



Doctoral Dissertation Defense Announcement

“Transcriptomic Diversity of Innate Lymphoid Cells During Their Developmental in Human Lymph nodes”



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Date: Wednesday, April 17, 2024

Time: 1 pm (CST)

Defense Location: BRI Conference room

Zoom: <https://mcw-edu.zoom.us/j/92991701932?pwd=S1FsT0RIQTNXU0ZTWmNGZ3pEd0g3dz09>

Meeting ID: 929 9170 1932 Passcode: 2Th0Aqv4

Graduate Studies:

Biochemistry of the Cell

Intro to Biomedical Research

Techniques in Molecular & Cell Biology

Molecular and Cellular Biology

Mechanism Cellular Signaling

Classical & Molecular Genetics

Ethics & Integrity in Science

Research Ethics Discussion Series

Cellular & Molecular Immunology

Immunology Journal Club

Tumor Immunology

Immunological Tolerance

Microbiology & Immunology Seminar Series

Biostatistics

Reading and Research

Doctoral Dissertation

Dissertation

“Transcriptomic Diversity of Innate Lymphoid Cells During Their Developmental in Human Lymph nodes”

Innate lymphoid cells (ILCs) are largely tissue-resident and do not express clonotypic receptors. In humans, ILCs are primarily described within the mucosal tissues. However, their presence and function(s) in the human draining lymph nodes (LN) are unknown. Here we performed single-cell RNA sequencing to unravel the tissue-specific transcriptional profiles of 47,287 ILCs within the human abdominal and thoracic LNs and compared them with that of bone marrow (BM) and spleen.

LNs contained a higher frequency of CD127+ ILCs than in BM or spleen. We found LN as the site for the early development of ILCs. A naïve ILCs population exists in the human LNs that can differentiate into other ILC subtypes. We identified highly heterogeneous sub-clusters of ILC1 and ILC3. Using unsupervised clustering we defined three ILC1, four ILC3, and one ILC2 sub-clusters in the LNs. Both cell types have clusters with a high level of heat shock protein genes, including HSPA1A, HSPA1B, and DNAJB, and clusters possibly trafficking from BM with a high level of the chemokine receptor, CXCR4. Finally, we isolated the NK cells from tumor-negative or tumor-bearing LNs from patients with head and neck squamous cell carcinoma (HNSCC) to unravel the tumor-specific transcriptional profiles of NK cells as the major population of innate lymphoid cells. Comparison of tumor-bearing LN with non-tumor-bearing LNs indicates that NK cells shifted the phase from circulatory to tissue-resident. They have higher expression of cytotoxic markers, including GZMs and perforin, while they express exhaustion markers, including PD1, LAG3, and CTLA4.

Our study is the in-depth characterization of human ILCs in LNs and understanding the transcriptome of ILCs under homeostasis. We extended our studies within the TME of Head and Neck Small Cell Carcinoma (HNSCC) Our findings will help to generate innovative methods to reinvigorate non-responsive ILCs.

Education

Ph.D. in Biomedical Science

Medical College of Wisconsin – Department of Microbiology & Immunology,
Milwaukee, WI

Master of Science in Medical Biotechnology

Thesis – Designing & Constructing a Biosensor (DNA ELISA) to detect *E. coli* ATCC
25922 using Genomic DNA
Tarbiat Modares University, Tehran, Iran

Bachelor of Science in Biology

Shiraz University, Shiraz, Iran

Professional Experience

Medical College of Wisconsin, Milwaukee, WI 2018 – Present

Research Assistant

Analyze and interpret transcriptomic data, single-cell, and bulk analysis as well as genomic data to identify relevant Transcriptomic and genome profile and genetic variations and their implications on immune cell function. Contribute to the collection and preparation of biological samples for both transcriptomic and genomic analysis while following established processing protocols. Perform transcriptomic data analysis, including preprocessing, quality control, differential gene expression analysis, developmental pathways, and functional enrichment analysis.

- Discovered breakthroughs in understanding critical immune cells by facilitating robust developmental techniques for dissecting transcriptomic diversity of innate lymphocytes in human lymph nodes through the application of advanced flow cytometry, PCR, and cloning techniques.
- Analyzed and interpreted data from cutting-edge methodologies, including single-cell, bulk RNA to understand and compare the immune profile in healthy humans and individuals with diseased conditions like cancer.
- Uncovered essential insights into root causes of immune dysfunction in Fanconi Anemia patients by conducting an in-depth analysis of transcriptome and genomic data with whole genome sequencing and advanced R-loop assessments using MAP-R and gene editing using CRISPR.

Genentech, Francisco, CA 2023

Internship Program

Contributed to the investigation of immune checkpoint molecule production by macrophages engaged in Antibody-Dependent Cellular Phagocytosis (ADCP), demonstrating proficiency in analyzing diverse sequencing data types, including single-cell, bulk, and whole-genome data, and uncovering critical insights into the role of immune cells in cancer immunology. Conducted statistical analysis to identify trends, correlations, and significant findings related to immune checkpoint molecule production in macrophages.

- Attained skills to isolate monocytes, induce their differentiation into distinct primary macrophage subtypes (M1 and M2), track phagocytic activity, label cells, and monitor kinetics using IncuCyte system during in vitro experiments.
- Delivered novel insights into disease-specific gene expression patterns and potential therapeutic targets through innovative application of MULTI-seq and CMO tag single-cell analysis.
- Revealed novel therapeutic targets by unveiling intricate gene expression profile patterns through the execution of large-scale RNA sequencing for ADCC macrophages.

