**BIOGRAPHICAL SKETCH**

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NAME: Shakirov, Eugene V.

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

POSITION TITLE: Assistant Professor of Biological Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Kazan State University, Russia | B.S. | 06/1997 | Microbiology |
| Kazan State University, Russia | Ph.D | 06/2000 | Microbiology |
| Texas A&M University, College Station, TX | Ph.D | 05/2004 | Biochemistry |

## A. Personal Statement

I am well-suited to successfully lead this project as I have the expertise, leadership, training, and motivation necessary to design and perform all proposed research efforts. I have an extensive background in plant biology, genetics and genomics, and I have made substantial contributions to plant telomere research. I first became interested in telomere biology upon joining Dr. Dorothy Shippen's laboratory at Texas A&M University as a Ph.D. student and working on several of her NIH-funded projects. I laid the groundwork for the proposed research by discovering that telomeres vary in length between natural populations of the model plant Arabidopsis thaliana. After further developing my skills in genomics, molecular evolution and bioinformatics through several postdoctoral appointments, I have joined Dr. Juenger's lab at UT Austin as a Research Associate (PI-level position) to further pursue my interests in genetic architecture of complex traits, including telomere length control. I have served as PI or co-PI on several non-profit and NIH-funded grants to investigate mechanisms of telomere length control in model organisms. In August 2019, I accepted the position of Assistant Professor of Biological Sciences at Marshall University, WV. In addition, I also serve as a Visiting professor at Kazan Federal University, Russia, where I direct projects related to plant phosphorus metabolism. Overall, this R01 proposal is designed to foster collaboration of two senior co-Investigators (Juenger, Shippen) and my own expertise to address fundamental questions regarding telomere length homeostasis in a novel way. With my long-standing interests in both quantitative genomic assays and telomere biology, I serve as a bridge to synergistically merge expertise of my collaborators. As part of my recently completed R03-funded project, we have already identified Arabidopsis NOP2A as a major regulator of telomere length. Importantly, the human NOP2 homologue is a tumor-associated marker whose abundance in many cancer types directly correlates with tumor progression and poor patient prognosis. Using a number of innovative approaches to quantitative analysis of telomere length variation, in this R01 proposal we intend to identify and characterize novel genetic and epigenetic factors involved in the establishment of telomere length polymorphism.


1. Shakirov E.V. and Shippen D.E. (2004) Length regulation and dynamics of individual telomere tracts in wild-type Arabidopsis. Plant Cell. 16(8):1959-67.
2. *Surovtseva Y.V., *Shakirov E.V., Vespa L., Osbun N., Song X. and Shippen D.E. (2007) Arabidopsis POT1 associates with the telomerase RNP and is required for telomere maintenance. EMBO J. 26:3653–3661. **Equal authorship*.
3. *Beilstein M.A., Renfrew, K.B., Song X., *Shakirov E.V., Zanis M.J. and *Shippen D.E. (2015) Evolution of the telomere-associated protein POT1a is characterized by positive selection to reinforce protein-protein interaction. **Corresponding authors*. Mol Biol Evol 32(5):1329-41.

4. Abdulkina L.R., Kobayashi C., Lovell J.T., Chastukhina I.B., Aklilu B., Agabekyan I.A., Valeeva L.R., Nyamsuren C., Aglyamova G.V., Sharipova M.R., Shippen D.E., Juenger T.J., and Shakirov E.V. (2019) Components of the ribosome biogenesis pathway underlie establishment of telomere length set point in Arabidopsis*. Nature Communications*. 10, 5479.

