Title: Developing a General Platform for Long Wavelength and Water Soluble BODIPY Photocages with Tunable Cell Permeability for Controlled Delivery of Biologically Relevant Molecules.

Abstract:

Photocages are light-sensitive protecting groups that functionally encapsulate molecule of interest (*MOI*) in an inactive form (Figure 1). Irradiation with light releases the trapped molecule, permitting targeted perturbation of a biological process. Photocages enable to control the spatial distribution and temporal release of *MOI* using light as an external, a non-invasive trigger. However, most caging groups available that operate by one-photon are excited with UV light. This results in potential tissue damage, limits tissue penetration and restricts the wavelength-window available for activation of multiple cues.

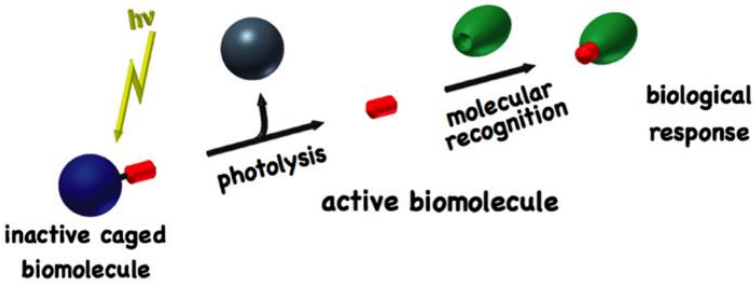

Figure 1: Schematic diagram illustrating the general photo-uncaging process.

Recently, Weinstain *et al.* [1] and others[2], introduced a novel photocage, excitable in the visible light range, based on the boron-dipyrromethene (BODIPY) core. In order for BODIPY cages to become more practical and functional for biological applications, three main issues were need to be addressed: (i) improving the photoreaction efficiency (ii) introducing cell organelle specificity and (iii) fine-tuning the structure's photophysical properties and water solubility as well as controlling cell membrane permeability

During this presentation, I will showcase our efforts and outcome to address above drawbacks. This work combines new synthetic routes to develop highly functionalized BODIPY photocages.

To improve photoreaction efficiency we have investigated a systematic structure activity relationship study on 32 mesomethyl BODIPY photocages and assessed their photophysical and photochemical properties. On the other hand, although photocaging facilitates non-invasive and precise spatio-temporal control over the release of biologically relevant *MOI* using light, subcellular organelles are dispersed in cells in a manner that renders selective light-irradiation of a complete organelle impractical. Organelle-specific photocages could provide a powerful method for releasing bioactive molecules in subcellular locations. We have developed a general platform for introducing cell organelle targeting groups on 2, 6 methyl groups of BODIPY photocages. To test general applicability, we have developed a general post-synthetic method for the chemical functionalization and the synthesis of endoplasmic reticulum (ER)-, lysosome-, and mitochondria-targeted derivatives. We also demonstrated that 2,4-dinitrophenol, a mitochondrial uncoupler, and puromycin, a protein biosynthesis inhibitor, can be selectively photoreleased in mitochondria and ER, respectively, in live cells by using visible light. We have also extended the application of this methodology to develop water-soluble BODIPY photocages with tunable cellular permeability.

References:

1) N. Rubinstein, P. Liu, E. W. Miller, R. Weinstain, *Chem. Commun.* **2015**, *51*, 6369–6372.
2) P. P. Goswami, A. Syed, C. L. Beck, T. R. Albright, K. M. Mahoney, R. Unash, E. A. Smith, A. H. Winter, *J. Am. Chem. Soc.* **2015**, *137*, 3783– 3786.