Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** Temple University – Of The Commonwealth System of Higher Education

2. **Reporting Period (start and end date of grant award period):** 1/1/2010-12/31/2013

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Germaine A Calicat, MA

4. **Grant Contact Person's Telephone Number:**215-204-7655

5. **Grant SAP Number:** 4100050909

6. **Project Number and Title of Research Project:** Project Number 5; *Targeted Multidrug Delivery System to Overcome Chemoresistance in Breast Cancer*

7. **Start and End Date of Research Project:** 12/1/2010 – 12/31/2011

8. **Name of Principal Investigator for the Research Project:** Bin Wang, PhD

9. **Research Project Expenses**.

   9(A) Please provide the total amount of health research grant funds spent on this project for the entire duration of the grant, including indirect costs and any interest earned that was spent:

   $ 75,269.14

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project	Cost
None			

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project
Bin Wang, PhD	Principal Investigator	100%
Mohan P. Achary	Co - Investigator	10%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
None		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No____x_____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes_____ No_____x_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _)			
	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)		$	$
	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)		$	$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes____x_____ No_____

If yes, please describe your plans:

I plan to apply additional funding in the field of cancer treatment.

12. **Future of Research Project.** What are the future plans for this research project?

I plan to use the preliminary data generated from this research project to apply grants from other funding agencies.

13. **New Investigator Training and Development**. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes_____ No____x_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				
Other				
Unknown				
Total				

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No____x_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes_____ No____x_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes_____ No_____x_____

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes_____ No____x_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No____x_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.
List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims <u>for the period that the project was funded (i.e., from project start date through end date).</u> Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research

goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

SPECIFIC AIMS:

1. *Synthesize and characterize the liposomes and immunoliposomes:* The liposome will be synthesized and then encapsulated with extracellular therapeutic drug (Bevacizumab). The immunoliposome will be synthesized and conjugated with a targeting moiety (Her-2/neu), and encapsulated with intracellular therapeutic drugs (Doxorubicin and Verapamil).

2. *Evaluate the therapeutic efficacy of the delivery systems in vitro against a breast cancer cell line:* The therapeutic effects of the synthesized delivery systems (liposomes and/or immunoliposomes) will be tested on a Her-2/neu positive breast cancer cell line either individually or in combination. Cellular uptake and intracellular retention will be assessed using fluorescence labeling techniques.

During this study period, a series of experiments have been conducted toward specific aims. The specific aims are achieved, and the results we got are what we have expected.

1. Preparation of Stealth Liposomes

The first step toward the final goal is to synthesize the liposomes we need. Long circulating liposomes were composed of 50 mole % hydrogenated soy L-α-phosphatidylcholine (HSPC), 45

mole % cholesterol, 3 mole % 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[(polyethylene glycol)2000] (DSPE-PEG2000), and 2 mole % DSPE-PEG-maleimide. In our experiment, a total of 40 nano mole lipids were dissolved in chloroform with. After mixing, the lipids were dried under vacuum overnight, and then the lipid film were rehydrated in 40 ºC deionized water to form vesicles. The lipids were then extruded 11 times using a thermobarrel extruder. Liposomes at different sizes were achieved by choosing filters with different sizes. Here we used 200, 100 and 80nm size filters respectively. Table 1 surmised the liposomes size distribution after passing them through different size filters.

Liposome size was measured by dynamic light scattering (DLS) using a Malvern Zetasizer. Size measurements were taken in triplicate at 25°C using a 1:100 (vol/vol) dilution of the liposome suspension in distilled water. The particle size was estimated from cumulant analysis once the correlation was determined. The polydispersity index was used as a measure of particle size distribution, scaled from 0 to 1, where bigger numbers indicating a wider size distribution.

As we can see from the table, the mean diameters of liposomes passing through 100 and 200 nm filters were 113.3 ± 0.6 nm and 192.1 ± 1.3 nm, respectively. Polydispersity index were 0.112 ± 0.012 and 0.047 ± 0.013 for both sizes respectively. The small polydispersity index indicates a tight size distribution around the mean.