## B. Positions and Honors

### Positions and Employment

| | | | |
|---|---|---|---|
| 05/2004 | – | 12/2009 | Postdoctoral Research Associate in the laboratory of Dr. Shippen, Texas A&M University, College Station, TX |
| 01/2010 | – | 10/2010 | Research Scientist in the laboratory of Dr. Ralph Quatrano, Department of Biology, Washington University, St. Louis, MO |
| 12/2010 | – | 06/2013 | Postdoctoral research associate in the laboratory of Dr. Timothy Hall, Department of Biology, Texas A&M University, College Station, Texas |
| 09/2013 | – | 08/2019 | Research Associate (*PI-level), Dr. Thomas E. Juenger laboratory, Department of Integrative Biology, University of Texas at Austin, Austin, Texas |
| 09/2012 | – | present | Visiting Professor, Institute of Fundamental Medicine and Biology, Kazan Federal University, Russia |
| 08/2019 - | | present | Assistant Professor, Department of Biological Sciences, Marshall University, WV |
| 09/2019 | – | present | Adjunct Assistant Professor, Department of Biomedical Sciences, Joan C. Edwards College of Medicine, Marshall University, Huntington WV, USA |

### Honors

| | |
|---|---|
| 1996 | Recipient, Russian Presidential Scholarship to Study Abroad. |
| 1996, 1997 | International George Soros Science Education Program Student Awards for Research Excellence. |

## C. Contributions to Science

1. My early publications provided the first evidence that telomerase activity and telomere length vary not only between plant species, but also between natural populations (ecotypes) of the same plant species. Although length of the telomeric DNA tract has been known to vary widely across evolution, we showed that a population-specific set point is established and maintained in Arabidopsis by unknown mechanisms. We discovered that telomere tracts in natural Arabidopsis populations range between 2 to 9 kb. F1 and F2 progeny of a cross between long and short telomere parents had intermediate telomeres, implying that telomere length in Arabidopsis is not controlled by a single genetic factor. We proposed that an optimal size for telomere tracts is established and maintained for each Arabidopsis ecotype. This research laid the groundwork for the proposed research, as it is built around the central ideas of my previous studies that the factors establishing population-specific telomere length can be successfully mapped in a QTL screen.

    a. Fitzgerald MS, Shakirov EV, Hood EE, McKnight TD, Shippen DE. Different modes of de novo telomere formation by plant telomerases. Plant J. 2001 Apr;26(1):77-87. PubMed PMID: 11359612.
    b. Shakirov EV, Shippen DE. Length regulation and dynamics of individual telomere tracts in wild-type Arabidopsis. Plant Cell. 2004 Aug;16(8):1959-67. PubMed PMID: 15258263; PubMed Central PMCID: PMC519188.

2. The major focus of my research is deciphering evolutionarily conserved mechanisms regulating telomere length in plants with the broader goal of integrating these results with animal systems. Using a combination of genetic and biochemical techniques, I characterized novel telomere-binding proteins POT1 in a number of plant species, providing important insight into evolutionary aspects of telomere biology. I discovered that, unlike the situation in most vertebrates, Arabidopsis harbors not one, but, surprisingly, three telomere-binding proteins, dubbed POT1a, POT1b and POT1c. I went on to demonstrate that each of these proteins specializes in a particular sub-function of the human POT1 protein. The apparent separation-of-function demonstrated by the Arabidopsis POT1 proteins allowed us to carefully characterize these functions.

a. Shakirov EV, Surovtseva YV, Osbun N, Shippen DE. The Arabidopsis Pot1 and Pot2 proteins function in telomere length homeostasis and chromosome end protection. Mol Cell Biol. 2005 Sep;25(17):7725-33. PubMed PMID: 16107718; PubMed Central PMCID: PMC1190295.

b. Surovtseva YV*, Shakirov EV*, Vespa L, Osbun N, Song X, Shippen DE. Arabidopsis POT1 associates with the telomerase RNP and is required for telomere maintenance. **Equal authorship* EMBO J. 2007 Aug 8;26(15):3653-61. PubMed PMID: 17627276; PubMed Central PMCID: PMC1949013.

c. Shakirov EV, McKnight TD, Shippen DE. POT1-independent single-strand telomeric DNA binding activities in Brassicaceae. Plant J. 2009 Jun;58(6):1004-15. PubMed PMID: 19228335.

d. Shakirov EV, Song X, Joseph JA, Shippen DE. POT1 proteins in green algae and land plants: DNA-binding properties and evidence of co-evolution with telomeric DNA. Nucleic Acids Res. 2009 Dec;37(22):7455-67. PubMed PMID: 19783822; PubMed Central PMCID: PMC2794166.

