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GRANT NUMBER DAMD17-97-1-7279

TITLE: Correlative Study of Tumor Hypoxia and Metastatic Potential in Breast Cancer

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REPORT DATE: September 1998

19981210 078

TYPE OF REPORT: Annual

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

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DTIC QUALITY INSPECTED 4

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 the 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 Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY <i>(Leave blank)</i>	2. REPORT DATE September 1998	3. REPORT TYPE AND DATES COVERED Annual (1 Sep 97 - 31 Aug 98)	
4. TITLE AND SUBTITLE Correlative Study of Tumor Hypoxia and Metastatic Potential in Breast Cancer		5. FUNDING NUMBERS DAMD17-97-1-7279	
6. AUTHOR(S) Varia, Mahesh A. M.D.			
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of North Carolina at Chapel Hill Chapel Hill, North Carolina 27599-1350		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	
<p>13. ABSTRACT <i>(Maximum 200 words)</i> Purpose: We propose a novel physiological approach using tumor hypoxia assessment to study the metastatic potential of primary breast cancer cells. Does the presence of hypoxia in breast primary detected by pimonidazole immunohistochemical binding, correlate with the presence of axillary lymph node metastases, and correlate the presence of hypoxia with markers of cell proliferation, p53, apoptosis, and VEGF in the primary breast tumor tissue. Scope: The specific aims are: I: Determine the presence and extent of tumor hypoxia in biopsies of primary breast cancer using pimonidazole binding to hypoxic tumor cells. II: Determine the patterns of pimonidazole binding in the breast cancer biopsies in relation to other landmarks such as blood vessels and necrosis. III: Correlate the presence and extent of tumor hypoxia in primary breast cancer with the presence of axillary node metastases. IV: Correlate the presence and extent of tumor hypoxia with the presence of other biological markers: p53, apoptosis, PCNA, Ki-67, and VEGF. V: Monitor adverse effects of pimonidazole. Major Findings: The clinical protocol has not been initiated. Please see the Annual Report Statement. We request deferral of the start date of the clinical research protocol to November 1st, 1998 or earlier pending Review Committee approval.</p>			
14. SUBJECT TERMS Breast Cancer		15. NUMBER OF PAGES 6	
		16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited

FOREWORD

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___ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

___ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

___ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

___ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Maheeh J. Venk 9.28.98
PI - Signature Date

Annual Report for Grant DAMD17-97-1-7279

Table of Contents

Front Cover

Standard Form 298

Foreword

Table of Contents

Annual Report Statement



THE UNIVERSITY OF NORTH CAROLINA
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September 28, 1998

**For Attention of MCMR-RMI-S
Research Data Management
SUBJECT: Annual Report for Grant DAMD17-97-1-7279**

Ms. Judy Pawlus
Office of the Deputy Chief of Staff for Information Management
U.S. Army Medical Research and Materiel Command
504 Scott Street,
Fort Detrick, MD 21702-5012

Dear Ms. Pawlus,

Enclosed please find the following in reference to the Annual Report for Grant DAMD17-97-1-7279.

1. Front Cover
2. Standard Form 298
3. Foreword
4. Table of Contents
5. Annual Report Statement

Please note that this research project has been delayed on account of issues related to the Consent for Human Subjects as described in the Annual Report Statement and we are hoping to commence patient entry this fall for research on this grant.

Request for Deferral of Protocol Start Date: We request a deferral of the start date of the clinical research protocol to November 1st, 1998 or earlier pending Review Committee approval. This should complete all the required approvals of the involved Human Research Review Boards and adherence to policies of applicable Federal Law 45 CFR 46. Explanation for this request is provided in the attached Annual Report Statement.

Sincerely,

A handwritten signature in black ink that reads "Mahesh A. Varia".

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Enc.

Annual Report Statement
Grant DAMD17-97-1-7279

There has been a lag in obtaining the approval of the Informed Consent Form for participation by breast cancer patients on the research study funded by this grant. After the initial award of the grant, a number of changes in the Consent Form approved by our Institutional Review Board were requested by the Surgeon General's Human Subjects Research Review Board (HSRRB, HURRAD Log. No. A-7766), USAMRMC Human Subjects Protection Division.

Although most of these changes could be addressed without significant difficulty, a major problem related to provision of financial compensation for research subjects in the event of research related **injury**. The required language of the two Review Boards were in direct conflict. In the Consent Form, our Review Board requires that in such a situation, provision will be made for medical care to the research subject but the institution cannot assume financial responsibility. HSRRB required that provision be made of financial responsibility. According to the Senior Legal Counsel of the University of North Carolina, the State of North Carolina does not permit the University to assume such responsibility.

After further discussions on this subject, language acceptable to both Review Boards was developed whereby Department of Defense as the sponsor of the research assumes the financial responsibility. These deliberations and required approval of the Consent Form has delayed entry of research subjects entry into the research protocol for this grant.

Pending final clarifications to the Clinical Research Advisory Committee our General Clinical Research Center (GCRC) regarding the cost of the research component of the tumor biopsy procedure, full approval of the clinical protocol is anticipated at the Committee's next meeting next month. The GCRC has indicated its enthusiastic approval of the protocol and unanimous support of the research proposal.

In view of the above deliberations and in order to comply with the requirements of the Human Research Review Boards of the DOD, University of North Carolina, and the GCRC, we have not embarked on the enrollment of patients.

Request for Deferral: We request a deferral of the start date of the clinical research protocol to November 1st, 1998 or earlier as expected with the GCRC approval. This should complete all the required approvals of the involved Human Research Review Boards and adherence to policies of applicable Federal Law 45 CFR 46.

We are extremely excited and enthusiastic about this innovative research and are very anxious to proceed with patient enrollment in compliance with the applicable approvals.

Revised, 9/30/98.
