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:** The Wistar Institute

2. **Reporting Period (start and end date of grant award period):** 01/01/2010 – 06/30/2011

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Russel E. Kaufman, MD

4. **Grant Contact Person's Telephone Number:** 215-898-3926

5. **Grant SAP Number:** **#** 4100050916

6. **Project Number and Title of Research Project:** *2: Characterizing Mechanisms of Transcriptional Activation Using Live Cell Imaging*

7. **Start and End Date of Research Project:** 01/01/2010 – 06/30/2011

8. **Name of Principal Investigator for the Research Project:** Susan M. Janicki, 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:

   $ $422,549.28

   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
Janicki	Principle Investigator	74%	151,458.22
Negorev	Staff Scientist	100%	19,131.36
Rafalska-Metcalf	Postdoctoral Fellow	100%	5,483.92
Newhart	Research Assistant	100%	17,249.20
Strumfels	Lab Assistant	100%	4,069.18
Bell	Lab Assistant	100%	3,754.32

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
Laser MM upgrade	An optimized integrated three-color laser module for confocal imaging	35,871.00

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

Yes_____ No_____x_____

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

11. Leveraging of Additional Funds

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

Yes_____ No_____x_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If

you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

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

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
None	☐NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)			

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

Yes___x_____ No_____

If yes, please describe your plans:

I am planning to apply to NIH for an RO1 to support our investigations into the functions of the chromatin assembly machinery using our live cell imaging system.

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

In the future, we will expand these studies to investigate the pathways that we have identified using this experimental system in the regulation of endogenous heterochromatin sites such as telomeres in order to elucidate the basic mechanisms of gene silencing in mammalian cells.

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				1
Unknown				
Total	**1**			**1**

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

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

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

    We were able to upgrade our imaging system and expand our research program into the area of chromatin assembly.

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.

Aim 1. Interrogate by shRNA depletion the requirement of known regulatory factors on (i) chromatin decondensation; (ii) pre-initiation complex assembly; and (iii) RNA synthesis, using kinetic, live cell imaging of single cells.

Our initial observation that the transgene array, stably integrated into the human osteosarcoma cell line, U2OS, is rapidly activated and that the array chromatin significantly decondenses led us to propose to use this system to delineate the recruitment timing of the transcriptional activation machinery. The conclusion of this study is that most of the activation factors are rapidly recruited to the site at the same time as the activator. Figure 1A shows the histone acetyltransferases (HATs) that are recruited to the transgene array; and Figure 1B shows that the HAT, GCN5, is recruited simultaneously with the activator during activation. This was the case with the majority of the activation factors that we examined. As such, it is not possible to temporally distinguish their recruitment timings. Our conclusion is that, using this system, it will be difficult to pursue questions about the timing of transcriptional activation events.

We also attempted to knock-down a number of transcriptional regulatory factors, including histone acetyltransferases and the bromodomain containing Brd proteins. However, we were not able to significantly reduce transcriptional activation in these assays. This led us to conclude that there is a lot of redundancy in the transcriptional activation machinery and that viruses, such as the herpes simplex virus through its VP16 activator (the activator used in this assay), exploit this cellular feature in order to ensure that the virus is able to induce high levels of transcription. The application of the RNA pol II inhibitor, alph-amanitin, to the cell prior to induction demonstrated that even though the activator can bind in the presence of the inhibitor, transcription is needed for chromatin decondensation (Figure 2).

Interestingly, the robust activation of this site, which is a multi-copy transgene array, is contrary to predictions of how a region of repetitive DNA should be regulated. Such regions are typically condensed and refractive to activation. As such, we have also been exploring the possibility of using this site to study mechanisms of gene silencing in mammalian cells.