3. The apparent differences in the number of POT1 genes between eukaryotic lineages led me to investigate evolution and co-evolution of telomeric DNA sequence, telomere organization and telomere-binding proteins. We discovered that many aspects of telomere biology are subject to change over time: the number of telomere-related genes, biochemical properties of telomere-binding proteins, even the telomere DNA sequence itself. We have also recently showed for the first time that positive selection can act on several amino acid residues of only one copy of a recently duplicated POT1 gene pair in Arabidopsis. To functionally test these residues in vivo, we developed a sensitive and quantitative genetic complementation assay, revealing a molecular role for these positively selected sites in reinforcing AtPOT1a protein-protein interactions. These research interests culminated in a 2015 paper on evolution of Arabidopsis POT1a protein by positive selection, where I served as a co-corresponding author. Furthermore, my expertise in comparative genomics was further enhanced by participation in genome projects for papaya and a model vascular plant Selaginella, and in gene expression and physiological genomics analyses of grasses.

   a. Shakirov EV, Perroud PF, Nelson AD, Cannell ME, Quatrano RS, Shippen DE. Protection of Telomeres 1 is required for telomere integrity in the moss Physcomitrella patens. Plant Cell. 2010 Jun;22(6):1838-48. PubMed PMID: 20515974; PubMed Central PMCID: PMC2910979.

   b. Banks JA, et al. [101 authors]. The Selaginella genome identifies genetic changes associated with the evolution of vascular plants. Science. 2011 May 20;332(6032):960-3. PubMed PMID: 21551031; PubMed Central PMCID: PMC3166216.

   c. *Beilstein MA, Renfrew KB, Song X, *Shakirov EV, Zanis MJ, *Shippen DE. Evolution of the Telomere-Associated Protein POT1a in Arabidopsis thaliana Is Characterized by Positive Selection to Reinforce Protein-Protein Interaction. **Corresponding authors*. Mol Biol Evol. 2015 May;32(5):1329-41. PubMed PMID: 25697340.

   d. Lovell JT, Shakirov EV, Schwartz S, Lowry DB, Aspinwall MJ, Taylor SH, Bonnette J, Palacio-Mejia JD, Hawkes CV, Fay PA, Juenger TE. Promises and Challenges of Eco-Physiological Genomics in the Field: Tests of Drought Responses in Switchgrass. Plant Physiology. 2016; 172(2):734-748. PubMed PMID: 27246097; PubMed Central PMCID: PMC5047078

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/eugene.shakirov.1/bibliography/48117442/public/?sort=date&direction=descending

## D. Additional Information: Research Support and/or Scholastic Performance

### Ongoing Research Support

**NIH/NIGMS 5R01GM127402-04** Shakirov (PI), 08/01/2018 – 05/31/2022.
Genetic and epigenetic architecture of natural telomere length variation.
Role: PI

The objective of this proposal is to elucidate the genetic and epigenetic causes of telomere length variation and to uncover pathways modulating natural telomere length polymorphism using the genetically facile plant *Arabidopsis thaliana* as a model.

### Completed Research Support:

**NIH/NIA (R03 AG052891)** Shakirov (PI); Juenger (co-PI). 04/2016-03/2019.
Identification and analysis of genetic determinants of natural telomere length variation.
Role: PI

The major goals of the project were to identify common genetic variants establishing telomere length polymorphism in the Arabidopsis recombinant inbred MAGIC population and to functionally characterize candidate genes.

**CRDF Global** (U.S.-Russian University Chem/Bio/Geo Research Competition), grant #25351. Shippen (PI), Shakirov (PI). 03/2018-04/2019). "A role for NOP2 in the control of telomere length".
Role: PI

The main goal of this collaborative proposal was to test the hypothesis that Arabidopsis NOP2A regulates telomere length set point by working in concert with DNA replication machinery.