ACS SyntheticBiology

In This Issue

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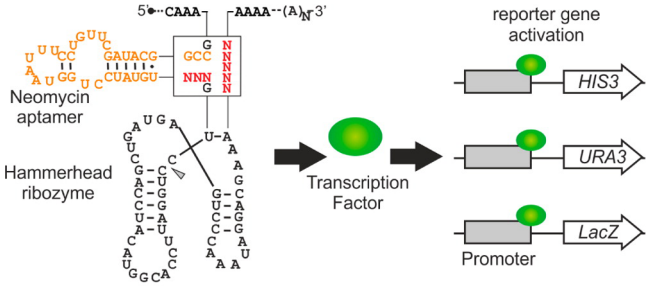
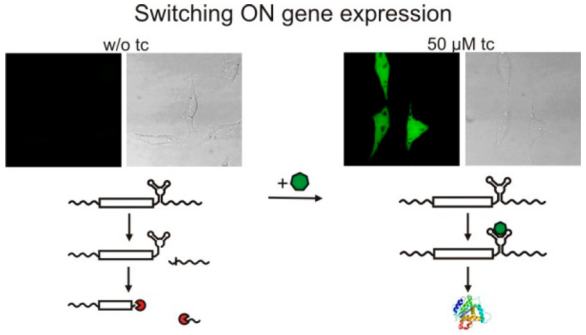
RIBOZYME-BASED AMINOGLYCOSIDE SWITCHES OF GENE EXPRESSION



In recent years, there have been increasing efforts to create synthetic biological devices capable of performing user-defined tasks. The functional complexity of these artificial genetic networks arises from the interplay of individual switches that can rapidly respond to environmental cues or cellular signals. The authors recently reported a series of hammerhead ribozyme-based artificial riboswitches that allow for post-transcriptional regulation of gene expression *via* switching mRNA, tRNA, or rRNA functions. Now, Klauser *et al.* (DOI: 10.1021/sb500062p) report the re-engineering of hammerhead ribozymes in order to respond efficiently to aminoglycoside antibiotics.

The authors first describe the development of an *in vivo* selection method previously not available in yeast, and then detail a new aptazyme design strategy. Combining these two methods, they develop neomycin-dependent genetic switches with very powerful performances. The work presented here has the potential to broaden the applicability of RNA switches and enable the development of many more aptazyme-based genetic controllers.

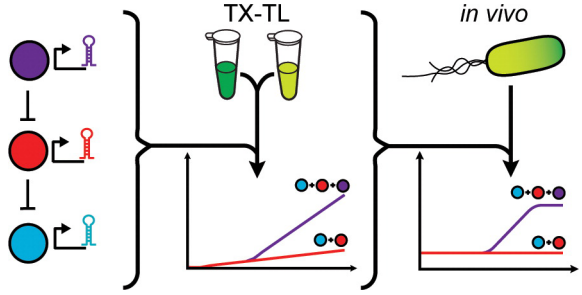
CONDITIONAL CONTROL OF MAMMALIAN GENE EXPRESSION BY TETRACYCLINE-DEPENDENT HAMMERHEAD RIBOZYMES



Robust synthetic devices are required for the construction of synthetic genetic circuits as well as important scientific and technological tools to control cellular processes. Here, Beilstein *et al.* (DOI: 10.1021/sb500270h) describe the development of tetracycline-dependent hammerhead ribozymes that can switch-on gene expression up to 8.7-fold upon addition of tetracycline.

A tetracycline aptamer was grafted onto the hammerhead in such a way that the ligand binding to the aptamers destroys a loop−loop interaction within the ribozyme, inhibiting hammerhead cleavage, and allowing gene expression. The advantage of this regulatory system is its independence from any regulatory proteins. The authors also show that stable integration into the genome of HeLa cells resulted in low background activity in the absence of ligand. Further, the ligand concentration required to robustly flip the switch does not affect cell viability and therefore allows a long-term application of the system. The work described here turns these tetracycline-dependent hammerhead ribozymes into promising tools for conditional gene expression in mammalian cells.

CELL-FREE TX-TL SYSTEMS FOR RAPID CHARACTERIZATION OF FAST DYNAMICS OF RNA GENETIC CIRCUITRY



The behavior of cells is governed by genetic networks—complex webs of interactions between cellular regulatory molecules that determine when different genes are expressed. In this work, Takahashi *et al.* (DOI: 10.1021/sb400206c) use a cell-free system to characterize network dynamics and further the case for RNA molecules as versatile regulators that can be used to construct synthetic gene networks.

Cell-free systems provide the cellular machinery to express genes without the need for actually growing cells. The authors start by showing that RNA genetic networks function the same in a cell-free system as in cells, and then show that RNA genetic networks work much quicker than networks made out of proteins. Finally, they develop a new RNA network by first testing its components in the cell-free system and then show that the complete network functions in cells. This new RNA network allows for the timed expression of two different genes inside cells, one after the other. This manuscript describes the utility of using a cell-free system to prototype gene networks, thus accelerating the pace at which new networks can be developed.

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