Highlighting fluorescence

Fluorescent proteins serve an integral role in chemical biology research. The 2008 Nobel Prize in Chemistry to Osamu Shimomura, Martin Chalfie and Roger Tsien "for the discovery and development of the green fluorescent protein, GFP" underscores the importance of this technology. In this issue, we go back to the basics, exploring the history and properties of GFP in our first Primer (http://www.nature.com/nchembio/journal/v5/n2/pdf/nchb-primer001.pdf; see also *Nat. Chem. Biol.* **5**, 1, 2009). Kai Johnsson looks to the future of the field, outlining questions that fluorescence-based visualization methods are poised to answer and calling for new advances to fill methodological gaps [**Commentary, p. 63**]. Finally, research by Subach *et al.* demonstrates that fluorescent protein methodology continues to tick forward. The authors identified mutations in the monomeric mCherry that convert this construct into a series of fluorescent timers with slow, medium or fast maturation rates. Attachment of the 'medium' timer to a membrane protein, LAMP-2A, enabled visualization of the protein at different locations in the cell. More importantly, correlating position with the color of the fluorescent timer allowed the authors to track the specific pathway of LAMP-2A progress. [**Articles, p. 118; News & Views, p. 70**] *CG*

Inhibitors probe where it Wnt

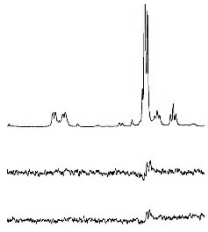
Despite its importance in cell fate decision making, little is known about how the Wnt/β-catenin signaling pathway functions in intact systems. A lack of chemical probes contributes to this lack of knowledge. Chen *et al.* performed a chemical genetic screen and identified two classes of inhibitors of the pathway. Several compounds block the pathway by preventing palmitoylation of Wnt proteins, which is required for their signaling ability and for Wnt secretion. A second class of inhibitors stabilize Axin, a major component of the complex responsible for β-catenin degradation. The compounds function to reversibly suppress the pathway *in vivo* in zebrafish tail fin regeneration and in cancer cell models where aberrant Wnt signaling has been implicated, which suggests that the compounds could be useful therapeutically in addition to allowing targeting of the pathway for biological studies. [**Articles, p. 100; News & Views, p. 74**] *MB*

Cytochrome *bd* resists NO

During aerobic respiration, cytochrome *bo* and cytochrome *bd* couple ubiquinol-8 oxidation with the reduction of molecular oxygen to water. Recent transcriptional data have revealed that cytochrome *bd* expression is induced by nitric oxide (NO) stress. Mason *et al.* have now found that deletion of cytochrome *bd* but not cytochrome *bo* results in greater NO-induced growth inhibition in *Escherichia coli*. In investigating the mechanistic basis for this resistance, the authors found that the NO dissociated faster from cytochrome *bd* than from cytochrome *bo* and that this faster NO dissociation rate corresponded to the rate of recovery of aerobic respiration. These results suggest a new role for cytochrome *bd* in supporting aerobic respiration during NO stress. [**Brief Communications, p. 94**] *JK*

Written by Mirella Bucci, Catherine Goodman, Joanne Kotz & Terry L. Sheppard

Rotavirus reception

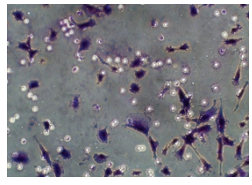


Rotavirus, a causative agent of acute and sometimes lethal gastroenteritis, is known to use a protein called VP8* to recognize carbohydrates on the host cell surface. These interactions, in combination with another protein, VP5*, mediate cell attachment and infectivity. Because the infectivity of some rotaviruses, but not others, can be reduced by treating the host cell with sialidase, these viruses have been characterized as either 'sialidase sensitive' or 'sialidase insensitive'. Haselhorst *et al.* now use saturation transfer difference NMR along with computational chemistry and binding and infectivity assays to demonstrate that both types of the virus recognize sialic acids, although the specific position of the carbohydrate residues, and thus the preferred substrates, vary. These results indicate that more detailed investigations of rotavirus selectivity may offer new insights into treatment of this prevalent illness. [Brief Communications, p. 91; News & Views, p. 71] *CG*

RNA completes the circle

The group I intron is a self-splicing RNA that excises itself from an RNA transcript and facilitates the ligation of the flanking exons. The splicing reaction requires a guanosine nucleotide cofactor that becomes attached to the 5′ end of the ribozyme during the reaction. After splicing is complete, group I introns typically undergo a deactivating intramolecular cyclization that releases a short oligonucleotide fragment from the 5′ end of the intron. Vicens and Cech now report a new cyclization reaction of group I introns. In assays designed to uncover new self-splicing introns, the authors found that a group I intron from *Anabaena* sp. *PCC 7120* produced a larger circular RNA than expected. Their analysis showed that the circularization reaction required guanosine 5′-triphosphate as the splicing cofactor and produced a closed RNA circle that contained a natural 3′,5′ linkage at the ligation site. The discovery of this new ribozyme ligase activity extends the catalytic versatility of group I introns but also supports the notion that RNA replicases could have arisen from established ribozymes. [**Brief Communications, p. 97; News & Views, p. 73**] *TLS*

Selectively stopping PLDs



Phospholipase D (PLD), which catalyzes the conversion of phosphatidic acid to phosphatidylcholine, is tightly regulated in cells and implicated in a number of cancers. A lack of chemical tools has hindered efforts to dissect the functional roles of the two mammalian isoforms, PLD1 and PLD2. Starting from a moderately potent nonselective PLD inhibitor scaffold, Scott *et al.* used a diversity-oriented synthetic approach to develop a library of PLD inhibitors. By screening this library *in vitro* and in cellular assays, the authors identified potent dual- and isoform-selective PLD inhibitors. Using these inhibitors in migration assays, in combination with selective PLD silencing, suggests distinct roles for the two PLD isoforms in cancer cell invasiveness. [Articles, p. 108] *JK*