-morbidity with cardiometabolic diseases heart disease and chronic kidney disease and understanding the basis of the relationship between gout and cardiometabolic disease, including shared molecular pathways, has proven elusive. Increasing our knowledge in this area will identify new therapeutic targets and improve management approaches. This project will address the question “What are shared pathogenic mechanisms between gout and cardiometabolic disease?” by integrating cutting edge experimental, analytic, and genetic epidemiological approaches.

Overlap: None

PREVIOUS

Title: Circuit dynamics of sensorimotor integration and decision making in octopus.

Time Commitments:

Year (2020-2023)	Person Months
1. 2020	0.23 academic 0.08 summer
2. 2021	0.23 academic 0.08 summer
3. 2022	0.2 academic 0.1 summer
4. 2023	0.2 academic 0.1 summer

Supporting Agency: NIH/NINDS (1UF1NS115817-01)

Address: 6001 Executive Boulevard, Rockville, MD 20852

Contracting/Grants Officer: David, Karen Kate

Performance Period: 04/15/2015 - 03/31/2023

Level of funding:

Project Goals / Specific Aims: The goal of this proposal is to identify fundamental sensorimotor circuits associated with goal-oriented gripping movement by using high-dimensional biological, analytical and robotics technologies. To pursue this, we will study the octopus that offers an unparalleled opportunity to study a functioning spinal cord in a disembodied arm. This novel research has the potential to bridge the gap between current BMI technologies and profound understanding of neural circuits associated with the gripping movement, that its impairment is most catastrophic and regaining this function is most desirable to patients. We expect that the sensorimotor circuits dynamics that we will discover will be later used to control locomotion and other adaptive movement in lower extremities. Additionally, this work will establish unparalleled new resources to the scientific community for studying unconventional species, and will fuel the developments of intelligent sensors, methods and frameworks to acquire high-dimensional biological data, and novel approaches to fabricate essential elements of soft robots to build the next generation of bionic limbs.

Overlap: None

Title: Investigations in Gout, Hyperuricemia, and ComorbidiTies (Translational Genomics of Hyperuricemia. (INSIGHT) Center of Research Translation (CORT). Project 3 – Translational Genomics of Hyperuricemia (Mount, Project Lead)

Time Commitments:

Year (2017-2022)	Person Months
1. 2017	0.36 academic
2. 2018	0.82 academic
3. 2019	0.82 academic
4. 2020	0.82 academic
5. 2021	0.82 academic
6. 2022	0.82 academic

Supporting Agency: NIH NIAMS (5P50AR060772-09)

Address: 1 AMS Circle. Bethesda, MD 20892-3675

Contracting/Grants Officer: Park, Heiyoung

Performance Period: 09/20/2017 - 8/31/2022

Level of funding:

Project Goals / Specific Aims: The goal of this project is fill in key knowledge gaps in the functional genomics of hyperuricemia (HU) and its causality with chronic kidney disease (CKD) to yield novel tools for translational urate research, novel insight into shared pathways in CKD and HU, and potential therapeutic targets.

Overlap: None

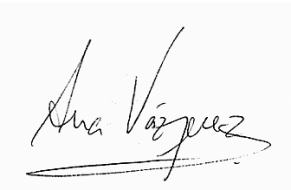
IN-KIND SUPPORT

None

*OVERLAP

No active or pending grant has any overlap with the current proposal.

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.



*Signature: Vazquez, Ana I.

Date: Sep 11, 2022

Positions/Scientific Appointments

2015-present Associate Professor, Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School, Boston, MA
2016-present Associate Professor, Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA

Marked in red indicates a change

COMPLETED

Title: The Boston Center for Endometriosis / Women's Health Study: from Adolescence to Adulthood / Progression Study 2.0
Supporting Agency: The Marriott Foundation
Grant Number: NA
Role: Subaward Principal Investigator (PI: Laufer)
Grants Specialist: Jenny Sadler Gallagher, MPH

Email: jenny.sadler@childrens.harvard.edu
Performance Period: 01/01/2021-12/30/2021
Level of funding:
This initiative encompasses three projects: Progression 2.0, A2A Infrastructure, and Proof of Concept.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2021	1.8 CM

Title: Redefining normal: Personalized CA125 cutpoints for ovarian cancer screening
Supporting Agency: National Institutes of Health
Grant number: 5R01CA193965-03
Role: Principal Investigator
Grants Specialist: Nicole Franklin

Email: nicole.franklin@nih.gov
Performance Period: 06/01/2016-05/31/2020
Level of funding:
Goals: We propose to develop personalized CA125 cutpoints using individual characteristics to improve the sensitivity and specificity of this important ovarian cancer marker and lead the way to population screening that could save lives.
Specific Aims:

1. Develop and validate a predictive model of CA125 in women without ovarian cancer.
2. Calculate personalized cutpoints and evaluate discriminatory ability compared to a single threshold in PLCO, NHS, and EPIC.
3. Evaluate whether the addition of personalized CA125 improves ovarian cancer risk prediction by adding adjusted CA125 to established ovarian risk models.

Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year		Person Months
1.	2017	3.60 CM
2.	2018	3.60 CM
3.	2019	3.60 CM

4. 2020	2.86 CM

Title: Comparing Options for Management: Patient—centered Results for Uterine Fibroids (COMPARE-UF)
Supporting Agency: Duke University / PCORI
Grant Number: 1P50HS023418
Role: Co-Investigator (PI: Myers)
Grants Specilaist: Bryan Luce PhD, MS, MBA

Email: bluce@pcori.org
Performance Period: 09/30/2014 – 09/29/2019 NCE
Level of funding:
Goals: The objective of the national collaborative project is to develop a multicenter registry that is geographically, racially, and clinically diverse that will generate high quality data that will enable women with fibroids to make informed decisions about treatment options. Specific research questions will focus on how treatment options impact symptom relief, preserving reproductive function, and other outcomes important to participants.
AIM 1: Develop the infrastructure necessary to implement large-scale observational comparative effectiveness research (CER) studies of management options for women with UF, including (a) a governance structure, policies, and procedures conducive to collaborative research involving patients, clinicians, methodologists, and other stakeholders, (b) an experienced Research and Data Coordinating Center, and (c) nine geographically diverse Clinical Centers (CCs) representing a broad range of patients and providers.
AIM 2: Use this infrastructure to implement three projects addressing high-priority evidence gaps related to the effect of different management strategies on patient-centered outcomes. These include PROJECT 1: Comparing management options for symptom relief PROJECT 2: Comparing management options for preserving reproductive function PROJECT 3: Comparing effectiveness in different subpopulations.
AIM 3: Evaluate innovative methods for the design, conduct, and analysis of observational comparative effectiveness research in this population.
AIM 4: Translate research results into improved patient care, through both traditional peer-reviewed publications and collaborations with stakeholders to integrate the research findings into evidence-based patient decision making tools, clinical practice guidelines, and quality.
Overlap: None

1.2015	1.2 CM
2.2016	1.2 CM
3.2017	1.2 CM
4.2018	1.2 CM
5.2019	1.2 CM

Title: High-throughput proteomics profiling for identification of early detection biomarkers of high-grade serous ovarian cancer
Supporting Agency: Minnesota Ovarian Cancer Alliance
Grant Number: N/A
Role: Co-Investigator (PI: Sasamoto)
Grants Specialist: Kathleen Gavin

Email: kgavin@mnovarian.org
Performance Period: 07/01/2019-06/30/2020
Level of funding:
The major goals of this project are to identify biomarkers that predict high grade serous ovarian cancer and elucidate etiologic pathways of development. Specifically, we plan to:
Aim 1. Identify proteins associated with early stage HGSOC in prospectively collected samples. We hypothesize that Pro-inflammatory and immunosuppression-related proteins in blood drawn one to three years

prior to diagnosis of late stage HGSOC will be higher compared to healthy controls. In addition, untargeted proteomics profiling considering all 1,305 proteins will identify novel candidate biomarkers for early stage HGSOC using blood drawn one to three years prior to diagnosis of late stage HGSOC compared to healthy controls. Aim 2. Elucidate potential biological pathways relevant to early stage HGSOC. We hypothesize that: Inflammatory and immunosuppression pathways are enriched among the circulating proteins associated with early stage HGSOC using blood drawn one to three years prior to diagnosis of late stage HGSOC compared to healthy controls.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2020	.24CM

Title: Dietary and Hormonal Determinants of Cancer in Women
Supporting Agency: National Institutes of Health
Grant Number: P01 CA87969
Role: Project 3 Leader (PI: Stampfer)
Grants Specialist: Somdat Mahabir

Mail: mahabir@mail.nih.gov
Performance Period: 07/01/2015-06/30/2021 (NCE)
Level of funding:
Goals: The goal of this project is to improve ovarian cancer prevention, which is key for reducing morbidity and mortality. This proposal examines two key, but understudied putative pathways in ovarian carcinogenesis, metabolism and inflammation. We will examine several key lipid classes using a metabolomics profiling platform as well as an agnostic evaluation of all measured metabolites. For inflammation, we propose to focus on modifiable factors, such as diet, sedentary behavior, premenopausal NSAID use, as well as biomarkers of prostaglandins and chlamydia antibodies. We also will consider tumor characteristics including mRNA expression with inflammatory exposures. Finally, for the first time, we will consider post-diagnosis modifiable exposures with ovarian cancer survival.

1. Project 1. Diet, exogenous hormones, and breast cancer risk. A series of analyses is being conducted that relates specific aspects of hormone replacement therapy and diet and nutritional status to breast cancer incidence and survival among women with the disease.
2. Project 2. Diet hormones, and colorectal cancer risk. A series of analyses is being conducted that relates specific aspects of hormone replacement therapy and diet and nutritional status to colorectal cancer incidence and survival among women with the disease.
3. Project 3. Hormones diet, and ovarian cancer risk. Repeated measurement of diet, body weight, and hormone use are permitting evaluation of relationships between these variables and risk for ovarian cancer.
4. Project 4. Statistical innovations in risk modeling. The rich body of epidemiologic data available through the cohort and the statistical expertise of the investigators provide opportunities to develop methods for prediction of cancer risk and analysis of multiple endpoints

Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2016	.96CM
2.2017	.96CM
3.2018	.96CM
4.2019	.96CM
5.2020	.96CM
6.2021	.96CM

Title: Harnessing biomarker and phenotypic diversity among adolescents and women with endometriosis to advance personalized medicine for diagnosis and pain remediation
Supporting Agency: Michigan State University / National Institutes of Health
Grant Number: R21HD096358
Role: Subcontract PI (PI: Missmer)
Grant Specialist: Candace Tingen, PhD

Email: tingencm@mail.nih.gov
Performance Period: 05/01/2019 – 04/30/2021
Level of Funding:
Goals: Within the Women's Health Study: from Adolescence to Adulthood (A2A; a prospective cohort of >1200 adolescents and young women, oversampled for those with surgically-confirmed endometriosis, followed for >4 years), we will combine WERF EPHect compliant data from participant surveys, electronic medical records, and stored blood samples collected annually. These data will capture informative changes in pain experience, inflammatory and oxidative stress milieu, and central sensitization to advance our understanding of phenotypic diversity among adolescents and women with endometriosis –the foundation for successful personalized, precision medicine to shorten diagnostic delay and maximize successful pain remediation.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2020	.47 CM
2.2021	.47 CM

