

July 16, 2024

## ***CURRICULUM VITAE***

### **ZEMFIRA N. KARAMYSHEVA, Ph.D.**

Associate Professor

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**CITIZENSHIP:** U.S.A.

### **EDUCATION:**

**Ph.D. in Molecular Biology**, Moscow State University, Moscow, Russia

**M.Sc. Biology**, Kuban State University, Krasnodar, Russia

**FIELD OF SPECIALIZATION:** Molecular and Cellular Biology, Biochemistry, Microbiology.

### **RESEARCH POSITIONS:**

*Associate Professor (tenure-track)*, Department of Cell Biology and Biochemistry (2023-present), Texas Tech University Health Sciences Center, Lubbock, Texas

*Adjunct Associate Professor*, Department of Biological Sciences (2023-present), Lubbock, Texas

*Research Associate Professor*, Department of Biological Sciences (2022-2023), Texas Tech University, Lubbock, Texas

*Research Assistant Professor*, Department of Biological Sciences (2016-2022), Texas Tech University, Lubbock, Texas

*Research Faculty (Instructor)*, Department of Physiology (2011-2016), Department of Pharmacology (2006-2010), University of Texas Southwestern Medical Center, Dallas, 75390.

*Assistant Research Scientist* (2004-2006), *Postdoctoral Research Associate* (2000-2003), Department of Biochemistry and Biophysics (mentor Dr. Dorothy Shippen), Texas A&M University, College Station, TX 77843.

*IMSUT Postdoctoral Fellow* (1997-1999), *Pre-postdoctoral Fellow* (1996-1997), Department of Tumor Biology (mentor Dr. Yoshikazu Nakamura), Institute of Medical Science, University of Tokyo (4-6-1 Shirokanedai, Minato-ku, Tokyo 108) and Department of Biochemistry II (mentor Dr. Senya Matsufuji), Jikei University School of Medicine Minato-ku, Tokyo 105-8461, Japan.

### **RESEARCH INTERESTS:**

- Fundamental mechanisms of regulation of gene expression and its dysregulation in human diseases

- Translation control in protozoa and mammalian organisms
- Ribosome specialization
- Specialized ribosomes in *Leishmania* and their role in survival and adaptation of parasites during development and change of the host
- Drug resistance in *Leishmania* parasites
- RNA degradation pathways in protozoa and mammals
- mRNA translation regulation in health and disease
- Protein/mRNA quality control at the ribosome

#### **AWARDS, HONORS, etc.:**

2024 Featured in the Office of Research and Innovation Annual Report. Shared Efforts, Stellar Outcomes. *TTUHSC-TTU Research Collaborations Leads to Possible Drug Targets for Leishmaniasis*. p. 10.

2023 Featured in TTUHSC EurekAlert: <https://www.eurekalert.org/news-releases/993169>

2023 Featured in Daily Dose by Mark Hendricks: <https://dailydose.ttuhsu.edu/2023/june/research-collaboration-Leishmaniasis.aspx>

2023 Featured in Texas Tech Today on June 1, 2023 *Finding Possible Solutions Through Working With Parasites* by Doug Hensley: <https://today.ttu.edu/posts/2023/06/Stories/Finding-Possible-Solutions-Through-Working-With-Parasites>

2023 Article *Translational Reprogramming as a Driver of Antimony-drug Resistance in Leishmania* (published in *Nature Communications*) has been chosen by Senior Editor Madlen Luckner as the best research article for the Editors' Highlights *Microbiology and Infectious Diseases*.

2022 Awarded certificate for the top downloaded papers in *IJMS* for the review article: "*Translational Control of Secretory Proteins in Health and Disease*"

2021 Outstanding research mentor award recipient from Center for Transformative Undergraduate Experiences (TrUE) at TTU

2018 Top 5.0 % most viewed and downloaded articles: "*Lost in Translation: Ribosome-Associated mRNA and Protein Quality Controls*" published in *Frontiers in Genetics* was in the top 5.0 % of most viewed and downloaded articles in 2018.

2014 Featured in *Nature Reviews Genetics*: Research highlights: *Novel mRNA quality control mechanism*, vol. 15 (3), p. 144.

2014 Featured in *Trends in Biochemical Sciences*: Popp, M. W.-L. and Maquat L. E. *Defective secretory-protein mRNAs take the RAPP*, vol. 39 (4), p. 154-156.

2003 Paper published in NAR (2003) selected as a technical advance by Faculty 1000.

2003 Featured in preview in *Cell*: Cristofari G, Lingner J. *Fingering the ends: how to make new telomeres* 113:552-554.

2003 Selected speaker at Cold Spring Harbor, *Meeting on Telomeres and Telomerase*, NY.

2003 Selected speaker at FASEB Summer Research Conference, The Tenth International *Meeting on Ciliate Molecular Biology* (Vermont).

2000 Fellowship for participation in the summer school on *Structure and Function of Macromolecular Complexes* (Greece, Spetses).

## **RESEARCH SUPPORT**

**NIH/NIGMS 1R15GM146171-01.** 05/01/2022 – 04/30/2025

*Ribosome remodeling as a mechanism of translational control during stress.*

The major goal of this project is to investigate the fundamental concept of ribosome specialization in protozoa parasites using *Leishmania* as a model organism.

\$ 459,000.00

Role: PI

This grant has been recently transferred to Dr. Salazar-Bravo due to my relocation to TTUHSC. I became a co-PI and subaward has been issued to me.

**NIH/NIGMS 3R15GM146171-01S1. Karamysheva (PI)** 05/01/2022 – 04/30/2025

*Ribosome remodeling as a mechanism of translational control during stress.*

\$ 99,658.00

Administrative supplement grant to purchase equipment (Cytation-5).

Role: PI

This grant has been transferred to Dr. Salazar-Bravo due to my relocation to TTUHSC.

**Multi-PI Grant, Foundation for Prader-Willi Research** 04/01/2022 – 04/31/31/2024

(in collaboration with TTU SVM and TTUHSC)

Multi-PIs: Fon Tacer (PI), **Karamysheva (PI)**, Ponomarev (PI).