2. <u>Bevacizumab ELISA</u>

In order to be able to determine the Bevacizumab concentration, a direct Enzyme-Linked Immunosorbent Assay (ELISA) method was developed. Briefly, a serial dilution of Bevacizumab solution with known concentration was made using 50 mM carbonate buffer, pH 9.6 (15 mM Na_2CO_3 and 35 mM $NaHCO_3$). 100 µL of Bevacizumab at each concentration was added to an ELISA plate, duplicate. The plate was placed in 4 ºC refrigerator overnight to allow for Bevacizumab attachment. Unbound Bevacizumab was then removed with 100 mM pH 9.2 $NaHCO_3$ wash (5 minutes each, on shaker, repeat 3 times). Remaining uncovered plate area was occupied with blocking buffer (3% BSA + 0.1% Tween 20 in HBSS) for 2 hours. Excessive blocking buffer was then removed by 3 times wash with washing buffer (1% BSA + 0.05% Tween 20 in HBSS). After applying anti-human IgG (Fc specific)-peroxidase detection antibody (1.5 µg/mL, 100 µL/well) for 1.5 hours at room temperature, the plate was ready for color development. After 3 times wash, color development was achieved by adding peroxidase substrate 3.3.5.5′-tetramethylethylenediamine (TMB) to each well and let it develop at room temperature for 30 minutes. Finally, color development was stopped by adding 50 µl of 1N sulfuric acid to each well. The resulting yellow color can be read at 450 nm in a plate reader.

Figure 1 shows the results of the ELISA assay. This direct Bevacizumab ELISA can test as low as 0.5 µg/mL concentration. Beyond 8 µg/mL concentration, the absorbance value started to saturate and became not linear. Below 8 µg/mL, the ELISA assay showed a good linearity as indicated by the R square value.

3. Bevacizumab Percentage of Entrapment

A dehydration/rehydration method was used to encapsulate Bevacizumab into liposomes. Plain liposome particles were made as described in section 1. Bevacizumab was added to the liposome suspension at a concentration of 250 µg/mL, with a 1:1 volume ratio of Bevacizumab : liposomes. The mixture was first flash frozen in a dry ice/2-propannol/acetone bath and then lyophilized to powder form. To resuspend the powder, a two step rehydration procedure was employed. First, 0.2 mL of Tris/saline buffer was added to the powder at temperature <40 °C; second, the flask was lightly rotated/vortexed to wet and resuspend the liposomes. Finally, we added additional Tris/saline buffer slowly up to 1 mL.

The separation of liposome entrapped Bevacizumab and free Bevacizumab was achieved by centrifugation 1 mL liposome sample at 80,000 *g* for 60 minutes in an ultracentrifuge. After centrifugation, the supernatant was removed and the liposome pellet was resuspended in 1 mL of Tris/saline buffer. To release all the entrapped Bevacizumab, high-frequency ultrasound was used to disrupt the liposomes. The percentage of Bevacizumab entrapment was determined by calculating the ratio of entrapped Bevacizumab to the total amount of Bevacizumab added. According to our calculation, 93.73 nano mole of Bevacizumab was entrapped, since the total amount added was 250 nano mole, the calculated percentage of entrapment was 93.73/250 = 37.5%.

4. Bevacizumab Release Profile

Bevacizumab release profile was obtained by calculating the amount of Bevacizumab remaining in the liposome 1, 2, 3, 4, 5, 6, 24, and 48 hours after the centrifuge. The results are shown in Figure 2. Bevacizumab presented two phases of release from the liposomes. The first phase was the burst release; a burst release of 21.13% was estimated from the curve fitting. This fast phase was due to the release of Bevacizumab that was adsorbed onto the surface during the liposome formulation process. Following burst release, the release was mediated by diffusion from the liposome core and degradation of the liposomes, which is much slower compared to the burst release. The total Bevacizumab released in 48 hours was 55.13%.

The attachment of Her-2/neu targeting moiety to the liposomes had been established in our lab and reported in the proposal for this grant. Therefore, this part is not included in this report. We are also currently synthesizing DOX & Verapamil encapsulated liposomes.

