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):** 1/1/2009 – 12/31/2012

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Germaine A 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:** 14 - Small Animal Model of Medulloblastoma for Translational MR Neuroimaging at 3 Tesla

7. **Start and End Date of Research Project:** 07/01/2009 – 7/31/2010

8. **Name of Principal Investigator for the Research Project:** Kamel Khalili, Ph.D.

9. **Research Project Expenses**.

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

   $ 51,719.90

   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
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	Position Title	% of Effort on Project
Khalili	PI	<1%
Gordon	Co-PI	<1%

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
digital imaging software, camera, and data workstation	microscopic analysis of experimental tissue samples, photodocumentation, archiving and preparation of images for publication	$ 51,719.90

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____X_____ No_____

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:
Comprehensive NeuroAIDS Core Center	X NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	01/2011	$8,428,771	$8,342,445

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:

We will seek additional funding from NIH for this project.

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

We will continue our investigations on neuroimaging of brain tumor and neurodenerative disease models to determine the molecular mechanisms involved in disease progression and new methods for non-invasive diagnosis and therapeutic delivery.

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____X_____ No_____

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

This project has allowed us to provide state-of-the-art imaging capabilities to our research team and has enabled us to secure NIH funding for related projects.

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 application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. 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. Acquisition, installation, and testing of the equipment and integrated accessories, imaging system software and hardware.

2. MR imaging of transgenic mouse model of medulloblastoma.
T-antigen transgenic mice which spontaneously develop brain tumors will be imaged at high field strength. We will perform initial studies to determine the optimal MR imaging and post-processing parameters, and perform histopathological validation of acquired images.

Medulloblastomas and primitive neuroectodermal tumors (PNETs) are highly cellular malignant primary brain tumors representing the most common solid tumors arising in children. The major limitations of the current state of the art clinical Magnetic Resonance Imaging and Spectroscopy to diagnose this disease include the inability to clearly define the parenchymal interface between normal and tumor regions; to differentiate tumoral edema from infiltration; to diagnose small primary or metastatic lesions; and to differentiate medulloblastomas or PNETs from other primary central nervous system (CNS) neoplasm.

Currently, to our knowledge, realistic animal models to study these medulloblastoma tumors are lacking. It is therefore necessary to develop and study the imaging characteristics of these CNS tumors using spontaneous brain tumor animal models that mimic human disease, as well as develop image processing tools to quantitatively analyze these tumors to improve diagnostic accuracy. Spontaneous tumor models in mice are generally thought to be more realistic models of human cancer than xenografts, and the lesions these animals develop present special challenges for imaging.

We are utilzing high field Magnetic Resonance (MR) imaging to develop optimal characteristics to image these spontaneous CNS tumors. Quantitative methods for tissue segmentation based on fuzzy connectedness and medical image data mining techniques are being developed and tested to analyze these tumors. The imaging and image post processing methods will be validated using histological staining and immunohistochemistry for the transgene T-antigen, the viral oncoprotein expressed in these tumors.

Drs. Khalili, Faro, Gordon, and Mohamed have a long-standing collaboration on in vivo imaging of JCV-induced brain tumors. Recently, we have focused our efforts on developing MR imaging protocols to optimize imaging parameters for the CNS using the spontaneous JCV T-antigen transgenic medulloblastoma mouse model. MRI scans were performed at field strength of 7 Tesla, with a Bruker DRX300 console and micro-imaging accessory. Experiments are now performed on a state-of-the-art 3 Tesla MRI available in house. Pilot scans in the axial, sagittal, and coronal orientations are performed to choose imaging sections to cover the whole brain. Based on these scans an internal anatomic landmark in the mouse brain (Bregma –2) is then used to prescribe axial slices perpendicular to this landmark and covering the whole brain. After the scanning, animals are euthanized, tissue harvested, and the images are transferred to the MR Physics laboratory for post-processing. The images are initially converted into a generic format for compatibility with the software used for visualization and analysis. The BioImaging Suite developed at Yale University is often used for visual inspection of the images. A

neuroradiologist reviews all the MR images and characterizes the normal and tumor areas of the mouse brain images. This is primarily based on the signal characteristics of the tumor visualization on various imaging sequences used (T2, pre, and post T1), as well as morphological characteristics of the normal and abnormal structures in the mouse brain. MR imaging results are then correlated with the histological findings imaged using the digital imaging software equipment obtained through this project. Co-registration of the MR images with regions of fixed brain tissue is then performed for validation of the radiological findings based on histogical data.

