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):** 01/01/2009 – 12/31/2012

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

4. **Grant Contact Person's Telephone Number:** 215.204.7655

5. **Grant SAP Number:** 4100047651

6. **Project Number and Title of Research Project:** 3- *C/EBP(s) and the Transcription of Dihydrodiol Dehydrogenase 1 in Human Ovarian Cancer Cells*

7. **Start and End Date of Research Project:** 7/1/2009 - 5/10/2010

8. **Name of Principal Investigator for the Research Project:** Hemant K. Parekh, Ph.D.

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:

   $ 25,000

   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	Position Title	% of Effort on Project	Cost
Pallai	Graduate Student	100	$ 25,000

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	Position Title	% of Effort on Project
Parekh, Hemant K.	PI	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:
None	☐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_____ No____X_____

If yes, please describe your plans:

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

No future plans.

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___X_____ No_____

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

	Undergraduate	Masters	Pre-doc	Post-doc
Male			1	
Female				
Unknown				
Total			**1**	

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic			1	
Unknown				
Total			**1**	

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian			1	
Other				
Unknown				
Total			**1**	

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 for the period that the project was funded (i.e., from project start date through end date). 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.

Project Overview

Ovarian cancer is one of the leading causes of female mortality in the United States. Chemotherapy with platinum-containing compounds is often effective in the treatment of this disease. However, ovarian cancers can develop resistance to these drugs via diverse mechanisms. Preliminary studies from our lab have demonstrated that overexpression of dihydrodiol dehydrogenase (DDH) is intimately involved in the development of the cisplatin resistance phenotype. Dihydrodiol dehydrogenases (DDH) are a family of aldo-keto reductase enzymes involved in the *de novo* detoxification of xenobiotics, steroids and

polycyclic aromatic hydrocarbons (PAH). Increased expression of Dihydrodiol dehydrogenase 1 (DDH1) protein has been demonstrated to induce cisplatin/carboplatin resistance in human ovarian carcinoma cells. The observed increase in protein expression was associated with the changes in the transcription of the DDH gene. In order to identify the factors that control the expression of DDH1 gene in human ovarian cancer cells, we cloned approximately 3000 bps of the 5'-end of the human DDH1 gene. Promoter deletion analysis indicated a complex control mechanism with the proximal -181 bp postively associated with basal transcription of the DDH1 gene in human ovarian carcinoma cells. This proximal promoter region contains overlapping binding sites for the following transcription factors; Sp1, CP1, C/EBP as well as USF. Further results from site-directed mutageneis indicated that C/EBP may be involved in the basal transcription levels of DDH1 gene in ovarian cancer cells (2008).

CCAAT/enhancer binding proteins (C/EBPs) are a family of transcription factors involved in regulation of cellular differentiation and proliferation, control of apoptosis and inflammatory process. The six different members of the C/EBP family are C/EBPα, C/EBPβ, C/EBPγ, C/EBPδ, C/EBPε and C/EBPζ. All six proteins share the conserved dimerization bZIP region at the C-terminus responsible for DNA binding. *In vitro* experiments and mouse knockout models have identified the importance of each of these specific TFs in various cellular processes. *This project aims to identify and decipher the role of specific C/EBP member(s) involved in regulating the transcription of DDH1 gene in ovarian cancer cells.* The results obtained herein will aid in our understanding of the role of C/EBPs involved in control of DDH1 gene expression.

Expected Research Outcomes and Benefits

Ovarian cancer is an important cause of death in women. Unfortunately, it is generally discovered late when the cancer has spread from the ovary to other parts of the body. This means that surgery, while important to remove most of the tumor, has to be followed by treatment with anticancer drugs. The side effects of the anti-cancer drugs are controlled to a certain extent by enzymes (that metabolize the drug) synthesized in the host. These enzymes act upon the anticancer drug and control the associated toxicity. In cases of cancer cells developing resistance to anticancer drugs an increased production of ezymes metabolising the drug has been observed. We have recently demonstrated in a series of human cancer cell lines that the protein Dihydrodiol Dehydrogenase (DDH) produces resistance to platinum drug based chemotherapy. In order to identify the mechanisms that control the expression of DDH in human ovarian tumor cells we have characterized the DDH1 gene promoter region. This has led to the identification of the several potential transcriptional elements that may be invovled in upregulating DDH1 expression in drug-resistant human ovarian carcinoma. This project is aimed at characterizing the C/EBP transcription factor that will influence the expression of DDH1 in ovarian cancer cells.

