RUSH

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Advancement of Medicine

In 2024, we strengthened our drug repurposing effort in our area of research on multiple sclerosis, or MS, in which myelin components are particularly targeted by the immune system, resulting in demyelination of axons and a range of neurological problems.

Gemfibrozil, also known by its brand name Lopid, is an FDA-approved lipid-lowering drug that has been well tolerated in human and animal studies. Establishing molecular mechanisms for anti-MS activities of gemfibrozil may help in repurposing this drug for MS. Using an animal model of MS, we have demonstrated that oral gemfibrozil attenuates the disease process, preserves the integrity of the blood-brain barrier, inhibits brain inflammation, and stimulates remyelination via peroxisome proliferator-activated receptor β (PPARβ) but not PPARα, highlighting a novel immunomodulatory role of gemfibrozil-PPARβ pathway for therapeutic intervention in MS.

In another study, we have delineated a new autoimmune function of IL-12p40 homodimer ($p40_2$), the so-called biologically inactive molecule, via stimulating the production of immunomodulatory cytokine IL-2 from T cells and macrophages, highlighting the possibility of controlling the disease process of MS through neutralization of $p40_2$.

Research

Funds from the endowment have gone toward supporting my innovative research work and allowed us to support a postdoctoral student, who is undertaking exciting studies on gemfibrozil, PPARβ and $p40_2$.

Grants

- Grant (1 I01 BX005613) titled “Remyelination by intranasal TIDM peptide” from the U.S. Department of Veterans Affairs.

- Grant (R01AT010980) titled “Muscle building supplement HMB for remyelination” from the National Institutes of Health.

Invited Presentations

- “A new intranasal option for progressive supranuclear palsy,” Zynext Ventures, Oct. 1, 2024.
- “Intranasal MAD peptide for Parkinson’s disease,” SPARK NS, Sept. 13, 2024.
- “Glial-neuronal signaling in neurodegenerative disorders,” Neurology Grand Rounds, Rush University Medical Center, Aug. 13, 2024.
- “Innate immune signaling in neurodegenerative disorders,” Department of Anatomy and Cell Biology, University of Illinois Chicago, June 17, 2024.
- “Targeting TLR2 to stop tauopathy,” the 28th Scientific Conference of the Society on Neuroimmune Pharmacology, March 12, 2024.

Publication Highlights — Abbreviated

- “Muscle-building supplement β-hydroxy β-methylbutyrate stimulates the maturation of oligodendroglial progenitor cells to oligodendrocytess,” *Journal of Neurochemistry* (2024)
- “Amelioration of experimental autoimmune encephalomyelitis by gemfibrozil in mice via PPARβ/δ: implications for multiple sclerosis,” *Frontiers in Cellular Neuroscience* (2024).
- “Induction of IL-2 by interleukin-12 p40 homodimer and IL-12, but not IL-23, in microglia and macrophages: Implications for multiple sclerosis,” *Cytokine* (2024).
- “Build muscles and protect myelin,” *Neuroimmune Pharmacology and Therapeutics* (2024).
- “Is it possible to maintain a plaque-free healthy brain by treadmill?” *Neural Regeneration Research* (2024).
- “Identification of Cinnamein, a Component of Balsam of Tolu/Peru, as a New Ligand of PPARα for Plaque Reduction and Memory Protection in a Mouse Model of Alzheimer's Disease,” *Journal of Alzheimer’s Disease Reports* (2024).
- “Therapeutic efficacy of cinnamein, a component of balsam of Tolu/Peru, in controlled cortical impact mouse model of TBI,” *Neurochemistry International* (2024).
- “Nebulization of low-dose aspirin ameliorates Huntington's pathology in N171-82Q transgenic mice,” *Neuroimmune Pharmacology and Therapeutics* (2024).

- “Cinnamic acid, a natural plant compound, exhibits neuroprotection in a mouse model of Sandhoff disease via PPARα,” *Neuroimmune Pharmacology and Therapeutics* (2024).
- “IL-12p40 Monomer: A Potential Player in Macrophage Regulation,” *Immuno* (2024).

The Year Ahead: 2025 and Beyond

Trainees conduct 95% of the research work in our laboratory. Therefore, we will continue training and mentoring 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 am extending my deep appreciation and sincere thanks for your generous contribution, which honors the legacy of Dr. Floyd A. Davis and enables us to perform innovative MS research at Rush. Due to this magnanimous support of our translational research, we are able to demonstrate a leadership role at both national and international levels.