Progress related to Specific Aims

Specific Aim 1. Acquisition, installation, and testing of the equipment and integrated accessories, imaging system software and hardware.
During the project period, the equipment was selected, confirmation of integration with existing microscopy equipment was verified and the equipment was purchased and installed.

Specific Aim 2: MR imaging of transgenic mouse model of medulloblastoma.
Tissues from T-antigen induced brain tumors were imaged. We performed histopathological validation of the acquired images.

Summary of Research Findings

We determined that T-antigen is downregulated by glucose deprivation in ex vivo tumor slice cultures. JCV T-antigen is a potent oncogenic protein that can interact with a variety of cellular proteins to promote tumorigenesis. In light of our findings of T-antigen downregulation by glucose deprivation, we examined the metabolic regulation of T-antigen in a semi-*in vivo* system. For these studies, we used an *ex vivo* tumor slice culture model with HJC-2 glioblastoma xenografts implanted into the brains of nude mice. Following tumor growth, brain slices containing tumor were prepared and were then grown *in vitro*. Tumor slice cultures were then exposed to various time-courses of glucose deprivation or rescue in normal medium before harvesting for western blot or immunohistochemical analysis. To reinforce our previous findings, we found that T-antigen is downregulated by 1 hour and 8 hours of glucose deprivation only appreciably after 24 hours of rescue in normal medium (1 g/L D-glucose) . We were also able to identify reduction in T-antigen expression in HJC-2 tumor tissue exposed to 1 hour and 8 hours glucose deprivation plus rescue. The changing pattern of T-antigen expression during the time course of GD and rescue paradigm suggests that mechanisms controlling the regulation of T-antigen expression may have alternative long-term and short-term effects and understanding these effects will require further study. These data indicate that T-antigen is also downregulated by glucose deprivation within tumor tissue and may provide useful information to develop strategies against T-antigen-positive brain tumors.

In parallel, we examined human brain tumor samples for the presence of T-antigen and two critical tumor suppressor proteins, p53 and NF2 to determine whether they interact in human glioblastomas. NF2, T-antigen, and p53 were previously shown to form a ternary complex in T-antigen positive tumors derived from JCV T-antigen transgenic mice. Yet, it has not been determined if these proteins interact in human tumors or if NF2 and p53 can bind together in the absence of T-antigen. To this end, Co-IP assays were conducted using antibodies against both T-

antigen and Myc-tagged p53 (Myc-p53) in extracts from transfected U-87 MG glioblastoma cells. T-antigen was observed to bind to both NF2 and p53, individually and in complex. Interestingly, binding between NF2 and p53 independent of T-antigen was not observed, although there is mounting evidence of a tumor suppressive synergy that exists between them. We then assayed human high grade gliomas resected from patients for the presence of these proteins. Using immunoblotting of fresh tumor tissue, we observed the presence of significant levels of NF2 in three of four high grade glioma tumors analyzed while p53 levels were more variable . In addition, we detected T-antigen protein in one anaplastic oligodendroglioma (AO812B) and one grade IV glioblastoma (Gli1105). Interestingly, high levels of NF2 and p53 were detected in another glioblastoma sample (Gli906A) in the absence of T-antigen. Immunohistochemical analysis of parallel sections from one of the T-antigen positive samples (Gli1105) revealed a predominantly cytoplasmic pattern for NF2, while T-antigen and p53 were detected in the nuclei of a subset of tumor cells. NF2 is typically examined in tumor tissues at the gene level to screen for gene deletion, i.e. LOH or mutational inactivation. However, here we examine the role of the NF2 protein as a tumor suppressor, rather than its loss of function. We were able to detect NF2 by immunohistochemistry and Western blotting in Gli1105, and as shown in Figure 5C, varying levels of NF2 are seen in the tumor tissues including some with a more prominent upper band likely representing the phosphorylated form of the protein, suggesting that total levels, as well as phosphorylation status may affect its function in human tumors. Visualizing the interactive nature of these proteins in human samples provides us with a better understanding of the complex interplay among tumor suppressors and oncoproteins that shape glioblastoma growth.

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, listed in the table, in a PDF version 5.0.5 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____X_____ No_____

If yes, please describe your plans:

Manuscripts in preparation were not included in the above table. We plan to submit articles to peer-review journals for publication in the near future.