Title: Inflammation and the Malignant Transformation of Endometriosis
Supporting Agency: Fred Hutchinson Cancer Center / DOD Congressionally Directed Medical Research Programs
Grant: W81XWH-19-1-0128
Role: Co-Investigator (PI: Harris)
Grants Specialist: Patricia Modrow, PhD

Email: patricia.modrow@amedd.army.mil.
Performance Period: 04/01/2019-09/30/2020
Level of funding:
Goals: We will examine the association between inflammatory markers in peritoneal fluid and cancer driver mutations (ARID1A, PIK3CA, PPP2R1A, CTNNB1, PTEN, KRAS, BRAF, ERBB2) and immunohistochemical (IHC) markers of cell proliferation (Ki67) and invasiveness (E-cadherin, α- and ß-catenin) in endometriosis tissue. We hypothesize that women with higher levels of peritoneal fluid inflammatory markers will have endometriosis tissue with higher numbers of cancer driver mutations and increased invasive/proliferative activity. We will evaluate whether inflammation-related factors (ovulatory cycles, NSAID use, BMI, dysmenorrhea, tubal ligation, IUD use, pelvic infections) and systemic inflammation (e.g., CRP, IL-6 plasma levels) are associated with inflammatory markers in peritoneal fluid, taking into account menstrual cycle phase.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2020	.85 CM

Title: PREDICT: The Prospective Early Detection Consortium for Ovarian Cancer
Supporting Agency: German Cancer Research Center / DOD Congressionally Directed Medical Research Program
Grant Number: W81XWH1910307

Role: Subcontract PI (PI: Kaaks)
Email: a.nelson@dkfz.de
Performance Period: 09/01/2019-08/31/2020
Level of funding:
Goals: To develop a worldwide collaboration to assemble a sufficient number of EOC cases, with blood samples collected relatively shortly before diagnosis, to enable the development of accurate diagnostic algorithms for multi-marker panels. The aim of this consortium is to identify and cross-validate biomarker panels that, combined with TVUS and CA125, will allow diagnosis of EOC in earlier stages of disease. To achieve this aim, we propose to:

1. Establish an international consortium of large-scale prospective cohort studies and biobanks with blood samples collected prior to diagnostic surgery - "PREDICT", the Prospective Early Detection Consortium for Ovarian Cancer - for the application of state-of-the-art "omics" technologies for biomarker discovery and validation. Prospective cohorts will contribute more than 450 EOC cases with blood samples collected ≤18 months prior to diagnosis, and from cancer-free controls, for biomarker discovery and validation. Cohorts contributing to the consortium include the European Prospective Investigation into Cancer [EPIC], Women's Health Initiative [WHI], Nurses' Health Studies [NHS and NHSII], Finnish Maternity Cohort [FMC], Norwegian Janus Serum Bank cohort, and Prostate, Lung, Colorectal and Ovarian Cancer screening trial [PLCO]. Pre-operative blood samples from a large, established biorepository at the Brigham and Women's Hospital [BWH], including patients with invasive EOC (n=548) and borderline tumors (n=131), and benign pelvic disease, plus population-based based controls, will be available for additional cross-validation.
2. Leverage existing data in individual cohorts to provide preliminary data for future studies. In silico cross-validation of miRNA patterns with diagnostic potential (discovery studies ongoing or recently completed by individual consortium members).
3. Initiate a "proof of concept" study validating a set of candidate tumor associated autoantibodies (TAAbs) identified in an immuno-proteomics scan for antibodies against 768 candidate proteins. Preliminary data are being generated in the EPIC cohort, with findings to be validated in the consortium.

Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2020	.35 CM

Title: Integrative analysis of genomic, epigenomic and phenotypic data for disease stratification of endometriosis
Supporting Agency: University of California San Francisco / National Institutes of Health
Grant Number: R01 HD089511-01
Role: Subcontract PI (PI: Guidice)
Grant Specialist: Candace Tingen, PhD
Email: tingencm@mail.nih.gov

Performance Period: 09/26/2016 – 04/30/2021
Level of funding:
Goals: This global project that includes collaborative sites in the US, UK, and Australia proposes to perform genome-wide DNA methylation analyses and genotyping of nearly 1000 existing, phenotypically well-annotated eutopic endometrium tissue samples of women with endometriosis and controls, collected by standard operating procedures, to test the hypothesis that environmental and genetic influences contribute to endometriosis and leave long-term signatures in the DNA methylome in the uterine endometrium contributing to disease pathogenesis and pathophysiology, with promise for translational diagnostics and therapeutic target development. Specifically, we will address the hypotheses that 1) environmental and genetic influences contribute to endometriosis and leave long-term signatures in the DNA methylome in the eutopic endometrium that contribute to disease pathogenesis and pathophysiology, and 2) these can serve to stratify disease risk and inform new avenues for drug target discoveries and diagnostic development.

Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2017	.56 CM
2.2018	.56 CM
3.2019	.56 CM
4.2020	.56 CM
5.2021	.56 CM

Title: Defining the Role for Descending Pain Modulation and Reward-Aversion Processes Towards the Development of Chronic Pain in Endometriosis
Supporting Agency: Boston Children's Hospital / Department of Defense
Grant Number: W81XWH1910560
Role: Subaward Principal Investigator (PI: Seiberg)
Grants Specialist: Stephanie Davis

Email: stephanie.p.davis12@civ@mail.mil
Performance Period: 08/15/2021-08/14/2022
Level of funding:
Goals: The goals are to define changes in brain structure and function as a correlate of subjective measures of pain and psychophysical functioning in adolescent, young adult, and adult women with surgically confirmed endometriosis vs. healthy controls; to correlate psychophysical measures and brain changes with levels of Offset Analgesia (OA) and to compare brain metrics of adolescents, young adults, and adult women with endometriosis with female patients ages 12-44 with migraines.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	.12 CM

Title: Metabolomic signatures of pain and progression among women with endometriosis
Supporting Agency: Marriott Family Foundation/ Peery Foundation
Grant Number: Marriott Family Foundation/Boston Center for Endometriosis Investigator Grant
Role: Principal Investigator
Grants Specialist: Jenny Sadler Gallagher, MPH

Email: Jenny.Sadler@childrens.harvard.edu
Performance Period: 01/01/2018-12/31/2019
Level of funding:
Goals: The objective of this project is to identify metabolites and metabolite signatures in women with endometriosis that are associated with pain and progression which may aid in monitoring disease, lead to personalized treatment, and provide insight into the biology of the disease that may lead to new therapeutic targets.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

1.2018	.36 CM
2.2019	.36 CM

Title: Identifying early detection metabolomics biomarkers for high-grade serous ovarian cancer
Supporting Agency: Sperling Family Foundation (Broad Institute/BWH)
Grant: 2021A001681
Role: Co-Investigator (PI: Sasamoto)

Contracting/Grants Officer: Ashlin Bolton
Time Commitments: .6 CM
Performance Period: 03/01/2021-12/28/2022 (NCE)
Level of funding:
Project Goals: To discover novel early detection metabolomic biomarkers for ovarian cancer and elucidate the systemic metabolomic profiles in the early phase of ovarian cancer development. Specific Aims: The primary objective of this innovative application aims to discover novel early detection metabolomic biomarkers for ovarian cancer and elucidate the systemic metabolomic profiles in the early phase of ovarian cancer development utilizing the biospecimens and clinical data at the Brigham and Women's Hospital and applying the world-class innovative technology of the highly reproducible, highthroughput, multiplex metabolomics technology at the Broad Institute.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	.6 CM

Title: Mucins and immune cell interactions in ovarian cancer pathogenesis & progression
Supporting Agency: National Institutes of Health
Grant Number: R35 CA197605
Role: Co-Investigator (PI: Cramer)
Grants Specialist: Neeraja Sathyamoorthy Ph.D.
Email: ns61r@nih.gov

Performance Period: 03/01/2016-02/28/2023
Level of funding:
Goals: The goal of this proposal is to study the inflammatory pathway leading to the development ovarian cancer and to further understanding mechanisms of risk that may lead to early detection.
Specific Aims: Review obstacles to cancer prevention and early detection including the needs:

1) to reconcile individual risk factors for ovarian cancer with the totality of epidemiologic evidence
2) to find unifying explanations for risk factors common to different cancers
3) to demonstrate that mucin tumor antigen levels are changed not only by the tumor but also by risk factors for the tumor
4) to be able to consider serum biomarkers in the context of the white blood count (WBC).

Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2017	3 CM
2. 2018	2.4 CM
3. 2019	2.4 CM
4. 2020	2.4 CM
5. 2021	.6 CM
6. 2022	.6 CM
7. 2023	.0 CM

Current Research Support

Title: The Boston Center for Endometriosis: A First-in the World Care and Research Program for Women of all Ages
Supporting Agency: J. Willard and Alice S. Marriott /The Boston Center for Endometriosis
Grant Number: NA

Role: Subcontract PI (PI: Laufer)
Grants Specialist: Jenny Sadler Gallagher, MPH

Email: Jenny.Sadler@childrens.harvard.edu
Performance Period: 07/01/2012-12/31/2024
Level of funding:
Project Goals: Design and conduct for study enrollment and data and biologic sample collection within Brigham and Women's Hospital and Boston Children's Hospital
Specific Aims: Establish a longitudinal cohort of girls and women with endometriosis and appropriate comparison girls/women with detailed life course data and extensive biologic samples storage.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2013	1.18 CM
2. 2014	1.18 CM
3. 2015	1.18 CM
4. 2016	1.18 CM
5. 2017	1.18 CM
6. 2018	1.18 CM
7. 2019	1.20 CM
8. 2020	1.20 CM
9. 2021	1.18 CM
10. 2022	2.40 CM
11. 2023	1.18 CM
12. 2024	1.20 CM

Title: Changing contraceptive patterns and ovarian cancer risk
Supporting Agency: National Institutes of Health
Grant Number: 1R01CA258679
Role: Principal Investigator
Grant Specialist: Goli Samimi
9000 Rockville Pike, Bethesda, MD 20892

Email: goli.smimi@nih.gov
Performance Period: 04/01/2021-03/31/2026
Level of Funding:
Goals: Changing contraceptive patterns, specifically the decline of oral contraceptives and rise intrauterine devices, could have important implications for future ovarian cancer risk. Leveraging consortium data including more than 700,000 women (>20,000 cases) as well as blood (n~1,500) and tissue (n~2,000) on women to examine systemic and local immune mechanisms with cutting-edge multiplex immunofluorescence technology, we will evaluate how this highly prevalent and modifiable risk factor may impact the population burden of this extremely fatal disease.
Aim 1. Estimate the association between IUD use and risk of ovarian cancer, including by histotype, in 17 case-control studies (20,314 cases, 26,099 controls) and 7 cohort studies (678,650 participants, 1,891 cases) with prospectively collected data.
Aim 2. Describe how timing and type of IUD use influence ovarian cancer risk in 13 case-control and 4 cohort studies.
Aim 3. Evaluate whether the association between IUD use and ovarian cancer risk differs by the tumor immune microenvironment, utilizing 3,530 cases on tissue microarrays.
No Overlap
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	3.00 CM
2. 2023	1.92 CM
3. 2024	2.40 CM
4. 2025	2.40 CM
5. 2026	2.40 CM

