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## Dual control system - a novel scaffolding architecture of an inducible regulatory device for the precise regulation of gene expression

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## Abstract

Here, we present a novel scaffolding architecture of an inducible regulatory device. This dual control system is completely silent in the off stage and is coupled to the regulation of gene expression at both the transcriptional and translational levels. This system also functions as an AND gate. We demonstrated the effectiveness of the cumate-riboswitch dual control system for the control of pamamycin production in Streptomyces albus. Placing the cre recombinase gene under the control of this system permitted the construction of synthetic devices with nonvolatile memory that sense the signal and respond by altering DNA at the chromosomal level, thereby producing changes that are heritable. In addition, we present a library of synthetic inducible promoters based on the previously described cumate switch. With only one inducer and different promoters, we demonstrate that simultaneous modulation of the expression of several genes to different levels in various operons is possible. Because all modules of the AND gates are functional in bacteria other than Streptomyces, we anticipate that these regulatory devices can be used to control gene expression in other Actinobacteria. The features described in this study make these systems promising tools for metabolic engineering and biotechnology in Actinobacteria.

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