

Genetically encoded tags and indicators are molecular spies that reveal specific gene products and biochemical processes in living cells and organisms. Fluorescent proteins from jellyfish and corals have been bred to eliminate multimerization and cover the entire visible spectrum. Somatic hypermutation in B lymphoma cells can offer a powerful new way to evolve protein properties. Indicators constructed from fluorescent proteins can report local dynamic signals such as redox potential, kinase vs. phosphatase activities, protein-protein interactions, and ion and neurotransmitter concentrations. Improved reporters for protein kinase A and Src are revealing localized kinase activation in cells that are locomoting or feeling external tensions. A new glutamate indicator is showing promise for imaging glutamate release and reuptake and their modulation during synaptic plasticity.

Short tetracysteine motifs are complementary tags, which can be labeled in live cells with membrane-permeant biarsenical dyes. These labels are far smaller and sometimes less perturbative than fluorescent proteins. Unique applications include green vs. red pulse-chase labeling of old vs. new copies of the same protein, electron-microscopic localization, chromophore-assisted light inactivation of a chosen protein without the problems of antibody penetration, and measurement of local  $\text{Ca}^{2+}$  within nanometers of proteins such as  $\text{Ca}^{2+}$  channels.