Title

Synthetic Cell Biology of Primary Cilia

Abstract

Primary cilium is a small, ubiquitous organelle that functions as a sensory antenna for surrounding physical and chemical stimuli. To do this, primary cilia must accumulate specific signaling molecules. Defects in protein trafficking to primary cilia cause a plethora of disorders, collectively termed ciliopathies, which include loss of smell and sight, polycystic kidney or liver disease, obesities, and developmental defects. However, these protein trafficking mechanisms, which are fundamentally significant to cell biology and pathophysiology, are poorly understood, mainly due to the lack of techniques to specifically probe and visualize dynamic protein diffusion to the primary cilia. We integrate expertise in organic chemistry, biophysics, cell biology, biochemistry, advanced imaging and computational modeling, and deploy newly developed chemically-inducible molecular probes to unravel ciliary protein trafficking mechanisms at the molecular level. Our multidisciplinary research will provide a powerful technology that extends conventional techniques in ciliary biology, and offer far-reaching insights into ciliopathies.

Recent Publications:

1. Komatsu T. Kukelyansky I, McCaffery JM, Ueno T, Varela LC and Inoue T. “Organelle-Specific, Rapid Induction of Molecular Activities and Membrane Tethering” *Nature Methods* 7, 206-208 (2010)
2. Umeda N., Ueno T., Pohlmeyer C., Nagano T. and Inoue T. “A photocleavable rapamycin conjugate for spatiotemporal control of small GTPase activity” *Journal of American Chemical Society* 133(1), 12-14 (2011)
3. Ueno T., Falkenburger B.H., Pohlmeyer C., and Inoue T. “Triggering Actin Comets Versus Membrane Ruffles: Distinctive Effects of Phosphoinositides on Actin Reorganization” *Science Signaling* 4(203), ra87 (2011)
4. DeRose R., Pohlmeyer C., Umeda N., Ueno T., Nagano T., Kuo S., and Inoue T. *Journal of Visualized Experiments*, e3794 (2012) “Moving molecules by light; Spatio-temporal manipulation of small GTPase activity at subcellular level and on timescale of seconds in living cells”
5. Miyamoto T., DeRose R., Suarez A., Ueno T., Chen M., Sun T.-p., Wolfgang M.J., Mukherjee C., Meyers D. and Inoue T. “Rapid and Orthogonal Logic Gating with a Gibberellin-induced Dimerization System” *Nature Chemical Biology* 8, 465-470 (2012)