Docket #: S20-414

High-Multiplexed Genome Engineering Using Synthetic CRISPR Arrays

Genetic engineering of biological systems is a fundamental tool for both basic and translation research, where up- and down-regulation of gene expression is necessary to drive cellular phenotypes and evaluate gene function. However, modulating the expression of multiple genes is difficult and labor-intensive.

Researchers in Stanley Qi's laboratory at Stanford have developed a CRISPR-based tool for multiplexed genome engineering. The inventors have combined multiple Cas enzymes and developed guide sequences to drive multi-gene silencing and activation in mammalian cells. While existing CRISPR arrays are limited by interference between adjacent RNAs, the inventors have optimized linker sequences to minimize interference between guide RNA sequences.

Among its many applications, the technology can be used to control developmental transcriptional programs, and differentially modulating gene signatures related to immune response. It can be used with different delivery methods including transfection or transduction to aid cell engineering and manufacturing.

Applications

- Cellular reprogramming across cell lineages
- Multiplex screening of genetic interactions
- Optimization of cell therapies across therapeutic areas, including oncology and regenerative medicine
- Simultaneous targeting of multiple genetic loci

Advantages

- Simultaneous modulation of many genes with the transfection of a single plasmid
- Enables multiple types of genetic engineering
- Eliminates the need to troubleshoot transfection/delivery of multiple individual cDNAs or RNAis
- No stoichiometry concerns from multiple transfections
- Shorter sequences than traditional cDNA overexpression systems
- Greater specificity than RNAi
- Array structure reduces interference between guide RNAs

Publications

- Enhanced Cas12a multi-gene regulation using a CRISPR array separator Jens Magnusson et al., bioRxiv

Patents

- Published Application: WO2022159402
- Published Application: 20240110175

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