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:** 20 - *Cellular Transformation and Transcriptional Regulation of JC Virus in a Human Brain Tumor Model*

7. **Start and End Date of Research Project:** 9/15/2009 – 6/30/2010

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

9. **Research Project Expenses**.

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

   $ 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
Sariyer, Ilker	Graduate Assistant	70%	$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
Khalili, Kamel	Principal Investigator	<1%
Gordon, Jennifer	Co-Investigator	<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
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____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:
Neuroimmune regulation of neurotropic JC virus by SF2/ASF in glial cells	X NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	July 2011	$ 1,912,496	$1,912,500

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:

Will pursue additional research grants from NIH to continue the project.

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

We will continue to pursue our studies to determine the pathways involved in the regulation and progression JC virus-associated demyelinating disorders. This will assist us in understanding the specific mechanism by which the JCV can be reactivated in infected brain cells which results in cytolytic destruction of host oligodendrocytes leading to the development of demyelination. Indeed, this information will be beneficial for the development of therapeutic approaches that can inhibit JC virus replication and progression of CNS and biomarkers to measure at risk individuals.

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			1	
Black				
Asian				
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.

JCV is a human polyomavirus that infects greater than 80% of the human population during childhood. Replication of the neurotropic strain of JCV in glial cells causes the fatal demyelinating disease of the central nervous system, progressive multifocal leukoencephalopathy (PML), which is seen in patients with underlying immunocompromised conditions, notably among AIDS patients. Recently, several cases of PML have been reported in patients under treatment with immunomodulatory drugs including Natalizumab, Rituximab, and Efalizumab, indicating that alterations in immune status may lead to reactivation of latent and/or passing virus in human brain. Like other polyomaviruses, the JCV genome is composed of double-stranded circular DNA of approximately 5 kb in size with a bi-directional non-coding control region that is located between the early and late coding sequences. The early coding region is responsible for expression of large T-antigen, small t-antigen, and a group of T' proteins, all of which are produced upon alternative splicing of a specific primary transcript. Similarly, alternative splicing of the late transcript results in production of the viral capsid proteins VP1, VP2, and VP3 all of which are important for completion of the viral lytic cycle and formation of viral particles. Processing of both early and late primary transcripts requires participation of splicing factors including SF2/ASF, an ubiquitous factor which plays a pivotal role in alternative and constitutive splicing of precursor mRNAs of mammalian cells. Of particular interest, the notion that SF2/ASF was first discovered as a cell type-specific regulator of another well-studied member of the polyomavirus family, SV40, based on its ability to modulate splicing of the viral early gene, thus effecting the expression of large T-antigen and small t-antigen expression at the post transcriptional level. The non-coding control region of the neurotropic strain of JCV, Mad-1, is composed of two 98 bp tandem repeats that have cell type-specific characteristics and its activation primarily occurs in glial cells such as oligodendrocytes and astrocytes. Earlier results from our laboratory and others led to the identification of several constitutive and inducible cellular factors with the ability to positively and negatively control JCV gene transcription. These observations led us to postulate that transcription of the JCV promoter is controlled by a group of transcription factors that universally silence expression of the viral genome under normal conditions and the level of their expression and/or activities are changed under certain physiological conditions such as immunosuppression, thus providing an opportunity for the virus to replicate in the permissive cells of the CNS. Here, we examined the possible effect of SF2/ASF on the regulation of JCV gene expression and viral replication in glial cells. Our results show that while SF2/ASF plays a role, similar to that seen in SV40, in splicing viral transcripts, it has a profound impact on transcription of the viral genome and replication of JCV in glial cells. Our results show that overexpression of SF2/ASF suppresses JCV gene transcription in human glial cells. Accordingly, suppression of SF2/ASF enhances the level of viral replication in astrocytic cells. These observations provide the first evidence for regulation of a promoter activity by the splicing factor, SF2/ASF, and shed new light onto regulation of JCV gene transcription and replication.