Title: Using genetic predictors of CA125 to improve personalized ovarian cancer screening
Supporting Agency: Marsha Rivkin Center for Ovarian Cancer Research
Grant Number: NA
Role: Co-Investigator (PI: Sasamoto)
Grants Specialist: Jackie Lang
1200 12th Ave S, Suite 110, Seattle, WA 98144

Email: Jackie.Lang@Swedish.org
Time commitment: .0 CM
Performance Period: 04/01/2021-03/31/2024 NCE
Level of funding:
Goals: Aim 1. Identify genetic predictors of CA125 using data on 4,391 women without ovarian cancer in PLCO, EPIC, NHS/NHSII, and NEC.
Aim 2. Examine whether adding genetic predictors of CA125 will improve the discriminatory performance of personalized CA125 cutpoints in blood collected months prior to diagnosis in prospective cohorts of PLCO, EPIC, and NHS/NHSII.
No Overlap
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	.60 CM
2. 2023	0 CM
3. 2024	0 CM

Title: What is Endometriosis? Deep Phenotyping to Advance Diagnosis and Treatment
Supporting Agency: Michigan State University / National Institutes of Health
Grant Number: R01HD094842
Role: Subcontract PI (PI: Missmer)
Grants Specialist: Margaret Young

Email: Margaret.young@nih.gov
Performance Period: 08/01/2018 - 04/30/2024 NCE
Level of funding:
Goals: We will utilize three existing diverse studies of adolescents and women for whom surgical, clinical and participant data as well as blood and tissue samples have been harmonized via the WERF EPHect tools. The goal of our study will be to identify unique classifications of endometriosis patients that inform non-invasive diagnostics, response to current treatments, and novel treatment pathways - stratifying discoveries by participant symptom presentation, and for the cases, by surgical and imaging visualized disease characteristics to capture the full heterogeneity of endometriosis.
Specific Aims: Aim 1: Identify plasma markers of endometriosis across independent and synergistic pathways; Aim 2: Quantify informative heterogeneity in associated transcriptomic and milieu-related plasma markers by disease phenotype; Aim 3: Further identify informative disease phenotypes by symptom presentation; Aim 4: Evaluate heterogeneity in plasma markers, disease phenotype, and symptom presentation by participant characteristics
No Overlap

Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2019	1.20 CM
2. 2020	1.20 CM
3. 2021	1.20 CM
4. 2022	.98 CM
5. 2023	.91 CM

Title: Using affinity based proteomics to identify diagnostic and plasma biomarkers for endometriosis
Supporting Agency: Department of Defense
Grant Number: W81XWH1910318
Role: Principal Investigator (Partnering PI: Libermann at Beth Israel Deaconess Medical Center)
Grants Specialist: Chris Baker

Email: christopher.l.baker132.civ@mail.mil
Performance Period: 09/01/2019-08/31/2023 (NCE)
Level of funding:
The major goals of this project are to identify proteomic markers associated with early detection and progression of endometriosis using data and specimens from the Nurses' Health Study II cohort and the Boston Center for Endometriosis Women's Health Study: Adolescence to Adulthood.
Aim 1. In prospectively collected plasma samples obtained up to 6 years before diagnosis, identify proteins that differentiate women who will be diagnosed with endometriosis from controls.
Aim 2. Determine whether proteins differ between endometriosis subtypes.
Aim 3. In pre and post-operative samples, identify proteins and pathways that discriminate between those who continue to be impacted by the disease, characterized by continued chronic pain and poor quality of life, and those who improve after surgery.
No Overlap
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2020	1.80 CM
2. 2021	1.80 CM
3. 2022	1.80 CM
4. 2023	1.38 CM

Title: Relating molecular subgroups of endometriosis-associated ovarian cancers to survival and risk factors
Supporing Agency: Mayo Clinic / National Institutes of Health
Grant Number: R01-CA248288
Role: Subcontract PI (PI: Goode)
Grant Specialist: Ashley Salo

Email: ashley.salo@nih.gov
Performance Period: 01/13/2021-12/31/2025
Level of funding:
Goals: Aim 1. To characterize molecularly defined subgroups of ENOC and CCOC, we will statistically integrate sequencing and array data from gene expression, somatic mutations, and differentially methylated regions from 523 ENOC and 344 CCOC. Clustering approaches will use samples divided into training and test sets.
Aim 2. To identify subgroup-specific survival associations, we will relate molecular subgroups defined in Aim 1 to overall survival using Cox regression models.
Aim 3. To identify subgroup-specific risk factor associations, we will relate molecular subgroups defined in Aim 1 to lifestyle risk factors.

Aim 4. To identify opportunities for overlapping treatments in patient care, we will statistically compare the patterns of molecular features of the ENOC and CCOC subgroups with various TCGA cancer subgroups.
No Overlap
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2021	1.2 CM
2. 2022	1.86 CM
3. 2023	1.02 CM
4. 2024	1.2 CM
5. 2025	1.2 CM

Title: Identifying Proteomic Profiles and Biological Networks of Early-Stage Ovarian Cancer
Supporting Agency: Department of Defense W81XWH2110320
Address: 1120 Fort Detrick – CDMRP
Frederick MD 21702
Contracting/Grants Officer: Abigail Strock
email: abilgail.l.strock.civ@mail.mil

Role: Mentor (PI: Sasamoto)
Performance Period: 05/01/2021-04/30/2025
Level of funding:
Goals: To identify circulating proteins and biological networks associated with ovarian cancer in blood collected 1 to 7 years before diagnosis of overt invasive disease
Specific Aims: We propose to leverage existing samples and data from the Nurses' Health Studies (NHS/NHSII), a prospective cohort of women, and the Preoperative Pelvic Mass (PreOP) Study, a clinic-based study of women who donated blood samples before surgery for a suspicious pelvic mass and apply next generation proteomics technology that has excellent reproducibility and reliability.
Aim 1. In prospectively collected plasma samples obtained up to 7 years before diagnosis of overt invasive disease, identify proteins associated with preclinical disease in the NHS/NHSII.
Aim 2. In pre-surgical plasma samples, identify proteins associated with early-stage disease in the PreOP.
Aim 3. Identify biological networks related to early-stage disease and disease progression.
No Overlap
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2021	.6 CM
2. 2022	.6 CM
3 .2023	.48 CM
4. 2024	.6 CM

Title: Using biomarkers to elucidate the breastfeeding and ovarian cancer risk association
Supporting Agency: National Institutes of Health
Grant: R03CA259659-01A1
Role: Co-Investigator (PI: Sasamoto)
Grants Specialist: Tram K. Lam

Email: lamt@mail.nih.gov
Performance Period: 03/07/2022-02/29/2024
Level of funding:
Goals: To elucidate the breastfeeding ovarian cancer association using circulating biomarker, tumor marker expression, and detailed questionnaire data from more than 800,000 women.

Aim 1. Identify factors that mediate and modify the association between breastfeeding and ovarian cancer risk in 12 case-control and 10 prospective cohort studies.
Aim 2. Characterize the impact of breastfeeding on circulating inflammatory and metabolic markers in NHS/NHSII.
Aim 3. Examine the association between breastfeeding and tumor immunity in NHS/NHSII and NEC.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	.48 CM
2. 2023	.48 CM

Title: Defining Endometriosis Physiologic Sub-Phenotypes and Subsequent Cancer and Comorbidities Risk Through Discovery of Novel Genetic Variants
Supporting Agency: Michigan State University / Department of Defense
Role: Subaward Principal Investigator (PI: Missmer)
Grant Number: W81XWH2110744
Grants Specialist: Abigail Strock

Email: abigail.l.strock.civ@mail.mil
Performance Period: 08/15/2021-08/14/2025
Level of funding:
Goals: The overall hypothesis of this study is to identify novel germline genetic variants associated with subphenotypes in endometriosis and examine how these genetic variants relate the subsequent risk of gynecologic and non-gynecologic comorbidities including cancer, as well how they interact with the inflammatory context. These goals will be achieved using data from an international consortium, and separately, three longitudinal studies. We hypothesize that subphenotypes in endometriosis are associated with unique genetic loci above and beyond those identified in prior studies of endometriosis as a homogenous entity. We further hypothesize that some loci may be shared between specific subphenotypes and comorbidities, suggesting either a common etiology, or progression via endometriosis which we hope to elucidate in our study. Finally, we hypothesize that the disease progression from the genetic risk factor to the long-term high risk-sub phenotypes and comorbidities may be modified by the inflammatory context. To advance the two areas targeted in in FY 2020 PRMRP, we will use cross-sectional data from the International Endometriosis Genome Consortium (IEGC), and three ongoing prospective cohort studies—Nurses' Health Study II (NHS II), Women Health Study (WHS), and Women's Health Study Adolescence to Adulthood (A2A). We will leverage genomic and phenotypic data collected in multiple well-established cohort populations as well as more recent case-control studies that launched with harmonized data and sample collection via the Endometriosis Phenome and Biobanking Harmonization Project (WERF-EPHect) tools.53 For longitudinal analysis we will include three ongoing cohorts with existing whole-genome, phenotypic and comorbidity data (1) Nurses' Health Study II, a cohort of 116,429 female nurses aged 25-42 years in 1989 among whom 2,230 endometriosis cases have been genotyped, (2) Women's Health Study, including 23,294 female health professionals ≥45 years at enrollment among whom 1494 have been diagnosed with endometriosis, (3) Women's Health Study: from Adolescence to Adulthood (A2A), a cohort of 1,550 adolescents and young women with median age of 22 at enrollment. A2A is a deeply-phenotyped cohort with detailed assessment of symptoms including pain types, severity, other life-impacting symptoms, and other disease diagnoses.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	1.20 CM
2. 2023	.91 CM
3. 2024	1.20 CM

4. 2025	1.20 CM
5. 2026	1.20 CM

Title: Aspira Endometriosis Project
Supporting Agency: Aspira Women's Health / Dana Farber Cancer Institute
Grant Number: SRA 2022A006361
Role: Subaward Co-Investigator (SubAward PI: Elias) (PI: Chowdhury)
Grants Specialist: Thomas Greco (CEO)
Email/Phone: tgreco@aspirawh.com
Performance Period: 08/02/2022-08/03/2024
Level of funding:
The proposed application for this technology is to guide clinical management for women without a pelvic mass presenting with symptoms (e.g., chronic pelvic or abdominal pain, infertility, dysmenorrhea, dyspareunia, dysuria) suggestive of possible endometriosis. The intended uses are to 1) eliminate endometriosis from the differential diagnosis among women for whom this diagnosis is unlikely; 2) allow empiric medical treatment for endometriosis among women for whom endometriosis is almost certain; and 3) to limit surgical evaluation for possible endometriosis to those few cases where the non-invasive test is equivocal or in whom surgical excision of endometriosis is clinically indicated.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.2 CM
2. 2024	1.2 CM

Title: Menstrual health during the Covid-19 pandemic: A longitudinal study among young people with and without endometriosis (Wise Supplement)
Supporting Agency: Michigan State University / National Institutes of Health
Grant Number: 3R01HD094842-04S1
Role: Subaward Principal Investigator (PI: Missmer)
Grants Specialist: Jessica Lemke

