

**AWARD NUMBER: W81XWH-20-1-0280  
LC190500**

**TITLE: Cell-Free DNA for Diagnosis of Malignancy, Genetic Mutations and  
Prognosis in Lung Cancer Related Pleural Effusions**

**PRINCIPAL INVESTIGATOR: Kamran Mahmood, MD, MPH**

**CONTRACTING ORGANIZATION: Duke University**

**REPORT DATE: JULY 2021**

**TYPE OF REPORT: ANNUAL**

**PREPARED FOR: U.S. Army Medical Research and Development Command  
Fort Detrick, Maryland 21702-5012**

**DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited**

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

**REPORT DOCUMENTATION PAGE***Form Approved*  
*OMB No. 0704-0188*

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

**1. REPORT DATE**

JULY 2021

**2. REPORT TYPE**

Annual

**3. DATES COVERED**

1JUL2020 - 30JUN2021

**4. TITLE AND SUBTITLE**

Cell-free DNA for Diagnosis of Malignancy, Genetic Mutations and Prognosis in Lung Cancer Related Malignant Pleural Effusions

**5a. CONTRACT NUMBER****5b. GRANT NUMBER**

LC190500 (W81XWH-20-1-0280)

**5c. PROGRAM ELEMENT NUMBER****6. AUTHOR(S)**

Kamran Mahmood, MD, MPH

**5d. PROJECT NUMBER****5e. TASK NUMBER****5f. WORK UNIT NUMBER****E-Mail:**

k.mahmood@duke.edu

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**Duke University  
2200 W Main St, Ste 710  
Durham NC 27703-4677**8. PERFORMING ORGANIZATION REPORT NUMBER****9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**U.S. Army Medical Research and Development Command  
Fort Detrick, Maryland 21702-5012**10. SPONSOR/MONITOR'S ACRONYM(S)****11. SPONSOR/MONITOR'S REPORT NUMBER(S)****12. DISTRIBUTION / AVAILABILITY STATEMENT**

Approved for Public Release; Distribution Unlimited

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**

The objectives of this project is to assess if cell-free DNA in pleural effusions of patients with lung cancer can help establish diagnosis, assess targetable genetic mutations, and response to therapy. For aim 1, we recruited 20 patients with benign pleural effusions and 30 patients with lung cancer pleural effusions. Based on cfDNA, we determined integrity index as the ratio of concentration of long (247 bp) to short (115 bp) DNA fragments. The mean integrity index of benign vs. malignant pleural effusions was 0.29 vs. 0.42, t-test P value of 0.01.

For aim 2, we determined targetable mutations using cfDNA in 30 patients with lung adenocarcinoma pleural effusions. With next generation sequencing, we were able to detect mutations in 26 out of 30 patients.

For aim 3, we have recruited 13 patients with lung cancer pleural effusions. Once, we have recruited the target 30 patients, we will determine if cfDNA can inform about the response to therapy.

**15. SUBJECT TERMS**

NONE LISTED

**16. SECURITY CLASSIFICATION OF:**

a. REPORT

b. ABSTRACT

c. THIS PAGE

Unclassified

Unclassified

Unclassified

**17. LIMITATION OF ABSTRACT**

Unclassified

**18. NUMBER OF PAGES**

18

**19a. NAME OF RESPONSIBLE PERSON**

USAMRMC

**19b. TELEPHONE NUMBER** (include area code)

**Standard Form 298 (Rev. 8-98)**  
Prescribed by ANSI Std. Z39.18

## TABLE OF CONTENTS

Page

1. Introduction
2. Keywords
3. Accomplishments
4. Impact
5. Changes/Problems
6. Products
7. Participants & Other Collaborating Organizations
8. Special Reporting Requirements
9. Appendices

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

In this project, we are assessing if cell-free DNA (cfDNA) can be used to diagnose malignancy, genetic mutations and prognosis in lung cancer related pleural effusions. We will use integrity index of cfDNA in lung cancer associated pleural effusion to determine if the effusion is malignant. We will also perform next-generation sequencing on cfDNA to assess if it can give information about the targetable mutations. We will also use cfDNA to predict prognosis.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Cell-free DNA (cfDNA); lung cancer; pleural effusion

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

**What were the major goals of the project?**

*List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.*

**Specific Aim/Goal 1. To determine if pleural and plasma cell-free DNA integrity index has a higher yield compared to cytology to detect malignancy in pleural fluid.**

Target Recruitment: 30 patients with malignant pleural effusions (PE) and 30 patients with benign pleural effusions.

