

**BIOMEDICAL & VETERINARY SCIENCES**

**GRADUATE PROGRAM**



**ANNOUNCES**

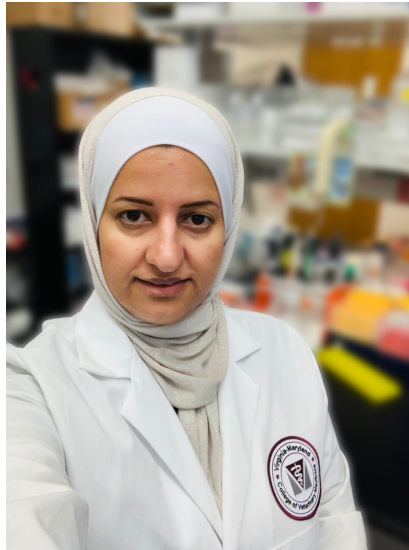
The Doctor of Philosophy Seminar and Examination of

**Razan Mefleh Alajoleen**  
**“Gut Microbiota Regulation of SLE Pathogenesis”**

**Monday, November 27th, 2023**

**10:00AM**

**VMIA 220**



## **Bio**

Razan Alajoleen is originally from the enchanting city of Madaba, Jordan, where she embarked on a remarkable academic trajectory. She earned her foundational knowledge in genetics through a bachelor's degree before delving into the intricate world of toxicology, where she secured a master's degree. These diverse academic pursuits have equipped Razan with a unique interdisciplinary perspective, enriching her ability to tackle complex scientific challenges. Razan's Ph.D. research journey is firmly rooted in the profound realm of immunology, with a specific focus on unraveling the mysteries of lupus disease. Under the expert guidance of her Principal Investigator, Dr. Xin Luo, Razan's research endeavors are pushing the boundaries of what we know about lupus and its underlying immunological mechanisms. Her work is paving the way for innovative approaches to diagnosis, treatment, and understanding the factors that contribute to this challenging autoimmune disease.

Apart from her academic pursuits, Razan is a loving mother to three wonderful daughters, embodying the values of balance, hard work, and determination in both her personal and professional life. Her journey in academia is not only a testament to her passion for learning but also serves as an inspiration to her family and peers.

In addition to her academic pursuits, Razan is an active volunteer, demonstrating her commitment to giving back to her community and making a positive impact on society. Her desire to create a better world extends beyond her academic and family life, exemplifying her strong sense of social responsibility.

## **Funded by**

NIAMS, NIH  
VMCVM Office of Research and Graduate Studies  
Virginia Tech Graduate School

## **Academic Awards and Achievements**

May 2023 American Association of Immunology  
Abstract Trainee Award.

April 2023 Sigma Xi Graduate Research Award.

## Lay Language Abstract

Systemic Lupus Erythematosus (SLE) is characterized by a range of health issues and the body attacking itself. In this exploration, we journey through the intricate landscape of SLE, uncovering key players and unexpected twists. In this dissertation, we closely examine these immune cells, revealing how different types of B cells contribute to SLE's development. We also introduce the enigmatic regulatory B (Breg) cells, which act as potential peacekeepers in this autoimmune reaction. Our results illuminate the complex relationship between B cells and SLE, offering insights that benefit both researchers and those seeking new treatments. We employ cutting-edge technology, single-cell RNA sequencing, to scrutinize the genetic fingerprints of B cells in mice with SLE. The results unveil changes in Breg cells during active disease, providing critical clues about how B cells impact SLE progression. In addition, this dissertation takes us into the microscopic world of our gut inhabitants, the microbiota. We dive into a treasure trove of research, focusing on how interactions between bacterial flagellin and various microbiota elements affect immune cells through a special receptor called Toll-Like Receptor 5 (*TLR5*). These interactions, like hidden clues, have piqued scientists' interest for their potential role in SLE development. We synthesize existing research, offering valuable insights into the complex interplay between SLE and our microbiota. The discussion also suggests promising paths for future research and potential therapies. In the final study, we encounter a plot twist. We anticipated that deleting the *Tlr5* gene would improve lupus-like disease in mice. To our surprise, the opposite happened. Lupus-like symptoms worsened, especially in female mice lacking *Tlr5*. Clinical signs included enlarged spleens and lymph nodes, increased immune cell activity, and kidney inflammation. But *Tlr5* deletion didn't change the mice's metabolism or the leaky gut. Instead, it reshaped their gut's microbial residents. Future research aims to uncover how *Tlr5* deletion alters the interactions between the host and gut microbes, ultimately making lupus-like disease more severe. In a nutshell, this journey through SLE's complex world has provided a deeper understanding of its intricacies. We've met the B cells, explored the microbiota, and encountered surprises along the way. These discoveries are vital pieces of the puzzle, bringing us closer to unlocking the secrets of SLE and, perhaps, finding new ways to manage and treat this challenging autoimmune disorder.

