AD_____

Award Number: DAMD17-01-1-0284

TITLE: Serum FAS and the Early Detection of Breast Cancer

PRINCIPAL INVESTIGATOR: Craig J. Newschaffer, Ph.D.

CONTRACTING ORGANIZATION: Johns Hopkins University
Baltimore, Maryland 21205

REPORT DATE: August 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel 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. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	August 2002	Annual (15 Jul 01 -14 Jul 02)

4. TITLE AND SUBTITLE
Serum FAS and the Early Detection of Breast Cancer

5. FUNDING NUMBERS
DAMD17-01-1-0284

6. AUTHOR(S)
Craig J. Newschaffer, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Johns Hopkins University
Baltimore, Maryland 21205

E-Mail: cnewscha@jhsph.edu

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. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

This study will explore the potential usefulness of measuring blood levels of fatty acid synthase (FAS) as a means of breast cancer early detection. Fatty acid synthase (FAS) is associated with poor breast cancer prognosis and is elevated in both breast cancer and *in situ* disease compared to normal breast tissue. Recently, serum FAS assays have been developed and higher serum FAS levels have been found in women with breast cancer compared cross-sectionally to women without the disease. In this nested case-control study we will analyze FAS levels in blood samples donated in 1974 and 1989 by women from Washington County Maryland participating in the CLUE studies. Samples from 129 incident breast cancer cases detected between 1990 and 1998, a like number of women diagnosed with benign breast disease during these same years, and a group of controls not diagnosed with any breast disease will be analyzed. Associations between absolute, and change over time in, serum FAS levels with subsequent breast cancer risk will be estimated as will the ability of these measures to correctly classify women with breast cancer, benign breast disease, and no diagnosed breast disease.

14. SUBJECT TERMS
FAS, breast cancer, serum

15. NUMBER OF PAGES
5

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Introduction

The specific aims of the proposed study are to:

1. Estimate the association between absolute, and change in, serum FAS levels measured in blood drawn during the preclinical period and subsequent breast cancer risk.
2. Determine whether these associations are modified by time from blood draw to diagnosis or eventual severity of breast cancer.
3. Determine whether serum FAS levels measured in blood drawn during the preclinical period discriminate between breast cancer and benign breast disease.
4. Conduct preliminary assessments of the performance of preclinical serum FAS levels as a test for breast cancer and to estimate optimal cutpoints for categorizing high and low risk women based on serum FAS levels.

Capitalizing on the existing serum bank of the CLUE research program, we will carry out a population-based nested case-control study of the association between pre-diagnostic serum FAS measures and beast cancer. Study groups will include breast cancer patients diagnosed from 1990-98, benign breast disease patients diagnosed from 1990-98, and women without breast disease all of whom had blood drawn and banked in both 1974 and 1989. For serum-FAS to be a useful biomarker for early detection of breast cancer, preclinical FAS levels must be associated with disease risk. If this is true, it will be useful to know how the strength of the association changes with time from blood draw to diagnosis of clinical cancer. The earlier in the preclinical period the marker is associated with disease, the more attractive the marker is as an early detection tool. In addition, it will be useful to know whether the marker is associated with all breast cancer or only a certain subset. In breast cancer tissue studies, FAS level has been positively correlated with several markers of tumor severity. Consequently, we suspect that serum-FAS may be more strongly associated with cancer in individuals whose lesions ultimately have a more aggressive profile. We also would like to determine whether the marker is specific to cancer and not capturing some more general feature of breast tissue anomalies. For this reason, estimating whether serum FAS levels are associated with breast cancer when the reference group is women with benign breast disease is important. Finally, we will shift analyses from an association measurement framework to a cancer detection framework and provide summary measures of the ability of serum-FAS to detect breast cancer. However, if FAS serum levels are incorporated into early-detection algorithms, discrete risk categories based on serum-level cutpoints would need to be developed. Therefore, we will explore various categorizations and present conventional performance measures (i.e., sensitivity and specificity) for these alternative cutpoints.

Report Body

Although the official funding period for this project began May 15, 2001 because it took a considerable amount of time for the project to clear Human Subjects Protection review, the authorization to begin the work was not received until October of 2001. Following that authorization the following steps have been completed:

- The CLUE database was queried to select eligible breast cancer cases and nondiseased controls. Relevant data from baseline and follow-up questionnaires have been incorporated into analytic data sets.
- Women in the CLUE cohort reporting a history of benign breast disease and/or past biopsy on follow-up questionnaires have been identified. Confirmation of BBD diagnosis is underway. Selection of BBD sample will proceed thereafter.

- Sample aliquots stored at the Washington County Public Health Training Center for 50 breast cancer cases and 50 breast cancer controls (eligible for this analysis but already matched and aliquoted for a previous study) who had prediagnostic samples available from both 1974 and 1989 were sent to Dr. Kuhajda's lab for FAS assay.
- Results from the assays on this initial sample were returned to JHSPH and preliminary analyses on this group have been completed.
- A second group of cases and controls were sent to Dr. Kuhajda's laboratory and assays were performed. (These data need to be analyzed.)

Results of the preliminary analysis on the initial samples from the 50 breast cancer cases and breast cancer controls are as follows. For the 1989 samples, mean FAS levels were 17.7 (sd 30.1) and 14.7 (sd 15.7) for cases and controls respectively. The p-values for the paired t-tests of case-control differences were 0.36 for the earlier and 0.53 for the latter samples. The mean change 1974-to-1989 among cases was 7.0 ng/ml (sd 29.5) and among controls was 1.7 (sd 16.4). The p-value for the paired t-test of the case-control difference was 0.28. Mean 1989 serum FAS levels and 1974-to-1989 serum FAS level change was higher in cases than in controls. However, at this sample size, these differences were not large enough to attain statistical significance at conventional alpha error tolerances. Of more importance, was the substantial observed overlap of the serum FAS distributions across case and controls. Adjusted analyses of these preliminary data are in progress, and results from the second batch of case and control samples are ready for analysis.

Key Accomplishments

Research is still in the implementation phase, as described above.

Reportable Outcomes

An abstract describing findings from the preliminary comparison was submitted to the Era of Hope Meeting and was accepted for poster presentation.

Conclusions

No definitive conclusions, as yet.

References

NA

Appendices

None.