Title: *MAGEL2 role in adaptive stress response: New insights into MAGEL2 function and pathogenesis of PWS.*

\$108,000.00, to ZK \$32,400.00

Renewal for another year is available, and it will be submitted in 2024.

Role: multi-PI.

**NIH/NIAAA R03 AA028370.** Ponomarev (TTUHSC, PI); **Karamysheva (TTU, Co-I)**

05/01/2020 – 04/30/2023

*Effects of chronic alcohol consumption on the synaptic translationalome.*

\$153,000, to ZK \$39,000.00.

Role: Co-I.

**CMPR (Center for Membrane Protein Research) Seed Grant** 04/01/2020 – 04/30/2021

MacDonald (TTUHSC, PI); - **Karamysheva (TTU, Co-I)**

*Synaptic Membrane Proteins in the Brain are Regulated by the CSTF2 Polyadenylation Protein.*

\$ 20,000 to Dr. MacDonald.

Role: Co-I

**Grant # 5P30AG01230019. Karamysheva (PI) 07/2013- 06/2015**

**UT Southwestern Medical Center Pilot Project Research Grant** for two years from the **National Institute on Aging (NIA) Alzheimer's Disease Center (ADC) grant.**

*Characterization of RNA bound to tau protein in Alzheimer's disease brain samples and in vitro*.  
\$30,000.

Role: PI

### **Pending Research Support**

#### **Internal One Health Seed Grant**

**Karamysheva (PI), TTUHSC; Caleb Phillips (co-PI), TTU**

Submitted 06/20/2024.

Title: *Establishment of a new model to study persistence in leishmaniasis, an emerging zoonotic disease*

#### **Internal One Health Seed Grant**

**Maria Onyango (PI), TTU; Danielle Levitte (co-PI), TTU; Karamysheva (co-PI), TTUHSC;**

**Karamyshev (co-PI), TTUHSC;**

Submitted 06/30/2024.

Title: *Establishment of a new model to study persistence in leishmaniasis, an emerging zoonotic disease*

### **RESEARCH and TEACHING STATEMENT**

**Research.** I have expertise in molecular and cellular biology, microbiology, molecular parasitology, biochemistry, and molecular genetics. During my career I worked on studying several major cellular processes including mRNA translation, secretion, telomere maintenance and genome stability. Therefore, I have a comprehensive understanding how cells function and how different processes are interconnected in the cells. My major life-time scientific accomplishment is the discovery of programmed gene elimination in ciliated protozoa *Euplotes crassus* as a novel mechanism of gene expression regulation that was published in *Cell*. This discovery was highlighted in *Cell* preview: Fingering the ends: how to make new telomeres. I am an author of **36 papers** and **59 abstracts**. Publications include papers in the high-impact scientific journals such as *Cell* (two papers), *EMBO J.*, *Nucleic Acids Research*, and many others. Recently, paper on molecular mechanisms of drug resistance has been published in *Nature Communications*. Our recent review articles are among top the most viewed and downloaded articles in *Frontiers*. My major research interests lie in the areas of translational regulation in eukaryotes (protozoa parasites, mammalian organisms). I have several ongoing collaborative projects supported by grants and described under **Current Collaborations**.

**Teaching.** My teaching experience includes cellular and molecular biology, microbiology, general biology, biology seminars and CRISPR course. I was first to establish a gene editing technology at Texas Tech University, wrote a manual on gene editing and developed a new undergraduate research class **"Editing of microbial genomes using CRISPR technology"**. This is a project-based research course allowing undergraduate students to get hands-on research experience in the class setting and stimulate an interest in research. Students are exposed to cutting-edge research and learn how to edit genomes using CRISPR technology. Students are assigned either to knock-out an uncharacterized gene or perform gene-tagging. This class will develop scientific reasoning and critical thinking in undergraduate students and make them better prepared for graduate school.

During my career I mentored students and researchers from different countries (USA, Mexico, China, India, Korea, Colombia, Russia), so I have ability to work with and instruct culturally diverse students and researchers.

## RESEARCH OVERVIEW:

### ***1. Protein Synthesis (mRNA Translation)***

During my postdoctoral studies at the University of Tokyo and the Jikei University School of Medicine (Japan) I was involved in research on molecular mechanism of protein synthesis. As a result, we have found that re-initiation of translation is regulated by the distance between stop and initiation codons. I have cloned termination factors eRF1 and eRF3 from rabbit and developed frameshifting assay to measure eukaryotic translational termination *in vitro*. One of the publications resulting from this study was selected by faculty 1000 as a technical advance article.

### ***2. Regulation of Telomerases' Switch by Programmed Gene Elimination During Development***

During my postdoctoral studies at Texas A&M under mentorship of Dr. Shippen I have made a fundamental discovery of completely new type of gene expression regulation through gene elimination in protozoa. I have found that telomerase expression in *Euplotes crassus* is controlled by unique regulatory mechanisms that culminate in a developmental switch to a different catalytic subunit with properties suited to *de novo* telomere addition. More importantly this process is regulated by programmed gene elimination in order to achieve this switch. This work changed the view how gene silencing is achieved in the eukaryotic cells and was published in *Cell*.

### ***3. Gene Networks to Maintain Genome Stability in Human Cells***

As a research faculty at UT Southwestern Medical Center I was involved in several projects including work on genome-wide siRNA screen for increased survival of human cells arrested in mitosis. This screen allowed us to identify several human gene networks important for maintenance of genomic stability including spindle checkpoint, spliceosome, DNA replication and apoptosis.

### ***4. Novel Mechanism of Translational Regulation and Protein Quality Control***

At UTSW Medical Center I participated in the teamwork on the project that led to discovery of the novel pathway where aberrant protein production leads to the elimination of its own mRNA template. I was involved in providing ideas and experimental design for the project, as well as I performed crucial experiments on the specificity of the mechanism and conducted exceptionally challenging RNA immunoprecipitation experiments for this project. This fundamental discovery was published in *Cell*. The paper was highlighted in *Trends in Biochemical Sciences* and *Nature Reviews Genetics* and recommended by Faculty of 1000.

