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Fluorescent Proteins show the bright fluorescence in the absence of exogenous substrates and cofactors, thus they are very useful for monitoring gene expression, localization of proteins and so on even in living cells, and actually used for many purposes in the various fields of bioscience.

The red fluorescent protein DsRed from Discosoma coral undergoes oligomerization as essential and highly rate-limiting step of its fluorescence maturation. While trying to overcome this apparent drawback, we found that DsRed is rapidly degraded through the ubiquitin-proteasome pathway in mammalian cells, but its tandem-linked dimer can escape this proteolysis to show markedly enhanced fluorescence. Taking advantage of this dimerization-dependent stabilization of DsRed, we have developed a new versatile two-hybrid vector system that can directly trace protein-protein interactions in living cells by only using conventional types of flow cytometers and fluorescent microscopes. This RFP-using bimolecular fluorescence yielding (RUBY) system has been successfully utilized to visualize the intracellular assembledge and localization of two known heteromeric protein pairs, Runx2-PEBP2β and p65RelA-IκBα. Furthermore, we have developed new variants of DsRed1 and established multicolor system to detect alternative protein-protein interactions among three proteins in living cells.