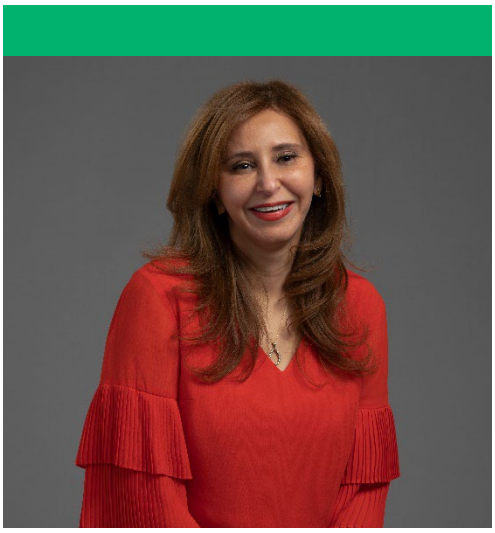
RUSH

Lena Al-Harthi, PhD



Thomas J. Coogan Sr., MD,

Professor of Immunology

Advancement of Medicine

Over the last 22 years, I have participated in the research, administration and education mission of Rush. My research has focused on virus/host interactions, with a special emphasis on bridging basic and clinical science. Specifically, I study three viruses and their impact on the brain. They are human immunodeficiency virus, or HIV, ZIKA virus and COVID-19. All cause neurologic damage that is mediated by inflammation in the brain.

Research

In 2023, we conducted a study that garnered recognition from the National Institutes of Mental Health, or NIMH, at the National Institutes of Health, or NIH. This study demonstrated how immune cells carry the virus into the brain. We identified a unique population of T cells called $CD4^{dim}CD8^{bright}$ T cells and showed that they mediated HIV invasion of the brain. We also showed that they can be silently infected with HIV. This is critical, as HIV remains dormant in the body and once drug treatment stops it resurfaces. Continuing to characterize $CD4^{dim}CD8^{bright}$ T cells and how they enter the brain and contribute to HIV persistence will help us move toward strategies to better treat HIV, which could include maintaining it in a latent state or removing it altogether.

Further, I have leveraged the Coogan endowment to continue my collaboration with Dr. Dino Samartzis through a common PhD student and have a publication regarding the impact of the human microbiome (natural bacterial flora) and its association with musculoskeletal disorders, or MSDs. Variations in the makeup of the gut's natural bacterial flora may be related to chronic MSDs. Our research explores potential connections between chronic MSDs and variations in the composition of the human microbiome.

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Clinical Trials

In 2023, we assessed the relationship between $CD4^{dim}CD8^{bright}$ T cells and neuroinflammation and found that these cells protect against neuroinflammation in the brain. As such, these cells on one hand carry HIV, but silence its expression, while being neuroprotective against inflammation in the brain, a hallmark of HIV in the brain.

I have continued to leverage the valuable resources provided by the Coogan endowment to continue my research focus and expand into a new area of clinical relevance. Specifically, I have initiated studies to assess the role of COVID autoantibodies in neurologic COVID. A number of COVID patients have neurologic disorder that continues long after the infection is cleared. What mediates this condition is not known. My group initiated studies to identify COVID autoantibodies and assess their impact on resident brain cells. Preliminary data generated allowed for the submission of an NIH grant that was well reviewed.

Outreach and Education

In 2023, I was honored to be named head of the Division of Translation Science at Rush University Medical College. This new division contains all the programs from Rush University's Graduate College.

I have continued my outreach efforts over the past year. I was a co-organizer of the 2023 International Symposium on NeuroVirology, where a number of my faculty gave talks on their research. Also, I was invited to present, "Role of T-cells in CNS Reservoir Seeding, Persistence and Neuropathogenesis," at the NIMH conference in Naples, Italy. Due to a scheduling conflict, one of my lab's staff scientists presented this research.

Finally, our group hosted high school students who are interested in careers in science and medicine for a week-long internship at Rush MPI and in other Rush departments.

Publication Highlights – Abbreviated

- HIV infection of non-classical cells in the brain. Retrovirology. 2023.
- The Human Microbiome and Its Role in Musculoskeletal Disorders. Genes (Basel). 2023.
- Hyperactivity of Medial Prefrontal Cortex Pyramidal Neurons Occurs in a Mouse Model of Early-Stage Alzheimer's Disease Without β-amyloid Accumulation. Frontiers in

Pharmacology. 2023.

- An Efficient and Cost-Effective Approach to Generate Functional Human Inducible Pluripotent Stem Cell-Derived Astrocytes. Cells. 2023.
- An Efficient Humanized Mouse Model for Oral Anti-Retroviral Administration. Cells. 2023.

The Year Ahead: 2024 and Beyond

In 2023, I received a competitive score for a R01 NIH grant looking at the role of COVID autoantibodies in COVID-associated neurologic disease. This grant is expected to be funded, either this cycle or next, pending NIH congressional budget approval, per my NIH program officer.

Also, I will continue to emphasize studies to assess the interface between viral pathogen and host, as it relates to neuroimmunology. We submitted a PhD training grant in pathogen-host interaction. Depending on the outcome, I will engage in those activities and re-submit the application, if needed.

With Gratitude

I am profoundly grateful for the ongoing and generous support from the Coogan endowment. Your contributions have not only allowed us to delve into innovative realms of research but have also paved the way for securing national funding, enabling us to expand our work on a larger scale. This significant progress and impact would have been unattainable without the invaluable commitment and dedication of the Coogan family. Your role as champions for research is truly commendable, and it stands as a testament to honoring the esteemed legacy of Dr. Coogan Sr.