### ***5. Molecular mechanisms of translational control in Leishmania***

In 2023 I joined Department of Cell Biology and Biochemistry at Texas Tech University Health Science Center as an Associate Professor and continued a research project on molecular mechanisms of translational control in *Leishmania* which was originally initiated at TTU Department of Biological Sciences. It is aimed towards elucidation of the role of specialized ribosomes in *Leishmania* life cycle as well as the role of translational control in the development of drug resistance (see *Research Statement* for details). *Leishmania* parasites alternate between promastigotes living in the midgut of sandflies and amastigotes residing in the mammalian host. The change between hosts involves dramatic temperature, pH and nutritional stresses. The adaptation to each host and parasite survival in harsh environment is achieved through differential gene expression. Interestingly, *Leishmania major* lacks promoter-

mediated regulation of transcription and its gene expression is predominantly controlled at the level of mRNA translation and stability. My major project is based on hypothesis that *Leishmania* ribosomes undergo change in their composition in order to promote parasite survival and withstand environmental insults during change of host. We use polysome profiling technique to analyze changes in protein composition of ribosomes by proteomic approach and identify transcripts engaged in translation during stress using advances of next generation sequencing (NGS). Our data reveal a dramatic change in the ribosome composition supporting our hypothesis and the feasibility of the approach. Currently, we examine the role of specialized ribosome components in parasite survival and differentiation using CRISPR/Cas9 gene knock-out screen. The second project is focused on the molecular mechanisms of drug resistance in *Leishmania* parasites. Specifically, we explore the role of translational reprogramming in the development of drug resistance. Current studies on drug resistance in *Leishmania* are mostly limited to the research at genomic level. However, changes at genomic level cannot explain all possible mechanisms of resistance and treatment failures without genetic-based resistance are very widespread. Our data demonstrate that *Leishmania* parasites undergo a dramatic reprogramming of mRNA translation during development of drug resistance. It leads not only to changes in proteome but also to lipidome and metabolome remodeling thus contributing to drug resistance. We propose a novel concept just published in *Nature Communications* that establishes translational control as a major driver of antimony drug resistance in *Leishmania*. Two additional papers on drug resistance have been published (on lipidome and metabolome) in 2021. My team is also developing a project on molecular mechanisms of persistence in *Leishmania* parasites.

#### CURRENT COLLABORATIONS:

*Dr. Carlos Muscus*, University of Antioquia, Colombia, project: Drug resistance in *Leishmania* parasites, 3 articles have been published including one in *Nature Communications*.

*Dr. Kai Zhang*, TTU, Department of Biological Sciences, project: Role of sterols in RNA stability and protein homeostasis in *Leishmania* parasites. 3 papers have been published in collaboration.

*Dr. Klementina Fon Tacer*, School of Veterinary Medicine, TTU, Amarillo. Project 1: *MAGEL2 role in adaptive stress response: New insights into MAGEL2 function and pathogenesis of PWS*, supported by **Multi-PI grant** (Fon Tacer (PI), Karamysheva (PI), Ponomarev (PI) from Prader-Willi foundation. This project is of high interest for the foundation and is likely to get renewed for the next year.

*Dr. Igor Ponomarev*, Department of Pharmacology and Neuroscience, TTUHSC, project: Effects of chronic alcohol consumption on the synaptic translatome. Our collaborative project has been supported by **R03 grant**.

*Dr. Andrey Karamyshev*, Department of Cell Biology and Biochemistry, TTUHSC, projects: mRNA translation regulation in health and disease, RAPP pathway. Long-term collaborator. The collaboration already led to publication of 17 papers including articles in *Cell*, *NAR*, *JMB*, *Front. Genet.*, *JoVE*, *Nature Communications* and others. Co-investigator on awarded R15 NIH grant.

*Dr. Clinton MacDonald*, Department of Cell Biology and Biochemistry, TTU HSC, project: Regulation of synaptic membrane proteins by polyadenylation, was supported by CMPR grant. Two papers have been published in collaboration.



### **TEACHING EXPERIENCE:**

**Texas Tech University** (Lubbock, Tx):

**Cell Biology lectures**, 183 students (BIOL-3320-001: F2022)

**Microbiology lectures and labs** for science majors, 208 students (MBIO-3401-001: F2021; MBIO-3401-501-508: F2021); Microbiology lab (MBIO 3400-501: S2019).

**Advanced Topics in Biology:** *Editing of microbial genomes using CRISPR technology* (BIOL 6301-017: F2022)

**Topics in Biology:** *Editing of microbial genomes using CRISPR technology* (BIOL 4301-017: S2020, S2021, F2022)

**Biology Seminar** (BIOL 4101: S2019; F2019; S2020; F2020; S2021; F2021)

**Richland College** (Dallas, Tx)

**Biology 1406** for science majors – lectures and labs. (BIOL1406: F2006; S2007), Richland Community College.

### **Teaching innovations:**

Developed a new research course “*Editing of microbial genomes using CRISPR technology*” and wrote a manual for undergraduate and graduate students. The course teaches recent advances in gene editing using *Leishmania tarentolae* as a model organism. This is a project-based research course allowing undergraduate students to get hands-on research experience and stimulate an interest in research. Students are exposed to cutting-edge research and learn how to edit genomes (knock-out and gene tagging) using advanced CRISPR technology.

### **Teaching resources:**

Blackboard

Mastering biology

SmartWork for Cell Biology homework

### ***Graduate faculty***

2023-present: full member within Biochemistry, Cellular and Molecular Biology concentration of the Biomedical Sciences degree program in the Graduate School of Biomedical Sciences (GSBS).

2024-present: Biotechnology Program

### ***PhD student mentorship***

2023-present: PhD student Maria Camila Hoyos Sanchez. I co-mentor this student together with Dr. Klementina Fon Tacer, TTU SVM.

2022-present: PhD student Tara Bayat. I co-mentor this student together with Dr. Klementina Fon Tacer, TTU SVM. We have a multi-PI grant to support the project, and Tara works on the role of Magel2 in translation in different brain tissues.