Summary of Research Completed

Analysis of constitutive and cisplatin- induced differential expression of CCAAT enhancer binding protein (C/EBP) isoforms in human ovarian carcinoma cells 2008 (cisplatin-sensitive) and 2008/C13 (-resistant)*:

In order to analyze the differential expression of C/EBP isoforms (alpha (α), beta (β), delta (δ), gamma (γ) and zeta (ζ)), ovarian cancer cells 2008 and 2008/C13* were seeded at a density of $1x10^6$ cells in a 100mm dish 24 h before isolation of RNA using RNAzolB as described by Deng *et al*. In the case of treatment, cells were exposed to 10μM concentration of cisplatin for an additional 16-18h and RNA was isolated. One microgram of the RNA was to be utilized to generate cDNA using the Omniscript RT kit (Qiagen) as detailed by the manufacturer. Ten percent of the RT product was to be utilized for C/EBPs real-time PCR analysis with primers specific for C/EBPα, C/EBPβ, C/EBPδ, C/EBPγ and C/EBPζ (GADD153) (Table 1). The expression of C/EBPs were normalized relative to GAPDH gene expression.

The results clearly indicated that there were no significant changes in the basal expression levels of C/EBP isoforms in the cisplatin-sensitive (2008) and –resistant (2008/C13*) human ovarian carcinoma cells (Table 2). In contrast there was an 8-fold increase in the expression levels of C/EBPζ (GADD153) isoform in cisplatin treatment 2008 cells, whereas there was a two fold decrease in C/EBPζ in the case of 2008/C13* cells treated with cisplatin. Further it was identified that on treatment with cisplatin there was no significant change in the expression levels of other C/EBP isoforms in cisplatin-sensitive (2008) and –resistant (2008/C13*) human ovarian carcinoma cells (Table 2).

In-vitro binding of NF-Y and C/EBP to the DDH1 proximal promoter region:
Based on previous observations from site-directed mutagenesis, it was clearly identified that the tandem of transcription factor binding sites for NF-Y and C/EBP was critical in regulating the transcription of DDH1 proximal promoter in human ovarian carcinoma cells (2008 & 2008/C13*). In order to further substantiate the observations, electrophoretic shift assay (EMSA) was performed with nuclear extracts obtained from 2008 and 2008/C13* cells. The region between -120/-91 of the DDH1 gene promoter was utilized as the wild-type probe, along with NF-Y and C/EBP transcription factor consensus sequences. Results from EMSA clearly demonstrated that NF-Y is essential in regulating the basal transcription of DDH1 by binding to the -120 to -91 region of the DDH1 gene promoter, while C/EBP did not have any functional role. These results led us to concentrate on the functional role of NF-Y in regulating the transcription of DDH1 gene promoter.

To corroborate the results from EMSA, gel super-shift was performed. For the gel super-shift assay, following the incubation of the nuclear extracts with the 30bp WT DDH1 promoter fragment for 30 min, 2μg of NF-YA polyclonal antibody, 2μg of NF-YB polyclonal antibody and/or the three polyclonal antibodies (anti-NF-YA, -NF-YB and -NF-YC) (Santa Cruz Biotechnology, Santa Cruz, CA) were added to the binding reaction and the mixture incubated at for an additional 1h. The rabbit pre-immune IgG (Santa Cruz Biotechnology, Santa Cruz, CA) was utilized as negative control in the super-shift assay. The mixture was fractionated on a 5% nondenaturing polyacrylamide gel. Transfer and detection was performed utilizing chemiluminescence with charge-coupled device.

