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Award Number: W81XWH-10-1-0264

TITLE: Integrative Analysis of Genomewide Gene Expression for Prostate Cancer Prognosis

PRINCIPAL INVESTIGATOR: Jiyoung Ahn

CONTRACTING ORGANIZATION: New York University
New York, NY 10016

REPORT DATE: May 2012

TYPE OF REPORT: Annual

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

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) 01-05-2012		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 15 APR 2011 - 14 APR 2012	
4. TITLE AND SUBTITLE Integrative Analysis of Genomewide Gene Expression for Prostate Cancer Prognosis				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-10-1-0264	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Jiyoung Ahn E-Mail: jiyoung.ahn@nyumc.org				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) New York University New York, NY 10016				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel 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 We aim to examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with PSA recurrence and systemic progression (metastasis), in a consortium study based on Mayo and NYU prostate cancer cohorts. We have completed research steps as planned in Mayo cohort, but we have a 5-6 month unexpected delay in NYU samples. One year no cost extension has been approved by DOD.					
15. SUBJECT TERMS No subject terms provided.					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 5	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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INTRODUCTION

The specific aims of the project have not changed. Using the resources from the Mayo and NYU cohorts, we are conducting:

Aim 1. Examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with PSA recurrence in men who had prostate cancer. We will compare gene expression profile between 400 PSA recurrent men (defined as a follow-up PSA ≥ 0.20 ng/ml) and 400 non PSA recurrent men.

Aim 2. Examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with systemic progression in men who had a biochemical (PSA) recurrence of prostate cancer. We will compare gene expression profile between 200 systemic progressors (defined as a positive bone scan or CT scan with 5 years of PSA recurrence) and 200 non-progressors, who remained negative for at least 5 years.

Our underlying hypothesis is that mRNA transcription profile plays an important role in shaping phenotypic inter-individual differences in tumor behavior related to prostate cancer prognosis. The ultimate goal of this study is to identify biomarkers that can be used at the time of diagnosis to predict risk of recurrence and improve clinical treatment decision making.

Note that the time sequence of tasks is not necessarily the sequence of the study Aims.

BODY:

Task 2. Pathology Review and tissue biospecimen shipping:

Pathology review from Mayo and NYU samples was completed. Briefly, tumor blocks were characterized by pathologists with a standardized protocol. Foci highly enriched for prostate cancer (>90%) were identified by microscopic examination. Four freshly cut 10 um sections of FFPE tissue was deparaffinized and the Gleason dominant cancer focus was macrodissected.

Task 3. RNA extraction:

RNA was extracted using the High Pure RNA Paraffin Kit from Roche (Indianapolis, IN). RNA was quantified using ND-1000 spectrophotometer from NanoDrop Technologies (Wilmington, DE).

Task 4. DASL Assay:

DASL expression assay (Illumina Inc, San Diego, CA) was performed using 50 ng of cDNA according to manufacturer's instructions. DASL Assay for pre-study sample run (n=12) was completed. The RNAs were sent to the Mayo Clinic Expression Array Shared resource for Illumina 24,000 gene DASL expression analysis. Each plate contained 4 interplate replicates and 5 intra-plate replicates. Analysis of the DASL data in Mayo cohort data is currently in progress.

One Year No cost extension approved:

Because we had unexpected delay in year 1 of NYU prostate tissue procurement, overall project progress has been delayed. The one year no cost extension has been approved by DOD. The extension period will be between 5/15/2012 and 5/14/2013 (one year). We will complete the DASL 24,000 gene expression analysis, and submit manuscripts during this extension period.

We will complete the following tasks.

Task 5. DASL Assay (4 Months):
a. DASL Assay, n=200 subjects
Mayo Clinic, Rochester, MN

Task 6. Data Analysis (4 Months):
a. Create a master dataset merging gene expression data and clinical data
b. Gene expression data cleaning.
c. Analysis of the association between gene expression and PSA recurrence
d. Analysis of the association between gene expression and systemic progression.
NYU School of Medicine, New York, NY

Task 7. Manuscript Preparation (4 Months):

RESEARCH ACCOMPLISHMENTS in year 2

- Completed Pathology Review and RNA extraction.
- Completed DASL Assay for study samples.
- Ongoing data analysis of DASL Assay results.

REPORTABLE OUTCOMES: None

CONCLUSION:

We aim to examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with PSA recurrence and systemic progression (metastasis), in a consortium study based on Mayo and NYU prostate cancer cohorts. We have completed research steps as planned in Mayo cohort, but we have a 5-6 month unexpected delay in NYU samples in year 1. The one year no cost extension (5/15/2012 and 5/14/2013) was granted. We will complete the DASL 24,000 gene expression analysis, and submit manuscripts during this extension period.

REFERENCES: None

SUPPORTING DATA: None

APPENDICES: None