### ***PhD student committee:***

2024-present: PhD student Sofia Altamirano, Department of Surgery at TTUHSC

Role: Committee Member

2023-present: PhD student Caleb Boren, Biology at TTU

Role: Committee Member

2022-present: PhD student Maria Camila Hoyos Sanchez, School of Veterinary Medicine at TTU

Role: Committee Member

2022-present: PhD student Tara Bayat, School of Veterinary Medicine at TTU

Role: Committee Member

**Graduate and undergraduate student research training:**

2024-present: MD/PhD rotation student Francis Khuong.

2023-present: undergraduate student Wolfgang Volchenkov.

2022-present: undergraduate Honors College, UMSI student Isha Iqbal. She works on ribosome specialization project.

2021-present: undergraduate Honors College student Isaiah Sanchez. He works on drug resistance in *Leishmania* and presented his recent studies at the TrUE symposium in October, 2022 and recent URC, 2023 and 2024. He was selected for a very prestigious Amgen internship at UTSW in the summer of 2023 and recently got accepted into PhD program at John Hopkins University.

2022-2023: undergraduate student Plamin Zehe. She worked on CRISPR gene knock-out screen.

2020-2022: Undergraduate Honors College student Sohan Sanghani. He worked on ribosome specialization in *Leishmania* parasites.

2019-2022: Ph.D. student Sneider Alexander Gutierrez Guarnizo. He came from Colombia to do internship with me as a part of his PhD studies. He worked on drug resistance in *Leishmania* parasites. He published four papers under my supervision including paper in *Nature Communications*; currently several papers are in preparation for submission.

2018-2021: undergraduate Honors student Andrea Perez, Honors College, Department of Biological Sciences, TTU. She worked on gene editing of parasitic genomes. She presented her data multiple times at Undergraduate Student Research conference at TTU and TTU HSC, Lubbock and national level conferences such as SACNAS conference (California) etc. She is also a co-author in the paper published in *Biomedicines*.

2017-2018: undergraduate student James Huffman, Department of Biological Sciences, TTU.

James got CISER scholarship for his research on *Leishmania major* under my supervision. He also won Undergraduate Research Excellence Award (TAUREA). James is a co-author in the paper published in *Journal of Visualized Experiments (JoVE)*. He is doing residency in the medical school.

2015: high school student (internship with UT Southwestern Med. Center) Connor Gilliland

2013: STARS summer research program participant at UTSW, teacher at Forest Meadow Junior High School Kimberly Harkrider

2008: Ph.D. student Soonjoung Kim, Dept. of Pharmacology, UTSW

2006: undergraduate student Rabia Qamer Soleja, Dept. Biochemistry & Biophysics, Texas A&M University.

2005: Ph.D. student Leyva Dinorah, Dept. Biochemistry & Biophysics, Texas A&M University;

2005: Ph.D. student Maria Shubina, Dept. Biochemistry & Biophysics, Texas A&M University

2005: Research class, undergraduate student Rabia Qamer Soleja, Dept. Biochemistry & Biophysics, Texas A&M University

2004: Ph.D. students Kelly Williamson, Dept. Biochemistry & Biophysics, Texas A&M University.

2004: Ph.D. student Madhu Jasti, Dept. Biochemistry & Biophysics, Texas A&M University

2003: Ph.D. student Li Zhang, Dept. Biochemistry & Biophysics, Texas A&M University.

2002: Ph.D. students Yulia Surovtseva and Sudhakar Chintharlapalli, Dept. Biochemistry & Biophysics, Texas A&M University. Yulia earned co-authorship in JBC paper.

2001: Ph.D. student Jennifer Welch, Dept. Biochemistry & Biophysics, Texas A&M University.

**STUDENTS AWARDS UNDER MY MENTORSHIP:**

**PhD student Tara Bayat:**

2022, Fall - Study Abroad Competitive Scholarship

2022, Spring and Fall - TTU TA RA Ex Scholarship

2022, Summer - Graduated School Designated Scholarship



Undergraduate Honors student **Isaiah Sanchez:**

2023- Amgen Internship

2022- TTU Honors College undergraduate research scholarship

Undergraduate Honors student **Isha Iqbal:**

2024 – Lubbock Economic Development Alliance Commercialization award

2022 - TTU Honors College undergraduate research scholarship

Undergraduate Honors student **Sohan Sanghani:**

2021 - TrUE scholarship

Undergraduate Honors student **Andrea Perez:**

2021-Outstanding undergraduate researcher award from Center for Transformative Undergraduate Experiences (TrUE)

2020-Award at the national SACNAS conference promoting multidisciplinary and multicultural STEM diversity (Microbiology section) for presentation: *Study of Ribosome Specialization in Leishmania Parasites Using Polysomal Profiling and CRISPR-Cas9 Gene Editing Technology*.

Undergraduate student **James Huffman:**

2018-Tech Undergraduate Research Excellence Award (TAUREA)

2018-Scholarship from the Center for the Integration of Stem Education and Research (CISER)

**SERVICE:**

**University service:**

2024 – present: member of MD/PhD selection committee, TTUHSC

2020-present: member of Texas Center for Comparative Cancer Research (TC<sup>3</sup>R), TTU, Director Dr. Klementina Fon Tacer, my role: to address cancer biology on the level of protein homeostasis, translational regulation, and apply CRISPR genome editing to study cancer.

