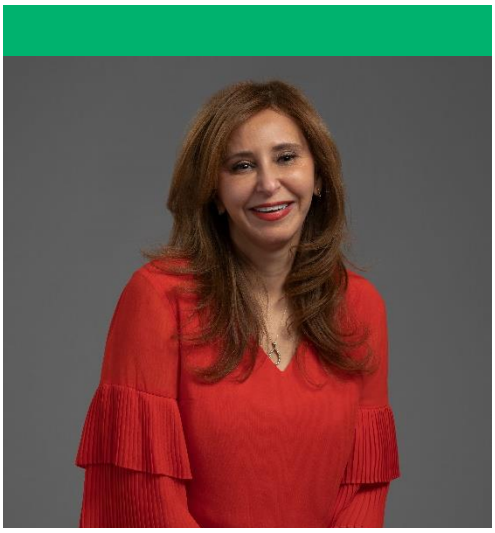
RUSH

Lena Al-Harthi, PhD



The 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: human immunodeficiency virus, or HIV, Zika virus and SARS-CoV-2 that causes COVID-19 and is associated with post-acute sequelae of SARS-CoV-2 infection, commonly referred to as PASC or long COVID.

Research

In 2024, I continued to advance my research focus on virus-host interactions in the brain. One critical area of investigation has been understanding how SARS-CoV-2 infection may lead to persistent neurologic complications. PASC describes a range of lingering symptoms and health complications that persist for weeks or months after the initial infection has resolved, even in people with mild or asymptomatic cases, including neurocognitive impairments. While many patients recover fully, a significant subset experience ongoing cognitive, mood and neurologic symptoms, even after clearing the infection. The underlying biological mechanisms remain poorly understood.

Through Coogan endowment support, we initiated studies to investigate whether autoantibodies — antibodies generated by the immune system that mistakenly target the body's own tissues — might play a role in driving these complications. Using brain-resident human cells, we discovered that circulating IgG antibodies from COVID-19 donors recognize self-antigens on neurons and astrocytes, indicating a break in immune tolerance. These autoantibodies not only bind to these cells but also

induce inflammatory responses, implicating them in the pathogenesis of PASC-related neurologic symptoms.

Our preliminary data strongly supported the idea that these brain-reactive autoantibodies may trigger neuroinflammation and neurocognitive impairment following SARS-CoV-2 infection. This work formed the foundation of a National Institutes of Health, or NIH, R01 application focused on the mechanistic role of these antibodies in neurologic COVID. While the proposal was well-reviewed, it fell short of the funding payline. However, its high-impact potential was recognized by the Office of Autoimmune Disease Research in partnership with the National Institute of Neurological Disorders and Stroke, resulting in a prestigious R56 Bridge Award. This interim funding allows us to further characterize these pathogenic antibodies and their effects on resident brain cells, with the goal of resubmitting a competitive R01.

Our project was one of a select few highlighted in a November 6, 2024, NIH news release, underscoring the urgency and promise of research into autoimmune mechanisms contributing to chronic disease. I am honored that our work was recognized nationally and proud that this line of inquiry — made possible through the Coogan endowment — is now at the forefront of efforts to understand and mitigate the long-term neurologic impact of COVID-19.

Additionally, I leveraged the Coogan endowment to expand my research into musculoskeletal and neuroinflammatory connections. A graduate student I co-mentored with **Dino Samartzis, DSc**, professor in Rush's Department of Orthopedic Surgery, completed his PhD and is now an instructor in the Department of Orthopedic Surgery, investigating the role of infections in orthopedic disease and implants. We published on how the human microbiome may influence musculoskeletal disorders.

Building on findings from Rush Orthopedics that metals like cobalt and titanium, released through wear and tear of orthopedic implants, can trigger inflammation, I launched a new project assessing the potential role of metal-induced neuroinflammation in Alzheimer's disease, or AD. These metals have recently been identified in the brains of AD donors. With the support of a Coogan-funded graduate student, we are examining how these metals affect brain-resident cells and whether they contribute to or exacerbate AD pathology. As with the SARS-CoV-2 work, this support positions us to generate pilot data for federal funding.

