A NanoBioLab Symposium 2021 Webinar

Dr. Luke Lavis, Howard Hughes Medical Institute

DESIGNING BRIGHTER DYES FOR ADVANCED FLUORESCENCE MICROSCOPY



Thursday, March 11, 2021
9:00 - 10:00 am SGT
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Dr. Luke Lavis

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ABSTRACT

Specific labeling of biomolecules with bright, photostable fluorophores is the keystone of fluorescence microscopy. An expanding method to label cellular components utilizes genetically encoded self labeling tags, which enable the attachment of chemical fluorophores to specific proteins inside living cells. This strategy combines the genetic specificity of fluorescent proteins with the favorable photophysics of synthetic dyes. However, intracellular labeling using these techniques requires small, cell-permeable fluorophores, thereby limiting utility to a small number of classic, unoptimized dyes. We discovered a simple structural modification to standard fluorophores that improves brightness and photostability while preserving other spectral properties and cell permeability. Inspired by computational experiments, we replaced the N,N-dimethylamino substituents in tetramethylrhodamine with a four-membered azetidine ring. This net addition of two carbon atoms doubles the quantum efficiency and improves the photon yield in living cells. The novel substitution is generalizable to fluorophores from different structural classes, yielding a palette of synthetically tractable chemical dyes with improved quantum efficiency and enabling multicolor single-molecule imaging experiments. These brighter versions of classic fluorophores can be further modified to fine-tune spectral and chemical properties for advanced imaging experiments in increasingly complex biological samples.

ABOUT THE SPEAKER

Luke D. Lavis was born and raised in the Applegate Valley area outside Jacksonville, Oregon. A first-generation college student, he received his B.S. in Chemistry at Oregon State University in 2000, where he performed undergraduate research in synthetic organic chemistry with James D. White. Uncertain about whether to pursue a research career or go to medical school, he took a four-year hiatus and worked in the biotechnology industry, first at Molecular Probes in Eugene Oregon (now a part of ThermoFisher) and later at Molecular Devices in Sunnyvale, California. Luke then entered graduate school at the University of Wisconsin–Madison and worked with Ronald T. Raines to develop strategies to trace the path of anticancer proteins in living cells. He received his Ph.D. in Organic Chemistry in 2008.

Circumventing a traditional postdoc, Dr. Lavis started his independent career as a Group Leader at the Howard Hughes Medical Institute's Janelia Research Campus a month after defending his thesis. His appointment was renewed in 2012 and Luke was named one of C&E News's "Talented 12" in 2015. Dr. Lavis was promoted to Senior Group Leader and Head of Molecular Tools and Imaging in 2017 where he runs his own research group and oversees a department of ~10 other labs. His research program focuses on the design and synthesis of small-molecule tools that interact with light. In particular, his efforts to modernize fluorescent dye chemistry have resulted in the development of the Janelia Fluor® dyes, which are being used in labs around the world for sophisticated imaging applications in cells, tissue, and animals. His work during his independent career has resulted in the publication of over 60 research papers to date and led to the founding of Eikon Therapeutics in 2019.

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