Run	Angle	KCps	ZAve	Poly
1	90	358.2	114	0.098
2	90	358.7	112.8	0.117
3	90	358.7	113.2	0.12
Average		358.6	113.3	0.112
+/-		0.3	0.6	0.012

(a)

Run	Angle	KCps	ZAve	Poly
1	90	214.1	193.6	0.038
2	90	215.4	191.5	0.062
3	90	211.9	191.3	0.042
Average		213.8	192.1	0.047
+/-		1.7	1.3	0.013

(b)

Table 1. Size distribution of liposomes (a) after passing through a 100 nm filter 11 times in a thermobarrel extruder; (b) after passing through a 200 nm filter 11 times in a thermobarrel extruder.

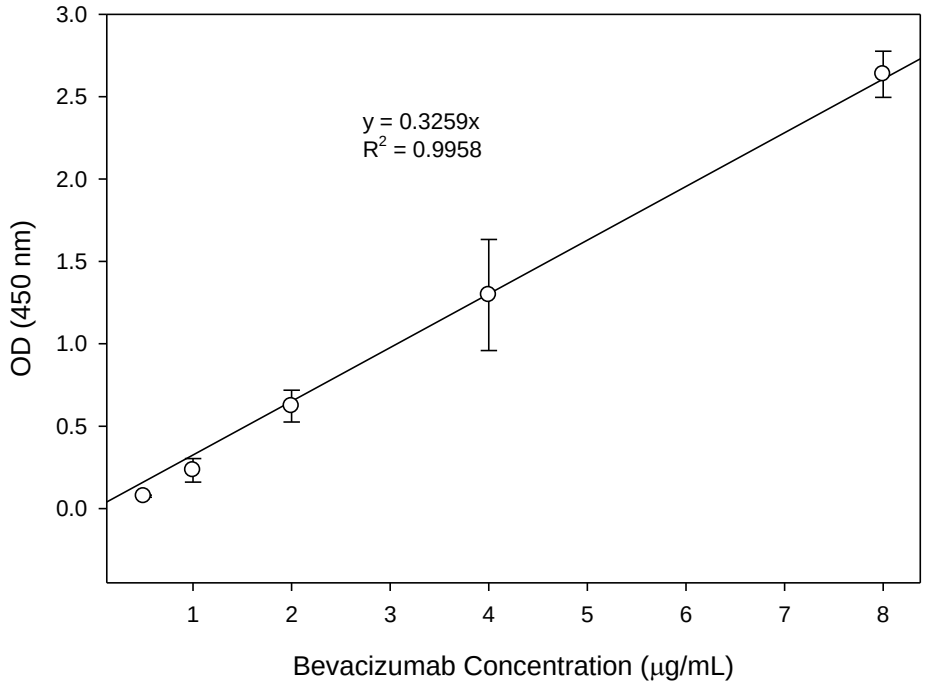

Figure 1. Absorbance value of 0.5, 1, 2, 4, 8 μg/mL Bevacizumab after ELISA assay.