Email: subawards@cga.msu.edu
Performance Period: 08/27/2021-04/30/2024 NCE
Level of funding
Goals: Dr. Terry and her team at the Ob/Gyn Epidemiology Center at Brigham and Women's Hospital will design a COVID-specific questionnaire to assess menstrual changes and other aspects of health that may have changed during the pandemic.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	.60 CM
2. 2023	.48 CM
3. 2024	.0 CM

Title: Systemic immune dysfunction assessed by methylation and endometriosis
Supporting Agency: Boston Children's Hospital, Marriott Foundation Grant: Boston Children's Hospital / J Willard & Alice S Marriott Foundation
Role: Principal Investigator
Grants Specialist: Jenny Sadler Gallagher, MPH
Email: jenny.sadler@childrens.harvard.edu
Performance Period: 08/01/2022-07/30/2024 NCE

Level of funding:
Goals/Aims: Aim 1. Assess reproducibility of circulating immune cell distributions duplicate samples from 10 endometriosis cases and 10 controls. Aim 2. Evaluate differences in circulating immune cell distributions in 40 A2A participants with endometriosis compared to 40 matched controls.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	.48 CM
2. 2024	.6 CM

Title: Oral microbiome profiling of adolescent endometriosis
Supporting Agency: Boston Children's Hospital / J Willard & Alice S Marriott Foundation
Grant: 2021A016418
Role: Co-Investigator (PI: Sasamoto)
Grants Specialist: Jenny Sadler Gallagher, MPH

Email: jenny.sadler@childrens.harvard.edu
Performance Period: 08/01/2022-07/31/2024 NCE
Level of funding:
Goals: The goal of this proposal is to improve early diagnosis and personalized treatment strategies for endometriosis through identifying novel oral microbiome profiles associated with adolescent and adult diagnosed endometriosis (Aim 1) and oral microbiome profiles predictive of persistent post-surgical pain among endometriosis patients (Aim 2) utilizing the deeply phenotyped cohort of The Women's Health Study: From Adolescence to Adulthood (A2A).
Aim 1. Identify oral microbiome profiles in adolescent and adult-diagnosed endometriosis.
Aim 2. Among endometriosis cases, identify oral microbiome profiles predictive of persistent post-surgical pelvic pain. Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	.24 CM
2. 2024	0 CM

Title: The role of neurotrophins in chronic pelvic pain and central sensitization among adolescents and women with endometriosis
Supporting Agency: Boston Children's Hospital / National Institutes of Health
Grant: R21HD107515
Role: Subaward Principal Investigator (PI: Shafrir)
Grants Specialist: Jaime Chan
Email: Jamie.chan@childrens.harvard.edu

Performance Period: 09/19/2022-08/31/2024
Level of funding
Goals/Aims: Aim 1: Determine the relationship between β-NGF and BDNF measured in peritoneal fluid and the occurrence of co-morbid pain conditions (e.g. migraines, fibromyalgia) that may be linked to central sensitization.
Aim 2: Investigate how β-NGF and BDNF levels measured in peritoneal fluid relate to pain remediation and quality of life within 2 years after laparoscopic surgery. We hypothesize that:
Aim 3: In exploratory analyses, evaluate interactions between neurotrophic (β-NGF and BDNF) and inflammatory markers in the peritoneal cavity to predict treatment response.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months

1. 2023	.48 CM
2. 2024	.48 CM

Title: Metabolomic profiling of adolescent endometriosis
Supporting Agency: National Institutes of Health
Grant Number: 1 R21 HD107266-01
Role: Co-Investigator (PI: Sasamoto)
Grant Specialist: Yvonne C. Talley

Email: talleyy@mail.nih.gov
Performance period: 08/01/2022-07/31/2024
Level of funding:
Goals: To improve early diagnosis and personalized treatment strategies for endometriosis through identifying novel (1) blood metabolomic profiles associated with adolescent endometriosis and (2) peritoneal fluid metabolomic markers predictive of persistent post-surgical pain.
Aim 1. Identify plasma metabolomics profiles that differ between 219 adolescent endometriosis cases and 210 controls.
Aim 2. Identify peritoneal fluid metabolites and pathways predictive of persistent pelvic pain following surgery despite hormonal therapy among 360 adolescent endometriosis cases.
No Overlap
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	.48 CM
2. 2024	.60 CM

Title: Endometriosis, pelvic pain, and covid-19 immunologic response
Supporting Agency: Michigan State University / Boston Children's Hospital, Marriott Foundation
Grant: Boston Children's Hospital / J Willard & Alice S Marriott Foundation
Role: Subaward Principal Investigator (PI: Missmer)
Grants Specialist: Jenny Sadler Gallagher, MPH

Email: Jenny.sadler@chilrens.harvard.edu
Performance Period: 08/01/2022-12/31/2023
Level of funding:
Goals: The overarching goal of this proposal is to elucidate biological mechanisms and risk defining biomarkers of SARS-CoV-2 infection comparing women with and without endometriosis or chronic pelvic pain and to explore the impact of social isolation and diminished access to healthcare on pain symptom severity and mental health progression using two longitudinal cohorts, which will further our understanding of the biological mechanisms of COVID-19 short- and long-term health in this large and oft ignored potentially high risk group.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	.0 CM*
2. 2024	.6 CM

Title: Erythrocyte fatty acids and risk of endometriosis
Supporting Agency: Fred Hutchinson Cancer Center / National Institutes of Health
Grant Number: R21HD107577
Role: Co-Investigator Sub Award (PI: Eliassen)
Grant Specialist: Virginia L. (Piaseczny) Hoekstra

Phone/Email: virginia.hoekstra@channing.harvard.edu
Performance period: 04/01/2023-03/31/2025
Level of funding:
Goal: This proposal is a novel first-step towards understanding the relationship between serum fatty acids and their association with uterine fibroids and endometriosis. Aim 1. Investigate whether levels of circulating fatty acids are associated with reproductive diseases. Aim 2. Among women with endometriosis and fibroids investigate whether circulating fatty acids are associated with cardio-metabolic disease. Aim 3. Using a Mendelian randomization approach assess whether genetic variants associated with poly unsaturated fatty acid levels are associated with risk of uterine fibroids and/or endometriosis.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	.36 CM
2. 2024	.36 CM

*recently activated at our institution, therefore the current effort is 0

PENDING

Title: Identification of ovarian cancer risk factors among women with endometriosis
Supporting Agency: Fred Hutchinson Cancer Research Center / Department of Defense
Grant Number: unknown
Role: Subaward Principal Investigator (PI: Harris)
Grants Specialist: unknown at this time
Phone: unknown at this time
Performance Period: 01/01/2024 - 12/31/2027
Level of funding:
Goals: Identifying women with endometriosis who are at elevated ovarian cancer risk
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	.6 CM
2. 2026	.6 CM
3. 2027	.6 CM
4. 2028	.6 CM
5. 2029	.6 CM

Title: Identifying plasma proteomic profiles of chronic pain development in endometriosis from adolescence to adulthood
Supporting Agency: National Institutes of Health
Grant Number: DP2-HD112176-01
Role: Co-Investigator (PI: Sasamoto)
Grant Specialist: Yvonne Talley

Email: talleyy@nih.gov
Performance period: 01/01/2023-12/31/2025
Goals: In this application, we propose a prospective study of adolescent endometriosis cases with up to 10-years of follow-up to elucidate predictors of chronic pain development from adolescence to adulthood. Status
Total Award Amount:
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.2 CM
2. 2024	1.2 CM
3. 2025	1.2 CM

Title: The role of biobehavioral factors and anti-inflammatory medications on the ovarian tumor immune response
Supporting Agency: H. Lee Moffitt Cancer Center / National Institutes of Health
Grant Number:
Role: Subaward Principal Investigator (PI: Tworoger)
Grants Specialist: Vaurice Starks

Email: starksv@mail.nih.gov
Performance Period: 07/01/2024 - 05/31/2029
Level of funding:
Goals: Goals: The primary objective of this proposal is to evaluate the hypothesis that distress enhances ovarian cancer progression by promoting recruitment and activity of immunosuppressive TAMs and MDSCs, while medications that intervene on the immunosuppressive biologic pathways triggered by distress, including aspirin and other non-steroidal anti-inflammatory drugs [NSAIDs], beta-blockers, and statins, abrogate these effects. Our innovative approach leverages unique population-based and experimental resources. First, we will use data from four long-term prospective cohorts, the Black Women's Health Study, Nurses' Health Study (NHS), NHSII, and Sister Study, and a population-based case-control study, the New England Case Control Study (NEC), that collected self-reported measures of distress (anxiety, depression, early life physical and sexual abuse) as well as ovarian tumor tissue (n=649; 400 high-grade serous carcinomas [HGSC], the most common histotype). Second, using an orthogonal and interactive approach, we will use syngeneic mouse models of HGSC to comprehensively examine the role of chronic stress in TAM/MDSC recruitment, activity, and tumor progression, as well as a potential abrogation by aspirin.

Year	Person Months
1. 2025	1.2 CM
2. 2026	1.2 CM
3. 2027	1.2 CM

Title: Dietary patterns, biological changes, and endometriosis-associated pelvic pain
Supporting Agency: Boston Children's Hospital / Department of Defense
Grant Number: unknown at this time
Role: Subaward Principal Investigator (PI: Shafrir)
Grants Specialist: unknown at this time
Phone: unknown at this time
Performance Period: 01/01/2024-12/31/2025
Level of funding: 99,650
Goals: The goal of this project is to investigate how dietary patterns (Alternative Healthy Eating Index and Empirical Dietary Inflammatory Pattern) influence pelvic pain and quality of life among adolescents and adults with and without endometriosis. Additionally, we will investigate how these dietary patterns may affect systemic inflammation and oxidative stress levels as well as local inflammation levels in the peritoneal cavity of endometriosis patients. Finally, we will assess how these dietary patterns are associated with trajectories of pelvic pain and quality of life over four years of follow-up.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Calendar Months
1. 2024	.36CM
2. 2025	.36CM

Title: A multi-omics approach to identifying novel early detection biomarkers for ovarian cancer in prospectively collected blood samples
Supporting Agency: American Cancer Society
Grant Number: Unknown
Role: Co-Investigator (PI: Sasamoto)
Grant Specialist: Unknown
Phone/Email: unknown at this time
Performance period: 07/01/2024-06/30/2027
Level of funding:
Goals: The overarching goal of this application is to identify circulating proteins and metabolites associated with ovarian cancer in blood collected up to five years before diagnosis, which will likely reflect biological changes related to preclinical to early stage disease.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2024	.6 CM
2. 2025	.6 CM
3. 2026	.6 CM
4. 2027	.6 CM

Title: Elucidating the biobehavioral pain mechanisms contributing to co-morbid endometriosis and migraines: A developmental perspective
Supporting Agency: Boston Children's Hospital / Department of Defense Expansion Award PRMRP
Grant Number: Unknown
Role: Subaward Principal Investigator (PI: Seiberg)
Grant Specialist: Unknown at this time
Phone/Email: Unknown at this time
Performance period: 10/01/2023-09/30/2027
Level of funding
Goals: Evaluate shared etiologic pathways between endometriosis and migraines using QST testing and proteomic biomarkers.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.20 CM
2. 2024	1.20 CM
3. 2025	1.20 CM
4. 2026	1.20 CM
5. 2027	1.20 CM

