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:** Thomas Jefferson University

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):** Theodore F. Taraschi, Ph.D.

4. **Grant Contact Person's Telephone Number:** 215-955-3900

5. **Grant SAP Number:** 4100047652

6. **Project Number and Title of Research Project:** 4 – Targeting the IGF-1 Receptor in Cancer

7. **Start and End Date of Research Project:** 1/1/2009 - 06/30/2012

8. **Name of Principal Investigator for the Research Project:** Renato Baserga, 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:

   $ $309,670.29

   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
Baserga	Professor	10% Yr 1,2,3	$49,899.16
De Angelis	Research Assistant 1	50% Yr 1,2; 100% Yr 3	$98,628.67
LaRocca	Post Doc Fellow	50% Yr 1,2	$31,906.85

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
None		

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:_)		$	$

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?

Principal Investigator retired.

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 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.

This project proposes to determine conditions which will maximize the therapeutic effect of antibodies to the insulin growth factor I (IGF-I) receptor (a receptor for a growth factor) in cancerous tumors. Many cancers (including lung, colon and breast cancers), have already shown susceptibility to this treatment, and these antibodies are currently being used in clinical trials. Clinicians are now anxious to know which human tumors are most sensitive to the antibodies to the IGF-I receptor. There are intra- and extra-cellular factors that condition

the response of tumor cells to treatment and the purpose of this project is to identify these conditions.

Specific Aim # 1: IRS-1 Acetylation and its Effect on IRS-1 Function. This aim focuses on the IGF-1 receptor (IGF-IR) and its docking protein, insulin receptor substrate I (IRS-1), and their role in colon cancer. The hypothesis is that IRS-1 is the key molecule in the role of the IGF-IR in cancer, and could possibly be a biomarker for sensitivity of colon cancer cells to antibodies to the IGF-IR.

Specific Aim # 2: Role of IRS-1 in oncogenesis and its relationship to the EGFR. A problem that confronts clinicians when using antibodies to growth factor receptors in cancer therapy is the ability to identify tumors that are particularly sensitive to targeting. This project will focus on why certain tumors become resistant to therapy with receptor antibodies. This is well illustrated in antibodies to the epidermal growth factor receptor (EGFR) that are currently used in clinical practice. This aim will study the problem of resistance to therapy in breast and lung cancer cells, based on the hypothesis that IRS-1 plays a major role in resistance. In addition, we will study the role of Stat proteins in cancer in relation to the interaction with IRS-1.

The objectives were accomplished using mass spectrometry, and molecular and cell biology methodologies with which this laboratory has over 20 years of experience. Levels of IRS-1 can be modulated by down-regulating it or by increasing it through ectopic expression. The outcome of this project is to provide new criteria for the treatment of human cancer with antibodies to the IGF-I receptor. The ongoing clinical trials have indicated that antibodies against the IGF-I receptor are effective against various forms of cancer, and Phase II clinical trials are now being carried out at several institutions in cancers of the lung, breast, and colon, brain tumors and bone sarcomas. No cancer treatment is effective against all forms of cancer, and resistance to treatment is unfortunately a frequent outcome with almost all therapies. The benefits of this research will allow clinicians to apply the specific therapy that will yield the best results when using antibodies to the IGF-IR. The project will also define the mechanisms of resistance of cancer cells to therapeutic interventions. This is an exquisitely translational research project, with basic science exploring modalities to be directly applied in clinical venues.

IRS-1 was targeted with microRNA 145, which was previously shown to down-regulate IRS-1 (but not IRS-2), and the IGF-I receptor by binding to the 3'UTR of their mRNAs. miR145 has been proposed as a tumor suppressor. We found that an IRS-1 lacking its 3'UTR is no longer down-regulated by miR145, and rescues colon cancer cells from miR145-induced inhibition of growth. An IGF-IR resistant to miR145 (again by elimination of its 3'UTR) is not down-regulated by miR145, but fails to rescue colon cancer cells from growth inhibition.

These results indicate that down-regulation of IRS-1 plays a significant role in the tumor suppressor activity of miR145. It also indicates that all-trans retinoic acid (ATRA) stops the growth of mammary cancer cells, and that the inhibition is tied to the down-regulation of IRS-1 (but not IRS-2). This suggests that ATRA may act on cell growth through miR145, that also down-regulates IRS-1 but not IRS-2. This hypothesis is now the focus of this project.

