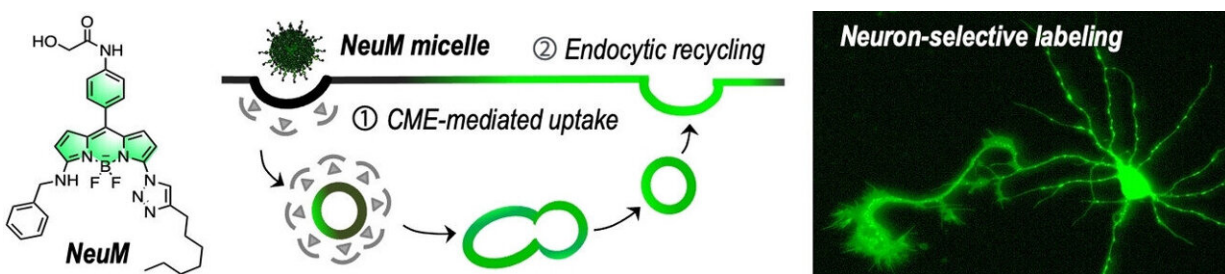# Next-generation neuron labeling technology may be key to unlocking the secret of degenerative brain disorders

April 8 2024

Graphical abstract. Credit: *Angewandte Chemie International Edition* (2023). DOI: 10.1002/anie.202312942

Alzheimer's disease and Parkinson's disease, along with stroke, are among the top three neurodegenerative disorders, characterized by the malfunction and progressive degeneration of neurons. Understanding the mechanisms underlying these neurological disorders and developing therapies requires labeling technologies that can visualize neuronal changes not only in normal conditions but also in disease states.

A research team led by Dr. Kim Yun Kyung from the Brain Science Institute at the Korea Institute of Science and Technology (KIST), in collaboration with Professor Chang Young-Tae's team from Pohang University of Science and Technology, has developed a next-generation

neuron labeling technology called NeuM. NeuM (Neuronal Membrane-selective) selectively labels neuronal membranes, visualizing neuronal structures and allowing real-time monitoring of neuronal changes. The research is published in the journal *Angewandte Chemie International Edition*.