One factor that we have been studying is the histone H3 variant, H3.3 and its role in replication independent transcriptional activation. Initially, we had been investigating the function of the histone H3.3 chaperone HIRA, which regulates H3.3 incorporation into active single copy genes. However, HIRA is not enriched at the transgene array. It was recently reported that Daxx and ATRX regulate H3.3 incorporation into heterochromatin. When we examined the recruitment of these factors to the transgene array, we found that they are, in fact, both enriched at the site, suggesting that they regulate it. This discovery, and the difficulty in studying transcription activation using this system, led us to change the direction of the project and to focus on this system as a model of how replication-independent histone assembly regulates gene silencing at a region of repetitive DNA using the same techniques proposed to study activation. This includes

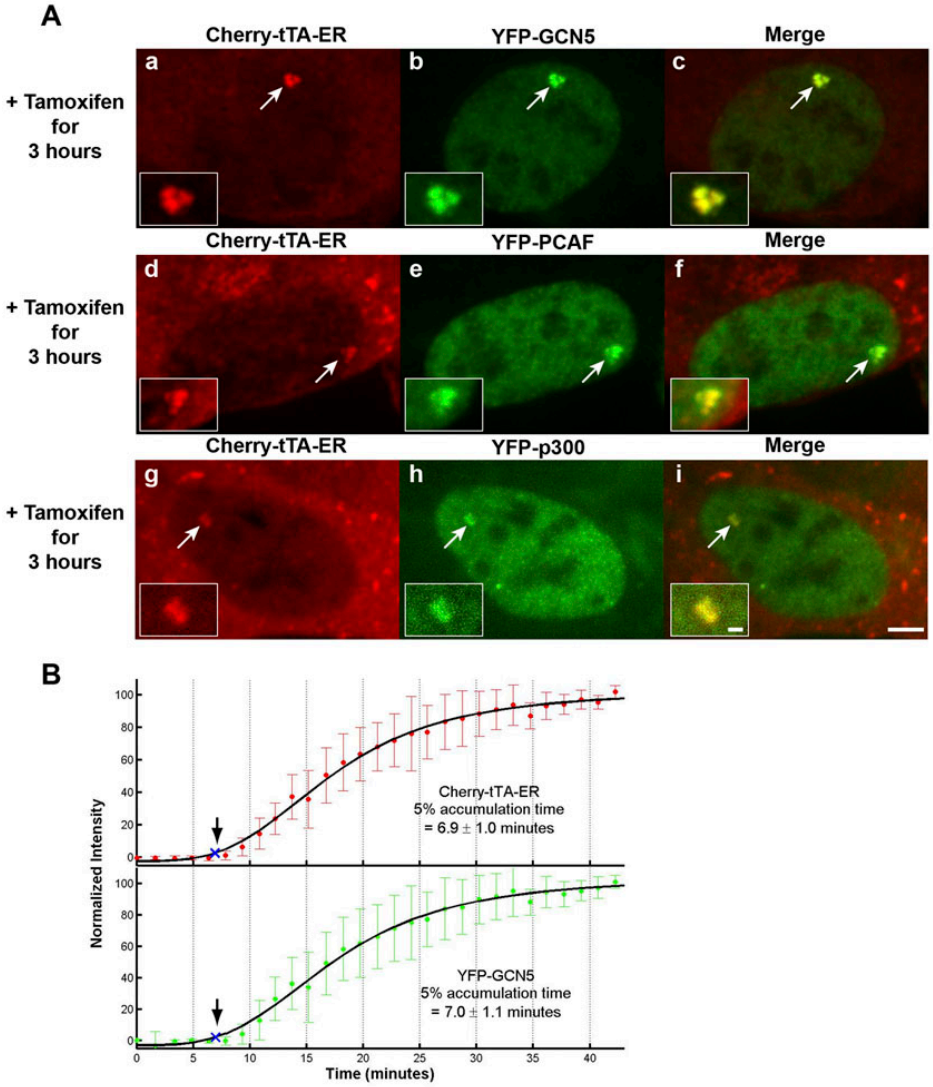
examining the effects of factor expression and knock down on chromatin decondensation, RNA accumulation and factor recruitment.