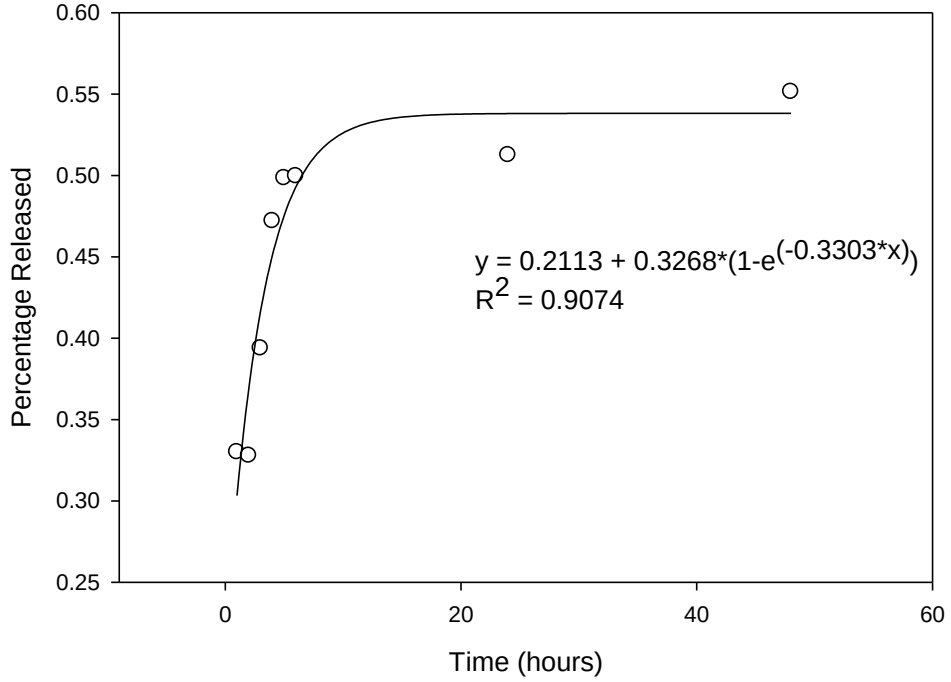

Figure 2. Cumulative Bevacizumab release during 48 hours.

A list of published abstracts, poster presentations and scientific meeting presentations

1. Targeted Delivery of Therapeutics to Diseased Tissue. Northeast Bioengineering Conference (2012).
2. Targeted Multidrug Delivery for Overcoming Chemoresistance in Breast Cancer. Biomedical Engineering Annual Meeting (2012).

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___x___No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___x___No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
___x___ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
___x___ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

Project 01 – Smith – Three cases of isolated
Project 01 – Smith – Investigation of NEB1 deletions
Project 03 – Zhang – Molecular profiling of aromatase
Project 04 – Bates – Neonatal intensive care

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):

1.				☐Submitted ☐Accepted ☐Published
2.				☐Submitted ☐Accepted ☐Published
3.				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes_____ No_____x_____

If yes, please describe your plans:

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

It is our expectation that development of this novel mode of breast cancer therapy will produce a new and exciting therapeutic option. Specific properties of the combination therapy (e.g. blocking a number of pathways rather than a single one) increase the efficacy of tumor treatment. This unique combination delivery system will significantly improve the treatment outcome of breast cancer by increasing treatment efficacy, reducing side effects, and overcoming drug resistance. The successful completion of this project will provide a better alternative for patients in the treatment of breast cancer and ultimately help in eradicating breast cancer mortality. In summary, this research will result in a new treatment for breast cancer that could beneficially impact survival and quality of life for patients with this disease.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

We have developed this novel mode of breast cancer therapy will produce a new and exciting therapeutic option. Nevertheless, there are still more work to do to advance to clinical trials.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___x_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No_____x_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME WANG, BIN	POSITION TITLE Assistant Professor of Mechanical Engineering
eRA COMMONS USER NAME BINWANG2DAY	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Qiqihar University, Qiqihar, China	B.S.	1995	Fermentation Engineering
Tianjin University of Science & Technology, Tianjin, China	M.S.	2001	Fermentation Engineering
University of Tennessee Health Science Center, Memphis, TN	M.S.	2004	Biomedical Engineering
Temple University, Philadelphia, PA	Ph.D.	2004-2007	Biomedical Engineering
Medical College of Georgia, Augusta, GA	Postdoc.	2007-2009	Vascular Biology Center

Professional Experience

1995-1998 Instructor, Department of Food Science & Engineering, Inner Mongolia Agricultural University, Inner Mongolia, China

1998-2001 Research Assistant, Department of Food Science & Engineering, Tianjin University of Science & Technology, Tianjin, China

2001-2004 Research Assistant, Department of Biomedical Engineering, University of Tennessee Health Science Center, Memphis, TN

2004-2007 Research Assistant, Department of Mechanical Engineering, Temple University, Philadelphia, PA

2007-2009 Postdoctoral Fellow, Vascular Biology Center, Medical College of Georgia, Augusta, GA