Our results indicated that in the presence of NF-YA or NF-YB or NF-Y (A, B and C)

antibodies, there was a shift in the protein-DNA complex from the nuclear extracts obtained from the cisplatin-sensitive (2008) and –resistant (2008/C13*) human ovarian carcinoma cells (Fig 1). These results confirm the *invitro* binding of transcription factor NF-Y to the -120/-91 region of DDH1 gene promoter.

Functional analysis of NF-Y in regulating the transcription of DDH1 gene:
To assess the effect of overexpression of NF-Y in regulating the DDH1 mRNA expression levels, 2008 (human ovarian carcinoma cells) were transiently transfected with 1µg of NF-YA, -YB and -YC cDNA expression vector or pCMV vector as negative control using lipofectamine 2000. After 24h, RNA was isolated from cells using Trizol (Invitrogen, CA) and used in the reverse transcription reaction and RT-PCR was performed.

Alternatively, the 2008 cells were transiently transfected with 500 picomoles of human NF-YA siRNA (siGENOME smart pool, Dharamacon, IL) or the control si-RNA (siGENOME Non-targeting siRNA pool#1, Dharamacon, IL). Transfection was performed utilizing siPORT NeoFX transfection reagent (Ambion, CA). RNA was isolated 24h after transfection using Trizol reagent (Invitrogen, CA) as instructed by the manufacturer. One microgram of the RNA was used in the reverse transcription reaction and RT-PCR was performed
Ectopic expression of NF-YA, -B and -YC also led to a 2-fold increase in DDH1 mRNA levels in 2008 human ovarian carcinoma cells (Fig 2A) compared to the pCMV control vector transfected cells. Furthermore, when 2008 cells were transfected with si-RNA directed against NF-YA, a 4-fold decrease in DDH1 mRNA expression levels was observed compared to control si-RNA (Fig 2B). Taken together these results confirm a direct role of NF-Y in regulating the basal transcription of DDH1 gene in human ovarian carcinoma cells.

Table 1 List of primers utilized for amplification of the gene(s) of interest by quantitative real-time RT-PCR assay

Gene	*Forward*	*Reverse*	*Annealing temperature*
GAPDH	5’-acccactcctccacctttg-3’	5’-ctcttgtgctcttgctggg-3’	55ºC
CEBPA	5’-gtccagaccctccaggtagt-3’	5’-gggaccaactgtatttgct-3’	58ºC
CEBPB	5’-tgaattgctgggttaccaaa-3’	5’-taggcatgagacccccata-3’	58ºC
CEBPD	5’-cccccgccatgtacgacgacgaga-3’	5’-gccgcccgcttgtgattgctgtt-3’	55ºC
CEBPG	5’-atggcgacaatgcaggacagtaga-3’	5’-gatcccagaaaatagcctccaatg-3’	55ºC
CEBPZ	5’-ggagctggaagcctggtatg -3’	5’-gctctgggaggtgcttgt-3’	55ºC

GAPDH- Glyceraldehyde-6-phosphate dehydrogenase; CEBPA- CCAAT enhancer binding protein alpha; CEBPB- CCAAT enhancer binding protein beta; CEBPD- CCAAT enhancer binding protein delta; CEBPG- CCAAT enhancer binding protein gamma; CEBPZ- CCAAT enhancer binding protein zeta. The PCR was performed with an initial denaturation at 95°C for 15 mins, followed by 45 cycles of 94°C for 15 s, annealing for 30s and extension at 72°C for 30s with a final melting curve analysis.

Table 2 Differential expression of C/EBP isoforms in human ovarian carcinoma cells (2008, 2008/C13*)

Genes	*2008 Ct values*	*2008T Ct values*	*2008/C13* Ct values*	*2008/C13*T Ct values*	***Fold difference between 2008T and 2008***	***Fold different between C13 and 2008***	***Fold difference between C13T and C13***
GAPDH	16.0±0.7	16.4±0.2	17.1±0.7	16.7±0.5	-	-	-
C/EBPα	26.0±0.6	25.3±1.0	28.0±1.2	26.2±1.8	**2.1**	**0.5**	**2.8**
C/EBPβ	22.7±0.9	21.9±0.1	23.7±0.7	23.0±1.6	**2.3**	**1.1**	**1.2**
C/EBPδ	25.9±0.7	26.7±0.8	26.3±0.6	25.6±1.2	**0.7**	**1.6**	**1.2**
C/EBPγ	22.8±0.5	22.6±1.5	23.4±1.7	23.3±1.9	**1.5**	**1.4**	**0.8**
C/EBPζ or GADD 153	26.3±0.5	23.7±1.1	27.0±0.6	27.5±0.4	**8.0**	**1.3**	**0.5**