Aim 2. Use p53 as a model transcriptional activator to interrogate the timing of its activation kinetics using live cell imaging analysis.

The goal of Aim 2 was to develop a single-cell imaging system to dissect the dynamics of the p53 activation domain during transcriptional activation. Interestingly, when we used the p53 activation construct that we engineered (Figure 3A), we found that the activator bound to the transcription site in fewer than 50% of cells and that the degree of chromatin decondensation was reduced compared to the VP16 activator (Figure 3B). The significance of this result is that it demonstrates that a weak activation domain (compared to the herpes simplex viral activator, VP16) cannot overcome the condensed chromatin structure of the multi-copy array transgene array stably integrated in U2OS cells (Figure 3F). It also demonstrates the importance of transcription in driving large-scale changes in chromatin organization.

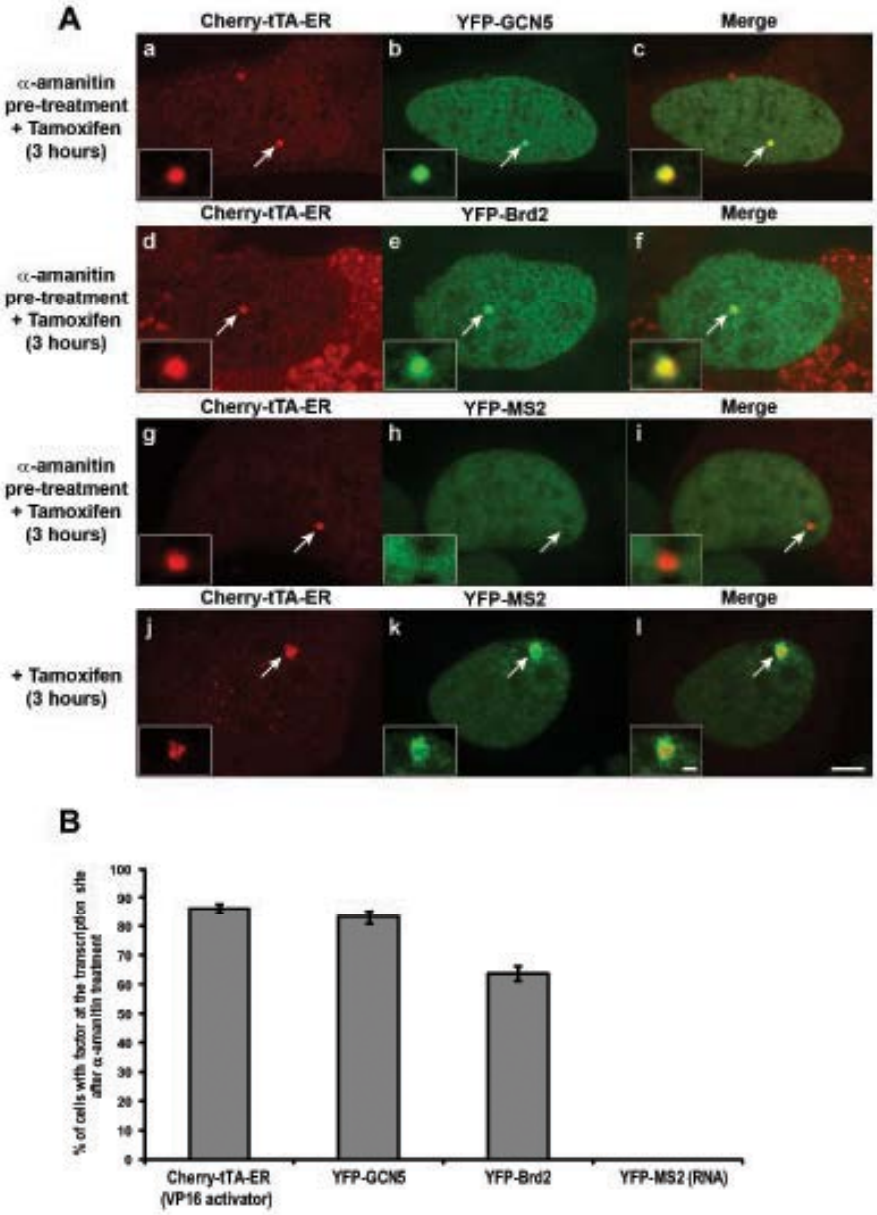
These experiments provided single cell data for the effects of a well characterized activator which had been tested using reporter constructs and cell population read-out assays. However, due to the limited activation potential of this construct, it is not possible for us to continue with this line of investigation using this model system.