We have also tried (in collaboration with Andrew Quong, PhD of this institution), to determine the IRS-1 residues acetylated. We have been able to determine that the acetylated residues are in the first 300 amino-acids of IRS-1, but more precise determinations were not conclusive at this point.

The research focused on optimizing the treatment of human cancers by the targeting of the insulin-like growth factor receptor-1 (IGF-IR). Our approach has followed two different avenues of investigation. The first approach has been to study how the IGF-IR relates to other oncogenes and tumor suppressors. We have shown that the insulin receptor substrate-1 (IRS-1), a docking protein for the IGF-IR, interacts directly (demonstrated by immuno-precipitation) with the oncogene c-met, the receptor for hepatocyte growth factor (HGF). IRS-1 and c-met do not only interact, but they de-stabilize each other. When IRS-1 is highly expressed, c-met is down-regulated, and when c-met is highly expressed, IRS-1 is down-regulated.

This surprising finding (two oncogenes down-regulating each other) has an important implication. c-met promotes motility (its ligand HGF was originally described as scatter factor for its ability to increase cell motility), while IRS-1 is known to inhibit motility. This finding may explain a paradox of IRS-1 expression. The literature shows unambiguously that IRS-1 is strongly mitogenic, anti-differentiating and anti-apoptotic. Yet, IRS-1 levels are often decreased, not in primary cancers, but in metastatic cancers. We and others, aware of the fact that IRS-1 inhibits cell motility, proposed that IRS-1 is decreased in metastatic human cancers (especially breast cancer metastases) because cells need motility to metastasize. The decrease in IRS-1 expression would be compensated by an increase in the oncogene c-met.

These results could have an immediate impact on future approaches to therapy. In the absence of IRS-1, the IGF-IR sends a differentiation signal; only when IRS-1 is well expressed, the IGF-IR sends a mitogenic, transforming signal. Targeting the IGF-IR in metastatic tumors (where IRS-1 is decreased or absent) could actually have an adverse effect, because it would attenuate the pro-differentiation signal originating from the IGF-IR. Our finding, available on line at the web site of the Journal of Cellular Physiology, was well documented, thanks to the wealth of cell lines and reagents we have accumulated in the more than 20 years we have dedicated to the study of the role of the IGF-IR in cancer. We have used as controls cells that do not express IRS-1 or c-met, or the IGF-IR, and the result is a solid result. The 2nd implication of this finding is more theoretical. Why would 2 oncogenes antagonize each other? We are pursuing an answer to this question and a clue may be found in another result we have obtained.

This second result has been the product of our collaboration with the laboratory of Dr. Richard Pestell, of the Kimmel Cancer Center, where they have shown repeatedly that DACH1 acts as a tumor suppressor in breast and prostate cells. DACH1 is the human homologous of Dachsund, a Drosophila gene required for the development of eye and limb. Clinical and experimental evidence have established DACH1 as a tumor suppressor, and we became interested in the possible role that the IGF-IR may have on DACH1 expression. Somewhat surprisingly, we have found that IGF-1 actually increases the expression of DACH1, under conditions in which IGF-1 is mitogenic. In this case, instead of two oncogenes antagonizing each other, we may have 2 growth factors antagonizing each other. We are actively pursuing this paradoxical finding.

Finally, we have continued our studies on microRNA 145, a tumor suppressor microRNA (miR) that targets the IGF-IR and IRS-1. We have discovered an unusual aspect of miR145 by isolating a genomic clone that, transfected into cells, expresses a mature miR145. The clone has two highly conserved sequences (from armadillo to man), one on the 5' side of the pre-miR sequence, the other on the 3' side of the pre-miR sequence. When the highly conserved sequence on the 3' side of the pre-miR is deleted, mature miR145 expression is abrogated. Deletion of the highly conserved sequence on the 5' side has no effect. Although this is an unabashedly basic science finding, one should remember tat miRs are now becoming possible players in a clinical setting. Previous research has shown that an injected tumor suppressor miR actually inhibited tumor growth in a xenotransplant in mice. In addition, miRs can now be detected in human plasma, and a recent publication has shown an increase in plasma levels of a specific miR in human prostate cancer cases. miR145 is an established tumor suppressor and may play a significant role in human cancers.

