ABSTRACT: The cells of higher eukaryotes utilize chromatin state to encode "permanent" epigenetic changes in gene expression. For example, signals received by a cell during the course of development can induce the partitioning of the genome into accessible (euchromatin) and inaccessible (heterochromatin) regions that specify the fate of that cell. This epigenetic profile, in which blocks of gene are "silenced" by heterochromatin, is stably maintained and inherited by daughter cells. Thus, chromatin state provides a higher level of gene expression control that is regional (acting on many genes at once), dominant over transcription factors, ultra-cooperative (all or none), and highly stable (memory). Engineerable control over chromatin state would clearly be a powerful tool for Synthetic Biology.

We have constructed and characterized a synthetic silencing system in *S. cerevisiae* in which we can inducibly silence specific loci in the genome. This foundational technology will facilitate the construction of complex genetic circuits with memory, and has potential application in the engineering of cell differentiation in higher eukaryotes.

**A** Natural silencing system in yeast

**B** Synthetic Chromatin System Design

**C** Inducible Silencing of Target Genes

**D** Silencing Dominant Over Transcription Factors

**E** Regional and Bidirectional Silencing

**F** Binary Switch

**G** Memory

Chromatin-based silencing is powerful mechanism to regulate gene expression in eukaryotes.

We have developed a synthetic chromatin switch with distinct properties:

1. **MODULAR**: can silence diverse promoters/genes
2. **REGIONAL**: can silence arrays of multiple genes
3. **DOMINANT**: overrides transcription factor control
4. **MEMORY**: silencing persists for multiple generations

**WHY IS THIS IMPORTANT FOR SYNTHETIC BIOLOGY?**

* A new, higher level of gene expression control
* Switch that encodes cellular memory

Foundation for many diverse synthetic biology applications