Title: Proteomics-based biological aging signature and long-term health outcomes of endometriosis
Supporting Agency: Department of Defense
Grant Number:
Role: Co-Investigator (PI: Sasamoto)
Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 06/01/2024 - 05/31/2028
Level of funding

Goals: Our long-term goal is to identify novel blood-based biomarkers that predict increased risk of long-term comorbidities among women with endometriosis and modifiable factors that will alter acceleration of biological aging.
Aims: Among endometriosis cases, determine the association between accelerated proteomic-based biological aging and long-term comorbidities in the NHSII cohort.
Aim 2. Identify endometriosis subphenotypes associated with accelerated proteomic-based biological aging in the A2A cohort.
Aim 3. Identify behavioral factors that alter proteomic-based biological aging in the NHSII and A2A cohorts.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	.6 CM
2. 2026	.6 CM
3. 2027	.6 CM
4. 2028	.6 CM

Title: Endometriosis and Lifelong Health
Supporting Agency: Michigan State University / Department of Defense
Grant Number: Unknown at this time
Role: Subaward Principal Investigator (PI: Missmer)
Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 09/01/2024 - 08/31/2028
Level of funding:
Goals: The main objectives of this study are: 1) To identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation. These novel sub-phenotype-specific variants will suggest distinct physiologic pathways that underlie the poorly understood endometriosis heterogeneity, potentially catalyzing discovery of precision medicine treatment and prevention targets. 2) To determine the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	1.2 CM
2. 2026	1.2 CM
3. 2027	1.2 CM
4. 2028	1.2 CM

Title: Macrophage phenotypes and endometriosis: Understanding their role in etiology and progression
Supporting Agency: National Institutes of Health
Grant Number: Unknown at this time
Role: Principal Investigator
Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 06/01/2024 - 05/31/2029
Level of funding:
Goals: In this application, we propose to evaluate endometriosis- specific gene expression profiles of circulating blood monocytes with upregulated phagocytosis pathways in endometriosis cases and controls from

the A2A and examine the peritoneal environment of adolescents and young women with endometriosis, using a state-of-the-art proteomics platform to measure 7000 proteins, including both inflammatory and immune markers, in peritoneal fluid.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	2.4 CM
2. 2026	2.4 CM
3. 2027	2.4 CM
4. 2028	2.4 CM
5. 2029	2.4 CM

Title: Hormone therapy use, local and systemic immune senescence, and ovarian cancer survival
Supporting Agency: Department of Defense
Grant Number: Unknown at this time
Role: Co Investigator (PI: Sasamoto)
Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 09/01/2024-08/31/2028
Level of funding:
Goals: The goal is to investigate (1) the association of MHT before and after ovarian cancer diagnosis, including type, timing, and duration, with ovarian cancer survival and (2) the effect of MHT on systemic and ovarian tumor immune profile
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	.36 CM
2. 2026	.36 CM
3. 2027	.36 CM
4. 2028	.36 CM

Title: Novel biomarkers and pathways of persistent endometriosis associated pain across the lifecourse
Supporting Agency: University of Michigan / National Institutes of Health
Grant Number: R01HD111242
Role: MPI (PI:As-Sanie; MPI:Terry)
Grant Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 12/01/2022-11/30/2027
Total Award Amount:
Goals: In this project, we propose to determine how changes in circulating proteins measured in blood are associated with endometriosis associated pain as well as baseline and serial proteomics profiles in peritoneal fluid to assess how local proteomic profiles relate to persistent (potentially nociplastic) endometriosis associated pain.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.2 CM
2. 2024	1.2 CM
3. 2025	1.2 CM
4. 2026	1.2 CM

IN-KIND: N/A

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award and accept the obligation to comply with Section 223(a) of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

Signature: Kathryn L Terry
Kathryn L Terry (Aug 24, 2023 08:31 EDT)

Date: Aug 24, 2023

Terry 2023_OS ProgRep ESP Final

Final Audit Report 2023-08-24

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Other Support **Progress Report YR2 8.24.23**

Naoko Sasamoto, MD PhD

Positions/Scientific Appointments

2022-Present	Assistant Professor, Obstetrics, Gynecology, and Reproductive Biology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA
2022-Present	Member, American Society of Reproductive Medicine
2020-Present	Member, World Endometriosis Society
2019-Present	Member, Metabolomics Association of North America
2021-Present	Active member, American Association for Cancer Research
2013-Present	Board-certified member, Japanese Society of Obstetrics and Gynecology (JSOG)
2013-Present	Board-certified member, Japanese Board of Cancer Therapy

COMPLETED

Title: Redefining normal: Personalized CA125 cutpoints for ovarian cancer screening
Supporting Agency: National Institutes of Health
Grant number: 5R01CA193965-03 (K. Terry)
Role: Co-Investigator (PI: Terry)
Grants Specialist: Franklin, Nicole

Email: nicole.franklin@nih.gov
Performance Period: 06/01/2016-05/31/2020
Level of funding:
Goals: We propose to develop personalized CA125 cutpoints using individual characteristics to improve the sensitivity and specificity of this important ovarian cancer marker and lead the way to population screening that could save lives.
Specific Aims:

1. Develop and validate a predictive model of CA125 in women without ovarian cancer.
2. Calculate personalized cutpoints and evaluate discriminatory ability compared to a single threshold in PLCO, NHS, and EPIC.
3. Evaluate whether the addition of personalized CA125 improves ovarian cancer risk prediction by adding adjusted CA125 to established ovarian risk models.

Overlap: none

Year		Person Months
1.	2017	.60 CM
2.	2018	.60 CM
3.	2019	.60 CM
4.	2020	.60 CM

Title: High-throughput proteomics profiling for identification of early detection biomarkers of high-grade serous ovarian cancer
Supporting Agency: Minnesota Ovarian Cancer Alliance
Grant Number: Memorandum of Understanding
Role: Principal Investigator
Grants Specialist: Kathleen Gavin

Email: KGavin@mnovarian.org
Time Commitment: 0.80 CM
Performance Period: 07/01/2019-01/31/2021
Level of funding:
The major goals of this project are to identify biomarkers that predict high grade serous ovarian cancer and elucidate etiologic pathways of development. Specifically, we plan to:
Aim 1. Identify proteins associated with early stage HGSOC in prospectively collected samples. We hypothesize that Pro-inflammatory and immunosuppression-related proteins in blood drawn one to three years prior to diagnosis of late stage HGSOC will be higher compared to healthy controls. In addition, untargeted proteomics profiling considering all 1,305 proteins will identify novel candidate biomarkers for early stage HGSOC using blood drawn one to three years prior to diagnosis of late stage HGSOC compared to healthy controls. Aim 2. Elucidate potential biological pathways relevant to early stage HGSOC. We hypothesize that: Inflammatory and immunosuppression pathways are enriched among the circulating proteins associated with early stage HGSOC using blood drawn one to three years prior to diagnosis of late stage HGSOC compared to healthy controls.
No Overlap

Year	Person Months
1. 2020	.80 CM
2. 2021	.80 CM
3. 2022	.80 CM
4. 2023	.80 CM

Title: Harnessing biomarker and phenotypic diversity among adolescents and women with endometriosis to advance personalized medicine for diagnosis and pain remediation
Supporting Agency: National Institutes of Health
Grant Number: R21HD096358
Role: Subaward Co-Investigator (PI: Missmer)
Grant Specialist: Candace Tingen, PhD

Email: tingencm@mail.nih.gov
Performance Period: 05/01/2019 – 04/30/2021
Level of Funding:
Goals: Within the Women's Health Study: from Adolescence to Adulthood (A2A; a prospective cohort of >1200 adolescents and young women, oversampled for those with surgically-confirmed endometriosis, followed for >4 years), we will combine WERF EPHect compliant data from participant surveys, electronic medical records, and stored blood samples collected annually. These data will capture informative changes in pain experience, inflammatory and oxidative stress milieu, and central sensitization to advance our understanding of phenotypic diversity among adolescents and women with endometriosis –the foundation for successful personalized, precision medicine to shorten diagnostic delay and maximize successful pain remediation.
No Overlap

Year	Person Months
1. 2022	.48 CM
2. 2021	.48 CM
2. 2022	.6 CM

Title: Identifying early detection metabolomics biomarkers for high-grade serous ovarian cancer
Supporting Agency: Sperling Family Foundation (Broad Institute/BWH)
Address: 415 Main Street

Cambridge, MA
Role: Principal Investigator
Contracting/Grants Officer: Ashlin Bolton

Performance Period: 03/01/2021-02/28/2023 (NCE)
Level of funding:
Project Goals: To discover novel early detection metabolomic biomarkers for ovarian cancer and elucidate the systemic metabolomic profiles in the early phase of ovarian cancer development.
Specific Aims: The primary objective of this innovative application aims to discover novel early detection metabolomic biomarkers for ovarian cancer and elucidate the systemic metabolomic profiles in the early phase of ovarian cancer development utilizing the biospecimens and clinical data at the Brigham and Women's Hospital and applying the world-class innovative technology of the highly reproducible, high-throughput, multiplex metabolomics technology at the Broad Institute.
Overlap: none

Year	Person Months
1. 2022	.36 CM
2. NCE	0 CM

CURRENT Changes to Other support noted in RED

Title: Using affinity based proteomics to identify diagnostic and plasma biomarkers for endometriosis
Supporting Agency: Department of Defense
Grant Number: W81XWH1910318 (Partnering PI's: Terry at Brigham and Women's Hospital and Libermann at Beth Israel Deaconess Medical Center)
Role: Co Investigator
Grants Specialist: Chris Baker

Email: christopher.l.baker132.civ@mail.mil
Performance Period: 09/01/2019-08/31/2024
Level of funding:
The major goals of this project are to identify proteomic markers associated with early detection and progression of endometriosis using data and specimens from the Nurses' Health Study II cohort and the Boston Center for Endometriosis Women's Health Study: Adolescence to Adulthood.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2020	3.6 CM
2. 2021	3.6 CM
3. 2022	0.12 CM
4.2023	.12 CM

Title: Using biomarkers to elucidate the breastfeeding and ovarian cancer risk association
Supporting Agency: National Institutes of Health
Grant: R03CA259659-01A1
Role: Principal Investigator
Grants Specialist: Tram K. Lam

Email: lamt@mail.nih.gov
Performance Period: 03/07/2022-02/29/2024

Level of funding:
Goals: To elucidate the breastfeeding ovarian cancer association using circulating biomarker, tumor marker expression, and detailed questionnaire data from more than 800,000 women.
Aim 1. Identify factors that mediate and modify the association between breastfeeding and ovarian cancer risk in 12 case-control and 10 prospective cohort studies.
Aim 2. Characterize the impact of breastfeeding on circulating inflammatory and metabolic markers in NHS/NHSII.
Aim 3. Examine the association between breastfeeding and tumor immunity in NHS/NHSII and NEC.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.176 CM
2. 2024	1.17 CM

Title: Relating molecular subgroups of endometriosis-associated ovarian cancers to survival and risk factors
Supporing Agency: Mayo Clinic / National Institutes of Health
Grant Number: R01-CA248288
Role: CoInvestigator Subcontract (Subcontract PI: Terry) (PI: Goode)
Grant Specialist: Ashley Salo