## Publications

**Razan M. Alajoleen**, David N. Oakland, Rana Estaleen, Aida Shakeri, Ran Lu, Michael Appiah, Sha Sun, Christopher M. Reilly, Xin M. Luo. *Tlr5* Deficiency Exacerbates Lupus-Like Disease in the MRL/*lpr* Mouse Model. **Manuscript under review.**

**Razan M. Alajoleen**, Liwu Li, Xin M. Luo. Isolation and Single-Cell Transcriptomic Analysis of Murine Regulatory B cells. Manuscript under review.

**Razan M. Alajoleen**, Xin M. Luo. Regulatory B Cells in the Pathogenesis of Systemic Lupus Erythematosus. **Manuscript under review.**

**Razan M. Alajoleen**, Xin M. Luo. Gut Microbiota and *TLR5* in the Pathogenesis of SLE. **Manuscript under review.**

Andrea R. Daamen#, **Razan M. Alajoleen**#, Amrie C. Grammer, Xin M. Luo, Peter E. Lipsky. Single-cell RNA sequencing analysis reveals the heterogeneity of IL-10 producing regulatory B cells in lupus-prone mice. **Manuscript under review.** #These authors contributed equally.

Leila Abdelhamid, **Razan M. Alajoleen**, Kathryn M. Kingsmore, Xavier Cabana-Puig, Ran Lu, Jing Zhu, James C. Testerman, Yaqi Li, A. Catharine Ross, Thomas E. Cecere, Christopher M. Reilly, Amrie C. Grammer, Peter E. Lipsky, Xin M. Luo. Hypovitaminosis A Drives the Progression of Tubulointerstitial Lupus Nephritis through Potentiating Predisease Cellular Autoreactivity. *ImmunoHorizons* 2023; 7(1): 17–29.

Cabana-Puig X, Lu R, Geng S, Michaelis JS, Oakes V, Armstrong C, Testerman JC, Liao X, **Alajoleen R**, Appiah M, Zhang Y, Reilly CM, Li L, Luo XM (2023) CX3CR1 modulates SLE-associated glomerulonephritis and cardiovascular disease in MRL/*lpr* mice. *Inflammation Research* 72(5):1083-1097.

Appiah MG, Oakland DN, Zhu J, Cabana-Puig X, Lu R, **Alajoleen R**, Armstrong C, Xu D, Reilly CM, Grammer AC, Shlomchik MJ, Lipsky PE, Luo XM. 1303 Bacterial DNA induces regulatory B cells and attenuates lupus through a B cell-extrinsic, TLR9-dependent mechanism. *Lupus Science & Medicine*. 2022;9(Suppl 3):A91-A2. doi: 10.1136/lupus-2022-lupus21century.93.

Awidi A, Ramahi M, Alhattab D, **Mefleh R**, Dweiri M, Bsoul N, Magablah A, Arafat E, Barqawi M, Bishtawi M, Haddadeen E, Falah M, Tarawneh B, Swaidan S, Fauori S. Study of mutations in Jordanian patients with haemophilia A: identification of five novel mutations. *Haemophilia* 2010 Jan;16(1):136-42.

