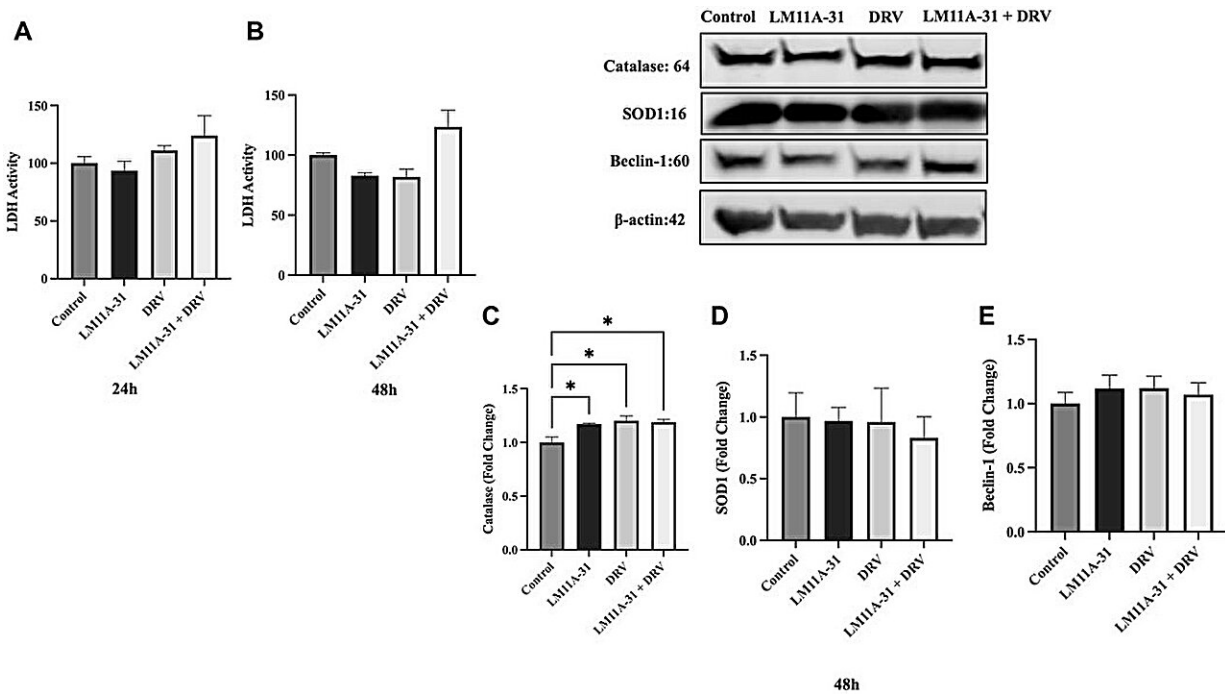


Study examines novel drug candidate for treatment of neuroHIV

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The effect of LM11A-31 on cytotoxicity, antioxidant enzymes, and autophagy marker in U937 macrophages. U937 macrophages were differentiated and then treated with DMSO, LM11A-31 (100 nM), DRV (5.5 μ M), and LM11A-31 + DRV for 48 h. The cytotoxicity was measured using CyQUANT LDH Cytotoxicity Assay Kit. Credit: *Experimental Biology and Medicine* (2024). DOI: 10.3389/ebm.2024.10123

A recently [published](#) article in *Experimental Biology and Medicine* titled

"LM11A-31, a modulator of p75 neurotrophin receptor, suppresses HIV-1 replication and inflammatory response in macrophages" highlights the potential of a novel drug candidate, 2-amino-3-methylpentanoic acid [2-morpholin-4-yl-ethyl]-amide (LM11A-31), which is a p75 neurotrophin receptor (p75NTR) modulator, in treating HIV in the brain (neuroHIV) and HIV-associated neurocognitive disorder (HAND).

The study, led by Dr. Kumar and his team, including recent graduate Dr. Mirzahosseini, from the Department of Pharmaceutical Sciences and the Department of Anatomy and Neurobiology at the University of Tennessee Health Science Center in Memphis, suggests that the LM11A-31 compound could be a promising new treatment for neuroHIV and HAND.

Despite the success in treating HIV over the past 25 years, the virus remains difficult to suppress in the [brain](#) because anti-HIV drugs do not efficiently cross the [blood-brain barrier](#) and therefore cannot reach therapeutic levels there. HIV hides in brain reservoirs shortly after entry and continues to infect brain macrophages and microglia. These cells are crucial for repairing and regenerating neurons and maintaining a healthy central nervous system (CNS).

However, persistent HIV infection in these [brain cells](#) not only reduces their ability to repair and regenerate the CNS but also causes them to release toxic agents ([inflammatory cytokines](#) and chemokines, oxidative stress agents, and viral proteins), which subsequently damage neurons.

Over time, the damaged neurons compromise CNS and impair cognitive functions, leading to a condition known as HAND. HAND is a growing concern among people living with HIV, particularly among the elderly, because as they age they develop other [neurological diseases](#) such as Alzheimer's Disease (AD) and AD-Related Dementias (ADRD).

Dr. Kumar and his colleagues, including Dr. Mirzahosseini, conducted a study on a novel drug candidate, LM11A-31, which can cross the blood-brain barrier and enter the brain. This drug candidate, which is orally available, is currently in [clinical trials](#) for treating mild-to-moderate AD. It has also shown potential in treating other neurological diseases such as stroke and traumatic brain injury.

The current study aimed to see if LM11A-31 could reduce HIV pathogenesis, including HIV replication and HIV-associated oxidative stress and inflammatory response in macrophages. The results were promising: LM11A-31, at a nanomolar range, effectively suppressed HIV in macrophages.

Impressively, its anti-HIV effects were comparable to the anti-HIV drug darunavir, which requires a much higher micromolar range to achieve the same effects. Additionally, LM11A-31 was found to be non-toxic and even reduced toxicity and [inflammatory response](#) in macrophages.

Overall, these findings suggest that LM11A-31 could be a valuable addition to HIV treatment regimens, particularly for managing the virus in the brain. However, further preclinical and clinical research is needed to validate these findings.

Dr. Kumar said, "LM11A-31 shows promise as a new treatment for neuroHIV and HIV-associated neurocognitive disorder (HAND), offering effective suppression of HIV in the brain."

Dr. Goodman, Editor-in-Chief for *Experimental Biology and Medicine* said, "This exciting study by Dr. Kumar and colleagues will lead to further clinical research to determine whether LM11A-31 can be developed as a novel therapy to suppress HIV-1 neuropathogenesis and HAND, and possibly have a dual benefit in HIV-1-AD comorbidity."

More information: Golnoush Mirzahosseini et al, LM11A-31, a modulator of p75 neurotrophin receptor, suppresses HIV-1 replication and inflammatory response in macrophages, *Experimental Biology and Medicine* (2024). [DOI: 10.3389/ebm.2024.10123](https://doi.org/10.3389/ebm.2024.10123)

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