MCW
GRADUATE SCHOOL

Doctoral Dissertation Defense Announcement

"Unraveling the complexity of the human peripheral blood B cell compartment through multiomic CITE-seq analyses"

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Committee in Charge:

Bonnie Dittel, PhD (Mentor)

Vera Tarakanova, PhD

Demin Wang, PhD

Aron Geurts, PhD

John Corbett, PhD

Date: Wednesday, May 8, 2024

Time: 1:00pm (CST)

Defense Location: VBRI Seminar Room

Zoom: link available upon request (nmeinhardt@mcw.edu)

Graduate Studies:

Foundations in Biomedical Sciences I-IV

Professional Development I-II

Statistics for Basic Sciences

Techniques in Molecular & Cell Biology

Fundamentals of Neuroscience

Graduate Neuroanatomy

Writing a Scientific Paper

Writing Individual Fellowship

Integrated Microbiology & Immunology

Ethics & Integrity in Science

Research Ethics Discussion Series

Neuroscience Journal Club

Immunological Tolerance

Microbiology & Immunology Seminar Series

Reading and Research

Doctoral Dissertation

Dissertation

"Unraveling the complexity of the human peripheral blood B cell compartment through multiomic CITE-seq analyses"

Classifying the heterogeneous human B cell compartment into discrete subsets based on surface phenotype alone remains a major challenge in the field of B cell biology. Our lab has discovered a novel mouse splenic $IgM^{+}IgD^{low/-}$ B cell subset (BD_L) that induces Treg proliferation, making it a potentially significant therapeutic target for autoimmune diseases. But due to their rarity and lack of sufficient cell surface identifiers, a more definitive phenotype is required to track this B cell subset in humans.

The objective of these studies was to develop a pipeline to characterize human $IgD^{low/-}$ B cells using peripheral blood (PB) B cells and multiomic cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq) analysis. Here, we adapted a standardized flow cytometry gating scheme (CD27 versus IgD and CD24 versus CD38) that captures all the major canonical human PB B cell subsets. This scheme allowed us to analyze FACS-purified $CD19^{+}IgM^{+}IgD^{low/-}$ PB B cells using CITE-seq targeting those four protein markers and recreate biaxial plots similar to our flow cytometry analyses. Utilizing this strategy, we successfully identified naïve, transitional, and memory B cell subsets. Further trajectory analysis of naïve B cells revealed three distinct cell states, one of which included a newly matured subset.

It is increasingly understood that mRNA levels within a cell do not correlate well with cell surface protein expression. This represents a major drawback to using a transcriptome-only scRNA-seq approach because any 'novel' cell populations discovered based on the upregulation of surface protein transcripts may prove impossible to validate. The studies herein overcame that caveat by establishing a multiomic approach workflow to identify discrete human B cell subsets based on cell surface expression that can then be analyzed for transcriptional differences.

Nathan Meinhardt
Curriculum Vitae
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Education

Ph.D. in Biomedical Science

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

Master of Science in Biological Sciences

University of Wisconsin – Milwaukee, WI

Bachelor of Science in Biology

Saint Louis University, St. Louis, MO

Honors and Awards

Travel award ($2000) from Center for Immunology (C4I) MCW, Wisconsin for AAI conference, 2024

Travel award ($1000) from Graduate School of MCW for AAI conference, 2023

Presentations

Oral presentation (upcoming 5/2024), "Unraveling the complexity of the human peripheral blood B cell compartment through multiomic CITE-seq analyses", American Association of Immunology (AAI) Conference, Chicago, IL, 2024

Oral presentation, "Phenotyping the complex human B cell compartment using CITE-seq analyses", Autumn Immunology Conference, Chicago, Illinois, 2023

Oral presentation, "Phenotyping the complex human B cell compartment using CITE-seq analyses", The Upper Midwest Chapter for Society for Neuroscience Conference, Green Bay, WI, 2023

Poster presentation, "Phenotyping the complex human B cell compartment using CITE-seq analyses", Autumn Immunology Conference, Chicago, Illinois, 2023

Poster presentation, "Phenotyping the complex human B cell compartment using CITE-seq analyses", American Association of Immunology (AAI) Conference, Washington, DC, 2023

Poster presentation, "Phenotyping the complex human B cell compartment using CITE-seq analyses", ACTRIMS Young Scientist Summit, Scottsdale, AZ, 2023

Poster presentation, "Phenotyping the complex human B cell compartment using CITE-seq analyses", Center for Immunology Symposium, Milwaukee, Wisconsin, 2022