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TITLE: Genomics of Early Lung Cancer Among Military Personnel (GELCAMP)

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14. ABSTRACT
Lung cancer is a leading cause of death worldwide, and improvements in morbidity and mortality hinge on continued investigation into the biology of cancer. Whole genome sequencing can uncover cancer-associated mutations that can meaningfully impact clinical care and decision-making. In this study, blood, bronchial epithelial cells and tumor tissue (as applicable) will be sequenced from 50 cases with confirmed cancer and 50 non-cancer controls. The resulting profiles will be analyzed for genetic markers that that may enable earlier diagnosis, guide therapy decisions and improve patient outcomes.

15. SUBJECT TERMS
Lung cancer, whole genome

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Table of Contents

Page

- **INTRODUCTION:**

  Currently several biomarkers are being validated on the DECAMP specimen, but none of these use the whole genome sequencing (WGS) technology. WGS offers a novel view of mutational changes in early lung cancer. We are testing for genomic biomarkers for the detection of early lung cancer using whole genome sequencing of DNA specimens from blood, endobronchial brushings and lung tumor specimens (for those with lung cancer). While genomic testing of lung cancer has been performed in other studies, testing other sites within the lung as well as peripheral blood for these biomarkers has not been attempted. The DEAMP cohort is unique for several reasons. The DECAMP cohort is the only cohort that specifically enrolls military personnel and offers the potential to identify mutations that might be linked to military specific exposures. It is also one of the most comprehensive and detailed cohorts associated with bronchoscopic brushings and tissue matched with CT imaging, clinical history in a longitudinal cohort.

- **KEYWORDS:**
  Cancer
  Lung
  Biomarkers
  Genomic
  Genome
  Tumor
  DNA
  Whole Genome Sequencing
  WGS

- **ACCOMPLISHMENTS:**
  - **What were the major goals of the project?**
    - Aim 1: Evaluate DNA copy number alterations and somatic mutations in the airway and tumor as well as germline polymorphisms that can distinguish benign vs. malignant nodules**.**
    - Aim 2: Characterize DNA copy number alterations and somatic mutations in the airway and tumor that associate with prognosis among those with lung cancer.

  - **What was accomplished under these goals?**
    - Obtained USU approval for budget reallocation from ODC (Vendor contract with American College of Radiology) to Personnel
    - Obtained HPRO approval to begin research activities at WRNMMC
    - Obtained HPRO approval for research activities at Brown University
    - Initiated meetings with Boston University and Investigators at USU and WRNMMC to coordinate study activities
    - Submitted Continuing Review package to WRNMMC IRB
    - Worked with WRNMMC IRB and HPRO to amend protocol due to change in requirement for consent waiver for non-exempt studies (WRNMMC IRB deferred approval of CR)

- Amended and resubmitted protocol to include a de-identification of samples by relabeling samples.
- Received WRNMMC IRB and HPRO approval of amended protocol changing protocol from NGTMR study to Exempt
- Resumed study meetings between Investigators at USU, WRNMMC and Boston University.
    - Discussed new requirements for re-labeling of samples
    - Discussed quantities and types of DECAMP samples available for selection
    - Discussed GELCAMP requirements for sample selection and shipping
    - Discussed ability to extract DNA and RNA material from tissue slides and number of samples needed to isolate enough DNA/RNA for whole genome sequencing
- Decision made to start with pilot sample of tissue slides to determine amount of material that can be extracted. Samples have been selected and are ready for shipment.

- **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?**
    - Ship pilot samples from Boston University to USU for extraction
    - Perform test DNA and RNA extraction to determine number of slides needed to have enough material to isolate DNA and RNA for sequencing
    - Finalize sample selection requirements and identify sample for shipping
    - Continue routine teleconferences between Investigators at Boston University, USU and WRNMMC
    - Modify existing USUHS array processing SOP for GELCAMP protocol
    - Finalize existing DECAMP shipping SOP for GELCAMP requirements
    - Modify and finalize data tracking / sharing mechanism between WRNMMC and USUHS
    - Finalize iMedidata Rave access
    - Modify and maintain electronic mail distribution lists and postal directories for correspondence and communication between the coordinating center and subcontractors and service providers
    - Continue operational teams and routine teleconferences to discuss study progress and timelines

- **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.

- **CHANGES/PROBLEMS:**
  - **Changes in approach and reasons for change**
    - Nothing to Report.
  - **Actual or anticipated problems or delays and actions or plans to resolve them**
    - *IRB Delays:* Significant IRB delays have adversely affected research activities. Initially, the study was approved by the WRNMMC IRB on September 18, 2018 with an exempt determination. However, in their second-level review, HPRO disapproved the protocol as they did not agree with the WRNMMC's exempt determination. The protocol was then revised and resubmitted to WRNMMC's IRB for review and re-approval. We finally received full HPRO approval on August 12, 2019 as a NGTMR study.

      The study then encountered additional IRB delays with the WRNMMC IRB deferring approval of the continuing review due to a change of requirement for consent waiver. As a result of the CR deference, all study activities had to cease. We worked with both HPRO and WRNMMC IRB to amend the protocol to include a de-identification of samples by relabeling samples with a unique GELCAMP identifier and removing the DECAMP identifier. The amended protocol was approved by the WRNMMC IRB on October 24, 2019 and by HPRO on November 1, 2019 with an exempt determination.

    - *COVID19 Research Priorities:* A pilot lot of tissue slides have been selected for shipment to USU for extraction. It was planned that USU would perform DNA and RNA extraction using these slides to determine the amount of material that could be extracted from each slide. This will finalize the number of slides/samples that should be sent to extract enough material for whole genome sequencing.

Unfortunately, the research efforts and sample shipments are currently on hold as the USU Genome Center has been assigned to COVID-19 efforts. We will resume research activities once the research facilities are open again.

- **Changes that had a significant impact on expenditures**
  - Delays in protocol approval have delayed collaborators contributions,
- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
  - Nothing to Report.

- **PRODUCTS:** Nothing to Report.

- **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**
  - **What individuals have worked on the project?** Individuals supporting the project for the past year in excess of 160 hours are:
    - Dr. Robert Browning, PI
    - Maggie Nellissery, Research Coordinator
    - Luis Rojas, Research Coordinator
    - Folashade Akani, Research Assistant

  - **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?**
    - Uniform Services University, Bethesda MD
      - Facilities: The American Genome Center
      - Collaboration: Dr. Clifton Dalgard
    - Brown University, Providence, RI
      - Collaboration: Dr. Fenghai Duan (no contributions thus far due to protocol delay)
    - Boston University, Boston, MA

- **SPECIAL REPORTING REQUIREMENTS**
  - COLLABORATIVE AWARDS: Nothing to Report

- **APPENDICES:**
  - Quad Chart