**Departmental service:**

TTUHSC:

Department of Cell Biology and Biochemistry:

Judge at the CMPR poster session (2023)

TTU:

Department of Biological Sciences: graduate students award committee member (2022-2023)

Safety, security and emergency action committee member (2019-2023)

Biology seminar committee member and coordinator (2019-2023)

Judge at URC (2017-2019, 2021, 2022)

Judge at the 10th Annual Texas Tech Biological Sciences Symposium (2019)

Judge at South Plains Regional Science and Engineering Fair (2017- 2019)

**Memberships:**

Center of Excellence for Translational Neuroscience and Therapeutics, member

**Professional service:**

*Ad-Hoc* NIH grant reviewer at *Pathogenic Eukaryote (PTHE)* study section

*Ad-Hoc* NSF grant reviewer

Wellcome Funding, England

*Ad-Hoc* grant reviewer for Strasbourg Institute for Advanced Study, France

Associate editor in *Frontiers in Molecular Biosciences*

Editorial board member in journals: *Current Genetics*, *Vector Ecology and Control*

<https://spphllc.com/jvec/about/editorialTeam>

*Ad-Hoc* Reviewer for Journals:

*Clinical and Translational Medicine*

*Frontiers in Cellular and Infection Microbiology*

*Tropical Medicine and Infectious Disease*

*International Journal of Molecular Sciences*

*Genes*

*Biochimie*

*Pathogens*

*Pediatrics and Child Health*

### **Faculty development activities**

Attended a personal meeting with representative from Lewis-Burke Consultants to identify federal funding opportunities and priorities (August 16, 2024)

Visited Louis Paster Institute in France to discuss collaboration with Dr. Gerald Spaeth, (July 2024)

Attended an event *Discoveries to impact innovation*, (April 2024)

Early career (ECR) reviewer training at NIH (2020)

Attended grant writing seminar with Dr. Robertson, applied and was accepted to participate in grant proposal writing workshop (2021)

Attended NIH virtual seminar on program funding and grant administration (October 27-30, 2020)

Attended NIH grant writing seminar at TTU (2019)

Attended online seminars, Proteostasis Consortium Seminar Series organized by the scientists from the Northwestern University, Stanford University, Harvard Medical School, the University of California, San Francisco, and the Scripps Research Institute, during 2020, 2021.

Attended seminars, TTUHSC CBB Department, during 2016-2021

Attended seminars, TTU DBS Department, during 2016-2021

### **Outreach**

Presented interactive seminar on CRISPR gene editing for high school students in Highland Park High School in Dallas (January 2023).

### **INVITED TALKS AND SEMINARS:**

2024: *Translational reprogramming as a major driver of drug resistance in Leishmania parasites*. The National Centre for Scientific Research (CNRS), Montpellier, France.

2024: *Molecular mechanisms of translational control*. Graduate School of Biomedical Sciences, TTU Health Science Center, Lubbock, Texas.

2024: *mRNA translation regulation in health and disease*. Obesity Research Institute, Academic Event Center, TTU Health Science Center, Lubbock, Texas.

2024: *Translational control and drug resistance in Leishmania parasites*. Department of Immunology & Molecular Microbiology, TTU Health Science Center, Lubbock, Texas.

2023: *Translational control, ribosome specialization and drug resistance in Leishmania*. Department of Cell Biology and Biochemistry, TTU Health Science Center, Lubbock, Texas.

2023: *Leishmania pathogenesis and drug resistance: new frontiers in understanding molecular mechanisms*. Department of Biological Sciences, TTU, Lubbock, Texas.

2021: *Molecular mechanism of Leishmania pathogenesis and drug resistance*. Department of Cell Biology and Biochemistry, TTU Health Science Center, Host: Dr. Clinton MacDonald Lubbock, Texas.

2016: *Mechanistic role of SLC6A14 in inflammation, infection and cystic fibrosis disease*. Department of Cell Biology and Biochemistry, TTU HSC, Lubbock, Texas.

2014: *Role of amino acid transporter SLC6A14 as a gene modifier of cystic fibrosis disease* Cystic fibrosis meeting, UTSW, Host: Dr. Raksha Jain Dallas, Texas.

2012: *Amino acid transporter SLC6A14 potentiates inflammatory response in lung epithelial Calu-3 cell line*. Host: Dr. Klementina Fon Tacer. University of Ljubljana, Slovenia.

2012: *A family of TERT genes in Euplotes crassus facilitating a switch in telomerase activity*. Furano conference, Japan.

2012: *Differentially expressed TERT genes facilitate a switch in telomerase activity during development in Euplotes crassus*. Department of Molecular Biology, Jikei University School of Medicine, Tokyo, Japan. Invited talk. Host: President of Jikei University Dr. Senya Matsufuji.

2006: *A family of TERT genes in Euplotes crassus: evidence for developmentally programmed gene elimination to facilitate a switch in telomerase activity*. Seminar at the Department of Cell Biology, UT Southwestern Medical school. Hosts: Dr. Jerry Shay and Dr. Woody Wright, Dallas, Texas.

2006: *Euplotes crassus and Arabidopsis thaliana provide useful models to study telomerase and telomere structure and function*. Seminar at the Department of Pharmacology, UT Southwestern Medical school. Host: Dr. Hongtao Yu, Dallas, Texas.

2003: *A family of TERT genes in E. crassus – Evidence for developmentally programmed gene elimination to facilitate a switch in telomerase activity*. Meeting on Telomeres and Telomerase. Cold Spring Harbor, NY.

2003: *Developmentally programmed gene elimination in Euplotes crassus facilitates a switch in the telomerase catalytic subunit*. FASEB Summer Research Conference. The Tenth International Meeting on Ciliate Molecular Biology, Vermont.

2003: *Expression of the catalytic subunit of telomerase in Euplotes crassus is regulated during development*. Seminar at Baylor College of Medicine. Host: Dr. Vicki Lundblad, Houston.

## **PERSONAL LAB EXPERIENCE:**

**Cell Biology:** Gene editing using CRISPR/Cas9, culturing of Leishmania parasites, mammalian cells, yeast and bacteria, genome-wide siRNA screen, DNA and siRNA transfection of mammalian cell cultures, generation of stable cell lines, analysis of cell cycle defects by FACS (propidium iodide staining and MPM2 staining), luciferase activity assay in mammalian cell cultures, chromosome spreads, staining of mitotic cells using cytospin, different drug treatments including taxol, nocadovol, Etopozide, thymidine, MG 132.

**Animal work:** Mice infection experiments, animal imaging to monitor infection progression using luciferase assay, limited dilution assay.

