Recent News

A novel platform for neurodegenerative disease studies: Applying photocontrollable probe to induce pathological proteins into amyloid fibers in live cells

Despite hyperphosphorylated TDP-43 has been confirmed as one of the major components in the inclusion bodies of patients with Amyotrophic Lateral Sclerosis (ALS) or Frontotemporal lobar degeneration (FTLD), the underlying disease mechanism has not yet been fully elucidated. Dr. Joseph Jen-Tse Huang, an associate research fellow at the Institute of Chemistry in Academia Sinica, Dr. Hsien-Ming Lee, an assistant research fellow at the Institute of Chemistry in Academia Sinica, and Dr. Eric Hwang, an associate professor at Department of Biological Science and Technology in National Chiao Tung University, developed a photocontrollable probe to induce TDP-43 aggregates in live cells. This platform enables researchers to spatiotemporally control the formation of the neurotoxic fibrils and directly observe the TDP-43 amyloidogenic process. The research was published in ACS Nano on June 27th, 2017.

Dr. Joseph Jen-Tse Huang was the first to discover the specific TDP-43 C-terminal peptide was able to form amyloid fibers and published his research findings in Journal of American Chemical Society (JACS) in 2010. Later on, he further identified the amyloidogenic core sequence of TDP-43. Based on these findings, Dr. Huang and his collaborators developed a fluorescence-labeled, membrane-permeable, photocontrollable probe which can spatiotemporally controlled the formation of endogenous TDP-43 aggregation in the cytosol and impaired the nuclearcytoplasmic transport without using laborious microinjection. In addition, this probe induced TDP-43 aggregation subsequently triggered neuron degeneration and neurite fragmentation. The observed phenomenon indicated that this probe can be applied as a model platform to mimic the pathological phenotype of neuron in neurodegenerative disease.

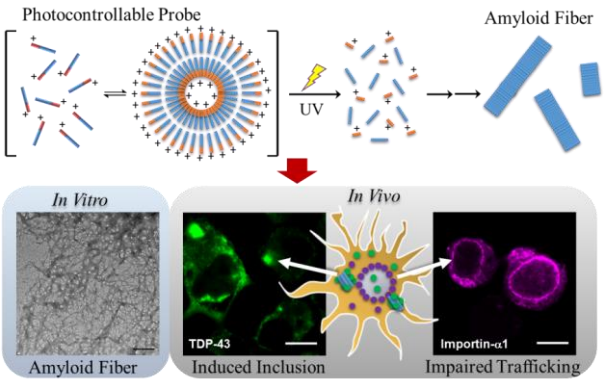

Figure 1. The photocontrollable probe can self-assemble into spherical vesicle but rapidly develop massive nanofibrils with amyloid properties upon photoactivation. In cellular experiments, this cell-penetrable probe can seed endogenous TDP-43 into aggregates upon irradiation and interfere with nucleocytoplasmic protein transport.

Dr. Huang remarked that "Within many currently developed photochemical toolboxes, light would be one of the best triggers to initiate and directly observe the process of TDP-43 amyloidogenesis in vivo. This platform can be widely applied in the studies of aggregation-induced protein mislocalization, amyloid-induced pathogenesis, and protein misfolding in neurodegenerative diseases." The related results are now under patent application.

In addition, Dr. Huang also collaborated with other principal investigators from Academia Sinica, National Yang-Ming University, and Taipei Veterans General Hospital to extend the use of this platform. In the future, the research team aims to apply the photocontrollable probe both in basic research and clinical science in ALS and other neurodegenerative diseases.

The full article entitled "Photocontrollable Probe Spatiotemporally Induces Neurotoxic Fibrillar Aggregates and Impairs Nucleocytoplasmic Trafficking" can be found at the ACS NANO website at: http://pubs.acs.org/doi/full/10.1021/acsnano.7b01645

Personnel

Dr. Chien-Ming Yu has been appointed Adjunct Research Fellow of the Institute of Modern History, effective from September 1, 2017 to July 31, 2019.