Email: ashley.salo@nih.gov
Performance Period: 01/01/2021-12/31/2025
Level of funding:
Project Goals: Aim 1. To characterize molecularly defined subgroups of ENOC and CCOC, we will statistically integrate sequencing and array data from gene expression, somatic mutations, and differentially methylated regions from 523 ENOC and 344 CCOC. Clustering approaches will use samples divided into training and test sets.
Aim 2. To identify subgroup-specific survival associations, we will relate molecular subgroups defined in Aim 1 to overall survival using Cox regression models.
Aim 3. To identify subgroup-specific risk factor associations, we will relate molecular subgroups defined in Aim 1 to lifestyle risk factors.
Aim 4. To identify opportunities for overlapping treatments in patient care, we will statistically compare the patterns of molecular features of the ENOC and CCOC subgroups with various TCGA cancer subgroups.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
2. 2022	2.27 CM
3. 2023	.726 CM
4. 2024	.96 CM
5. 2025	.96 CM

Title: Identifying Proteomic Profiles and Biological Networks of Early-Stage Ovarian Cancer
Grant: W81XWH2110320
Role: Principal Investigator
Supporting Agency: Department of Defense
Address: 1120 Fort Detrick – CDMRP
Frederick MD 21702
Contracting/Grants Officer: Abigail Strock
email: abilgail.l.strock.civ@mail.mil

Performance Period: 05/01/2021-04/30/2025
Level of funding:
Project Goals: To identify circulating proteins and biological networks associated with ovarian cancer in blood collected 1 to 7 years before diagnosis of overt invasive disease
Specific Aims: We propose to leverage existing samples and data from the Nurses' Health Studies (NHS/NHSII), a prospective cohort of women, and the Preoperative Pelvic Mass (PreOP) Study, a clinic-based study of women who donated blood samples before surgery for a suspicious pelvic mass, and apply next generation proteomics technology that has excellent reproducibility and reliability.
Aim 1. In prospectively collected plasma samples obtained up to 7 years before diagnosis of overt invasive disease, identify proteins associated with preclinical disease in the NHS/NHSII.
Aim 2. In pre-surgical plasma samples, identify proteins associated with early stage disease in the PreOP.
Aim 3. Identify biological networks related to early stage disease and disease progression.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	4.5 CM
2. 2023	2.706 CM
3 .2024	3 CM
4. 2025	3 CM

Title: Using genetic predictors of CA125 to improve personalized ovarian cancer screening
Supporting Agency: Marsha Rivkin Center for Ovarian Cancer Research
Address: 801 Broadway, Suite 701, Seattle WA 98122
Contracting/Grants Officer: Jackie Lang, PhD
Role: Principal Investigator
Performance Period: 04/01/2021-03/31/2023
Level of funding:
Project Goals: To identify genetic predictors of CA125 and examine whether adding genetic predictors of CA125 will improve the discriminatory performance of personalized CA125 cutpoints in blood collected months prior to diagnosis in prospective cohorts of PLCO, EPIC, and NHS/NHSII.
Specific Aims: Aim 1. Identify genetic predictors of CA125 using data on 4,391 women without ovarian cancer in PLCO, EPIC, NHS/NHSII, and NEC.

a. Identify novel genetic variants associated with blood CA125 levels by menopausal status.
b. Determine whether genetic variants associated with blood CA125 levels differ by race.
c. Secondarily, identify genetic predictors associated with change in CA125 over time.

Aim 2. Examine whether adding genetic predictors of CA125 to our model of personalized CA125 cutpoints will improve the discriminatory performance in blood collected months prior to diagnosis in prospective cohorts of PLCO, EPIC, and NHS/NHSII.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2022	0.40 CM
2. 2023	2.304 CM

Title: Changing contraceptive patterns and ovarian cancer risk
Supporting Agency: National Institutes of Health 1R01CA258679
Address: NIH/NHLBI Information center
P.O Box 30105

Bethesda, MD 20824-0105
Role: Co Investigator (PI: Terry)
Contracting/Grants Officer: Goli Smimi; email: goli.smimi@nih.gov

Performance Period: 04/01/2021-03/31/2026
Level of funding:
Project Goals: To examine the impact of changing contraceptive patterns of intrauterine device on ovarian cancer risk and to examine its impact on the local immune mechanisms.
Specific Aims: Aim 1. Estimate the association between IUD use and risk of ovarian cancer, including by histotype, in 17 case-control studies (20,314 cases, 26,099 controls) and 7 cohort studies (678,650 participants, 1,891 cases) with prospectively collected data. We hypothesize that:

a. IUD use is associated with a decreased risk of invasive ovarian cancer, particularly low grade serous and clear cell histotypes.
b. Secondarily, we will evaluate these associations by race and birth cohort.

Aim 2. Describe how timing and type of IUD use influence ovarian cancer risk in 13 case-control and 4 cohort studies. We hypothesize that:

a. IUD use before oral contraceptive use, particularly in nulliparous women, attenuate the inverse association or even increase ovarian cancer risk.
b. Progesterone-releasing IUDs decrease the risk of ovarian cancer more than other IUD types.

Aim 3. Evaluate whether the association between IUD use and ovarian cancer risk differs by the tumor immune microenvironment, utilizing 3,530 cases on tissue microarrays. We hypothesize that:

a. IUD use is associated with an increased risk of ovarian tumors with low stromal expression of CD163.
b. IUD use versus OC use alone will be differentially associated with ovarian cancer risk by the proportion of immune cell types in the tumor, including cytotoxic T cells, Tregs, or macrophages, identified by expression of CD3, CD8, CD4, CD69, FOXP3, and CD163.

Overlap: None

Year	Person Months
1. 2022	0.9 CM
2. 2023	2.706 CM
3. 2024	2.4 CM
4. 2025	2.4 CM
5. 2026	2.4 CM

Title: Aspira Endometriosis Project
Supporting Agency: Aspira Women's Health / Dana Farber Cancer Institute
Grant Number: SRA 2022A006361
Role: Subaward Co-Investigator (SubAward PI: Elias) (PI: Chowdhury)
Grants Specialist: Thomas Greco (CEO)
Email/Phone: legal@aspirawh.com and tgreco@aspirawh.com
Performance Period: 08/04/2022-08/03/2024
Level of funding:
The proposed application for this technology is to guide clinical management for women without a pelvic mass presenting with symptoms (e.g., chronic pelvic or abdominal pain, infertility, dysmenorrhea, dyspareunia, dysuria) suggestive of possible endometriosis. The intended uses are to 1) eliminate endometriosis from the differential diagnosis among women for whom this diagnosis is unlikely; 2) allow empiric medical treatment for endometriosis among women for whom endometriosis is almost certain; and 3) to limit surgical evaluation for possible endometriosis to those few cases where the non-invasive test is equivocal or in whom surgical excision of endometriosis is clinically indicated.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	.846 CM
2. 2024	1.2 CM

Title: Metabolomic profiling of endometriosis in adolescents and adults
Supporting Agency: National Institute of Health
Grant Number: R 21 HD107266-01A1
Role: Principal Investigator
Grant Specialist: Yvonne C. Talley

Email: talleyy@mail.nih.gov
Performance Period: 08/10/2022-07/31/2024
Level of Funding:
Goals: To improve early diagnosis and personalized treatment strategies for endometriosis through identifying novel (1) blood metabolomic profiles associated with adolescent endometriosis and (2) peritoneal fluid metabolomic markers predictive of persistent post-surgical pain.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.176 CM
2. 2024	1.56 CM

Title: Defining Endometriosis Physiologic Sub-Phenotypes and Subsequent Cancer and Comorbidities Risk Through Discovery of Novel Genetic Variants
Supporting Agency: Michigan State University / Department of Defense
Role: Subaward Co-Investigator (PI: Missmer)
Grant Number: W81XWH2110744
Grants Specialist: Abigail Strock

Email: abigail.l.strock.civ@mail.mil
Performance Period: 08/15/2021-08/14/2025
Level of funding:
Goals: The overall hypothesis of this study is to identify novel germline genetic variants associated with subphenotypes in endometriosis and examine how these genetic variants relate the subsequent risk of gynecologic and non-gynecologic comorbidities including cancer, as well how they interact with the inflammatory context. These goals will be achieved using data from an international consortium, and separately, three longitudinal studies. We hypothesize that subphenotypes in endometriosis are associated with unique genetic loci above and beyond those identified in prior studies of endometriosis as a homogenous entity. We further hypothesize that some loci may be shared between specific subphenotypes and comorbidities, suggesting either a common etiology, or progression via endometriosis which we hope to elucidate in our study. Finally, we hypothesize that the disease progression from the genetic risk factor to the long-term high risk-sub phenotypes and comorbidities may be modified by the inflammatory context. To advance the two areas targeted in in FY 2020 PRMRP, we will use cross-sectional data from the International Endometriosis Genome Consortium (IEGC), and three ongoing prospective cohort studies—Nurses' Health Study II (NHS II), Women Health Study (WHS), and Women's Health Study Adolescence to Adulthood (A2A). We will leverage genomic and phenotypic data collected in multiple well-established cohort populations as well as more recent case-control studies that launched with harmonized data and sample collection via the Endometriosis Phenome and Biobanking Harmonization Project (WERF-EPHect) tools.53 For longitudinal analysis we will include three ongoing cohorts with existing whole-genome, phenotypic and comorbidity data (1) Nurses' Health Study II, a cohort of 116,429 female nurses aged 25-42 years in 1989 among whom 2,230 endometriosis cases have been genotyped, (2) Women's Health Study, including 23,294 female health professionals ≥45 years at enrollment among whom 1494 have been

diagnosed with endometriosis, (3) Women's Health Study: from Adolescence to Adulthood (A2A), a cohort of 1,550 adolescents and young women with median age of 22 at enrollment. A2A is a deeply-phenotyped cohort with detailed assessment of symptoms including pain types, severity, other life-impacting symptoms, and other disease diagnoses.
Overlap: None

Year	Person Months
1. 2022	0 CM
2. 2023	0 CM*
3. 2024	1.20 CM
4. 2025	1.20 CM

Title: Oral microbiome profiling of adolescent endometriosis
Supporting Agency: Boston Children's Hospital / J Willard & Alice S Marriott Foundation
Grant: 2021A016418
Role: Principal Investigator
Grants Specialist: Jenny Sadler Gallagher, MPH

Email: jenny.sadler@childrens.harvard.edu
Performance Period: 08/01/2022-07/31/2024 NCE
Level of funding:
Goals: The goal of this proposal is to improve early diagnosis and personalized treatment strategies for endometriosis through identifying novel oral microbiome profiles associated with adolescent and adult diagnosed endometriosis (Aim 1) and oral microbiome profiles predictive of persistent post-surgical pain among endometriosis patients (Aim 2) utilizing the deeply phenotyped cohort of The Women's Health Study: From Adolescence to Adulthood (A2A).
Overlap: None

Year	Person Months
1. 2023	.12 CM

Title: Systemic immune dysfunction assessed by methylation and endometriosis
Supporting Agency: Boston Children's Hospital, Marriott Foundation Grant: Boston Children's Hospital / J Willard & Alice S Marriott Foundation
Role: Co-Investigator (PI: Terry)
Grants Specialist: Jenny Sadler Gallagher, MPH
Email: jenny.sadler@childrens.harvard.edu
Performance Period: 08/01/2022-07/30/2024 NCE
Level of funding:
Goals: Aim 1. Assess reproducibility of circulating immune cell distributions duplicate samples from 10 endometriosis cases and 10 controls. Aim 2. Evaluate differences in circulating immune cell distributions in 40 A2A participants with endometriosis compared to 40 matched controls.
Overlap: None