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

NAME: Kamel Khalili

POSITION TITLE: Professor and Chair Department of Neuroscience

eRA COMMONS USER NAME (credential, e.g., agency login): kkhalili

EDUCATION/TRAINING :

School of Medicine, Univ. of PA, Phila., PA	Ph.D.	1983	Microbiology
Wistar Institute, Phila., PA	Postdoc	1984	Molecular Biology
National Cancer Institute, Bethesda, MD	Postdoc	1987	Molecular Virology

A. PERSONAL STATEMENT

Describe why your expertise and qualifications make you particularly well-suited for your role in the project

Dr. Khalili has been actively studying the molecular biology and pathogenesis of brain tumors and diseases associated with neurotropic viruses including JCV and HIV-1 for more than twenty-five years. In this regard, he has unraveled a variety of host functions ranging from cytokine expression, cell cycle communication, activation of latent opportunistic pathogens, cell cycle dysregulation and DNA repair pathways. He has more than thirty years' experience working with oncogenic viruses, more specifically, SV40 (while at NCI in the late George Khoury's laboratory) and JCV since 1986 in his own laboratory and has uncovered several regulatory events that participate in the oncogenicity of JCV, developed unique experimental animal models using the JCV genome to investigate its tumorigenicity in vivo, and published in top ranked journals related to the association of JCV with human cancer. his experience and knowledge over the last three decades and the record of his accomplishments makes him a valuable asset as co-investigator on this project.

B. POSITIONS

1979-1980 Predoctoral Research Fellow, University of Pennsylvania, Philadelphia PA. Gene fusion strategy to study regulation of purin synthesis in E. coli. (Advisor: Joe Gotes)

1980-1983 Predoctoral Research Fellow, Wistar Institute, Philadelphia, PA. Regulation of human actin genes in adenovirus-infected Hela cells at transcriptional and post-translational stages. (Advisor: Roberto Weinmann)

1983-1984 Postdoctoral Research Fellow, Wistar Institute, Philadelphia, PA. Isolation and characterization of the genes encoding RNA-polymerase II in humans. (Advisor: Roberto Weinmann)

1984-1987 Postdoctoral Research Fellow, Laboratory of Molecular Virology, National Cancer Institute, National Institutes of Health, Bethesda, MD. Molecular Biology of DNA tumor viruses. Analysis of SV40 early gene transcription and translation. (Advisor: George Khoury)

1987-1991 Assistant Professor, Department of Biochemistry and Molecular Biology, Institute of Molecular Medicine, and Department of Microbiology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA.

1991-1995 Associate Professor, Department of Biochemistry and Molecular Biology, and Department of Microbiology and Immunology, Thomas Jefferson University, Philadelphia, PA.

1991-1996 Director, Molecular Neurovirology Section, Jefferson Institute of Molecular Medicine, Thomas Jefferson University, Philadelphia, PA.

1991-1996 Member, Jefferson Cancer Institute, Thomas Jefferson University, Philadelphia, PA.

1995-1996 Professor, Department of Biochemistry and Molecular Biology, and Department of Microbiology and Immunology, Thomas Jefferson University, Philadelphia, PA.

1996-1999 Founder and Director, Center for NeuroVirology and NeuroOncology, MCP Hahnemann University School of Medicine, Philadelphia, PA

1996-1999 Professor and Vice-Chairman for Research, Department of Neurology, MCP Hahnemann University School of Medicine, Philadelphia, PA

1994-Present Editor-in-Chief, Journal of Neurovirology (First Year, January 1995).

1999-2005 Founder and Director, Center for Neurovirology and Cancer Biology, Temple University, Philadelphia, PA.

1999-Present Professor (tenured), Department of Biology and Department of Microbiology Temple University, Philadelphia, PA.

2005-Present Professor (tenured) and Founding Chair, Department of Neuroscience and Director, Center for Neurovirology, Temple University School of Medicine, Philadelphia, PA

C. Selected Peer-reviewed publications (in chronological order from more than 374 publications).

Sariyer IK, Merabova N, Patel PK, Knezevic T, Rosati A, Turco MC, Khalili K. (2012) Bag3-induced autophagy is associated with degradation of JCV oncoprotein, T-Ag. *PLoS One* 7(9):e45000. PMID: 22984599.

Festa M, Del Valle L, Khalili K, Franco R, Scognamiglio G, Graziano V, De Laurenzi V, Turco MC, Rosati A. (2011) BAG3 protein is overexpressed in human glioblastoma and is a potential target for therapy. *Am JPathol.* 178(6):2504-12. PMID: 21561597.

Gentilella A, Khalili K. (2011) BAG3 expression in glioblastoma cells promotes accumulation of ubiquitinated clients in an Hsp70-dependent manner. *J Biol Chem.* 286(11):9205-15. PMID: 21233200.

Gentilella A, Khalili K. (2010) BAG3 expression is sustained by FGF2 in neural progenitor cells and impacts cell proliferation. *Cell Cycl.* 9(20):4245-7. PMID: 20962586.

