

## Biomolecular Phase Separation Suppresses Gene Expression in Bacteria

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Past studies on biomolecular phase separation (PS) have suggested it as a new engineering tool to control cellular processes. Specifically, once biomolecules undergo PS, membraneless organelles (MLO) will form, where concentrations of biomolecules become higher than those outside. Hence, it has been speculated that PS plays an important role in regulating biochemical processes such as gene regulations. By co-enrichment of regulatory proteins, PS may enhance the overall gene expression level. However, previous experimental studies yielded contradictory results in this regard.

Motivated by this, this study aims to unravel relationships between PS and gene expressions. In *E. coli*, we constructed synthetic genetic circuits to probe the relationship: each genetic circuit contains a transcription factor (TF) fused with a fluorescent protein (FP) and an intrinsically disordered protein (IDP). This TF-FP-IDP will undergo PS. Also, there is another FP placed under a promoter inducible by the TF. Consequently, we quantitatively map the functional landscape of PS in terms of the gene expression through FP levels. By testing various TF activators with many IDPs, we found that TF activators become TF repressors due to PS in *E. coli*. Such results demonstrate that PS does not guarantee the enhancement in gene expression as commonly expected.

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