**Biochemistry:** protein expression, purification and analysis, polysome profiling, affinity purification of telomerase, RNA pull-down using biotinylated oligonucleotides, RNA-immunoprecipitation, gel-shifts, telomerase activity assay, transcription and translation *in vitro* (rabbit reticulocyte and wheat germ systems), yeast two-hybrid system, nuclei isolation, SDS-polyacrylamide gel electrophoresis, non-denaturing electrophoresis, *in vitro* frameshifting and readthrough assay, pulse-chase analysis of protein processing, alkaline phosphatase assays, viral particles preparation, killer yeast activity assays, thin-layer chromatography, assay for RNA polymerase activity in viral particles.

**DNA and RNA technologies:** gene cloning, genotyping, DNA sequencing, site-directed mutagenesis, amber-suppressor mutagenesis, PCR, Q-PCR, RT-PCR, overlapping PCR to connect different DNA fragments, 5' and 3' RACE (Rapid Amplification of cDNA Ends), gene library screening, Southern and Northern blotting, preparation of plasmid and bacteriophage DNA, isolation of RNA and genomic DNA from different organisms, preparation of radiolabeled DNA, RNA and oligonucleotides, ECL nucleic acid labeling and detection, agarose and polyacrylamide gel electrophoresis.

**Gene expression:** expression of cloned genes in *E. coli*, yeast, plants and mammalian cell cultures.

**Immunology methods:** antibody preparation and purification, co-immunoprecipitation, Western blotting, ECL detection, immunofluorescence, ELISA, large scale IP for mass spec.

## GENE SEQUENCES SUBMITTED TO THE DDBJ/EMBL/GENEBANK

- **AB029089** *Oryctolagus cuniculus* mRNA for eukaryotic polypeptide chain release factor 1 (eRF1).
- **AB035256** *Oryctolagus cuniculus* mRNA for eukaryotic polypeptide chain release factor 3 (eRF3).
- **AY267543** *Moneuplotes crassus* micronuclear telomerase reverse transcriptase (TERT-2) gene, complete cds.
- **AY267544** *Moneuplotes crassus* micronuclear telomerase reverse transcriptase (TERT-3) gene, complete cds.

## LIST OF PUBLICATIONS

(\* = corresponding author).

1. Gutierrez Guarnizo, S. A., Kellogg, M. K., Miller, S. C., Tikhonova, E. B., Karamysheva, Z. N. **Karamyshev, A. L.** (2023) Pathogenic Signal Peptide Variants in the Human Genome. *NAR Genomics and Bioinformatics*, 5(4). <https://doi.org/10.1093/nargab/lqad093>.
2. Tarannum, A., Rodríguez-Almonacid, C.C., Salazar-Bravo, J., **Karamysheva, Z.N.\*** Molecular Mechanisms of Persistence in Protozoan Parasites. *Microorganisms*. Published September 7, 2023, 11, 2248. <https://doi.org/10.3390/microorganisms11092248>.
3. **Karamysheva, Z. N.\***, Karamyshev, A. L.\* (2023) Aberrant Protein Targeting Activates Quality Control on the Ribosome. *Frontiers in Cell and Developmental Biology*. Volume 11. Published June 6, 2023. doi: 10.3389/fcell.2023.1198184.

4. Gutierrez Guarnizo S. A., Tikhonova E. B., Karamyshev A. L.\*, Muskus C.E.\*, **Karamysheva Z. N.\*** Translational reprogramming as a driver of antimony-drug resistance in *Leishmania*. *Nature Communications* 2023 May 5;14(1):2605. doi: 10.1038/s41467-023-38221-1. PMID: 37147291; PMCID: PMC10163012. **Impact factor 17.69**

The article has been chosen by the Senior Editor Madlen Luckner as the best research article in the Editors' Highlights in *Microbiology and Infectious Diseases*.

The article has been featured in Texas Tech Today on June 1, 2023. *Finding Possible Solutions Through Working With Parasites* by Doug Hensley.

<https://today.ttu.edu/posts/2023/06/Stories/Finding-Possible-Solutions-Through-Working-With-Parasites>

*TTUHSC Daily Dose* by Mark Hendricks. *TTUHSC-TTU Research Collaboration Leads to Possible Drug Targets for Leishmaniasis* (by Mark Hendricks). <https://dailydose.ttuhsu.edu/2023/june/research-collaboration-Leishmaniasis.aspx>

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7. Tikhonova, E. B., Gutierrez Guarnizo, S. A., Kellogg, M. K., Karamyshev, A., Dozmorov, I. M., **Karamysheva, Z. N.**, Karamyshev, A. L. (2022) Defective Human SRP Induces Protein Quality Control and Triggers Stress Response. *Journal of Molecular Biology*, vol. 434, Issue 22. <https://doi.org/10.1016/j.jmb.2022.167832>
8. **Karamysheva, Z. N.\***, Moitra S., Perez A., Mukherjee S., Tikhonova E.B., Karamyshev A.L., Zhang K.\* (2021). "Unexpected Role of Sterol Synthesis in RNA Stability and Translation in *Leishmania*." *Biomedicines*, 9(6): 696; <https://doi.org/10.3390/biomedicines9060696>
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11. **Karamysheva, Z. N.\***, Gutierrez Guarnizo, S. A., Karamyshev, A. L.\* (2020) Regulation of Translation in the Protozoan Parasite *Leishmania*, *Review, Int. J. Mol. Sci.*, 21, 2981; doi:10.3390/ijms21082981.

12. Karamyshev A. L.\*, Tikhonova, E. B., **Karamysheva, Z. N.\*** (2020) Translational Control of Secretory Proteins in Health and Disease. *Review, Int. J. Mol. Sci.*, 21, 2538; doi:10.3390/ijms21072538.

