Department of Health and Human Services
Public Health Service
Ruth L. Kirschstein National Research Service Award
Termination Notice

1. NAME OF FELLOW OR APPOINTEE (Last, First, Middle)
Bower, Brian, D

2. GRANT NO.
2T32GM007092-36

3. NAME OF SPONSORING INSTITUTION
UNIVERSITY OF NORTH CAROLINA at CHAPEL HILL

4. SOCIAL SECURITY NO.
XXX-XX-XXXX

5. DEGREE(S) EARNED/COMPLETION DATE(S)
BS(06/2008)

6. DATES OF SUPPORT UNDER THIS AWARD (Month, day, year): FROM: 08/01/2010 TO: 07/31/2011

7. TOTAL KIRSCHSTEIN-NRSA STIPEND RECEIVED AND NUMBER OF MONTHS SUPPORTED UNDER THIS AWARD (See specific instructions for Amount of Stipend)

YEAR OF SUPPORT	AMOUNT OF STIPEND	ARRA	NUMBER OF Months	Days	YEAR OF SUPPORT	AMOUNT OF STIPEND	ARRA	NUMBER OF Months	Days
YEAR 36	21,180.00		12	0	**TOTALS**	**21,180.00**			

8. Provide a summary of training received and research undertaken during fellowship or trainee tenure. List publications, if any, resulting from the research during this period. List grants and career awards pending and received. If fellowship or training appointment is being terminated early, state reason.

- see attached document

9a. POST-AWARD INFORMATION: Please mark a single box in each of the categories below

Activity	Organization	Type of Position
☒ Further Education/ Training	☒ Academic	☒ Student
☐ Teaching	☐ Industry	☐ Resident/Clinical Fellow
☐ Research	☐ Government	☐ Postdoctoral Researchers
☐ Administration	☐ Hospital	☐ Research Scientist (non faculty)
☐ Clinical Practice	☐ Non-profit	☐ Faculty: Tenure-Track
☐ Unknown	☐ Unknown	☐ Faculty: Other
☐ Other	☐ Other	☐ Clinical Staff/ Private Practice
		☐ Unknown
		☐ Other

9b. POST-AWARD POSITION TITLE, FIELD, NAME OF ORGANIZATION, CITY, AND STATE

10a. MAILING ADDRESS AFTER TERMINATION OF THIS KIRSCHSTEIN-NRSA SUPPORT (Street, city, state, zip code)
135 Dixie Garden Drive, Chapel Hill, NC, 27516

10b. TEL NO. 9192654431

9c. TEL NO.

E-MAIL: bdbowe@email.unc.edu

11. OTHER PHS SERVICE OBLIGATION SUPPORT
☐ NHSC Scholarship: No of months: 0
☐ Kirschstein-NRSA: No. of months: 0

Period of Support Grant No

☐ LRP

12. SIGNATURE OF FELLOW OR TRAINEE (See specific instructions)
Electronically certified via eRA xTrain system by Trainee

DATE
09/23/2011

13. Certification of Sponsor or Program Director: that to the best of my knowledge all the above information is correct.

SIGNATURE OF SPONSOR OR PROGRAM DIRECTOR Electronically certified via eRA xTrain system by PI	DATE 09/28/2011	TYPED NAME OF SPONSOR OR PROGRAM DIRECTOR DURONIO, ROBERT	
14. Business Official's Verification of Items 6 and 7. (Not applicable to individual fellows at Federal or foreign institutions.)			
SIGNATURE Electronically verified via eRA xTrain system by BO	DATE 10/05/2011	TYPED NAME OF BUSINESS OFFICIAL Hess, Frances	TEL: 9199663411 FAX: 9199625011
15. (For Government use only) The information provided in Items 6 and 7 is in agreement with PHS records.			
SIGNATURE Electronically signed via eRA xTrain system	DATE 10/17/2011	TYPED NAME AND AWARDING OFFICE Fleisher, Nicole - NIH	

PHS 416-7

During the training period the recipient's work was split between two unrelated projects. The primary project was an attempted characterizing the gross organization of complexes containing nucleic acid templates and either heterogenous ribonucleoprotien A1 (hnRNP A1) or a proteolytic fragment thereof, unwinding protein 1 (UP1). The secondary project was a characterization of adeno-associated virus (AAV) genome organization and structure via electron microscopy that was additionally supported through separate funding from a collaborating laboratory. The primary project was abandoned after intractable difficulties with the experimental method were identified and after the project began to face completion from more conventional biochemical characterization. The secondary project has been successful and the electron microscopy results will be included in a publication being written by a collaborating laboratory.

The goal of the primary project was to elucidate whether N-terminally hexahistidine tagged recombinant hnRNP A1 and UP1 with intact nucleic acid binding activity could form an ordered structure on the single-stranded tail of model telomeres or on G-rich telomere derived RNA (TERRA). Examination of particles generated in reactions wherein hnRNP A1 or UP1 had been incubated with any of several nucleic acid templates via transmission electron microscopy revealed that the proteins formed unexpectedly large and unordered complexes of heterogeneous size on available single-stranded nucleic acid regardless of buffer or incubation conditions. Analysis of the purified proteins via dynamic light scattering revealed that the proteins were present predominately as monomers in storage buffer, suggesting that the complexes observed might be due to aggregation during incubation. Communication with Dr. Adrian Krainer revealed that the N-terminal hexahistidine tag on these proteins has been found to reduce the proteins' DNA binding activity – possibly by promoting the aggregation suspected in the reactions. Attendance of the 2011 Meeting on Telomeres and Telomerase at Cold Spring Harbor Laboratory revealed that a number of competing groups had made good progress in characterizing the role hnRNP A1 and UP1 in telomere biology. Due to uncertainty that the project would be fruitful even if it were re-attempted with untagged proteins and the high probability that the results of the project would face competition from several other groups, the project was suspended and all reagents were stored for future use or disposal.

The goals of the secondary project were to characterize the thermal stability of AAV particles containing either a double-stranded (dsDNA) or single-stranded DNA (ssDNA) genome and to characterize the intra-capsid genome organization and structure of dsDNA AAV genomes. This project is undergoing in collaboration with Doctors Aravind Asokan and Eric Horowitz of the University of North Carolina at Chapel Hill, and was partially funded through an NIH ARRA supplement grant (R01HL089221-S2). Characterization of the thermal stability of the AAV capsid was accomplished by partially heat denaturing the AAV particles at varying temperatures then examining the resulting particles via conventional transmission electron microscopy to assay the degree of capsid disruption and genome release. Characterization of the intra-capsid genome structure was attempted via psoralen crosslinking of the double-stranded potions of genome and coating of non-crosslinked portions go the genome with an extremely thermostable single-stranded binding protein. The results of these experiments remain inconclusive, but may be taken to suggest that the genome is maintained in a predominately single-

stranded state inside the capsid. The results of this collaboration are being written for publication at the time of this submission. Further collaboration is likely.