Ammirante M, Rosati A, Arra C, Basile A, Falco A, Festa M, Pascale M, d'Avenia M, Marzullo L, Belisario MA, De Marco M, Barbieri A, Giudice A, Chiappetta G, Vuttariello E, Monaco M, Bonelli P, Salvatore G, Di Benedetto M, Deshmane SL, Khalili K, Turco MC, Leone A. IKK{gamma} protein is a target of BAG3 regulatory activity in human tumor growth. (2010) *Proc Natl Acad Sci U S A* 107(16):7497-502. PMID: 20368414.

Rom I, Darbinyan A, White MK, Rappaport J, Sawaya BE, Amini S, Khalili K. (2010) Activation of HIV-1 LTR by Rad51 in microglial cells. *Cell Cycle* 9(18):3715-22. PMID: 20890127.

Gentilella A, Khalili K. (2009) Autoregulation of co-chaperone BAG3 gene transcription. *J Cell Biochem.* 108(5):1117-24. PMID: 19777443.

Stettner MR, Nance JA, Wright CA, Kinoshita Y, Kim WK, Morgello S, Rappaport J, Khalili K, Gordon J, Johnson EM. (2009) SMAD proteins of oligodendroglial cells regulate transcription of JC virus early and late genes coordinately with the Tat protein of human immunodeficiency virus type 1. *J Gen Virol.* 90(Pt 8):2005-14. PMID: 19420158.

Basile A, Darbinian N, Kaminski R, White MK, Gentilella A, Turco MC, Khalili K. (2009) Evidence for modulation of BAG3 by polyomavirus JC early protein. *J Gen Virol.* 90(Pt 7):1629-40. PMID: 19282432.

Rosati A, Khalili K, Deshmane SL, Radhakrishnan S, Pascale M, Turco MC, Marzullo L. (2009) BAG3 protein regulates caspase-3 activation in HIV-1-infected human primary microglial cells. *J Cell Physiol.* 218(2):264-7. PMID: 18821563.

Gentilella A, Passiatore G, Deshmane S, Turco MC, Khalili K. (2008) Activation of BAG3 by Egr-1 in response to FGF-2 in neuroblastoma cells. *Oncogene* 27(37):5011-8. PMID: 18469860.

Darbinian N, Darbinyan A, Czernik M, Peruzzi F, Khalili K, Reiss K, Gordon J, Amini S. (2008) HIV-1 Tat inhibits NGF-induced Egr-1 transcriptional activity and consequent p35 expression in neural cells. *J Cell Physiol.* 216(1):128-34. PMID: 18247371.

Rosati A, Leone A, Del Valle L, Amini S, Khalili K, Turco MC. (2007) Evidence for BAG3 modulation of HIV-1 gene transcription. *J Cell Physiol.* 210(3):676-83. PMID: 17187345.

Darbinian N, Popov Y, Khalili K, Amini S. (2008) Creation of a bi-directional protein transduction system for suppression of HIV-1 expression by p27SJ. *Antiviral Res.* 79(2):136-41. PMID: 18378326.

Kaniowska D, Kaminski R, Amini S, Radhakrishnan S, Rappaport J, Johnson E, Khalili K, Del Valle L, Darbinyan A. (2006) Cross-interaction between JC virus agnoprotein and human immunodeficiency virus type 1 (HIV-1) Tat modulates transcription of the HIV-1 long terminal repeat in glial cells. *J Virol.* 80(18):9288-99. PMID: 16940540

BIOGRAPHICAL SKETCH

NAME : Jennifer Gordon, Ph.D.

POSITION TITLE: Associate Professor

eRA COMMONS USER NAME: gordonjj

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

Albright College,	Reading, PA	B.S.	1990	Biology
MCP-Hahnemann School of Medicine,	Philadelphia, PA	Ph.D.	1999	Molecular Pathobiology
Temple University,	Philadelphia, PA	Postdoc	2001	Molecular Neurovirology

A. POSITIONS AND HONORS

Professional experience:

1991 - 1995 Research Assistant, Molecular NeuroVirology Section, Jefferson Institute of Molecular Medicine, Thomas Jefferson University, Philadelphia, PA. Molecular biology of viral-glial gene interaction in the central nervous system.

1995 - 1996 Predoctoral Fellow, Department of Pathology, Anatomy, and Cell Biology, Thomas Jefferson University, Philadelphia, PA. Viral models for tumor pathogenesis in the central nervous system.

