RUSH

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Advancement of Medicine

Discovery of a New Barrier to Remyelination

In 2025, we engineered a new small molecule to promote remyelination in multiple sclerosis, or MS. Although we have well-defined machinery for the remyelination of axons during insult or injury, many axons remain demyelinated in the brains of MS patients. Therefore, outlining new technologies to overcome the barrier and promote remyelination is an important area of research. While looking for new barriers and/or facilitators of remyelination, we found that the levels of mixed lineage kinase 3, or MLK3, and the enzyme peptidyl-prolyl cis-trans isomerase NIMA-interacting 1, or PIN1, are higher in the brains of a mouse model of MS than in those of ordinary mice.

Although there are inhibitors of MLK3 and PIN1, many molecules are phosphorylated by MLK3, and PIN1 is phosphorylated by many different kinases. As a result, pan-inhibition of MLK3, PIN1 or both by available inhibitors should affect multiple pathways. Therefore, we adopted a precision approach to inhibit the association between PIN1 and MLK3 without blocking the function and basal level of either MLK3 or PIN1. We have designed a small peptide corresponding to the MLK3-associated domain, or MAD, of PIN1 that binds to MLK3 but not other MLKs. Interestingly, we have seen that wild-type (wt)MAD, but not mutated (m)MAD peptide stimulates the generation of myelin-forming oligodendrocytes and remyelination. We have applied for a patent on wtMAD and remyelination.

Research

This endowment supports a postdoctoral fellow who is performing stimulating studies on wtMAD and remyelination. Therefore, funds from the endowment directly support innovative research to develop new technologies that could transform care for people with MS.

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Grants

- Grant (1 I01 BX005613) entitled “Remyelination by intranasal TIDM peptide” from the U.S. Department of Veterans Affairs
- Grant (IK6 BX004982) entitled “Research Career Scientist Award” from the U.S. Department of Veterans Affairs
- Grant (R01NS146220) entitled “MLK3-associated domain of PIN1 for remyelination” from the National Institutes of Health (pending)

Invited Presentations

- “Paying tolls is not good for the brain,” Recent Advances in Medical Sciences and Technology, Indian Institute of Technology, Kharagpur, India, December 17, 2025.
- “A possible treatment for MS on amino acid shelves!” Neurology Grand Rounds, Rush University Medical Center, July 22, 2025.
- “CNS innate immunity in neurodegenerative disorders,” Nevada Institute of Personalized Medicine, University of Nevada, Las Vegas, April 28, 2025.
- “A new intranasal option for Progressive Supranuclear Palsy,” Zynext Ventures, October 1, 2024.

Publication Highlights — Abbreviated

- “Activation of PPARα by gemfibrozil lowers tau-associated neuropathology in the MAPT mouse model of Alzheimer's disease,” *Brain Research* (2025)
- “L-Leucine upregulates lysosomal biogenesis and autophagy to lower plaques in 5XFAD mouse model of Alzheimer’s disease,” *Journal of Neurochemistry* (2025)
- “Selective inhibition of TLR2 stimulates the maturation of oligodendroglial progenitor cells to oligodendrocytes,” *Journal of Neuroimmune Pharmacology* (2026)
- “Benzoate drugs for traumatic brain injury,” *Brain and Behavior* (2026)
- “Selective inhibition of TLR2 inhibits microglial activation induced by low-molecular-weight hyaluronan,” *Neuroimmune Pharmacology and Therapeutics* (2026)
- “Regulation of neuronal ceroid lipofuscinosis genes by PPARα and RXRα” *Children* (2026)

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The Year Ahead: 2026 and Beyond

Trainees conduct the majority of the research work in our laboratory. We will continue to train and mentor medical students, graduate students and postdoctoral fellows. Many of our trainees are now either medical doctors in different clinics or faculty members in academic institutions.

With Gratitude

I want to extend my deepest gratitude and heartfelt appreciation for the generous contribution to respect the legacy of Dr. Floyd A. Davis and support our pioneering MS research at Rush University Medical Center. It is due to the noble support provided by this endowment that we have been able to exhibit leadership in translational research at both the national and international levels.