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Award Number: W81XWH-11-1-0455

TITLE: Cytokine Response to Subclinical Cytomegalovirus Reactivation as a Cause of Severe Fatigue in Women Undergoing Chemotherapy for Breast Cancer

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Fort Detrick, Maryland 21702-5012

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**14. ABSTRACT**

This is the annual report for the first year of this grant. The goal of this grant is to study 26 women undergoing chemotherapy for breast cancer, assessing their fatigue levels before, during and after treatment, and correlating fatigue with CMV serostatus, the immune response to CMV, and cytokine levels. During this first year we completed the technical arrangements for the study and enrolled the first 9 patients. 4 are CMV seronegative, and 5 are seropositive. Fatigue survey data, serum, PBMC and urine have been collected and stored. We will collect four time points on each patientt. One patients has completed the study, the others are in progress. During this year we performed quality control tests on PBMC preservation, and established our initial panel of antibodies to be used for intracellular cytokine staining and FACS analysis. Patient recruitment has been proceeding at an acceptable pace and no problems are anticipated in recuiriting the full study cohort within the allotted time. Furthermore, our patients are fairly equally distributed between CMV serpositives and seronegatives, which gives best statistical power for the study and optimizes our likelihood of recruiting the full patient cohort.

**15. SUBJECT TERMS**

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**INTRODUCTION**

This is the first annual report for this award, which is for a small clinical study of breast cancer treatment related fatigue, and specifically the role of CMV reactivation in causing fatigue. Here we report on our initial recruitment of subjects for this study.

**BODY**

Herein we list the statement of work from the grant application (in italics), and describe progress.

1. *Obtain IRB approval for the study including design of study flyer (pre award, month -6-0). (**Wood**: Torgrimson, Nail*)
   DONE.
2. *Recruitment (Months 0-18):*
   a. *Distribute recruitment materials to all OHSU oncologists. (Months 0-1) (**Wood:**Torgrimson)*
   b. *Screen potential study participants for eligibility. Include individuals who will receive at least 6 weeks of cytotoxic chemotherapy for breast cancer. Exclude individuals with known inflammatory diseases (RA, SLE, UC, Crohn's disease, etc) and metastatic disease. (Months 0-18). (**Wood:** Torgrimson, Chui)*
   c. *Contact potential study participants after the treatment planning meeting with their medical oncologist to assess interest in participating in the study. (Months 0-18). (**Wood:** Torgrimson)*
   d. *Arrange a home visit prior to the start of chemotherapy to obtain informed consent, collect demographic and fatigue data, clinical history for major co-morbid conditions, and blood and urine. (Months 0-18). (**Wood:** Torgrimson)*

   Nine patients have been recruited to date, consented, and home visit achieved.
3. *Obtain fatigue data, blood and urine at each clinic visit. Additional fatigue data, and blood and urine will be collected twice per treatment cycle (one week after infusion, and one week later) during home visits. Additional fatigue data, blood and urine will be collected from each study participant at the 3 month clinical follow-up appointment with their medical oncologist. (Months 1-24)( **Wood:** Torgrimson, **Hill:**Bonnett)*
   Data and samples have been collected as plnned for all 9 patients.
4. *Process and store blood and urine samples on day of collection (months 0-22)(**Hill:** Bonnett, van den Worm)*
   Serum, urine and PBMC samples have been collected and stored.
5. *Monthly meetings of both research teams; organized by Torgrimson and attended by Wood, Torgrimson, Hill, van den Worm and Bonnett. (Months 1-24)*
   Monthly meetings have been held involving all personnel. We have found during the accumulation stage that more frequent meetings were needed, and key clinical personnel have met weekly for the second half of the year.

6. *Determine CMV seropositivity for each patient following first visit (months 1-18)(**Hill:** van den Worm)*
   CMV serology has been performed; 4 patients are negative and 5 positive.

   The remaining items had not yet begun during this reporting period.

7. *Identify candidate CMV peptide epitopes (months 1-20) (**Hill:** van den Worm)*
   a. *Order HLA typing on CMV+ patients*
   b. *Based on HLA alleles, order synthesis of candidate CMV peptide epitopes*
   c. *Test peptides with patient's blood to identify the epitopes that will be used in serial analyses.*
8. *Measure serum cytokines by multiplex immunoassay on pre-chemotherapy infusion blood draw and all blood draws collected at home visit samples. This analysis will be performed in batches throughout the study period (months 1-22) (**Wood**)*
9. *Measure serum neopterin and hepcidin. This analysis will be performed in batches throughout the study period (months 1-22) (**Hill:** Bonnett)*
10. *Measure CMV DNA in urine and blood. This analysis will be performed in batches throughout the study period (months 1-22)( **Hill:** van den Worm)*
11. *Measure T cell subsets and CMV-specific T cell responses in CMV seropositives This analysis will be performed in batches throughout the study period (months 1-22) (**Hill:** Bonnett/van den Worm)*
12. *Obtain data from clinical records: CBC, relevant clinical history during study period. This data will be collected throughout the study period. (**Wood:** Torgrimson)*
13. *Data collation, cleaning and analysis (months 20-24) (**Hill, Wood**: Leo will be responsible and perfom statistical analyses, van den Worm to perform data cleaning and collation)*
14. *Preparation of reports to BCRP (Month 12 for first annual report; month 24 for final*

## KEYS RESEARCH ACCOMPLISHMENTS

- *Subject recruitment*
- *Sample preparation and storage*
- *CMV serology*
- *Fatigue data collection**.***

## REPORTABLE OUTCOMES

None to date.

## CONCLUSION

The study is progressing as planned, with subject recruitment and home visits proceeding smoothly, in large part due to the wonderful work of the study co-ordinator (Torgrimson).

## REFERENCES

**N/A/**