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In This Issue

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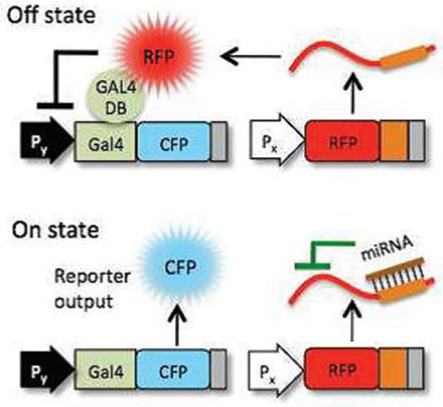
VISUALIZATION OF GENE SILENCING

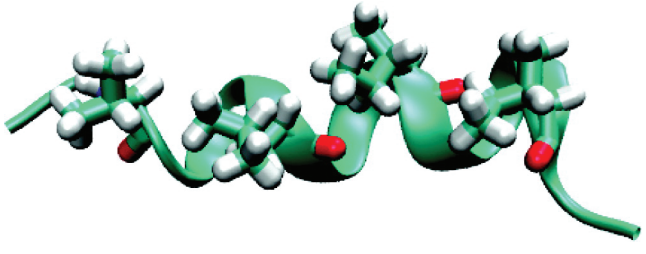
RNA interference (RNAi) is involved in several key cellular processes such as cell-cycle regulation, apoptosis, and cellular differentiation during development and disease. Thus, it is important to be able to accurately measure microRNA (miRNA) activity and, consequently, RNAi dynamics in living cells. Methods available to date either require cells to be lysed at different time points or employ the loss of fluorescence signal as a read-out. Haynes *et al.* (DOI: 10.1021/sb3000035) now describe the development of a novel artificial repressor that can regulate a switch to produce a positive, visible fluorescent signal in the presence of RNAi activity in living cells.



This engineered RNAi sensor is sensitive to even low levels of miRNA activity, like that of mir-34, often implicated in cancers. Here, the authors provide the first evidence of cell-cycle arrest associated miR-34 activity in proliferating osteosarcoma cells. This circuit design can further be engineered and may prove to be a useful biological tool for use in research and medical applications like cancer therapy.

INCREASING TARGET-PEPTIDE AFFINITY

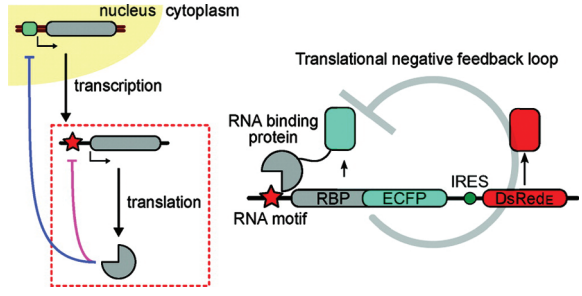
The family of Bcl-2 proteins regulates apoptosis via heterodimeric interactions between its pro-death and pro-survival members. These interactions are mediated by the binding of BH3 domains of pro-death proteins to the surface of pro-survival proteins. However, peptides corresponding to the BH3 domain have only modest affinities toward their cellular targets. Zhang *et al.* (DOI: 10.1021/sb200002m) now describe mechanisms that significantly increase the target affinity of the BH3 peptide from the pro-death protein, Bak.



Using two different methods, the authors demonstrate a 15-fold increase in affinity of the Bak BH3 peptide to its cellular targets, with no change in its cytotoxicity toward HeLa cells. Since pro-survival proteins are present in abundance in many cancers, the affinity-matured variants of the Bak BH3 domain have possible implications in the design of cancer therapeutics.

SYNTHETIC INHIBITION OF PROTEIN EXPRESSION

Feedback regulation, which is commonly observed in both biological and nonbiological systems, is often used to stabilize output signals against system fluctuations. In cells, dynamic gene expression is dependent on feedback control. Researchers until now have constructed and characterized transcriptional feedback systems in which protein-feedback inhibits further transcription of its encoding gene. However, a synthetic translational feedback system in which a protein feedback-inhibits translation of its encoding mRNA is lacking. Stapleton *et al.* (DOI: 10.1021/sb200005w) now describe one such synthetic system in which a RNA/protein binding pair enables translational feedback regulation, tightly controlling expression of proteins of interest.



The authors developed modified ribosomal fusion proteins that regulate the translation of their own mRNA in HeLa cells. They also report the ability to control feedback repression strength by altering RNA/protein pairs. In addition to being a useful synthetic biology tool, the system described here has applications in the study of natural regulation.

A PHOTO-ACTIVATED INDUCER OF CELL DEATH

Caspase-dependent apoptosis is a mechanism of programmed cell-death. This process plays a role in the development of multicellular organisms as well as in the progression of several diseases like cancer and HIV/AIDS. During apoptosis, the activation of initiator caspases results in the activation of executioner caspases such as caspase-7, which induces apoptosis. While previous studies have explored the regulation of apoptosis, specific spatiotemporal control of the apoptotic cascade was never achieved. Now, Mills *et al.* (DOI: 10.1021/sb200008j) describe the development of a photoactivated protein switch that can specifically activate caspase-7 in the presence of blue light.

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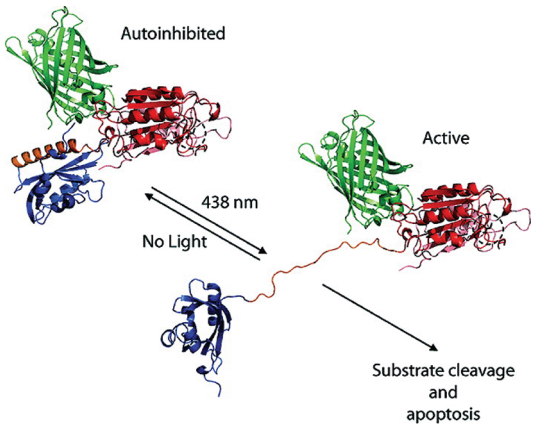

By fusing the light sensing domain of the *Avenas sativa* phototropin to the catalytic domain of caspase-7, the authors were able to engineer a photoactivated variant which can be used to study apoptosis on a single-cell level. Additionally, since cell death can now be spatiotemporally regulated, this fusion protein holds promise in the field of gene therapy.

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