BIOGRAPHICAL SKETCH

NAME: Roxane Khoogar
eRA COMMONS USERNAME: Khoogarr2
POSITION TITLE: Postdoctoral Fellow at the Cancer Research Center, NCI, NIH

EDUCATION:

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Azad University of Iran	B.S.	08/2001	05/2007	Cell & Molecular Biology
University of Alabama at Birmingham	M.S.	08/2011	05/2012	Biotechnology
UT Health San Antonio	Ph.D.	08/2012	05/2019	Molecular Medicine (Pharmacology)

A. Personal Statement

My long-term goal is to develop a comprehensive understanding of key developmental pathways and investigate how alterations in gene expression contribute to human disease. My academic training and research experience have provided me with an excellent foundation in molecular biology, RNA biology, and cancer genetics.

As a master's student, I was awarded an NIH-funded internship at the University of Alabama at Birmingham in Dr. Karen Iles' laboratory, studying cytoprotective Phase II gene polymorphisms in lung cancer. During my PhD at UT Health San Antonio, I conducted projects on prostate and colon cancer under Drs. Tim Huang and Wargovich, culminating in a review publication and a poster presentation at AACR. I also generated genome-wide methylation data using MBD-cap. For my dissertation, under Dr. Peter Houghton—an internationally recognized leader in pediatric therapeutics—I investigated the transcriptional deregulation mediated by EWSR1-FLI1 in Ewing sarcoma using single-cell RNA-seq. This work resulted in a first-author publication titled "Single-cell RNA profiling identifies diverse cellular responses to EWSR1/FLI1 downregulation in Ewing sarcoma cells" (2021).

My first postdoctoral fellowship was at Dana-Farber Cancer Institute, Harvard Medical School, where I studied genomic and transcriptomic heterogeneity contributing to relapse in pediatric sarcomas. I then joined the RNA Biology Laboratory at the NIH under Dr. Colin Wu's mentorship, where I investigate the impact of TET2 loss on tRNA methylation dynamics and translation rates in K562 leukemia cells. This work aims to uncover the role of 5mC and its oxidation in tRNA biology and gene regulation.

In parallel, I collaborated with Dr. Jordan Meier to study the effects of NAT10/ThumpD1 loss on tRNA stability and translation. Our collaborative work, integrating ribosome profiling and tRNA-seq data from engineered cell and animal models, has been published in Science Advances (2024), where I am a co–first author alongside Dr. Supuni Thalalla. This collaboration has since concluded, and I continue to pursue new directions exploring tRNA quality control and ribosome selectivity through reporter assays, CRISPR screens, and structural approaches such as cryo-EM.

Through my current and past experiences, I have developed a multifaceted expertise in post-transcriptional gene regulation and translational control, and I am now focused on building a robust, independent research program dedicated to understanding how RNA modifications shape cellular states and contribute to disease.

1. Supuni Thalalla Gamage, Roxane Khoogar, et al.Transfer RNA acetylation regulates in vivo mammalian stress signaling. BioRxiv, 2024.
2. Roxane Khoogar, Fuyang Li, Yidong Chen, Myron Ignatius, Elizabeth R. Lawlor, Katsumi Kitagawa, Tim H-M Huang, Doris A. Phelps, Peter J. Houghton. Cell Single-cell RNA profiling identifies diverse cellular responses to EWSR1/FLI1 downregulation in Ewing sarcoma cells. Oncol, 2022.
3. Yasaman Kalantarmotamedi, Roxane Khoogar, Doris A. Phelps, Peter Houghton, Andreas Bender. A Promising Computational Personalised Medicine Approach Enabled Identification of Highly Active and Selective Compounds for Childhood Sarcoma Cell Lines. SSRN Electronic Journal. January 2021.
4. Roxane Khoogar, Peter Houghton. Single-cell RNA-seq reveals heterogeneity for stem cell markers, LRG5 and CD271 to predict a subpopulation in Ewing sarcoma cells with lower levels of BRAF. AACR meeting. Cancer Research 78 (13 Supplement): 2074-2074. July 2018.
5. Roxane Khoogar, Doris Phelps, Peter Houghton. Shedding light on the unknown of Ewing sarcoma: Single cell study shows a co-expression pattern between TAPA-1 and EWSR1-FLI1. AACR meeting. April 2017.
6. Roxane Khoogar, Byung-Chang Kim, Jay Morris, Michael Wargovich. Targeting the progression of cancer with natural products: A focus on gastrointestinal cancer. AJP Gastrointestinal and Liver Physiology 310(9). February 2016
7. Supercritical extract of Azadirrachta indica in chemoprevention of colon cancer. Roxane Khoogar, Keys Mukhophadyay, Jay Morris, Michael Wargovich. AACR meeting. 74(19 Supplement): 3210. October 2014