Year	Person Months
1. 2023	.12 CM

*0 effort reporting as award was just set up

PENDING

Title: Novel biomarkers and pathways of persistent endometriosis associated pain across the lifecourse
Supporting Agency: University of Michigan / National Institutes of Health
Grant Number: R01HD111242

Role: Co-Investigator MPI (PI:As-Sanie; MPI:Terry)
Grant Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 12/01/2022-11/30/2027
Total Award Amount:
Goals: In this project, we propose to determine how changes in circulating proteins measured in blood are associated with endometriosis associated pain as well as baseline and serial proteomics profiles in peritoneal fluid to assess how local proteomic profiles relate to persistent (potentially nociplastic) endometriosis associated pain.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	1.2 CM
2. 2024	1.2 CM
3. 2025	1.2 CM
4. 2026	1.2 CM
5. 2027	1.2 CM

Title: A multi-omics approach to identifying novel early detection biomarkers for ovarian cancer in prospectively collected blood samples
Supporting Agency: American Cancer Society
Grant Number: Unknown
Role: Principal Investigator
Grant Specialist: Unknown
Phone/Email: Unknown
Performance period: 01/01/2024-12/31/2028
Level of funding:
Goals: The overarching goal of this application is to identify circulating proteins and metabolites associated with ovarian cancer in blood collected up to five years before diagnosis, which will likely reflect biological changes related to preclinical to early stage disease.

Year	Person Months
1. 2024	2.16 CM
2. 2025	2.16 CM
3. 2026	2.16 CM
4. 2027	2.16 CM

Title: Identification of ovarian cancer risk factors among women with endometriosis
Supporting Agency: Fred Hutchinson Cancer Research Center / Department of Defense
Grant Number: unknown
Role: Subaward Co-Investigator (PI: Harris)
Grants Specialist: unknown at this time
Phone: unknown at this time
Performance Period: 01/01/2024 - 12/31/2027
Level of funding:
Goals: Identifying women with endometriosis who are at elevated ovarian cancer risk
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2024	.6 CM
2. 2025	.6 CM
3. 2026	.6 CM

4. 2027	.6 CM

Title: Proteomics-based biological aging signature and long-term health outcomes of endometriosis
Supporting Agency: Department of Defense
Grant Number: Unknown at this time
Role: Principal Investigator
Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 06/01/2024 - 05/31/2028
Level of funding:
Goals: Our long-term goal is to identify novel blood-based biomarkers that predict increased risk of long-term comorbidities among women with endometriosis and modifiable factors that will alter acceleration of biological aging.
Aims: Among endometriosis cases, determine the association between accelerated proteomic-based biological aging and long-term comorbidities in the NHSII cohort.
Aim 2. Identify endometriosis subphenotypes associated with accelerated proteomic-based biological aging in the A2A cohort.
Aim 3. Identify behavioral factors that alter proteomic-based biological aging in the NHSII and A2A cohorts.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	1.8 CM
2. 2026	1.8 CM
3. 2027	1.8 CM
4. 2028	1.8 CM

Title: Hormone therapy use, local and systemic immune senescence, and ovarian cancer survival
Supporting Agency: Department of Defense
Grant Number: Unknown at this time
Role: Co Investigator (PI: Sasamoto)
Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 09/01/2024-08/31/2028
Level of funding:
Goals: The goal is to investigate (1) the association of MHT before and after ovarian cancer diagnosis, including type, timing, and duration, with ovarian cancer survival and (2) the effect of MHT on systemic and ovarian tumor immune profile
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	1.8 CM
2. 2026	1.8 CM
3. 2027	1.8 CM
4. 2028	1.8 CM

Title: Endometriosis and Lifelong Health
Supporting Agency: Michigan State University / Department of Defense
Grant Number: Unknown at this time
Role: Subaward Co-Investigator (PI: Missmer)

Grants Specialist: Unknown at this time
Phone: Unknown at this time
Email: Unknown at this time
Performance Period: 09/01/2024 - 08/31/2028
Level of funding:
Goals: The main objectives of this study are: 1) To identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation. These novel sub-phenotype-specific variants will suggest distinct physiologic pathways that underlie the poorly understood endometriosis heterogeneity, potentially catalyzing discovery of precision medicine treatment and prevention targets. 2) To determine the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	1.2 CM
2. 2026	1.2 CM
3. 2027	1.2 CM
4. 2028	1.2 CM

Title: Macrophage phenotypes and endometriosis: Understanding their role in etiology and progression
Supporting Agency: National Institutes of Health
Grant Number: unknown at this time
Role: Co-Investigator (PI: Terry)
Grants Specialist: unknown at this time
Phone: unknown at this time
Email: unknown at this time
Performance Period: 06/01/2024 - 05/31/2029
Level of funding
Goals: In this application, we propose to evaluate endometriosis- specific gene expression profiles of circulating blood monocytes with upregulated phagocytosis pathways in endometriosis cases and controls from the A2A and examine the peritoneal environment of adolescents and young women with endometriosis, using a state-of-the-art proteomics platform to measure 7000 proteins, including both inflammatory and immune markers, in peritoneal fluid.
Aim 1. Evaluate an endometriosis-specific gene expression signature in peripheral blood monocytes from newly collected blood samples from 100 endometriosis cases and 100 controls currently enrolled in the A2A study.
Aim 2. Evaluate the macrophage-related cytokine profiles in peritoneal fluid of 352 adolescents and young women with laparoscopically-confirmed endometriosis in the A2A in relation to endometriosis associated symptom progression over time.
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2025	1.8 CM
2. 2026	1.8 CM
3. 2027	1.8 CM
4. 2028	1.8 CM
5. 2029	1.8 CM

Title: Identifying plasma proteomic profiles of chronic pain development in endometriosis from adolescence to adulthood
Supporting Agency: National Institutes of Health

Grant Number: DP2-HD112176-01
Role: Principal Investigator
Grant Specialist: Yvonne Talley

Email: talleyy@nih.gov
Performance period: 01/01/2023-12/31/2025
Goals: In this application, we propose a prospective study of adolescent endometriosis cases with up to 10-years of follow-up to elucidate predictors of chronic pain development from adolescence to adulthood. Status
Total Award Amount:
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period

Year	Person Months
1. 2023	3 CM
2. 2024	3 CM
3. 2025	3 CM

Overlap Statement: None.

Signature Naoko Sasamoto
Naoko Sasamoto (Aug 24, 2023 11:59 EDT)

Date Aug 24, 2023

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Signer nsasamoto@bwh.harvard.edu entered name at signing as Naoko Sasamoto
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Document e-signed by Naoko Sasamoto (nsasamoto@bwh.harvard.edu)
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Agreement completed.
2023-08-24 - 3:59:06 PM GMT

Note: Changes from previous support are in red.
SUPPORT
SHAFIR, AMY L.

CURRENT

Title: Defining Endometriosis Physiologic Subphenotypes and Subsequent Cancer and Comorbidities Risk Through Discovery of Novel Genetic Variants
Time commitments: 1.2 CM
Supporting Agency: U.S. Department of Defense
Address: 1077 Patchel Street, Fort Detrick, MD 21702
Contacting/Grants Officer: Brittany N. Hebb
Email: Brittany.n.hebb.civ@mail.mil

Performance Period: 08/15/2021-08/14/2025
Level of Funding:
Project Goals/Specific Aims: This study will: 1) identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation; 2) determine the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis. We will capitalize upon our ongoing International Endometriosis Genome Consortium (IEGC) investigations and 3) in exploratory analyses, delve more deeply into the Women's Health Study: from Adolescence to Adulthood (A2A), which has measured an array of blood chemokine and cytokine markers.
Overlap: None

Title: The role of neurotrophins in relation to chronic pelvic pain and central sensitization among adolescents and women with endometriosis
Time Commitment: 4.9 CM
Supporting Agency: NIH/NICHD 1R21HD107515-01A1
Address: National Institutes of Health, 6710B Rockledge Drive, Bethesda, MD 20892-7004
Contracting/Grants Officer: Helena Ahn
Performance Period: 10/01/2022-09/30/2024
Level of Funding:
Project Goal: The goal of this project is to explore the relationship between neurotrophins and endometriosis, specifically in relation to chronic pelvic pain and central sensitization among adolescents and women and to assess interactions with the inflammatory environment to further our understanding of how nerve growth factors may influence pain symptoms among adolescents and adult women with endometriosis. Additionally, this grant will explore the role of nerve growth factor levels in relation to the occurrence of co-morbid pain conditions (e.g. migraines, fibromyalgia) that may be linked to central sensitization among adolescents and adult women with endometriosis.
Specific Aims: Aim 1: Determine the relationship between β-NGF and BDNF measured in peritoneal fluid and the occurrence of co-morbid pain conditions (e.g. migraines, fibromyalgia)

that may be linked to central sensitization. In exploratory analyses, higher β-NGF and BDNF levels will be associated with central sensization measures among a subset of participants (n=54) with post-surgery underlying pain sensitivity measurements. Aim 2: Investigate how β-NGF and BDNF levels measured in peritoneal fluid relate to pain remediation and quality of life within 2 years after laparoscopic surgery. Aim 3: In exploratory analyses, evaluate interactions between neurotrophic (β-NGF and BDNF) and inflammatory markers in the peritoneal cavity to predict treatment response.
Overlap: NoneLevel of Funding:

PENDING

Title: Dietary patterns, biological changes, and endometriosis-associated pelvic pain
Time Commitment: 1.8 CM
Supporting Agency: DoD RFA HT9425-23-PRMRP-DA
Address:
Contracting/Grants Officer: Not Assigned
Performance Period: 01/01/2024-12/31/2025
Level of Funding:
Project Goal: The goal of this project is to investigate how dietary patterns (Alternative Healthy Eating Index and Empirical Dietary Inflammatory Pattern) influence pelvic pain and quality of life among adolescents and adults with and without endometriosis. Additionally, we will investigate how these dietary patterns may affect systemic inflammation and oxidative stress levels as well as local inflammation levels in the peritoneal cavity of endometriosis patients. Finally, we will assess how these dietary patterns are associated with trajectories of pelvic pain and quality of life over four years of follow-up.
Specific Aims: Aim 1: Investigate how dietary patterns (AHEI and EDIP) influence pelvic pain symptoms, life interference due to pelvic pain and QoL among adolescents and adults with and without endometriosis within the A2A cohort. Aim 2: Evaluate AHEI and EDIP scores in relation to systemic oxidative stress and inflammation biomarker levels among participants with and without endometriosis as well as local inflammation levels in peritoneal fluid among endometriosis participants. Aim 3: Among endometriosis participants, determine how AHEI and EDIP scores are associated with pelvic pain and QoL trajectories over 4 years of follow-up
Overlap: None

Title: Endometriosis and Lifelong Health
Time Commitment: 1.2 CM
Supporting Agency: Department of Defense USAMRAA
Address:
Contracting/Grants Officer: Not Assigned
Performance Period: 09/01/2024-08/31/2028
Level of Funding:

Project Goal/Specific Aims: We will utilize two existing longitudinal cohort studies: the Nurses' Health Study II (NHSII) and the Women's Health Study: from Adolescence to Adulthood (A2A). Among 7,376 NHSII endometriosis participants, we will: Aim 1) Identify dynamic, modifiable, and static predictors of future chronic conditions known to have a higher incidence among those with endometriosis; Aim 2) Investigate dynamic, modifiable, and static mediators and modifiers of mental health disorders and QoL; Aim 3) Identify inflammatory, hormonal, and adipokine markers that are mediators and modifiers of chronic conditions including changes in these markers over a 10-year period. Exploratory analyses: For Aims 1 and 2, we will assess how behaviors and characteristics identified in the NHSII are similarly associated with indicators of endometriosis-associated conditions and QoL among 793 surgically-confirmed A2A endometriosis participants (72%, <26 years at enrollment). For Aim 3, we will investigate biological pathways that are informative of underlying risk of endometriosis-associated conditions among a younger population including change over 3 years of follow-up among 188 A2A endometriosis participants.
Overlap: None

PREVIOUS

Title: Epidemiologic Discovery Research Fund
Supporting Agency: Marriott Daughters' Foundation
Time commitments: 12.0 CM
Address:
10400 Fernwood Road, Department 901
Bethesda, MD 20817
Contracting/Grants Officer: Nancie Suzuki
Email: info@marriottdaughtersfoundation.org

Period: 10/1/2015-7/31/2018
Level of Funding:
Project Goals: The goal and aims of this project were to determine the factors that contribute to prognosis and improvement in adolescent endometriosis, including potential differences in symptom presentation and risk factors for women diagnosed with endometriosis during adolescence versus adulthood.
Overlap: None

Title: The Boston Center for Endometriosis: A First-in the World Care and Research Program for Women of all Ages
Time commitments: 1.8 CM
Supporting Agency: J. Willard and Alice S. Marriott Foundation
Address:

J. Willard and Alice S. Marriott Foundation
10400 Fernwood Road, Department 925
Bethesda, MD 20817
Contacting/Grants Officer: Sonnie Thuo
Email: marriott.family.foundation@marriott.com

Performance Period: 07/01/2012-12/31/2020
Level of Funding:
Project Goals: Design and conduct for study enrollment and data and biologic sample collection within Brigham and Women's Hospital and Boston Children's Hospital
Specific Aims: Establish a longitudinal cohort of girls and women with endometriosis and appropriate comparison girls/women with detailed life course data and extensive biologic samples storage.
Overlap: None

Title: Harnessing biomarker and phenotypic diversity among adolescents and women with endometriosis to advance personalized medicine for diagnosis and pain remediation
Time Commitments: 5.4 CM
Supporting Agency: NICHD R21HD096358
Address:
National Institutes of Health
6710B Rockledge Drive
Bethesda, MD 20892-7004
Contacting/Grants Officer: Vicky Haines
Performance Period: 04/01/2019-03/31/2022
Level of Funding:
Project Goal/Specific Aims: The goal and aims of this project are to (1) investigate a non-invasive diagnostic for endometriosis combining patient symptoms and characteristics with inflammatory, oxidative stress and central sensitization biomarkers; (2) assess changes in inflammatory, oxidative stress and central sensitization biomarkers before and after surgery; and (3) determine the optimal set of patient symptoms and characteristics in addition to inflammatory, oxidative stress and central sensitization biomarkers to advance personalized treatment selection.
Overlap: None

Title: What is Endometriosis? Deep Phenotyping to Advance Diagnosis and Treatment
Time Commitments: 2.3 CM
Supporting Agency: NIH R01HD094842 Contacting/Grants Officer: Margaret Young Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004

Email: margaret.young@nih.gov
Performance Period: 08/01/2018-08/22/2023
Level of Funding:
Project Goals: We will utilize three existing diverse studies of adolescents and women for whom surgical, clinical and participant data as well as blood and tissue samples have been harmonized via the WERF EPHect tools. The goal of our study will be to identify unique classifications of endometriosis patients that inform noninvasive diagnostics, response to current treatments, and novel treatment pathways - stratifying discoveries by participant symptom presentation, and for the cases, by surgical and imaging visualized disease characteristics to capture the full heterogeneity of endometriosis.
Specific Aims: Aim 1: Identify plasma markers of endometriosis across independent and synergistic pathways; Aim 2: Quantify informative heterogeneity in associated transcriptomic and milieu-related plasma markers by disease phenotype; Aim 3: Further identify informative disease phenotypes by symptom presentation; Aim 4: Evaluate heterogeneity in plasma markers, disease phenotype, and symptom presentation by participant characteristics.
Overlap: None

Title: Differences in Facilitators and Barriers of an Endometriosis Diagnosis Among Latina and non-Latina Adolescent and Adult Women: A Qualitative Assessment
Time Commitments: 3.8 CM
Supporting Agency: J. Willard and Alice S. Marriott Foundation
Address:
J. Willard and Alice S. Marriott Foundation
10400 Fernwood Road, Department 925
Bethesda, MD 20817
Contacting/Grants Officer: Sonnie Thuo
Email: marriott.family.foundation@marriott.com

Performance Period: 06/01/2022-08/22/2023
Level of Funding:
Project Goals: The main goals of this project are to identify facilitators and barriers to reaching an
endometriosis diagnosis from personal, social, and healthcare-related perspectives among Latina, non-Latina Black and Multiracial, and non-Latina White adolescent and adult women with surgically-diagnosed endometriosis.
Specific Aims: Aim 1: Investigate personal, cultural and societal differences in facilitators and barriers to reaching an endometriosis diagnosis among Latina, non-Latina Black and Multiracial, and non-Latina White adolescent and adult women. Aim 2: Elucidate facilitators and barriers in healthcare interactions among Latina,

non-Latina Black and Multiracial, and non-Latina White adolescent and adult women in reaching a diagnosis of endometriosis. Overlap: None

Title: Women's Health Study: from Adolescence to Adulthood
Time commitments: 0.96 CM
Supporting Agency: J. Willard and Alice S. Marriott Foundation
Address:
J. Willard and Alice S. Marriott Foundation
10400 Fernwood Road, Department 925
Bethesda, MD 20817
Contacting/Grants Officer: Sonnie Thuo
Email: marriott.family.foundation@marriott.com

Performance Period: 07/01/2017-08/22/2023
Level of Funding:
Project Goals: Design and conduct for study enrollment and data and biologic sample collection within Brigham and Women's Hospital and Boston Children's Hospital
Specific Aims: Continued support for the longitudinal cohort of girls and women with endometriosis and appropriate comparison girls/women with detailed life course data and extensive biologic samples storage.
Overlap: None

BUDGET OVERLAP
None

Signature: 

Date: 08/23/2023

PREVIOUS, CURRENT AND PENDING RESEARCH SUPPORT

KULKARNI, MADHAVI T.

CURRENT

Title: The Boston Center for Endometriosis
Time Commitments:

Years (2020-2024)	Person Months
1. 2020	9 Calendar
2. 2021	9 Calendar
3. 2022	4.2 Calendar
4. 2023	4.2 Calendar
5. 2024	4.2 Calendar

Supporting Agency: J.Willard and Alice S. Marriott
Address:
J Willard and Alice S. Marriott Foundation
10400 Fernwood Road, Department 925
Bethesda, MD 20817
Contracting/Grants Officer: Margaret Buckley
Performance Period: 07/01/2012-12/31/2024
Level of funding:
Project Goals: Design and conduct for study enrollment and data and biologic sample collection within Brigham and Women's Hospital and Boston Children's Hospital.
Specific Aims: Establish a longitudinal cohort of girls and women with endometriosis and appropriate comparison girls/women with detailed life course data and extensive biologic samples storage.
Overlap: None

Title: Defining Endometriosis Physiologic Sub-Phenotypes and Subsequent Cancer and Comorbidities Risk Through Discovery of Novel Genetic Variants
Time Commitments:

Years (2021-2025)	Person Months
1. 2021	6 Calendar
2. 2022	6 Calendar
3. 2023	6 Calendar
4. 2024	6 Calendar
5. 2025	6 Calendar

Supporting Agency: Department of Defense USMRAA (W81XWH2110744**)**
Address:
820 Chandler Street
Fort Detrick, MD 21702-5014
Contracting/Grants Officer: Brittany Hebb
Performance Period: 08/15/2021-08/14/2025
Level of Funding:
Project Goal / Specific Aims: This study will: 1) identify novel genetic variants associated with specific endometriosis sub-phenotypes defined by symptom and macro-surgically visualized presentation; 2) determine

the common and unique genetic variants that are associated with the higher risk of subsequent development of cancers, autoimmune and cardiovascular diseases among women with endometriosis. We will capitalize upon our ongoing International Endometriosis Genome Consortium (IEGC) investigations and 3) in exploratory analyses, delve more deeply into the Women's Health Study: from Adolescence to Adulthood (A2A), which has measured an array of blood chemokine and cytokine markers.
Overlap: None

Title: COVID-19 vaccination and menstrual health Time Commitments:

Year	Person Months
1. 2022	0.18 Academic 0.06 Summer
2. 2023	0.18 Academic 0.06 Summer

Supporting Agency: NIH (R01 HD096033-03S1) Address:
National Institutes of Health
6710B Rockledge Drive, Room 3219C, MSC 7004
Bethesda, MD 20892-7004
Contracting/Grants Officer: Vicky Haines
Performance Period: 08/27/2022-04/30/2023 (No Cost Extension started 5/1/2022)
Level of Funding
Project Goal / Specific Aims: The impact of SARS-CoV-2 infection or vaccination on menstrual health is unknown, despite anecdotal reports of post-vaccination change in menstruation. We will utilize two ongoing prospective cohorts (NHS3 and GUTS) with combined 17,000 female participants who have already answered a year-long series of COVID-19 focused questionnaires and have in-hand pre- and peri-pandemic gynecologic characteristics data. Accounting for change in menstruation impacting medications, medical conditions, or pandemic-related psychosocial upheaval, we will determine if infection or vaccination affect menstrual characteristics compared to pre-pandemic characteristics or to those neither infected nor vaccinated. **Overlap:** None

PENDING
Title: A Longitudinal study of the epidemiology of endometriosis after menopause
Role: PI
Time Commitments:

Year	Person Months
1. 2024	8.4 Calendar
2. 2025	8.4 Calendar

Supporting Agency: Department of Defense USMRAA
Address:
820 Chandler Street
Fort Detrick, MD 21702-5014
Contracting/Grants Officer: TBD
Performance Period: 01/01/2024-12/31/2025
Level of Funding:

Project Goal / Specific Aims: The **overall goal** of the proposed study is to identify predictive time-varying exposure-window-specific risk factors for PME, including inflammatory markers, to better understand the pathways of endometriosis among postmenopausal women. In addition, we propose to investigate the variation of risk factors by endometriosis diagnosis timing (pre vs postmenopausal), hypothesizing that the pathogenesis may differ between premenopausal and postmenopausal endometriosis. Ultimately this would establish risk groups who could be identified for pre- and perimenopausal surveillance and preventive care.

Overlap: None

PREVIOUS

None.

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

Signature: Madhavi Thombre Kulkarni