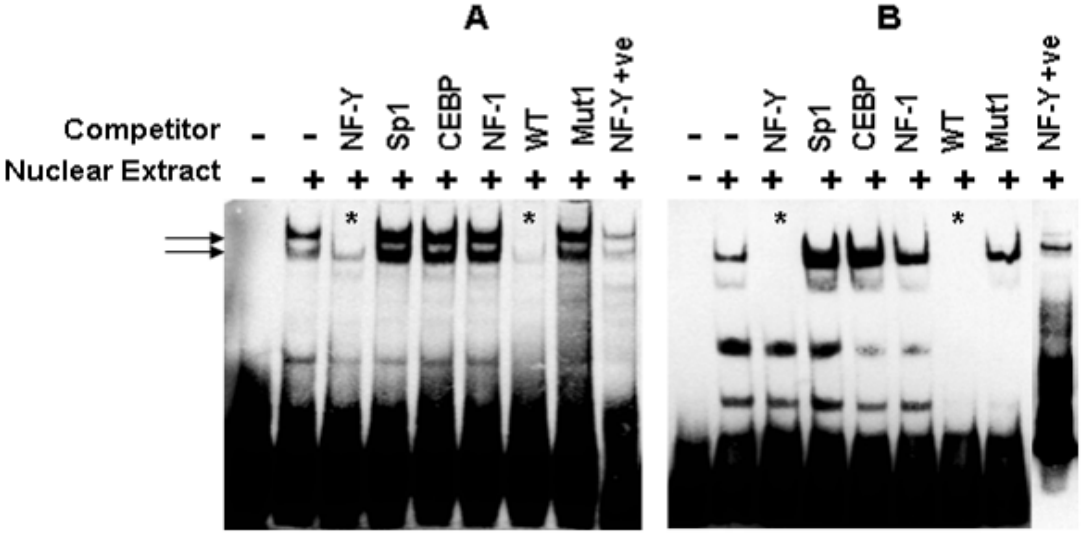

Figure 1. Confirmation of NF-Y binding to the proximal promoter region of the AKR1C1 gene. NF-Y is composed of three subunits NF-YA, NF-YB and NF-YC that are required for interaction with the CCAAT pentanucleotide sequence in the AKR1C1 gene promoter. Nuclear extracts (8μg) from (A) 2008, (B) 2008/C13*, were incubated with WT probe (-120 to -91) from DDH1 gene along with 2μg of polyclonal antibody directed towards NF-YA, NF-YB or NF-Y(NF-YA+NF-YB+NF-YC). The negative control consisted of rabbit pre-immune control IgG (C-IgG). The formation of DNA-protein complexes is designated by solid arrows and the loss of protein-DNA complex's and/or gel super-shift in the presence of the antibody is denoted by an asterisk. Each of the experiments was repeated at least three times with similar results.