Neurons continuously modify their structure and function to transmit information from sensory organs to the brain, regulating thoughts, memories, and behaviors. Therefore, to overcome degenerative neurological diseases, it is essential to develop techniques that selectively label living neurons for real-time monitoring. However, current gene-based and antibody-based labeling technologies, commonly used to observe neurons, suffer from low accuracy and difficulty in long-term tracking due to their dependence on specific gene expression or proteins.
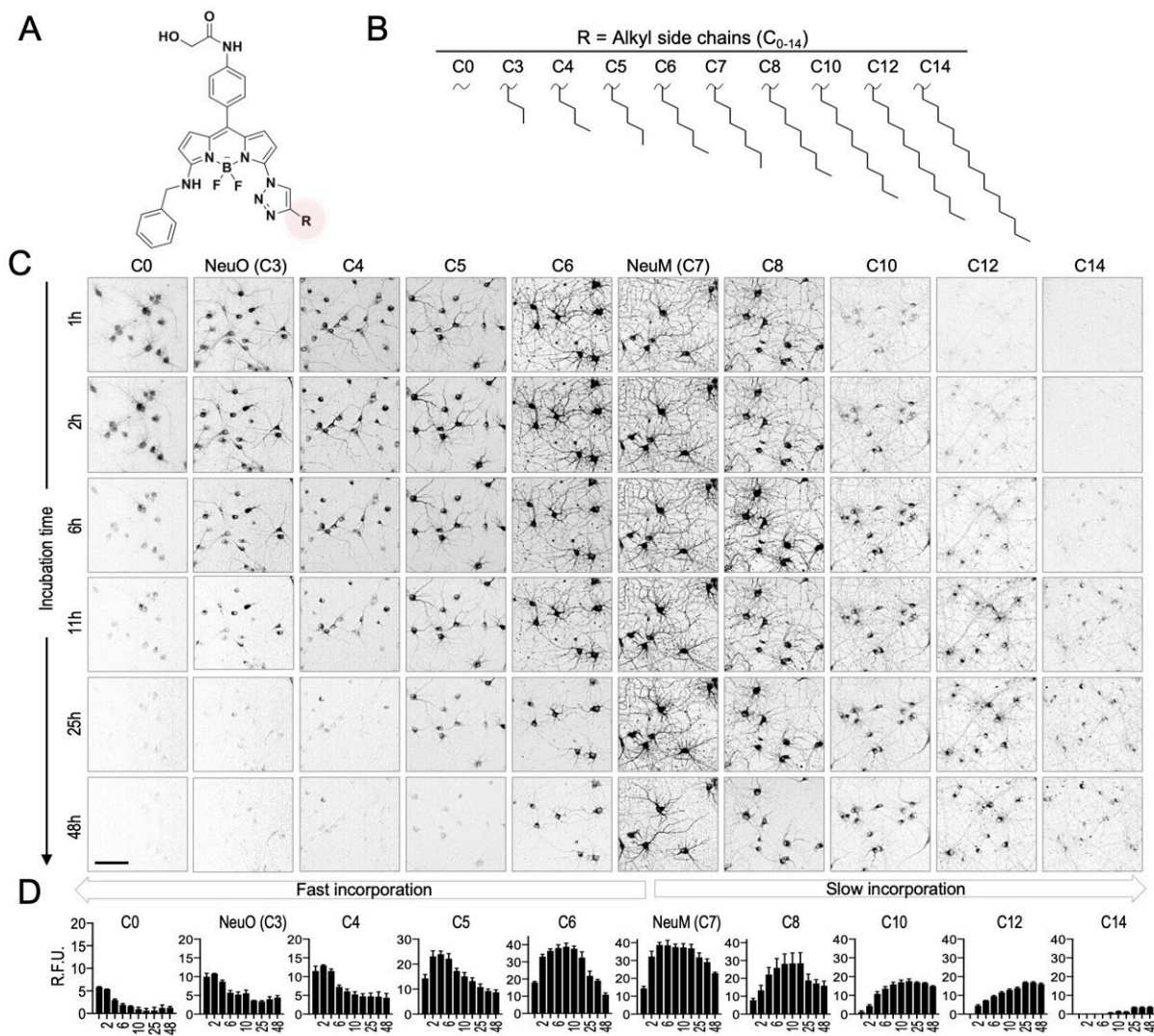
Molecular design for selective labeling of neuronal membranes. Credit: Korea Institute of Science and Technology

NeuM, developed by the research team through molecular design of neuronal cells, possesses excellent binding affinity to neuronal membranes, enabling long-term tracking and high-resolution imaging of neurons. The fluorescent probes within NeuM bind to neuronal membranes utilizing the activity of living cells, emitting fluorescent

signals upon excitation by specific wavelengths of light.

This visualization of neuronal membranes allows for detailed observation of neuronal terminal structures and high-resolution monitoring of neuronal differentiation and interactions.