2009-present Assistant Professor, Department of Mechanical Engineering, Temple University, Philadelphia, PA

Honors

American Heart Association Pre-doctoral Fellowship, 2006-2007
Genentech Research Contracts and Reagent Program Grant, 2006
The Duane F. Bruley Award, International Society of Oxygen Transport to Tissue, 2006
Temple University Doctoral Fellowship, Temple University, 2004-2006
Student Travel Scholarship, **Biomedical Engineering Society Annual Fall Meeting,** 2005
Student Travel Scholarship, **Biomedical Engineering Society Annual Fall Meeting, 2004**

Peer Reviewed Publications

Wu, W; Bao, B; **Wang, B**. (1998) The study on the optimizing design of the mixture oil used to fry fresh potato chip. Journal of Inner Mongolia institute of agriculture & animal husbandry. Vol. 19, NO. s, pp. 40-44

Wu, W; Bao, B; **Wang, B**. (1998) The effect of storage environment conditions on the soluble sugar content of wheat. Journal of Inner Mongolia institute of agriculture & animal husbandry. Vol. 19, NO. s, pp. 23-26

Wang, B; Zhang, G; Lu, F; Du, L. (2001) Progress on the ethanol tolerance mechanism in yeast. Journal of Tianjin university of light industry, NO. 1, Sum 36, pp. 18-24
Wang, B; Zhang, G; Lu, F; Du, L . (2001) Study on the Breeding of Saccharonyces cervisiae of *High Alcohol Gravity.* Journal of Tianjin university of light industry, NO. 3, Sum 38, pp. 33-37
Wang, **B**; Ansari, R; Sun, Y; Postlethwaite, AE; Weber, KT; Kiani, MF. (2005) The Scar Neovasculature Following Myocardial Infarction in Rats. Am. J. Physiol. Heart. Circ. Physiol. Jul;289(1):H108-13. Epub 2005 Feb 18
Ansari, R; Gaber, MW; **Wang**, B; Pattillo, CB; Miyamoto, C; Kiani, MF. (2007) Anti-TNF-α Treatment Abrogates Radiation Induced Bystander Changes in Vascular Density and Tissue Oxygenation. Radiat. Res.167, 80-86
Scott, RC; **Wang, B**; Nallamothu, R; Pattillo, CB; Perez-Liz, G; Issekutz, A; Del Valle, L; Wood, GC & Kiani, MF (2007) Targeted delivery of antibody conjugated liposomal drug carriers to rat myocardial infarction. Biotechnol. Bioeng., 96(4):795-802 (selected as a "Spotlight Article").
Wang, B; Scott, RC; Pattillo, CB; PrabhakarPandian, B; Sundaram, S & Kiani, MF. (2007) Microvasculature Transport Model of Myocardial Oxygenation for Guiding Angiogenesis in Infarcted Hearts. Am J Physiol Heart Circ Physiol 293: H3732-H3739
Wang, B (2007) Oxygen Delivery and Angiogenesis Post-Myocardial Infarction. Ph.D. Dissertation, Temple University, Philadelphia, PA.
Wang, B; Scott, RC; Pattillo, CB; Pandian, BP; Sundaram, S & Kiani, MF. (**2008)** Modeling oxygenation and selective delivery of drug carriers post-myocardial infarction. Adv. Exp. Med. Biol., **614** Pages: **333-343,**
Scott, RC; Rosano, JM; Ivanov, Z; **Wang, B**; Chong, PLG; Issekutz, AC; Crabbe, DL & Kiani, MF (2008) Targeting VEGF-encapsulated immunoliposomes to MI heart improves vascularity and cardiac function. FASEB, 2009 Oct;23(10):3361-7. Epub 2009 Jun 17.
Sullivan, JC; **Wang, B (Co-First Author);** Boesen, EI; D'Angelo, G; Pollock, JS; Pollock, DM (2009) Novel Use of Ultrasound to Examine Regional Blood Flow in the Mouse Kidney. Am J Physiol Renal Physiol. 2009;297 F228-F235
Wang, B; Rosano JM; Cheheltani, R; Achary, MP & Kiani, MF. Towards a targeted multi-drug delivery approach to improve therapeutic efficacy in breast cancer. Expert Opin Drug Deliv. 2010 Aug 25. [Epub ahead of print]
Tousi, N; **Wang**, B; Pant, K; Kiani, MF & Prabhakarpandian, B. Preferential adhesion of leukocytes near bifurcations is endothelium independent. Microvasc Res. 2010 Jul 20. [Epub ahead of print]