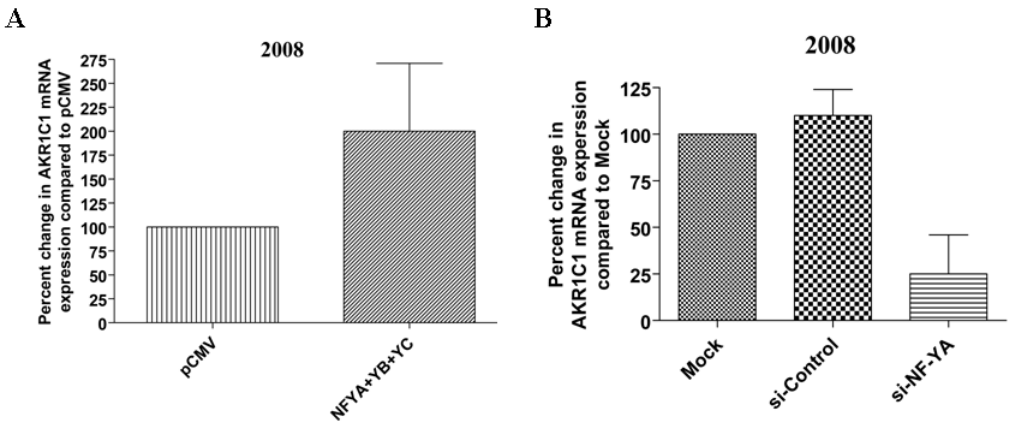

Figure 2. Functional analysis of NF-Y in regulating the transcription of human AKR1C1 in human ovarian, lung and liver carcinoma cells. (A) 1μg of NF-YA, -YB and -YC cDNA expression vector or pCMV control vector and **(B)** Five hundred picomoles of NF-YA siRNA or siRNA-scramble as the negative control. Twenty four hours after transfection RNA was isolated and the expression of AKR1C1 mRNA was assayed using real-time RT-PCR. Each experiment was performed in duplicates and repeated at least two times.

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

_____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, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

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.None				☐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.

None.

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.

None.

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	POSITION TITLE
Hemant K. Parekh	Professor
eRA COMMONS USER NAME Hparekh	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Bombay University, India	B.Sc	1986	Biochemist/Microbiology
Bombay University, India	M.Sc	1988	Biochemistry
Bombay University, India	Ph.D.	1990	Biochemistry
Univ. of Minnesota, Minneapolis, MN	Postdoc	1993	Drug resistance
Temple University, Philadelphia, PA	Postdoc	1996	Drug resistance

Postdoctoral Research Associate, Dept. of Pharmacology, University of Minnesota, 1991 - 1993. Dr. Parekh joined the Dept. in Feb. 1991. He purified the aldo-keto reductase family of enzymes and assessed their ability to catalyze reduction of aldophosphamide, the penultimate metabolite of the anticancer drug cyclophosphamide.
Postdoctoral Research Associate, Department of Pathology & Laboratory Medicine, Temple University, 1993 – 1996. Dr. Parekh joined the Dept. in Jan. 1993. He was involved in the characterization of resistance mechanisms of the anticancer drug, taxol and cisplatin.
Research Assistant Professor, Department of Pathology & Laboratory Medicine, Temple University, March 1996 - November 1997.
Assistant Professor, Department of Pathology & Laboratory Medicine, Temple University, December 1997 – June 2001.
Associate Professor, Department of Pathology & Laboratory Medicine, Temple University, July 2001 – June 2009.
Professor, Department of Pathology & Laboratory Medicine, Temple University, July 2009 – present.
Director, Molecular Pathology Laboratory, Department of Pathology and Laboratory Medicine, Temple University, July 1997 – present

Honors and Awards:
Junior Research Fellowship - Cancer Research Institute, Bombay, India. 1986-1988.
Senior Research Fellowship - Cancer Research Institute, Bombay, India. 1988-1990.
American Cancer Society Institutional Research Grant # 204, 01/01/96 - 12/31/96.
ACADEMIC HONORS AND AWARDS
R. K. Anjaria Award - 1st rank in Seth G.S. Medical College. M.Sc. (Biochemistry), 1986.
Special Certificate - 3rd rank in Bombay University. M.Sc.(Biochemistry), 1986.
Junior Research Fellowship - Cancer Research Institute, Bombay, India. 1986-1988.
Senior Research Fellowship - Cancer Research Institute, Bombay, India. 1988-1990.

Publications (FROM A TOTAL OF 35):

1. Hemant Parekh and Henry Simpkins. The differential expression of cytokeratin 18 in cisplatin-sensitive and -resistant human ovarian adenocarcinoma cells and its association with drug sensitivity. *Cancer Research, 55: 5203, 1995.*
2. Hemant Parekh and Henry Simpkins. Species-specific differences in taxol transport and its cytotoxicity against human and rodent cells. *Biochemical Pharmacology, 51: 301, 1996.*
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