Keivan Virology & Bacteriology Laboratory, Tehran, Iran 2015 – 2017

Scientific Expert

Utilized Real-Time PCR to accurately diagnose bacterial and viral diseases, delivering precise and timely results for effective patient care and management. Performed genotyping procedures for different types of bacteria and viruses including HPV and HCV. Executed microarray testing to analyze viral panels, facilitating comprehensive virus detection.

Teaching Experience

- Summer research program, Medical College of Wisconsin
Mentored high school in conducting and presenting research projects, 2020-2022.
- Instructure – High School Students, Summer School Conference, Shiraz University, Shiraz, Iran, 2011

Publications

Transcriptomic Diversity of NK cells in the patient with head and neck carcinoma, **Hashemi E**, McCarthy C, Zenga J, Anthony Veltri A, Sridhar Rao, Malarkannan S. In preparation.

A unique developmental program and transcriptomic diversity of Innate Lymphocytes in human Lymph Node using Single-cell RNA sequencing, **Hashemi E**, Malarkannan S. Under review, 2024

Methods for isolating and defining single-cell transcriptomes of tissue-resident human NK cells, **Hashemi E**, Mei A, Wang D, Khalil M, Malarkannan S. *Methods in Molecular Biology*, 2022

Isolation of Innate Lymphoid Cells from Murine Intestinal Lamina Propria, Mei A, **Hashemi E**, Khalil M, Wang D, Malarkannan S. *Malarkannan S. Methods in Molecular Biology*, 2022

Methods to Analyze the Developmental Trajectory of Human Primary NK Cells Using Monocle and SCENIC Analyses, Wang D, Burns R, Khalil M, **Hashemi E**, Malarkannan S. *Methods in Molecular Biology*, 2022

Implications of a Third Signaling NK Cells Khalil M, Wang D, **Hashemi E**, Terhune S, Malarkannan S. *cells*, 2021

NK Cell Development and Function in Patients with Fanconi Anemia, **Hashemi E**, Bjorgaard S, Wang D, Uyemura B, Thakar MS, Malarkannan S. *Critical Reviews in Immunology*, 2021

The role of GATA2 in human NK cell development, Wang D, Uyemura B, **Hashemi E**, Bjorgaard S, Thakar MS, Malarkannan S. *Critical Reviews in Immunology*, 2021

Conditional Deletion of PGC-1 Results in Energetic and Functional Defects in NK Cells, Gerbec ZJ, **Hashemi E**, Nanbakhsh A, Holzahuer S, Yang C, Mei A, Tsaih S, Lemke A, Flister MJ, Riese MJ, Thakar MS, Malarkannan S. *iScience*. 2020;23(9):101454, 2020

Tissue-Resident NK Cells: Development, Maturation, and Clinical Relevance, **Hashemi E**, Malarkannan S. *Cancers* 2020, 12(6), 1553, 2020

Designing DNA ELISA biosensor to detect Escherichia coli using genomic DNA and comparison of this method to PCR-ELISA, **Hashemi E**, Forouzndeh M. *Journal of Enzyme Inhibition and Medicinal Chemistry*, 33(1), 722-725, 2018

Honors & Awards

Travel award (\$2000) from Center for Immunology (C4I) MCW, Wisconsin for AAI conference, 2023

Travel award (\$1000) from Graduate School of MCW, 2023

Got ranked 13 in the Olympiad of Biology, 2012

Ranked among the top 5% of master's degree participants of Iran's Nationwide University Entrance Exam, 2012

Title of top Young Researcher by Iran Medical Proteomics Society in National Proteomics Conference, 2010

Member of management Council of Science Forum Shiraz University, 2009-2010

The forum was selected by the Ministry of Science, Research and Technology of Iran and selected by the national UNESCO-Iran commission in the third Harekat festival in research activity in this year, 2009-2010.

Undergraduates Full Scholarship from Iran Ministry of Science, Research & Technology

Presentations

Poster presentation, "Transcriptomic Diversity of NK cells in the patient with head and neck carcinoma" in Cancer Center 2nd annual Trainee Symposium, Wisconsin, 2024

Poster presentation, Single-cell transcriptome reveals the developmental progression of human ILCs from the bone marrow to lymph nodes in American Association of Immunology (AAI) Conference, Washington, DC, 2023

Poster presentation, Transcriptomic Diversity of ILCs in Human Lymph nodes in Autumn Immunology Conference, Chicago, Illinois, 2022

Poster presentation, Mutations in Fanconi Anemia Patients: Stochastic or Deterministic? in 5th Annual GSA Symposium, Milwaukee, Wisconsin, 2022

Poster presentation, Transcriptomic diversity of Innate Lymphoid Cells in Human Lymph Nodes in Center for Immunology Symposium, Milwaukee, Wisconsin, 2022

Oral presentation, " Designing and constructing a biosensor (DNA ELISA) to detect E. coli ATCC 25922 using genomic DNA in 7th International Congress, Iran, 2014

Poster presentation, Early Identification in Atherosclerosis by Proteomics in National Proteomics Conference, Iran, 2010

Poster presentation of review article Application of biosensors in medicine in the first national seminar on the role of basic science of health promotion