Figure 1: Analysis of histone acetyltransferase dynamics during transcriptional activation.



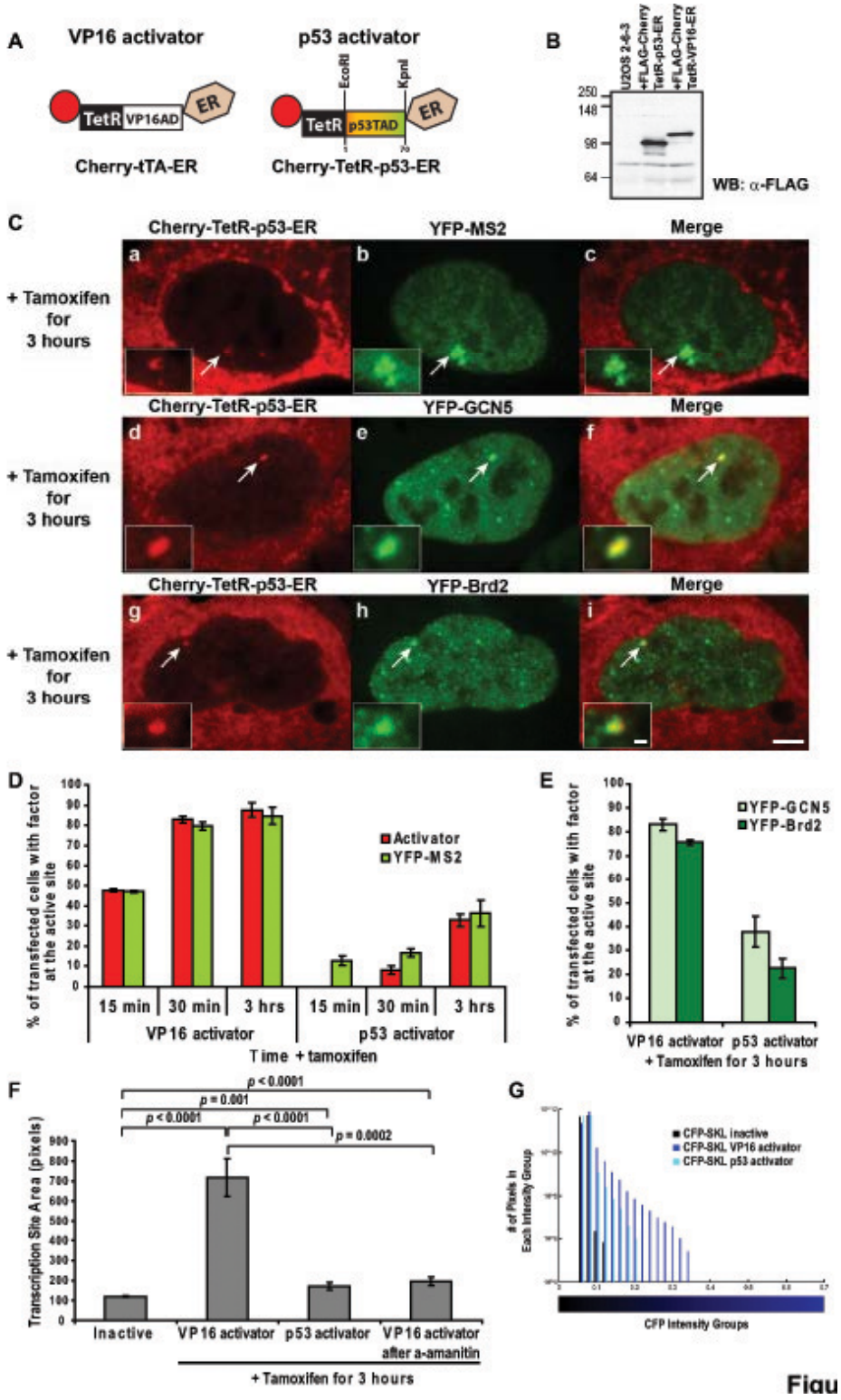
Legend: (**A**) YFP-GCN5 (panels **a**-**c**), YFP-PCAF (panels **d**-**f**), and YFP-p300 (panels **g**-**i**) are strongly recruited to the active transcription site, marked by Cherry-tTA-ER, 3 hrs post induction. Transcription was induced by the addition of tamoxifen. Scale bar represents 5 µm. Scale bar in the enlarged inset represents 1 µm. (**B**) Quantification of Cherry-tTA-ER (top panel, solid red circles) and YFP-GCN5 (lower panel, solid green circles) accumulation at the transcription site during activation. Tamoxifen was added to the media immediately after the first time point (~ 0 min). Images were collected every 1.5 min for ~40 min. Measured intensities were normalized to the high and low plateau values and fitted to a logistic fit (solid black line). The initial accumulation time (blue Xs and arrows) is the point when the fitted curve reaches 5% of the total accumulation. The graphs are the average of seven cells imaged from four different coverslips on four different days. Error bars represent the standard deviation.