NeuM, as the first [technology](link) to stain cell membranes through endocytosis in living neurons, exhibits selective reactivity towards living cells, excluding dead cells without internalization. Moreover, the research team has succeeded in extending the observation time of neurons from a mere six hours to up to 72 hours, enabling the capture of dynamic changes in living neurons over an extended period in response to environmental changes.
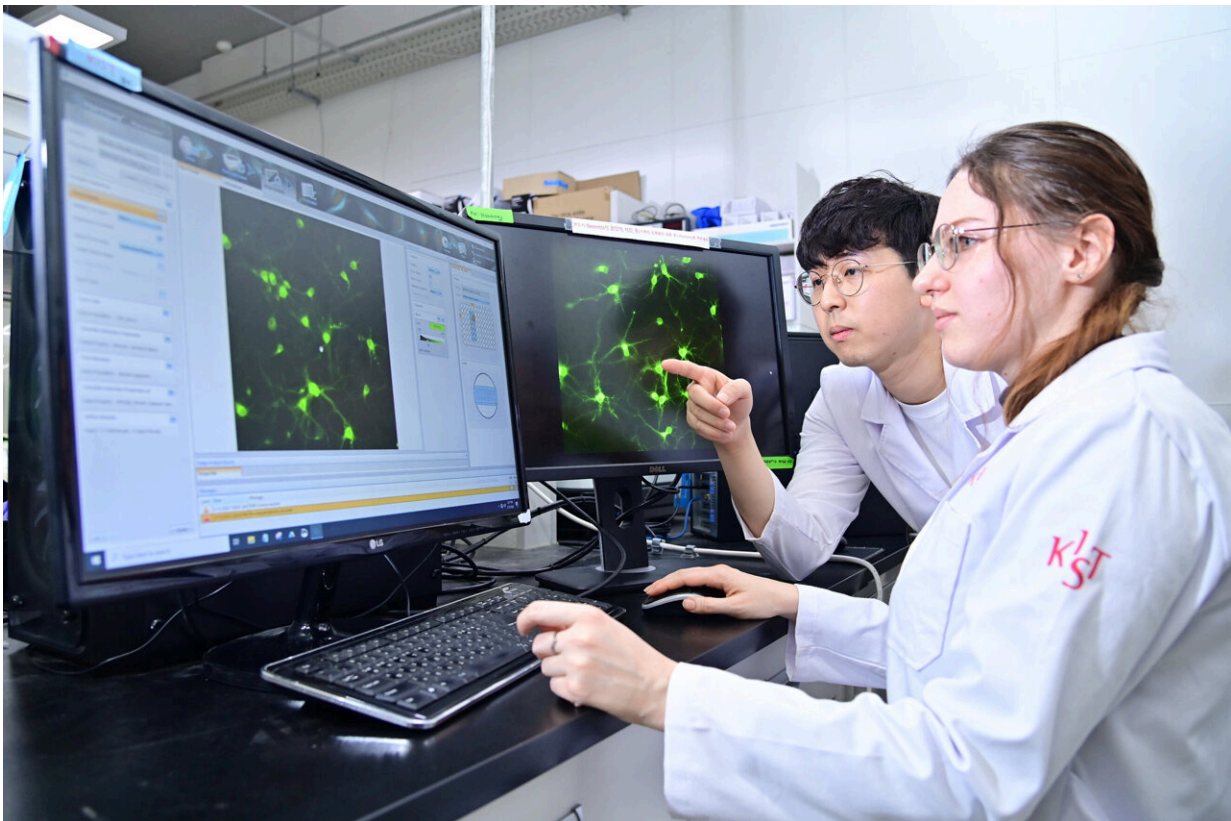
Researchers from Dr. Kim Yoon-kyung's team at KIST are utilizing the next-generation neuron labeling technology, 'NeuM,' to visualize neurons in real-time and examine high-resolution images. Credit: Korea Institute of Science and Technology

NeuM is expected to provide insights into research and therapy development for degenerative neurological diseases, for which there are currently no cures. These diseases, including Alzheimer's, result from neuronal damage due to the production of toxic proteins such as amyloid and the influx of inflammatory substances. NeuM's precise observation of neuronal changes can effectively facilitate the evaluation of candidate therapeutic compounds.

Dr. Kim said, "NeuM, developed this time, can distinguish aging and degenerating neurons, becoming a crucial tool in elucidating the mechanisms of degenerative brain disorders and developing treatments."

"In the future, we plan to refine NeuM for even more precise analysis of neurons by designing fluorescence wavelengths to distinguish colors such as green and red."

More information: Yoonsik Sung et al, NeuM: A Neuron-Selective Probe Incorporates into Live Neuronal Membranes via Enhanced Clathrin-Mediated Endocytosis in Primary Neurons, *Angewandte Chemie International Edition* (2023). DOI: 10.1002/anie.202312942

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