Chemigenetic Tools for Near-Infrared Imaging

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The combination of genetically encoded tags and their cognate small-molecule fluorophores is a powerful way to image specific protein targets. In the past decade, a large palette of fluorogenic dyes that emit in the visible range (400-650 nm) have been developed for the self-labeling protein tags HaloTag and SNAP-tag. These probes have been largely based on the xanthene scaffold (e.g., rhodamine, pyronine, silicon-rhodamine, etc.). So far, it has been challenging to tune this class of dyes to emit efficiently in the near-infrared (>700 nm), which is essential for in vivo applications. In this lecture, I will present our efforts to develop chemigenetic probes to reach such long wavelengths without compromising on the excellent contrast of visible-light probes. Towards this goal, we developed an intramolecular cyclization reaction in carbocyanine dyes that confers fluorogenicity to this class of fluorophores. Besides discussing the development of the small molecules, I will present recent results in the engineering of self-labeling proteins that work optimally with our new fluorogenic carbocyanine dyes.