B. Positions and Honors

<u>Positions, Scientific Appointments, and Employment</u>

2021 – Present **CRTA Postdoctoral Fellow, RNA Biology Laboratory, NCI-NIH**
2019 – 2021 **Harvard Fellow of Medicine, Dana-Farber Cancer Institute, Harvard**
2019-2021 **Postdoctoral Scholar, Broad Institute of MIT**
2012 – 2019 **Graduate Research Assistant, University of Texas Health San Antonio**

2011-2012 **Graduate Student, University of Alabama at Birmingham**
2012 – Present **Member, American Cancer Research Association**
2015 – Present **Member, Cancer Molecular Therapeutics Research Association**
2022 – Present **Member, Science Policy Group**
2022-2023 **Member, The NIH Fellows Editorial Board**
2022-Present **Member, NIAID-NCI Global Health Interest Group**

C. Contribution to Science

1. **Transcriptional and Epigenetic Regulation in Ewing Sarcoma**
   During my PhD training at UT Health San Antonio, I focused on the transcriptional and non-transcriptional regulatory roles of the oncogenic fusion protein EWSR1-FLI1 in Ewing sarcoma. Using single-cell RNA sequencing, I investigated how EWSR1-FLI1 regulates cellular subpopulations and uncovered potential biomarkers associated with quiescent, therapy-resistant cell states. This work illuminated key mechanisms of pediatric cancer cell survival and adaptation to stress and provided critical insights into tumor heterogeneity and transcriptional reprogramming during oncogenesis.
   - *Publication*: Khoogar et al. "Single-cell RNA profiling identifies diverse cellular responses to EWSR1/FLI1 downregulation in Ewing sarcoma cells." (2022) First author.
2. **Postdoctoral Research in Proteomic Analysis of Circulating Tumor Cells (CTCs)**
   At Dana-Farber Cancer Institute/Harvard Medical School, I designed and optimized a novel workflow to perform single-cell proteomics on liquid biopsy samples from sarcoma patients using mass cytometry (CyTOF). This approach, which involved GFP-tagged mimetic CTCs and heavy metal labeling, enabled the identification of key signaling proteins involved in treatment resistance and disease progression. This experience deepened my understanding of cancer heterogeneity and provided a platform to identify proteomic signatures of relapse.
3. **tRNA Dynamics and Translational Regulation in Hematologic Malignancies**
   In my current postdoctoral training at the NIH, I am investigating how loss of TET-mediated RNA demethylation (specifically 5mC to hmC) alters tRNA dynamics, codon usage, and translational pausing in leukemia cells. I developed an integrated pipeline that combines seCLIP-Mim-Seq with ribosome profiling to simultaneously capture ribosome stalling events and tRNA isoacceptor/isodecoder abundance. This project is revealing novel sequence-based determinants of translational regulation and offers mechanistic insight into tRNA quality control in response to epitranscriptomic perturbations. These findings may enable selective control of translation in metabolically distinct AML states.
4. **Discovery of Epitranscriptomic Signaling on tRNA**
   In collaboration with Dr. Jordan Meier's lab and postdoc, Supuni Thalala, I explored the role of acetylation-based signaling and post-transcriptional modifications in shaping tRNA function and translation outcomes. We conducted MimSeq profiling of tRNA modifications in THUMPD1 and TET2 knockout models, providing a high-resolution map of dynamic N4-acetylcytidine (ac4C) marks and their regulatory consequences. This collaboration culminated in a co–first author publication in *Science Advances* and led to the identification of potential mechanism regulating cellular fate when tRNA modifying enzyme are inactive with therapeutic relevance.

- *Publication: Thalalla, D., Khoogar, R. et al. Science Advances (2024).* First co-author.

Complete List of Published Work in My Bibliography:

https://pubmed.ncbi.nlm.nih.gov/?term=Roxane+Khoogar

https://connects.catalyst.harvard.edu/Profiles/display/Person/197706