Number of Presentations and Abstracts = 30

Ongoing Research Support
Targeting pro-angiogenic compounds to post-MI tissue, 1/2009-12/2010
P.I.: M.F. Kiani American Heart Association

Targeted Multidrug Delivery System to Overcome Chemoresistance in Breast Cancer
8/2010-8/2013 P.I.: Bin Wang Susan G. Komen Foundation Career Catalyst Research Grant

Targeted Multidrug Delivery System to Overcome Chemoresistance in Breast Cancer
7/2010-7/2011 P.I.: Bin Wang Temple University Provost Seed Grant (Internal Grant)

Targeting pro-angiogenic compounds to post-MI tissue, 1/2009-12/2010
P.I.: M.F. Kiani American Heart Association

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Achary Patnala Mohanrao	POSITION TITLE Assistant Professor Dept. of Radiation Oncology
eRA COMMONS USER NAME pachary	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Berhampur University, India	B.S.	1974	Biology
Berhampur University	M. S. First Class (Second Position)	1976	Cytogenetics
Calcutta University	Ph.D.	1987	DNA Replication
NIDDK/NIH, Bethesda, MD.	Postdoc.	1994-'95	Molecular Genetics

* Title of the Ph. D. degree thesis: *In vivo* synchronization of the DNA replication in the polytene chromosomes of *Drosophila,* Calcutta University, India.

Professional Experience

1987-88: Scientist, Council of Sci. and Industrial Research, Govt. of India, at Cal. Univ., India.
1988-98: Research Scientist, University Grants Commission, Govt. of India, at Cal. Univ., India.
1994-95: Guest Scientist, FAES Fellowship, at NIDDK, NIH, Bethesda, MD.
1995-97: Research Associate, Dept. of Radiation Oncology, Albert Einstein Coll. of Med., NY.
1997-04: Cancer Biologist, Dept. of Radiation Oncology, Albert Einstein Coll. of Medicine Bronx, NY.
1999-04: Assistant Professor, Dept. of Radiation Oncology, Albert Einstein Coll. of Med., NY.
2004-to date: Assistant Professor, Dept. of Radiation Oncology, Temple University, PA.

Professional Recognition:

1. Scientist award by C.S.I.R. (Govt. of India) in 1987 (1987-92)
2. Research Scientist (Faculty) award by U.G.C. (Govt. of India) in 1988 (1988-98).
3. Travel award by C.S.I.R. to Germany in 1991.
4. Fellow award of Zoological Society of India (FZS) in 1993.
5. Guest Scientist Award by the Foundation for Adv. Edu. in Sciences, USA, in 1994.
6. IDEA Award (US Army Breast Cancer Research Program) in 1999 (1999-03).
7. I. H. P. Klinger Fund award in 2001 (2001-04)
8. Member of editorial board of the Journal "Cytogenetic and Genome Research"
9. Member of Ph. D. thesis defense committee of Dept. of Pharmacy, TU (2004-06).
10. Member, Faculty candidate selection committee of College of Engineering (bio/electrical), TU (2006-07).
11. Member of Ph. D. thesis defense committee of Dept. of Engineering, TU (2006- Present).

Peer Reviewed Publications

P. Mohan R. **Achary**, W. Jaggernauth, E. Gross, A. Alfieri, H. P. Klinger and B. Vikram (2000). Cell lines from the same cervical carcinoma but with different radiosensitivities exhibit different cDNA microarray patterns of gene expression. **Cytogenetics and Cell Genetics** 91: 39-43.