Figure 2: Analysis of the effects of α-amanitin on regulatory factor recruitment.



Legend: Cells transfected with the indicated factors were pre-treated with α-amanitin for 2 hrs then incubated with tamoxifen for 3 hrs. **(A)** YFP-GCN5 (panels **a-c**) and YFP-Brd2 (panels **d-f**) were enriched at the transcription site marked by Cherry-tTA-ER. YFP-MS2 was not enriched at the transcription site after α-amanitin treatment (panels **g-i**) but did accumulate at the transcription site in untreated cells (panels **j-l**). Scale bar represents 5 µm. Scale bar in enlarged inset represents 1 µm. **(B)** Graph shows the percentage of cells with accumulations of each factor at the transcription site after α-amanitin pre-treatment followed by a 3 hr incubation with tamoxifen. 100 cells were analyzed from 3 independent experiments. SEM (in the form of error bars) are presented in the graphs.

Figure 3: Single cell analysis of transcriptional activation induced by VP16 and p53 activators.



[Legend on next page]

Legend: (**A**) Schematic representation of the VP16 and p53 activators. (**B**) Western blot analysis of Flag-tagged versions of the p53 and VP16 activators showing that they are expressed at comparable levels in 2-6-3 cells. (**C**) YFP-MS2 (panels **a-c**), YFP-GCN5 (panels **d-f**), and YFP-Brd2 (panels **g-i**) are enriched at the transcription site, marked by Cherry-tTetR-p53-ER. Scale bar represents 5 µm. Scale bar in enlarged inset represents 1 µm. (**D**) Analysis of the percentage of cells with the activators and YFP-MS2 enriched at the transcription site 15 min, 30 min, and 3 hrs after activation. 100 cells were analyzed from three independent experiments; SEMs (in the form of error bars) are presented in the graphs. (**E**) Analysis of the percentage of cells with accumulations of YFP-GCN5 and YFP-Brd2 at the transcription site 3 hrs after activation. 100 cells were analyzed from three independent experiments; SEMs (in the form of error bars) are presented in the graphs. (**F**) Measurement of the pixel area of the transcription site in the inactive state (marked by Cherry-lac repressor) and after 3 hrs activation by the VP16 activator (Cherry-tTA-ER with and without α-amanitin pre-treatment) and the p53 activator (Cherry-TetR-p53-ER). Inactive and VP16-activated transcription site data is the same as in Fig. 1D. Area values are averages of 10 cells. SEM (in the form of error bars) and *p* values are presented in the graph. (**G**) Frequency histogram showing the distribution of the blue pixel intensity levels (blue bars) as a measure of the CFP-SKL protein in cells activated for 3 hrs by the VP16 and p53 activators. Black bars represent the background signal. The x-axis is the average fluorescence pixel intensity in each bin on a scale from 0 to 1 and divided into bin sizes of 0.02; the y-axis is the number of pixels in each bin on a logarithmic scale. The bar beneath the histogram shows the intensity range. Measurements are from five independent experiments.

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. Regulation of transcriptional repression by Daxx and ATRX at a multi-copy transgene array	Rafalska-Metcalf IU, Newhart A, Strumfels ED, Joo LM, Powers SL, Yang T, Falk S, Bell LL, Lopez-Jones M, Singer RH, Negorev DG and Janicki SM	Proceedings of the National Academy of Science	July 2011	xSubmitted ☐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:

This work has provided us the foundation to investigate the mechanisms regulating the incorporation of histone H3.3 into heterochromatin. We found that there are a number of RNA processing factors that co-localize with H3.3 at the transcription site, and we will further delineate this pathway after the publication of this manuscript.

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	POSITION TITLE
JANICKI, Susan M.	**Assistant Professor**
eRA COMMONS USER NAME **SJANICKI**	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Tufts University, Medford, Massachusetts	B.S.	1993	Biology and English
University of Maryland, Baltimore, Maryland	Ph.D.	1999	Human Genetics

A. Personal Statement

My laboratory focuses on using live-cell imaging to study gene expression in single cells. We are taking a synthetic biology approach to develop tools for these studies by utilizing repeats sequences from bacteria and bacteriophage in combination with their auto-fluorescently label binding proteins. The application of live cell imaging to investigations of gene expression and nuclear organization is a very young discipline. However, these types of studies have already dramatically changed our perceptions regarding the dynamic nature of nuclear processes. My work builds on these foundations but with a specialized interest in establishing techniques that allow the regulation of specific genetic elements to be evaluated with high temporal and spatial resolution. The ultimate goal of my research is to bridge the gap between molecular and cellular analyses in order to obtain a comprehensive portrait of gene regulation. As a post-doctoral fellow in the Spector laboratory at Cold Spring Harbor, I established the system described in this application, which allows simultaneous visualization of DNA, RNA and proteins in single living cells. As an independent investigator, my efforts have been initially focused on making improvements to this system that now make me confident in the reliability and reproducibility of our results. We are using this technology to discover new mechanisms of gene regulation and to understand the pathogenic mechanisms of disease causing mutations.

B. Positions and Honors:

1993-1995	Research Assistant in the laboratory of Dr. Mervyn J. Monteiro, University of Maryland, Baltimore
1995-1999	Graduate Research in the laboratory of Dr. Mervyn J. Monteiro, University of Maryland, Baltimore. “Understanding the Function of the Presenilins in Apoptosis and Cell Cycle Progression”
1999-2005	Postdoctoral fellow in the laboratory of Dr. David L. Spector, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. Live cell imaging of gene expression.
2005-present	Assistant Professor, The Wistar Institute, Philadelphia, PA

Teaching experience:

2001 and 2002	Undergraduate Research Program, supervised research of summer students in the laboratory of Dr. David L. Spector
Summer 2006	Wistar Institute Undergraduate Research Program
Summer 2007	Wistar Institute Biotechnician Training (BTT) Program