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13. **Karamysheva, Z. N.\***, Tikhonova, E. B., Karamyshev, A. L.\* (2019) Granulin in Frontotemporal Lobar Degeneration: Molecular Mechanisms of the Disease. *Review, Frontiers in Neuroscience*, doi: 10.3389/fnins.2019.00395. PMID: 31105517 PMCID: PMC6494926.
14. Tikhonova, E. B., **Karamysheva, Z. N.**, von Heijne, G., Karamyshev, A. L. \* (2019) Silencing of aberrant secretory protein expression by disease-associated mutations. *Journal of Molecular Biology*. PMID: 31100385, doi: 10.1016/j.jmb.2019.05.011. PMID: 31100385.
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20. Karamyshev A.L., Patrick, A. E.\*, **Karamysheva, Z. N.\***, Griesemer D.S., Hudson H., Tjon-Kon-Sang S., Nilsson I., Otto H., Liu Q., Rospert S., von Heijne G., Johnson A.E., Thomas P.T. (2014) Inefficient SRP Interaction with a Nascent Chain Recruits Ago2 and Triggers Specific mRNA Degradation. *Cell*, 156(1-2), 146-157. **Impact factor 66.85.**

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## MEETINGS, CONFERENCES AND SYMPOSIA

Results were presented at various international, national and local meetings, conferences and symposia (total **59** abstracts).

1. Gutierrez Guarnizo, S. A., Tikhonova, E. B., Karamyshev, A. L., Muskus, C., **Karamysheva, Z. N.** *Development* of antimony drug resistance is dictated by translational reprogramming in *Leishmania*. Gordon Research Conference, June 9-14, 2024, Newport, Rhode Island, USA.
2. Tikhonova, E. B., Grozdanov, P. N., Gutierrez Guarnizo, S. A., **Karamysheva, Z. N.**, Karamyshev, A. L. Translational Repression Induced by the SRP Failure to Target Proteins to the Endoplasmic Reticulum. Abstracts of papers presented at the 2024 Cold Spring Harbor meeting on Protein Homeostasis in Health and Disease. April 24-28, 2024, p. 185. Cold Spring Harbor, New York, USA.
3. Iqbal, I., Moncada, J., Rodriguez, C., Sanchez I., **Karamysheva Z. N.** *Optimization of Transfection in Leishmania parasites*. 16<sup>th</sup> TTU Undergraduate Research Conference, April 9-11, 2024, Texas Tech University, Lubbock, Texas, USA.
4. Sanchez I., Iqbal, I., Moncada, J., Rodriguez, C., **Karamysheva Z. N.** *Optimization of CRISPR Gene Editing using AMAXA 4D-Nucleofector*. 16<sup>th</sup> TTU Undergraduate Research Conference, April 9-11, 2024, Texas Tech University, Lubbock, Texas, USA.
5. Fon Tacer, K., Hoyos Sanchez, M. C., Bayat T., Popy F., Ponomarev I., Castro-Piedras I., **Karamysheva, Z. N.**, Tikhonova, E. B., Karamyshev, A. L. *Magel2 Role in the Stress Response to Fasting: From Hypothalamic Single-cell Dynamics to Hormonal Balance Throughout the Body*. Foundation for Prader-Willi Research Symposium, October 5-7, 2023, Denver, CO.
6. Bayat T., Tikhonova, E. B., Hoyos Sanchez, M. C., Popy, F., Diab H., Thompson, J., Karamyshev, A. L., **Karamysheva, Z. N.**, and Klementina Fon Tacer. *Role of mRNA*

*Translational Regulation in Hormone Secretion Deficit in MAGE-L2 KO Mouse Model*. Foundation for Prader-Willi Research Symposium, October 5-7, 2023, Denver, CO.

7. Tikhonova, E., **Karamysheva, Z. N.**, Karamyshev, A. *Translational Repression Induced by the SRP Failure to Target Proteins to the Endoplasmic Reticulum*. EMBO Workshop on Protein quality control: From molecular mechanisms to therapeutic intervention. Srebreno-Dubrovnik, Croatia, 21 – 26 May 2023.
8. Sanchez I., Gutierrez Guarnizo, S. A., Tikhonova, E. B., Zhang K., Karamyshev, A. L., **Karamysheva, Z. N.** *Mechanism of antimony drug resistance in Leishmania parasites*, 15<sup>th</sup> Annual Undergraduate Research Conference, April 11<sup>th</sup>, 2023, Texas Tech University, Lubbock, Texas, USA.
9. Iqbal I., Gutierrez Guarnizo, S. A., Tikhonova, E. B., Karamyshev, A. L., **Karamysheva, Z.N.** *Ribosome specialization in Leishmania parasites*, 15<sup>th</sup> Annual Undergraduate Research Conference, April 11<sup>th</sup>, 2023, Texas Tech University, Lubbock, Texas, USA.
10. Tikhonova, E. B., Gutierrez Guarnizo S. A., Kellogg, M. K., Miller S. C., Orobets, K., **Karamysheva, Z. N.**, Karamyshev, A. L. *RAPP is a Co-Translational Quality Control for Secretory and Membrane Proteins*. Gordon Research Conference on Translation Machinery in Health & Disease: Protein Synthesis and Cellular Synergy. February 19-24, 2023, Galveston, Texas, USA.
11. Bayat T., Tikhonova E. B., Hoyos Sanchez M. C., Popy F., Andrey L. Karamyshev, **Karamysheva Z. N.**, and Fon Tacer K. *mRNA translational changes upon loss of MAGE-L2 in Prader-Willi syndrome mouse model*. 22<sup>nd</sup> annual graduate poster competition, March 2023, Texas Tech University, Lubbock, Texas, USA.
12. Sanchez I., Gutierrez Guarnizo, S. A., Tikhonova, E. B., Karamyshev, A. L., Muskus, C., **Karamysheva, Z. N.** *Translational control as a major driver of drug resistance in Leishmania parasites*, Transformative Undergraduate Experiences Symposium, October 14-15<sup>th</sup>, 2022, Texas Tech University, Lubbock, Texas, USA.
13. Gutierrez Guarnizo, S. A., Tikhonova, E. B., Karamyshev, A. L., Muskus, C., **Karamysheva, Z. N.** *Translational Reprogramming as Central Driver of Antimony Drug Resistance in Leishmania Parasites*, The 7<sup>th</sup> World Congress on Leishmaniasis (WorldLeish7), August 1-6, 2022, Cartagena, Colombia.
14. Sanghani, S., Zhang, K., Karamyshev, A.L., **Karamysheva, Z.N.** *CRISPR/Cas9 Gene Knock-out Screen to Explore the Translational Mechanisms in Leishmania parasites*, Undergraduate Research Conference, March 29-30, 2022, Texas Tech University, Lubbock, Texas, USA.
15. Perez A., Gutierrez Guarnizo S.A., Tikhonova E.B., Zhang K, Karamyshev A.L., **Karamysheva, Z.N.** *Ribosome Specialization as a Mechanism of Leishmania Parasite Survival in Mammalian Host*, April 12-14, 2021, NCUR, online.
16. Perez A., Gutierrez Guarnizo S.A., Tikhonova E.B., Zhang K, Karamyshev A.L., **Karamysheva, Z.N.** *Genome Editing using CRISPR-Cas9 to Study Ribosome Specialization in Leishmania Parasites*, Undergraduate Research Conference, March 29-30, 2021, Texas Tech University, Lubbock, Texas, USA.
17. Perez A., Gutierrez Guarnizo S.A., Tikhonova E.B., Zhang K, Karamyshev A.L., **Karamysheva, Z. N.** *Specialized ribosomes as a mechanism to remodel translation in protozoa parasites during*