Recruited to-date: 30 patients with malignant PE and 20 patients with benign PE.

**Specific Aim/Goal 2: To assess if cell-free DNA in pleural fluid and plasma has a better yield versus cytology to identify targetable genetic mutations in lung adenocarcinoma.**

Target Recruitment: 30 patients with targetable mutations.

Recruited to-date: We have enrolled and obtained PE samples from 30 lung adenocarcinoma patients.

**Specific Aim 3. To determine if cell-free DNA in pleural fluid and plasma can be used as a predictor of response to therapy.**

Target Recruitment: 30 patients

Recruited to-date: We have enrolled 13 patients.

**What was accomplished under these goals?**

*For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include*

*pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.*

Duke IRB and MRDC and HRPO approval obtained.

**Goal 1.**

We have recruited 30 patients with malignant PE, but 20 with benign PE.

Integrity Index: We have extracted cfDNA from PE. We ran different analyses using different kits and reagents for quality control and determined the most robust methodology using quantitative real time PCR. With this method, we have determined integrity index as the ratio of concentration of long (247 bp) to short (115 bp) DNA fragments. The mean integrity index of benign vs. malignant pleural effusions was 0.29 vs. 0.42, t-test P value of 0.01.

**Goal 2.**

We have enrolled and obtained PE samples from 30 patients.

Analysis: Targetable mutations are being assessed with next generation sequencing (NGS) by our industry partner, Inivata Inc.

NGS was successful to determine targetable mutations in 26 out of 30 samples. NGS for fusion mutations is being performed.

**Goal 3.**

We have enrolled 13 patients.

Serial total cfDNA and mutation allele frequency are being determined to assess if there are changes with therapy.

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

*If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.*

Nothing to report.

**How were the results disseminated to communities of interest?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

Awaiting completion of the project.

*Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.*

Goal 1.

Recruit 10 more patients with benign PE.

Complete the PCR analysis to assess integrity index for all patients.

Goal 2.

Complete the NGS for fusion mutations on the samples.

Goal 3:

Recruit 17 patients.

Assess the changes in total cfDNA and mutation allele frequency in response to treatment to use as predictors of response.

4. **IMPACT:** *Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

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

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

Nothing to Report. Awaiting completion of the project.

**What was the impact on other disciplines?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.*

Nothing to Report. Awaiting completion of the project.

**What was the impact on technology transfer?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report. Awaiting completion of the project.

**What was the impact on society beyond science and technology?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report. Awaiting completion of the project.

- 5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

We are currently resolving the following problems:

1. We are trying to assess ways to determine tumor mutation burden with the help of our industry partner, Inivata. Traditional tumor burden is not performed on cfDNA. However, we are assessing total cfDNA and changes in allele frequency of mutations as a surrogate of tumor burden, tumor response and progression.

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

*Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

1. Since our industry partner is not able to perform tumor mutation burden on cfDNA, we are looking at similar, novel tests to determine a prognostic marker. One of the markers that we are currently using is total cfDNA concentration and changes with therapy. We will also determine if changes in mutation allele frequency can be used as a surrogate of tumor burden, tumor response and progression, as being done for colorectal cancer. Salvianti, F., Gelmini, S., Mancini, I. et al. Circulating tumour cells and cell-free DNA as a prognostic factor in metastatic colorectal cancer: the OMITERC prospective study. *Br J Cancer* 125, 94–100 (2021).

**Changes that had a significant impact on expenditures**

*Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*

None.

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

*Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

**Significant changes in use or care of human subjects**

None
None

**Significant changes in use of biohazards and/or select agents**

None
------

**6. PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”*

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

*Report only the major publication(s) resulting from the work under this award.*

**Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal;*

*volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

**Books or other non-periodical, one-time publications.** *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

**Other publications, conference papers and presentations.** *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (\*) if presentation produced a manuscript.*

Nothing to report.