This project showed the crucial importance of IRS-1 on the growth of colon cancer cells. This project targeted IRS-1 with microRNA 145, which was previously shown to down-regulate IRS-1 (but not IRS-2), and the IGF-I receptor by binding to the 3'UTR of their mRNAs. miR145 has been proposed as a tumor suppressor. It was found that an IRS-1 lacking its 3'UTR is no longer down-regulated by miR145 and rescues colon cancer cells from miR145-induced inhibition of growth. An IGF-IR resistant to miR145 (again by elimination of its 3'UTR) is not down-regulated by miR145, but fails to rescue colon cancer cells from growth inhibition. These results indicate that down-regulation of IRS-1 plays a significant role in the tumor suppressor activity of miR145. This project also found that all-trans retinoic acid (ATRA) stops the growth of mammary cancer cells, and that the inhibition is tied to the down-regulation of IRS-1 (but, not IRS-2). This suggests that ATRA may act on cell growth through miR145, that also down-regulates IRS-1 but not IRS-2. This hypothesis is now being tested

Finally, this project investigated the relationship of the IGF-IR signaling pathway to DACH1, a tumor suppressor of breast cancer cells. The mammalian homologue of the Drosophila dachshund gene (DACH1) has been reported as a tumor suppressor in human breast and prostate cancers. It down-regulates the epidermal growth factor receptor (EGFR) and cyclin D1. The signaling pathway of the type 1 insulin-like growth factor receptor (IGF-IR) is known to be responsible for the development of resistance to treatment of human cancer with antibodies to the EGFR. This project investigated whether DACH1 still exerts its tumor suppressor activity in cells dependent on the IGF-IR for growth. The findings were that in cells growing in IGF-1 (and unresponsive to EGF), DACH1 is devoid of tumor suppressor activity.

The Drosophila dachsund (dac) gene is the founding member of the DACH subfamily encoding a nuclear protein essential for the development of Drosophila eye, limb and brain. The DACH1 protein of mammalian cells is decreased in human breast cancer compared to normal mammary gland. Analysis of over 2,000 human breast cancer samples showed an inverse correlation between levels of nuclear DACH1 expression and mitotic index and predicted survival. DACH1 levels are also decreased in prostate cancer and its ectopic expression inhibits prostate cancer cells proliferation in xenotransplants. Over-expression of DACH1 down-regulates both the EGFR and cyclin D1 levels; confirming its role as a growth inhibitor. DACH1 is considered a tumor suppressor.

The implications of these findings, although of a negative nature, are actually of considerable interest. The evidence is clear that nuclear DACH1 is down-regulated in human breast cancers, and its role as a tumor suppressor has been confirmed experimentally in breast and prostate cancers, both of epithelial origin. There is scattering in nuclear DACH1 levels in specimen of human breast cancer, and it is a legitimate question to ask how these cells manage to grow in the presence of normal levels of a tumor suppressor. For a number of years, investigators had noted that development of cancer cells resistance to EGFR targeting involved activation of the IGF-IR (see for instance Chakravarti et al. with many references). Sharma et al. went further and claimed that IGF-IR signaling is responsible for the development of drug-resistance in subpopulations of cancer cells in a more general way, including resistance to antibodies to the EGFR and chemotherapeutic agents.

In addition, a number of observations have shown that cancer cells switch to other growth factors when a growth factor receptor is targeted, for instance with an antibody. It has been known for some time that there is a cross talk between the IGF-IR and EGFR, and since then, numerous reports have appeared showing that the IGF-IR signaling pathway is often responsible for the development of resistance to treatment with antibodies to the EGFR. Since the IGF-IR is often antagonist to EGFR targeting, this project investigated whether in the case of DACH1, the IGF-IR also acted by evading the tumor suppressor activity in those cells with normal DACH1 levels. Our results show that the IGF-IR is independent of DACH1 action and that cells growing in IGF-1 are not subject to inhibition by DACH1.

This project proposed that the IGF-IR may provide the growth factor necessary to evade the tumor suppressor activity of DACH1. In addition, it was proposed that in mammary cancer cells where DACH1 is not down-regulated, or very little, cells may grow because they express substantial amounts of IGF-IR and respond to growth through IGF1. Our prediction is that cancer cells with normal levels of DACH1 will be found to express substantial levels of IGF-IR and/or IRS-1, its docking protein that sends a strong proliferative, anti-differentiation and transformation signal.