## Publications continued

Awidi A, Alhattab D, Bsoul N, Magablah A, **Mefleh R**, Dweiri M, Fauori AS. FIX mutation spectrum in haemophilia B patients from Jordan: identification of three novel mutations. *Haemophilia* 2011 Jan;17(1):162-3.

Awidi A, Ayed AO, Bsoul N, Magablah A, **Mefleh R**, Dweiri M, Ramahi M, Arafat E, Bishtawi M, Marie L.:Relationship of serum imatinib trough level and response in CML patients: long term follow-up. *Leukemia Research* 2010 Dec;34(12):1573-5.

Awidi A, Salem II, Najib N, **Mefleh R**, Tarawneh B Determination of imatinib plasma levels in patients with chronic myeloid leukemia by high performance liquid chromatography-ultraviolet detection and liquid chromatography-tandem mass spectrometry: methods' comparison. *Leukemia Research* 2010 Jun;34(6):714-7.

Awidi A, Ababneh N, Magablah A, Bsoul N, **Mefleh R**, Marei L, Abbasi S. ABL kinase domain mutations in patients with chronic myeloid leukemia in Jordan. *Genet Test Mol Biomarkers* 2012 Nov;16(11):1317-21

## **Presentations**

**Razan Alajoleen.** *Tlr5* Deficiency Exacerbates Lupus-Like Disease in the MRL/*lpr* Mouse Model. **RIP Seminar, Blacksburg, VA October 2023.**

**Razan Alajoleen.** Single-Cell RNA Sequencing Reveals Disease Stage-Dependent Transcriptomic Profiles of Regulatory B Cells in Systemic Lupus Erythematosus. **Oral presentation AAI May 2023.**

**Razan Alajoleen.** Single-Cell RNA Sequencing Reveals Disease Stage-Dependent Transcriptomic Profiles of Regulatory B Cells in Systemic Lupus Erythematosus. **RIP Seminar, Blacksburg, VA May 2023.**

**Razan Alajoleen.** Single-Cell RNA Sequencing Reveals Disease Stage-Dependent Transcriptomic Profiles of Regulatory B Cells in Systemic Lupus Erythematosus. **Poster presentation AAI 2023.**

**Razan Alajoleen.** Single-Cell RNA Sequencing Reveals Disease Stage-Dependent Transcriptomic Profiles of Regulatory B Cells in Systemic Lupus Erythematosus. **Poster presentation GPSS at VT 2023.**

**Razan Alajoleen.** Single-Cell RNA Sequencing Reveals Disease Stage-Dependent Transcriptomic Profiles of Regulatory B Cells in Systemic Lupus Erythematosus. **Poster presentation VCOM research day 2023.**

**Razan Alajoleen.** *Tlr5* Deficiency Exacerbates Lupus-Like Disease in the MRL/*lpr* Mouse Model. **Poster Presentation AAI 2023**

## Examination Graduate Committee

### Major Advisor/Chair:

Xin Luo, PhD  
Professor of Immunology  
Assistant Department Head for Graduate Studies  
Department of Biomedical Sciences and Pathobiology

### Graduate Advising Committee Members:

Christopher Reilly, PhD  
Research Associate Professor at VMCVM  
Department of Biomedical Sciences and Pathobiology  
Discipline Chair for Cellular Biology and Physiology  
Edward Via College of Osteopathic Medicine

S. Ansar Ahmed, BVSc, PhD  
Professor of Immunology  
Director, Summer Veterinary Scholars Research Program  
Professor, Faculty of Health Sciences  
Department of Biomedical Sciences and Pathobiology

Tanya LeRoith, DVM, PhD,  
DACVP–Anatomic Pathology  
Clinical Professor  
Anatomic Pathology  
Department of Biomedical Sciences and Pathobiology



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