Tuning the Coenzyme B12 Riboswitch sensor with a transcriptional repressor to invert and amplify the signal

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Genetic circuits are composed of input, logic, and output parts. Construction of complex circuits for practical applications requires numerous tunable genetic parts. However, the limited diversity and complicated tuning methods used for the input parts hinders the scalability of genetic circuits. Therefore, a new type of input part is required that responds to diverse signals and enables easy tuning. Here, we developed RNA-protein hybrid input parts that combine a riboswitch and orthogonal transcriptional repressors. The hybrid inputs successfully regulated the transcription of an output in response to the input signal detected by the riboswitch and resulted in signal inversion because of the expression of transcriptional repressors. Furthermore, the hybrid input detected both exogenous and endogenous signals, indicating potential applications in metabolite sensing. This hybrid input part could be highly extensible considering the rich variety of components.