

Functional Human-on-a-Chip® Model Reveals Peripheral Neuromuscular Pathology not CNS Dependent for Alzheimer's Disease

Study demonstrates that motor function deficits observed in patients can arise independently of the brain-related cognitive impairment traditionally associated with the disease.

Orlando, Florida — 16 April 2026 — Hesperos, Inc., a global leader focused on improving preclinical drug development with its Human-on-a-Chip® (HoaC) single- and multi-organ system platforms, today announced the publication of a new study conducted in collaboration with the University of Central Florida (UCF) in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*. The study titled “[Evaluating the peripheral nervous system pathology of Alzheimer's disease utilizing a functional human NMJ microphysiological system](#)” was funded by the National Institute on Aging and found that peripheral neuromuscular dysfunction caused by familial Alzheimer's disease (fAD) may occur independently of brain pathology.

Alzheimer's disease is traditionally characterized as a central nervous system (CNS) disorder. However, patients often experience significant motor deficits including impairments in gait, balance, and muscle tone, which involve the peripheral nervous system (PNS). It has been thought by researchers and clinicians that peripheral neuromuscular symptoms arise due to CNS neurodegeneration rather than reflect an independent pathology.

In this study, Hesperos researchers, in collaboration with scientists at the University of Central Florida's NanoScience Technology Center (NSTC), used a well-established neuromuscular junction (NMJ) HoaC, multi-organ construct was comprised of iPSC-derived fAD motoneurons and healthy human skeletal muscle. The NMJ HoaC system was used to measure changes in motoneuron signaling and skeletal muscle contraction over time. This collaboration had previously established a long-term potentiation (LTP) model of AD in the CNS that is currently being used to evaluate therapeutic candidates.

The results demonstrated that fAD-associated mutations caused significant, mutation-specific, impairments in NMJ function, including reduced synaptic fidelity, increased muscular fatigue, and decreased stability. Importantly, these deficits were observed in the absence of any CNS neurons, providing direct evidence that peripheral neuromuscular pathology may arise independently of CNS involvement in Alzheimer's disease. During peer review, the significance of these findings was highlighted, with one reviewer noting, “The finding that neuromuscular dysfunction occurs with fAD mutations independent of the brain is of high significance and will help push the field forward towards novel therapeutic strategies.”

The study also evaluated the effects of two commonly prescribed Alzheimer's therapies with different modes of action, memantine and galantamine, on the NMJ HoaC system. Neither treatment reduced the observed neuromuscular deficits, underscoring the need for drug development strategies that address peripheral nervous system aspects of Alzheimer's pathology separate from the CNS.

“This work shows that fAD mutations directly impair peripheral neuromuscular function, independent of the central neurodegenerative pathology; this should change the drug development paradigm for AD as

effective treatment will require therapeutics designed to separately address the peripheral pathology,” said James J. Hickman, PhD, Chief Scientist at Hesperos and senior author of the study.

Link to study: <https://doi.org/10.1002/alz.71281>

About Hesperos

Hesperos is a global contract research organization (CRO) specializing in preclinical drug development services utilizing its Human-on-a-Chip® platform. By replicating key aspects of human biology (and thus avoiding expensive, time-consuming, and often less informative animal testing), Human-on-a-Chip® organ-system models provide product development teams with more meaningful insights that can accurately predict an agent’s therapeutic profile while lowering costs and accelerating development timelines. For more information, <https://hesperosinc.com>.

About the UCF NanoScience Technology Center (NSTC)

The UCF NanoScience Technology Center (NSTC) is a multidisciplinary research hub at the University of Central Florida focused on advanced materials and nanotechnology. The center integrates research, education, and innovation across diverse areas including green energy, bioimaging, robotics, and nanoelectronics to address real-world technological challenges. Learn more at <https://nanoscience.ucf.edu/>.

Research reported in this press release was supported by the National Institute on Aging of the National Institutes of Health under award number 5R01AG077651. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.