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report.

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- data or databases;

- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### What individuals have worked on the project?

*Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".*

Example:

*Name: Mary Smith*  
*Project Role: Graduate Student*  
*Researcher Identifier (e.g. ORCID ID): 1234567*  
*Nearest person month worked: 5*

*Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.*

*Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name: Kamran Mahmood, MD, MPH  
 Project Role: PI  
 Research Identifier: 0000-0002-8643-2634

Nearest person month worked: 2.71

Contribution to Project: PI. Mahmood is leading and providing oversight of the entire project. He is helping with identifying and consenting the patients, obtaining the specimens, providing direction for analysis, quality control and interpretation of the findings. He is responsible for publishing and dissemination of the findings of the study.

Name: Parvathi Jampani, PhD

Project Role: Laboratory Personnel

Research Identifier: 0000-0002-8857-2307

Nearest person month worked: 3.39

Contribution to Project: Jampani conduct all laboratory-based experiments and oversee all molecular biology techniques employed. She is responsible for communicating with other groups and facilitating sample collection and shipping. She coordinates sample transfer, receipt, inventory, and processing of all biological samples, including maintaining of all chain-of-custody documents. Additionally, she works with the statistical team to assist with the final analyses and data interpretation.

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

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

**ACTIVE**

**Title:** Known Medicine Pleural Fluid Samples

**Time Commitment:** 1% 0.12 calendar months

**Supporting Agency:** Known Medicine

**Contracting/Grants Officer:** Known Medicine, Inc. 675 Arapeen Drive, Suite 103A-1, Salt Lake City, UT 84108

**Performance Period:** 02/19/2021-02/28/2022

**Level of Funding:**

**Project Goals/Specific Aims:** Objective is to validate that tumor organoid drug sensitivity is representative of patient treatment outcomes. The primary endpoint of this study is the validation of the hypothesis that the Known Medicine platform is predictive of tumor shrinkage at 3, 6, 9 and 12-months post-surgery. The secondary endpoint of this study is the validation of the hypothesis that the Known Medicine platform is predictive of patient survival time post-surgery.

**Overlap:** None

**(THIS AWARD)**

**Title:** W81XWH2010280 LC190500

**Time Commitment:** 26% 3.12 calendar months

**Supporting Agency:** Department of Defense

**Contracting/Grants Officer:** Amanda Carrera

**Performance Period:** 07/01/2020-06/30/2022 (NCE)

**Level of Funding:**

**Brief description of project’s goals:** Our central hypothesis is that cfDNA testing in pleural fluid has a better yield versus cytology to diagnose malignant effusions, and identify targetable mutations for lung adenocarcinoma.

**Specific Aims:** Aim #1: To determine if cfDNA integrity index in pleural fluid and plasma has a higher yield compared to cytology to detect malignancy in pleural fluid. Aim #2: To assess if cfDNA in pleural fluid and plasma has a better yield versus cytology to identify targetable genetic mutations and tumor mutation burden in lung adenocarcinoma. Aim #3: To determine if cfDNA in pleural fluid and plasma can predict response to therapy.

**Title:** Lymphocyte Exhaustion Markers in Malignant Pleural Effusions of Lung Cancer

**Time Commitment:** 0% 0.0 calendar months\*

**Supporting Agency:** Lung Cancer Initiative of North Carolina  
**Contracting/Grants Officer:** Jenni Danai, 5171 Glenwood Avenue, Suite 401, Raleigh, NC,  
NJDanai@LungCancerInitiativeNC.org

**Performance Period:** 07/01/2019-06/30/2022 (NCE 2)

**Level of Funding:**

**Brief description of project's goals:** The major goal of this project is to study markers of CD8+ T cells activity in malignant pleural effusions that may predict response to immunotherapy.