It is believed that JCV may enter many cell types, yet only under certain immunosuppressive conditions does it enter into a lytic infection cycle in glial cells. Earlier studies established that cell type-specific reactivation of JCV in glial cells is primarily regulated at the transcriptional level. In this respect, several transcription factors including YB-1, Purα, GF-1, Egr-1, c-jun, NF1, and others were identified based on their ability to modulate JCV promoter activities in glial cells. Of note, none of these regulators were restricted to glial cells, and their overexpression, in most areas, failed to stimulate transcription of JCV in non-glial cells,

suggesting that the JCV promoter in general is under a negative regulation in non-permissive cells. Accordingly, one may speculate on the involvement of inducible glial specific activator which becomes reactivated and promotes JCV gene transcription and replication during the course of immunosuppression. Thus, it is conceivable that the combination of ubiquitous negative and inducible positive glial specific factors determines the level of viral gene expression in glial and non-glial cells. Here, we identified an RNA splicing regulatory protein, SF2/ASF, which is ubiquitously expressed in all cell types as a negative regulator of JCV gene transcription. This is not a universal event for the other members of the polyomavirus family including SV40 and BKV and requires a specific DNA sequence located within the 98 bp tandem promoter region. Our results demonstrate that a decrease in the level of SF2/ASF increases the level of viral gene expression and replication in glial cells and has no positive impact on JCV expression in non-glial cells, suggesting that a positive glial-specific activator is required to initiate viral gene expression. SF2/ASF also suppresses expression of the JCV promoter in transformed cells whose viral genome is integrated in host chromosomes. Our DNA binding experiments identified a CR3 region of the JCV 98 bp repeat that is conserved in PML (Mad) and non-PML (archetype) strains of JCV as the primary target for SF2/ASF. This region encompasses several predicted binding sites for DNA binding proteins including Purα, NF-1, MF3, Elk-1, COE1, p300, and Zic3. At present, the importance of these transcription regulators and their potential interplay with SF2/ASF remains to be investigated.

SF2/ASF exhibits a modular structure consisting of two copies of RNA binding motifs (RRM1 and RRM2), followed by an arginine-serine rich (RS) domain. Whereas the RRM domains are responsible for RNA binding activity of ASF/SF2, the RS region interacts with the core-splicing components. Our results showed that the RRM1 domain has the capacity to interact with the DNA sequence of JCV and that this interaction is important for suppression of viral gene transcription.

Examination of SF2/ASF levels in several glial-derived cells including human astrocytic tumor cells, U-87 MG, primary human fetal astrocytes (PHFA) and primary human adult astrocytes (PHAA) showed higher levels of SF2/ASF expression in U-87 MG and PHAA where virus replicates poorly in comparison to PHFA, routinely utilized for virus propagation. Our results demonstrated that a decrease in the level of SF2/ASF in both PHFA and PHAA increases the level of viral replication. Altogether, results from the studies presented here identified a novel regulatory pathway involving splicing factor SF2/ASF in suppression of JCV gene transcription. This is a first report on the ability of SF2/ASF to control viral gene expression at the transcriptional level and suggests the operation of a novel regulatory event that controls reactivation of JCV in non-glial as well as glial cells.

In conclusion, the data represented here provides the first report of transcriptional suppression of JC virus, by an unusual candidate, SF2/ASF, a cellular alternative splicing factor. Our results suggest a novel role of SF2/ASF as a transcriptional inhibitor of JC virus. These observations may suggest a novel mechanism of JCV reactivation and a new approach for suppression of JCV infection.

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):
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.

Here, we investigated the possible impact of SF2/ASF on propagation of human polyomavirus, JC virus, in glial cells. Our results indicate that SF2/ASF might be an important cellular protein in control of JCV infection, since its expression in glial cells completely blocked viral propagation. Surprisingly, JCV gene expression is inhibited by SF2/ASF mostly at transcriptional stage of the gene expression rather than posttranscriptional. This provides evidence for SF2-mediated transcriptional regulation in addition to its roles in alternative splicing and translation, and suggests a novel approach for the suppression of JCV propagation.

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. 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 (tenured), 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 (tenured) 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

B. 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.

Johnson, E.M., Kinoshita, Y., Weinreb, D.B., Wortman, M.J., Simon, R., Amini, S., Khalili, K., Winckler, B., and Gordon, J. (2006) Role of Pur-alpha in targeting mRNA to sites of translation in hippocampal neuronal dendrites. *J. Neurosci. Res.* 83:929-43.

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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.