

AWARD NUMBER: W81XWH-20-1-0102

TITLE: Finding Metabolomic Signatures in Pregnancy that Predict Breast Cancer: 60-Year Prospective Study in the Child Health and Development Studies Pregnancy Cohort

PRINCIPAL INVESTIGATOR: Dr. Barbara Cohn, PhD

CONTRACTING ORGANIZATION: Public Health Institute, Oakland, CA

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14. ABSTRACT We propose to study 2nd and 3rd trimester archival serum samples of women in the Child Health and Development Studies (CHDS) pregnancy cohort who subsequently developed breast cancer, compared to 2nd and 3rd trimester archival serum samples from women who did not develop breast cancer, to identify predictive gestational biomarkers which could lead to new approaches to prevent breast cancer. For this, we will apply powerful high-resolution metabolomics (HRM) with advanced computational tools to identify chemicals and biochemical metabolic networks in pregnancy which are linked to subsequent breast cancer occurrence. There were minor delays caused by staff and offices transitioning to remote work due to the COVID-19 pandemic. We still accomplished all major tasks specified in the first year (obtaining all human subjects' approvals, sample selection, preparation and order of archived pregnancy serum for delivery to Site 2).					
15. SUBJECT TERMS Breast cancer, environmental chemicals, high-resolution metabolomics, metabolic pathways, metabolome-wide association study					
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1. INTRODUCTION:

We propose to study 2nd and 3rd trimester archival serum samples of women in the Child Health and Development Studies (CHDS) pregnancy cohort who subsequently developed breast cancer, compared to 2nd and 3rd trimester archival serum samples from women who did not develop breast cancer, to identify predictive gestational biomarkers which could lead to new approaches to prevent breast cancer. For this, we will apply powerful high-resolution metabolomics (HRM) with advanced computational tools to identify chemicals and biochemical metabolic networks in pregnancy which are linked to subsequent breast cancer occurrence. The sample population come from CHDS women with already measured levels of 3rd trimester steroid hormones, available placental morphology and clinical pregnancy measures.

2. **KEYWORDS:** Breast cancer, environmental chemicals, high-resolution metabolomics, metabolic pathways, metabolome-wide association study.

3. ACCOMPLISHMENTS:

○ What were the major goals of the project?

- This project is to use high-resolution metabolomics (HRM) to address the overarching challenges, to identify determinants of breast cancer initiation risk or susceptibility in order to prevent breast cancer. The objective is to establish proof of concept that Metabolome-Wide Association Studies (MWAS) patterns in pregnant women during the 2nd and 3rd trimesters predict subsequent breast cancer case status for individual women.
 - Aim 1 is to conduct MWAS to describe pathways in the 2nd and 3rd trimester that distinguish women who go on to develop breast cancer.
 - Aim 2 is to compare MWAS pathways by time to diagnosis after pregnancy, tumor characteristics (stage at diagnosis, receptor status), age at pregnancy, placenta morphology, and third trimester pregnancy estrogens (estradiol, estrone, estriol).
- Major Task 1: Institutional and DoD HRPO approval.
- Major Task 2, Site 1: Prepare archived pregnancy serum for delivery to Site 2 (Emory University)

○ What was accomplished under these goals?

- All sites have IRB and HRPO approval.
- The CHDS has chosen the target population and corresponding serum samples. Random batch order with cases and controls randomized within batches were created. Pregnancy sample QCs stored under identical conditions as samples will be inserted in duplicate into randomly selected batches to represent 5% of the total sample. A specimen and shipping request were submitted to the for National Institute of Child Health and Human Development (NICHD) repository. The repository is in the process of pulling and aliquoting the samples. We anticipate the shipment will be delivered to Emory University by early April 2021.

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

- Nothing to Report

○ 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?

- The Emory team expects to receive 1,179 serum samples from the NICHD repository by April 2021 and plans to analyze 1000 of these pregnancy serum samples within the next funding period. CHDS and Emory teams will work together in planning to ensure completion of the mass spectral analyses in time to complete the biostatistics and bioinformatics analyses. Emory will

share analysis data with the CHDS team. Both teams will work together to begin to test for associations of metabolites and environmental chemicals with breast cancer outcome.

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:**

Nothing to Report

6. **PRODUCTS:**

Nothing to Report

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

- **What individuals have worked on the project?**
 - Barbara Cohn, PhD
Project Role: MPI
Nearest Person month: 1
Contribution to the Project: As MPI she directed the overall study design and research methods.
 - Piera Cirillo
Project Role: Research Scientist
Nearest Person month: 1
Contribution to the Project: Study design and data guardian.
 - Nickilou Krigbaum
Project Role: Research Associate
Nearest Person month: 1
Contribution to the Project: PHI IRB completion, serum selection and serum ordering.
- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to Report
- **What other organizations were involved as partners?**

Nothing to Report

8. **SPECIAL REPORTING REQUIREMENTS**

See The award chart in Appendix

9. **APPENDICES:**

W81XWH2010102: Finding Metabolomic Signatures in Pregnancy that Predict Breast Cancer: 60-Year Prospective Study in the Child Health and Development Studies Pregnancy Cohort



PI: Barbara Cohn, Public Health Institute, California **Budget** \$521,718.00

Topic Area: DoD Breast Cancer Research Program **Mechanism:** FY19, BCRP, Breakthrough Award Levels 1 and 2 (Funding Level 1, Partnering PI Option)

Research Area(s): Breast Cancer

Award Status: March 1, 2020 – February 28, 2023

Study Goals:

We propose to study 2nd and 3rd trimester archival serum samples of women in the Child Health and Development Studies (CHDS) pregnancy cohort who subsequently developed breast cancer, compared to 2nd and 3rd trimester archival serum samples from women who did not develop breast cancer, to identify predictive gestational biomarkers which could lead to new approaches to prevent breast cancer. For this, we will apply powerful high-resolution metabolomics (HRM) with advanced computational tools to identify chemicals and biochemical metabolic networks in pregnancy which are linked to subsequent breast cancer occurrence.

Specific Aims:

Aim 1: Conduct MWAS to describe pathways in the 2nd and 3rd trimester that distinguish women who go on to develop breast cancer.

Aim 2: Compare MWAS pathways by time to diagnosis after pregnancy, tumor characteristics (stage at diagnosis, receptor status), age at pregnancy, placenta morphology, and third trimester pregnancy estrogens (estradiol, estrone, estriol).

Key Accomplishments and Outcomes:

Publications: none to date

Patents: none to date

Funding Obtained: none to date