



# **GRADUATE SCHOOL OF BIOMEDICAL SCIENCES**

## **BIOCHEMISTRY AND MOLECULAR PHARMACOLOGY**

### **Ph.D. THESIS DEFENSE**

**ADAM CHOI**

MENTOR: Stephen Miller, PhD  
Friday, 9/7/2018 10:00 a.m.  
LRB 816

#### **Illuminating Biology with Membrane Penetrating Sulfonate Delivery Scaffolds and Near-Infrared Azasiline Fluorophores**

Near-infrared (NIR) light, with wavelengths of 650 to 900 nanometers, effectively penetrates tissues. The high signal to noise ratio and low phototoxicity of NIR light makes this wavelength range ideal for deep tissue imaging. However, current NIR fluorophores are generally large hydrophobic molecules that are prone to aggregation. Sulfonation can enhance aqueous solubility, but their anionic nature prevents membrane diffusion, and thus, restricts the applications of sulfonated molecules to *in vitro* or fixed cells.

The repertoire of commercially available sulfonated NIR probes is mostly limited cyanines, which have low photostability. Moreover, larger cyanines require multiple sulfonates to maintain aqueous solubility. For example, Indocyanine Green is only sparingly soluble in PBS, despite having two sulfonates.

My work has focused on the delivery of sulfonated dyes into live cells and the development of a new, ultra-compact NIR dye scaffold. First, to expand the in-cell applications of sulfonated fluorophores, I designed reductively-labile sulfonate protecting groups. Using these scaffolds, I have successfully delivered the fluorophore dansyl sulfonate into live cells, where the cytosolic reducing environment unmasks the anionic sulfonate. Secondly, to create a compact, photostable NIR fluorophore, I pioneered the discovery of azasilines dyes. The two azasiline derivatives, ASiFluor710 and ASiFluor730, fluoresce over 700 nanometers and are among the most compact NIR fluorophores currently known. ASiFluor730 also retains the high photostability of oxazine dyes, highlighting their potential in long exposure applications. Beyond the immediate applications in fluorescence microscopy and *in vivo* imaging, I envision that my work will serve as a framework for the future design of soluble, membrane permeable, NIR fluorescent probes.

#### **Mentor(s)**

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#### **Dissertation Exam Committee**

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