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18. Tikhonova, E. B., **Karamysheva, Z. N.**, Karamyshev, A. L. *Regulation of aberrant protein production (RAPP) as a mechanism to maintain homeostasis of secretory and membrane proteins.* Cold Spring Harbor Meeting Protein Homeostasis in Health & Disease, November 11 - 14, **2020**, Abstracts of papers presented at the 2020 virtual meeting, p. 146, Cold Spring Harbor, New York, USA.
  19. Perez A., Gutierrez Guarnizo, S. A., Tikhonova, E. B., Zhang, K., Karamyshev, A. L., **Karamysheva, Z. N.** *Study of Ribosome Specialization in Leishmania Parasites Using Polysomal Profiling and CRISPR-Cas9 Gene Editing Technology.* 2020 SACNAS – The National Diversity in STEM Virtual Conference, October 19-24, 2020, online.
  20. Gutierrez Guarnizo, S. A., Perez, A. F., Tikhonova, E. B., Zhang, K., Karamyshev, A. L., **Karamysheva, Z. N.** *Ribosome Specialization as a Mechanism of Leishmania Parasite Survival During Infection.* Annual Student Research Week March 10-13, 2020. Texas Tech University Health Sciences Center, Lubbock, Texas, USA.
  21. Gutierrez Guarnizo, S. A., Tikhonova, E. B., Galeano, E., Muskus, C., **Karamysheva, Z. N.**, Karamyshev, A. L. *Mechanism of Antimony Drug Resistance in Leishmania Parasites.* Annual Student Research Week March 10-13, 2020. Texas Tech University Health Sciences Center, Lubbock, Texas, USA.
  22. Tikhonova, E. B., Karamyshev, A., **Karamysheva, Z. N.**, Karamyshev, A. L. The failure of co-translational targeting by signal recognition particle leads to complex cellular stress response. *11<sup>th</sup> Annual CMPR Symposium*, October 4, 2019 TTUHSC, Lubbock, TX, USA.
  23. Perez A., Zhang K. and **Karamysheva Z. N.** Lipid imbalance leads to reduced RNA and protein levels in Leishmania major parasites. April 2-3, 2019, *11th annual Texas Tech University Undergraduate Research Conference*, Lubbock, TX, USA.
  24. Karamyshev, A. L., Tikhonova, E. B., **Karamysheva, Z. N.** Ribosome associated mRNA degradation of aberrant proteins in human diseases. *The 20th Takeda Science Foundation Symposium on Bioscience.* February 1 - 2, 2019. Center for Learning and Innovation, Takeda Pharmaceutical Company, Ltd. (CLI) 50-2 Yamadamnamini, Suita Osaka 565-0823, Japan.
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  26. Karamyshev, A. L., Tikhonova, E. B., **Karamysheva, Z. N.** Quality Control of Secretory Proteins During Translation in Health and Disease. *FASEB conference on Protein Folding in the Cell.* July 22-27, 2018 St. Bonaventure University, NY, USA.
  27. Karamyshev, A. L., Tikhonova, E. B., **Karamysheva, Z. N.** Specific mRNA Degradation as a Mechanism to Silence Aberrant Protein Expression in Human Diseases. *FASEB conference on Post-transcriptional Control of Gene Expression: Mechanisms of RNA Decay.* June 24-29, 2018, Scottsdale, AZ, USA.
  28. Tikhonova, E. B., **Karamysheva, Z. N.**, Karamyshev, A. L. Inefficient SRP Interaction with Signal Sequences of Secretory Proteins Induces their mRNA Degradation by the RAPP Pathway and Causes Human Diseases. *Gordon Research Conference on Protein Transport Across Cell Membranes*, March 11-16, 2018, Galveston, Texas, USA.

29. Baca, K., **Karamysheva, Z.**, Tikhonova, E., Huffman, J., Karamyshev, A. Polysome Profiling in *Leishmania*, Human Cells and Mouse Testis, *10th annual Texas Tech University Undergraduate Research Conference*, March 27-29, 2018, 212, p.164, Lubbock, TX, USA.
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35. **Karamysheva, Z. N.**, Fon Tacer K., Shadaan A., Winter M.C., Potts R., Engelhardt J.F., Jain, R., Greenberg, D.E., Thomas, P.J. Mechanistic study of putative modifier of cystic fibrosis severity. *Abstract of NACFC 29<sup>th</sup> annual conference*, October 8-10, 2015, Phoenix, Arizona.
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40. Thomas P. J., Schmidt A., Mendoza J. L., Millen L., Richardson J., Fuller M., Patrick A., Vetter A., **Karamysheva Z.**, Karamyshev A. L. Mechanism of Action & Molecular Pathology: Matching Drugs & Mutants. *The 26th Annual North American Cystic Fibrosis Conference, Pediatric*

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