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Clinical Trials

Although our current research is not directly part of ongoing clinical trials, the scientific insights generated through our work have important implications for future clinical applications. In both the HIV and SARS-CoV-2 research spaces, our findings are helping to define the underlying immune and neuroinflammatory mechanisms that contribute to long-term neurologic complications. By identifying novel targets — such as brain-reactive autoantibodies in COVID or $CD4^{dim}CD8^{bright}$ T cells in HIV — we are building a foundation for future clinical trials aimed at mitigating neurocognitive impairment and improving patient outcomes. Our translational approach continues to bridge basic discovery with clinical potential.

Outreach and Education

In 2024, I continued to serve as vice dean of research and head of the Division of Translational Science, supporting research training across Rush Medical College. The Coogan endowment enabled support for an instructor and a graduate student, both exploring inflammatory triggers — one in the context of orthopedic research and the other in neurodegenerative disease.

I helped organize the inaugural Frontiers in Translational and Clinical Research: Insights from Early-Career Medical and Science Researchers Symposium, held on March 26, 2025. The symposium featured more than 100 research presentations spanning eight thematic tracks, including Neurodegenerative Diseases and Inflammation, Musculoskeletal Research and Orthopedics, Infectious Diseases and Immunology, Health Equity and Community Engagement, Clinical Practice (Case Studies, Cohort Studies and Education), and Cancer and Translational Medicine. Student awards were granted in each theme, including the NeuroInnovation Excellence Award, Excellence in Cancer and Translational Medicine Award, Excellence in Infectious Disease and Immunology Award, Excellence in Musculoskeletal Research and Orthopedics Award, Community Health Impact Award, Clinical Excellence Award, Medical Education Advancement Award, and Research Advancement Award.

This event reflects my commitment to building research capacity across the college and fostering early-career scholarship. The goal is to grow this into a regional — and eventually national — event.

I continue to serve on the Board of the International Society of NeuroVirology, support the Midwest Immunology Conference, and co-sponsor faculty and student participation in the Chicago Chapter of the Society for Neuroscience using Coogan funds.

Publication Highlights – Abbreviated

- **Discovery of circulating blood biomarkers in patients with and without Modic changes of the lumbar spine: a preliminary analysis.** *Eur Spine J. 2024 Apr;33(4):1398-1406.* PMID: 38451373
- **The anti-HIV drug abacavir stimulates β-catenin activity in osteoblast lineage cells.** *JBMR Plus. 2024 Mar 19;8(5):ziae037.* PMID: 38590756
- **CD4 ^{dim} CD8 ^{bright} T cells are inversely associated with neuro-inflammatory markers among people with HIV.** *AIDS. 2024 Jan 1;38(1):1-7.* PMID: 37792358
- **HIV infection of non-classical cells in the brain.** *Retrovirology. 2023 Jan 13;20(1):1.* PMID: 36639783
- **The Human Microbiome and Its Role in Musculoskeletal Disorders.** *Genes (Basel). 2023 Oct 14;14(10):1937.* PMID: 37895286
- **An Efficient Humanized Mouse Model for Oral Anti-Retroviral Administration.** *Cells. 2023 Mar 28;12(7):1034.* PMID: 37048107
- **An Efficient and Cost-Effective Approach to Generate Functional Human Inducible Pluripotent Stem Cell-Derived Astrocytes.** *Cells. 2023 Sep 26;12(19):2357.* PMID: 37830571
- **Hyperactivity of medial prefrontal cortex pyramidal neurons occurs in a mouse model of early-stage Alzheimer's disease without β-amyloid accumulation.** *Front Pharmacol. 2023 Jul 3;14:1194869.* PMID: 37465526

The Year Ahead: 2025 and Beyond

In 2025 and beyond, I will continue to lead investigations into the impact of metals on neuroinflammation in Alzheimer's disease, with the goal of submitting competitive grant proposals based on data generated by a Coogan-supported graduate student. This work builds upon interdisciplinary findings from Rush's Orthopedics, Microbial Pathogens and Immunity, and Neurological Sciences departments.

I remain committed to mentoring early-stage faculty and PhD students, supporting them in building independent research careers. I also aim to expand the Frontiers Symposium into a regionally recognized event, fostering broad collaborations and recognition of trainee excellence.

With Gratitude

In these chaotic and uncertain times — when the federal government is freezing or canceling funding streams, including programs I have led to support underrepresented students — this endowment is a lifeline. **The Coogan endowment has enabled me to explore bold, innovative research that has already led to externally funded projects and promising data pipelines.** Your continued support is not only appreciated but essential for protecting progress and fostering the next generation of scientific leaders.