**Specific Aims:** Specific Aim 1: Characterize the T-cell exhaustion profile in lung cancer associated malignant pleural effusions, and compare it with peripheral blood and non-malignant pleural effusions. Our working hypothesis is that T-cells in lung cancer associated malignant pleural effusions will exhibit increased inhibitory receptors and decreased cytokine production. Specific Aim 2: Assess the changes in T-cell exhaustion profile in lung cancer associated malignant pleural effusions in non-responders who have cancer progression on anti-cancer therapy. Working hypothesis: T-cells in lung cancer associated malignant pleural effusions will exhibit increased inhibitory receptors, and decreased cytokine production in non-responders when compared to pre-therapy. This can be a biomarker for immunotherapy response.

\*Note: Dr. Mahmood serving as mentor for PI-Fellow, Dr. Michael Dorry, and no effort for his role

**Overlap:** None

**Title:** Lymphocyte Exhaustion Markers in Malignant Pleural Effusions of Lung Cancer

**Time Commitment:** 1% 0.12 calendar months\*

**Supporting Agency:** Chest Foundation

**Contracting/Grants Officer:** Konstandina (Argryopoulos) Dulu, Manager, Grants & Awards, American College of CHEST Physicians, 2595 Patriot Blvd., Glenview, IL 60026; Email: dulu@chestnet.org, Phone #: 224-521-9522, Fax #: 224-521-9801

**Performance Period:** 11/15/2019-11/15/2022

**Level of Funding:**

**Brief description of project's goals:** The major goal of this project is to assess cytotoxic T cells exhaustion markers in malignant pleural effusions.

**Specific Aims:** Specific Aim 1: Compare the T-cell exhaustion profile in lung cancer associated malignant pleural effusions with primary lung cancer biopsies of the same patients; Specific Aim 2: Contrast the T-cell exhaustion profile in lung cancer associated malignant pleural effusions to benign pleural effusions; Specific Aim 3: Determine the changes in T-cell exhaustion profile in lung cancer associated malignant pleural effusions in non-responders to immunotherapy.

**Overlap:** None

\*Note: Pending allocation of effort anticipated approximately July/August 2021

**Title:** Airflow 3: Multicenter randomized sham-controlled study to evaluate safety and efficacy after treatment with the Nuvaira Lung Denervation System in subjects with COPD

**Time Commitment:** 1% 0.12 calendar months

**Supporting Agency:** Nuvaira, Inc.

**Contracting/Grants Officer:** Delanie Reller, Clinical Study Manager, NUVAIRA, Inc., 3750 Annapolis Lane North, Minneapolis, Minnesota 55447, 763-450-2800

**Performance Period:** 11/05/2019-04/30/2025

**Level of Funding:**

**Project Goals/Specific Aims:** TLD Therapy ablates the airway nerve trunks of the vagus nerves

that travel parallel to and outside of the main bronchi and into the lungs. These airway nerve trunks are ablated circumferentially near the distal end of each of the right and left main bronchi to denervate both the right and the left lungs in a targeted manner. The system and therapy delivery are designed to ablate airway nerve trunks that effect nerve input into the lungs and avoid disruption of nerve input to other organs. As observed with surgical resection of airway nerve trunks, TLD Therapy is intended to lead to sustained airway smooth muscle relaxation from the site of treatment all the way to the lung periphery.

The Nuvaira Lung Denervation System, manufactured by Nuvaira, Inc., is intended to deliver TLD Therapy using predetermined radiofrequency (RF) energy over a predetermined period of time to ablate airway nerve trunks which are located on the outside of the main bronchi. TLD Therapy ablates airway nerve trunks while minimizing damage to tissues of the main bronchi through the use of a dual cooling method.

**Overlap:** None

### **What other organizations were involved as partners?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

*Provide the following information for each partnership:*

*Organization Name:*

*Location of Organization: (if foreign location list country)*

*Partner’s contribution to the project (identify one or more)*

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site): and*

Inivata.

Research Triangle Park, NC, USA.

Inivata is a collaborator in this project and is performing the next generation sequencing (NGS) to assess genetic mutations in pleural effusions. Inivata is performing NGS free of charge and covering its cost.

## **8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:** *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ebrap.org/eBRAP/public/index.htm> for each unique award.*

**QUAD CHARTS:** *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil/Pages/Resources.aspx>) should be updated and submitted with attachments.*

**9. APPENDICES:** *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*