Professional Honors:

1996	American Society for Cell Biology Pre-doctoral Travel Award
2006	Beckman Young Investigator Award
2007	V Foundation Scholar
2007	March of Dimes Basil O’Connor Starter Scholar Research Award

C. Selected Peer-Reviewed Publications (in chronological order):.

1. Hsu C, **Janicki SM**, and Monteiro MJ. 1995. The first intron of the mouse neurofilament light gene NF-L. increases gene expression. *Molecular Brain Research* 32, 241-251.Darzacq X, Shenoy SM, Fusco D, **Janicki SM**, Spector DL and Singer RH. 2004. Dynamics of Single mRNPs in the Nuclei of Living Cells. *Science* 18, 1797-1800.
2. **Janicki SM** and Monteiro MJ. 1997. Increased apoptosis arising from increased expression of the Alzheimer's disease-associated presenilin-2 mutation N141I. *Journal of Cell Biology* 139, 485-495.
3. **Janicki SM** and Monteiro MJ. 1999. Presenilin overexpression arrests cells in the G1 phase of the cell cycle: arrest potentiated by the Alzheimer's disease PS2N141I mutant. *American Journal of Pathology* 155, 135-144.
4. Stabler SM, Ostrowski LL, **Janicki SM**, Monteiro M.J. 1999. A myristoylated calcium binding protein that preferentially interacts with the Alzheimer's disease presenilin-2 protein. *Journal of Cell Biology* 145, 1277-1292.
5. **Janicki SM**, Stabler SM, Monteiro MJ. 2000. Familial Alzheimer's disease presenilin-1 mutants potentiate cell cycle arrest. *Neurobiology of Aging* 21, 829-836.
6. Tsukamoto T, Hashiguchi N, **Janicki SM**, Tumbar T, Belmont AS, Spector DL. 2000. Visualization of gene activity in living cells. *Nature Cell Biology* 2, 871-878.
7. Muratani M, Gerlich D, **Janicki SM**, Gebhard M, Eils R, Spector DL. 2002. Metabolic-energy-dependent movement of PML bodies within the mammalian cell nucleus. *Nature Cell Biology* 4, 106-110.
8. **Janicki SM**, Tsukamoto T, Salghetti SE, Tansey WP, Sachidanandam R, Prasanth KV, Ried T, Shav-Tal Y, Bertrand E, Singer RH, Spector DL. 2004. From Silencing to Gene Expression: Real-Time Analysis in Single Cells. *Cell* 116, 683-698.
9. Shav-Tal Y, Darzacq X, Shenoy SM, Fusco D, **Janicki SM**, Spector DL, Singer RH. 2004. Dynamics of Single mRNPs in the Nuclei of Living Cells. *Science* 18, 1797-1800.
10. Shanbhag NM, Rafalska-Metcalf IU, Balane-Bolivar C, **Janicki SM**, and Greenberg RA. ATM-dependent chromatin changes silence transcription in cis to DNA double-strand breaks. *Cell* 141(6):970-81.
11. Rafalska-Metcalf IU, Joo LM, Powers SL, LeRoy G and **Janicki SM**. Single cell analysis of transcriptional activation dynamics. *PLoS ONE* 5(4):e10272.
12. Lan L, Ui A, Nakajima S, Hatakeyama K, Hoshi M, Watanabe R, **Janicki SM**, Ogiwara H, Kohno T, Kanno S, Yasui A. The ACF1 complex is required for DNA double-strand break repair in human cells. *Molecular Cell* 40(6):876-87.
13. Rafalska-Metcalf IU, Newhart A, Strumfels ED, Joo LM, Powers SL, Yang T, Falk S, Bell LL, Lopez-Jones M, Singer RH, Negorev DG and **Janicki SM**. Regulation of transcriptional repression by Daxx and ATRX at a multi-copy transgene array. (Submitted).