We have completed this year an investigation with Tiziana DeAngelis and Andrew Quong on growth factors present in the serum-free conditioned media of v-src transformed cells. v-src-transformed cells grow in serum-free medium, presumably because they secrete some growth factors that allow them to grow. We repeated experiments of 1997, and reproduced the observation that v-src transformed cells grow in serum-free medium. By mass spectrometry, followed by western blots and ELISAs, we have confirmed the presence in the conditioned media of osteopontin. We have also shown that addition of osteopontin make non-v-src transformed cells grow and that an addition to media of an antibody to osteopontin inhibits growth. These findings, repeated in 2 different cell lines, are now in preparation for publication in scientific journals.

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 **BASERGA, Renato** eRA COMMONS USER ID: **RXB008**	POSITION TITLE **PROFESSOR**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Liceo Gonzaga, Milan, Italy		1943	
Faculty of Medicine, Univ. of Milan Medicine	M.D.	1949	MEDICINE

A. PROFESSIONAL EXPERIENCE

11/2005-present Distinguished Professor, Department of Cancer Biology, Kimmel Cancer Center, Thomas Jefferson University
10/2004-11/2005 Interim Director, Thomas Jefferson University, Kimmel Cancer Center
1991-Pres. Distinguished Professor Micro./Immun., Thomas Jefferson Univ., Deputy Director, Kimmel Cancer Center
1980-1991 Professor and Chairman of Pathology, Temple University School of Medicine
1968-1973 Professor and Chairman of Pathology, Temple University School of Medicine
1965-1991 Professor of Pathology, Temple University School of Medicine
1965-1991 Senior Investigator, Fels Research Inst., Temple Univ. School of Medicine
1964-1965 Associate Professor in Pathology, Northwestern Univ. Med. School
1960-1964 Assistant Professor in Pathology, Northwestern Univ. Med. School
1959-1965 Consultant, Argonne National Laboratory
1958-1960 Instructor in Pathology, Northwestern University Medical School

Editorial Board Assignments

Laboratory Investigation, Experimental and Molecular Pathology, Cancer Research, Journal of Cellular Physiology, Experimental Cell Research, Molecular and Cellular Biology, Journal of Biological Chemistry,Cell Proliferation

Honors and Awards

1976 Searle Lectureship of the British Society for Cell Biology
1984 Welcome Visiting Professorship in Cell Biology
1984 Frontiers of Science Lectureship, Case-Western University
1988 Samuel Noble Foundation Research Award, Ardmore, OK
1990 Rous-Whipple Award, Am. Assoc. of Pathologists.
1990 Fred. W. Stewart Award, Memorial Sloan Kettering Cancer Center.
1993 Susan Swerling Lecture-Dana-Farber Cancer Institute, Harvard Medical School

B. SELECTED LATEST PUBLICATIONS (out of 430)

1. Prisco, M., Santini, Francesca, Baffa, Raffaele, Liu, M., Drakas, Robert, Wu, A. and Baserga, R. Nuclear translocation of IRS-1 by the SV40 T antigen and the activated IGF-I Receptor. JBC 277:32078-32085, 2002.
2. Tu, X., Batta, P., Innocent, N., Prisco, M., Casaburi, I., Belletti, B. and Baserga, R. Nuclear Translocation of Insulin Receptor Substrate-1 by Oncogenes and IGF-I: Effect on Ribosomal RNA Synthesis. JBC 277:44357-44365, 2002.
3. Sun, H-Z, Tu, X., Wu, A., Prisco, M., Casaburi, I., and Baserga, R. IGF-I Receptor Signaling and Nuclear Translocation of Insulin Receptor Substrates-1 and 2. Molecular Endocrinology, 17:472-486, 2003.

4. Tu, X, Baffa, R, Luke, S, Prisco, M, and Baserga, R. Intracellular Redistribution of Nuclear and Nucleolar Proteins during Differentiation of 32D Murine Hemopoietic Cells. Experimental Cell Research, 288:119-130, 2003.
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C. RESEARCH SUPPORT

Ongoing:

none