1996 - 1999 Predoctoral Fellow, Department of Pathology and Laboratory Medicine, Center for NeuroVirology and NeuroOncology, MCP-Hahnemann School of Medicine, Philadelphia, PA. Viral model for tumor pathogenesis in the central nervous system.

1999 - 2001 Assistant Scientist, Laboratory of Brain Tumor Biology, Center for Neurovirology & Cancer Biology, College of Science & Technology, Temple University, Philadelphia, PA.

2001 - 2006 Assistant Professor, Center for Neurovirology and Cancer Biology, College of Science and Technology, Temple University, Philadelphia, PA.

2006 - 2012 Associate Professor, Department of Neuroscience and Center for Neurovirology, Temple University School of Medicine, Philadelphia, PA.

2013- present Associate Professor (tenured), Department of Neuroscience and Center for Neurovirology, Temple University School of Medicine, Philadelphia, PA.

Honors and awards:

1995 - 1996 NRSA Predoctoral Fellowship, Thomas Jefferson University, Philadelphia, PA

1996 - 1999 Predoctoral Fellowship, MCP-Hahnemann School of Medicine, Philadelphia, PA

2000 International Society of NeuroVirology Investigator in Training Award

2001 Rodger C. Haggitt Memorial Award for Excellence in Translational Research, American Association for Cancer Research, Pathobiology of Cancer Workshop

2006 International Society for NeuroVirology President's Award for outstanding service as Conference Chair of the 7th ISNV, Philadelphia, PA

B. PUBLICATIONS (LIMITED TO 15 RELEVANT PUBLICATIONS)

Shollar, D., Del Valle, L., Otte, J., Khalili, K., and Gordon, J. (2004) JCV T-antigen interacts with the Neurofibromatosis Type 2 gene product in a transgenic mouse model of malignant peripheral nerve sheath tumor. *Oncogene* 23:5459-5467.

Radhakrishnan, S., Gordon, J., Del Valle, L., Cui, J., and Khalili, K. (2004) Intracellular approach for blocking JCV gene expression using RNA interference *J. Virol.* 78:7264-7269.

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(2008) Negative regulation of A®PP gene expression by Pur-alpha. *J. Alzheimer's Dis.* 15:71-82.
Stettner, M.R., Nance, J.A., Wright, C., Kinoshita, Y., Kim, W.-K., Morgello, S., Rappaport, J., Khalili, K., Gordon, J. and Johnson, E.M. (2009) SMAD Effectors of TGF-® Regulate Transcription of JC Viral Early and Late Genes in Glial Cells Coordinately with the Tat Protein Of Human Immunodeficiency Virus Type I. *J. Gen. Virol.* 90:2005-14.
Del Valle, L., Pina-Oviedo, S., Perez-Liz, G., Augelli, B.J., Azizi, A., Khalili, K., Gordon, J. and Krynska, B. (2010) Bone marrow-derived mesenchymal stem cells undergo JCV T-antigen mediated transformation and generate tumors with neuroectodermal characteristics. *Cancer Biol. Ther.* 9(4):286-294.
Noch, E., Gordon, J., and Khalili, K. (2012) JC virus T-antigen regulates glucose metabolic pathways in brain tumor cells. *PLoS One* 7(4):e35054.
Mishra, M., Del Valle, L., Otte, J., Darbinian, N., and Gordon, J. (2012) Pur-alpha regulates the developmental expression of RhoA and affects its downstream signaling ability in the mouse brain *J. Cell. Physiol.* 228:65-72.
Bouvard, H. et al, on behalf of the WHO International Agency for Research on Cancer Monograph Working Group. (2012) Carcinogenicity of malaria and of some polyomaviruses. (J. Gordon, member of the Working Group). *Lancet Oncol.* 13:339-40.
Beltrami, S., Branchetti, E., Sariyer, I., Otte, J., and Gordon, J. (2013) Neurofibromatosis Type 2 tumor suppressor protein, NF2, induces proteasome-mediated degradation of JC virus T-antigen in human glioblastoma. *PLoS One* 8(1):e53447.
Beltrami, S., Kim, R., and Gordon, J. (2013) Neurofibromatosis Type 2: An unconventional cell cycle regulator. *Anticancer Res.* 33:1-11.
Johnson, E.M., Daniel, D.C., and Gordon, J. (2013) The Pur family: Genetic and structural features in development and disease. *J. Cell. Physiol.* 228(5):930-7.
White, M.K., Gordon, J., and Khalili, K. (2013) The rapidly expanding family of human polyomaviruses: recent developments in understanding their life cycle and role in human pathology. *PLoS Pathogens* 9(3):e1003206. PMID: 23516356.