R. Yuan, S Fan, P. Mohan R. **Achary**, D. M. Stewart, I. D. Goldberg, and E.M.R. Rosen. 2001. Altered gene expression pattern in cultured human breast cancer cells treated with hepatocyte growth factor/scatter factor (HGF/SF) in the setting of DNA damage. **Cancer Research** 61: 8022-8031.

L. H. Herbst, R. Chakrabarty, P. A. Klein, and P. Mohan R. **Achary**. 2001. Differential Gene Expression Associated with Tumorigenicity of Cultured Green Turtle FP-Derived Fibroblasts. **Cancer Genetics and Cytogenetics** 129: 35-39.

B. Mukherjee, H. Zhao, B. Parashar, B. M. Sood, P. S. Mahadevia, H. P. Klinger, B. Vikram, P. Mohan R. **Achary**. 2003. Microsatellite dinucleotide (T-G) repeat: A candidate marker for breast metastasis. **Cancer Detection and Prevention** 27: 19-23.

P. Mohan R. **Achary**, Zhao H, Fan Z, Herbst L, Jones, J. Klinger HP, Vikram B. 2003. A candidate metastasis associated DNA marker for ductal mammary carcinoma. **Breast Cancer Research** 5: 52-58.

H. Zhao, Meena Jhanwar-Uniyal, Prasun K. Datta, Srishailam Yemul, Lap Ho, Gregory Khitrov, Ilya Kupershmidt, Giulio M. Pasinetti, Raghbir S. Athwal and P. Mohan R. **Achary**. 2004. Expression Profile of Genes Associated with Antimetastatic Gene, nm23-Mediated Metastasis Inhibition in Breast Carcinoma Cells. **International Journal of Cancer** 109: 65-70.

A. Agelan, A. Plante, S. Basak, L.H. Herbst, M. April and P. Mohan R. **Achary**. Animal models of selected diseases. In: "**Recent Research Developments in Life Sciences**" (Research Signpost) Pgs. 103-119.

Diana S. Woodruff-Pak, A. Agelan, L. D. Valle, and P. Mohan R. **Achary**. 2008. An Animal Model of Alzheimer's Disease Highlighting Targets for Computational Modeling. In: **Advances in Cognitive Neurodynamics** (Springer Science; Eds: Wang et al) Pgs: 903-907

Chi Zhang, P. Jia, X. Huang, G. Sferrazza, G. Athauda, P. Mohan P. **Achary**, J. Wang, S. L Lemansi, D. K. Dube and Larry F Lemanski. 2009. Myofibril-Inducing RNA (MIR) is essential for tropomyosin expression and myofibrillogenesis in axolotl hearts. **Journal of Biomedical Science, 16: 81-90**

Larry Lemanski; Zhang, Chi; Jia, Pingping; Jia, Yuanyuan; Weissbach, Herbert; Huang, Xupei; Lemanski, Sharon; **Achary**, P. Mohan; Webster, Keith. 2010. Methionine Sulfoxide Reductase A (MsrA) Protects Cultured Mouse Embryonic Stem Cells from H2O2-mediated Oxidative Stress" **Journal of Cellular Biochemistry** (**In Press**)

Ongoing Research Support

1. Research Program: Diangnostic Markers for Different Cancers Using Genomics and Proteomics Methods.
   Start-up funds from Radiation Oncology, Temple University School of Medicine
2. Title: Does Combination of Betulinic Acid with Ionizing Radiation have Any Synergistic Effect in Killing GBM Brain Tumor Cells
   Zaloga Brain Tumor Foundation 01/2007 to 12/2010 Co- PI.
3. Title: Isolation and Separation of Breast Cancer Cells from Biopsy Samples using a Microfluidic Cell Sorter.
   The Nanotechnology Institute, Philadelphia 3/2009 to 2/2010 Co- PI.
4. Title: Non-Destructive Detection and Separation of Radiation Damaged Cells in Miniaturized, Inexpensive Device
   NASA (STTR Phase II) 10/2009 to 9/2011 Co-Investigator
5. Title: A Myofibril-Inducing RNA Regulates Heart Development
   Funding agency: National Institutes of Health 12/2006 to 11/2010 Consultant