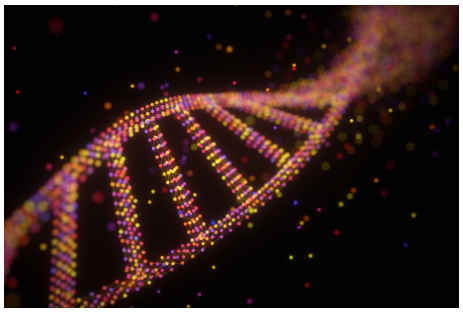

Novel epigenome editors for multiplexed gene regulation

Unmet Need

Epigenome editors activate or inhibit gene expression without modifying the underlying DNA sequence. Consequently, these editors can reversibly fine-tune gene expression without the risk of permanently altering the genome or off-target editing. Epigenome editors are currently in development for therapeutic purposes to restore gene function or to silence undesirable gene expression. However, most epigenome editors can only modulate one gene or regulatory region at a time, limiting its ability to achieve combinatorial gene regulation that underlies complex biological processes. There is a need for an epigenome editor that is compatible with multiplexed gene regulation.

Technology

Duke inventors have identified a novel epigenome editing method for multiplexed control of gene regulation. This is intended to be used in research and clinical applications. Specifically, the inventors have developed a toolbox of catalytically inactive Cas12a- and MS2-based epigenome editors to guide the p300 and SID effectors to targeted regions for gene activation and inhibition, respectively. This system is compatible with a multiplexed format using an array of guide sequences, allowing control of multiple genomic regions at once. In addition, the use of multiple guide sequences achieves a stronger gene activation or inhibition versus using a single guide. The inventors have also derived Cas12a proteins from a variety of bacterial species capable of different strengths of gene regulation. This method has been demonstrated to effectively control gene expression *in vitro* using human cell lines.

Other Applications

In addition to targeting specific genomic regions, this invention can be used as a screening tool to discover combinatorial interactions of genomic regions underlying a specific phenotype. This tool can also be adapted for use in other organisms (ex. improving yield in plants, increasing resistance to pathogens), enabling potential industrial applications.

Advantages

- Compatible with the activation and inhibition of multiple genomic regions at once
- Compatible with different strengths of gene regulations using diverse Cas12a proteins and an array of guide sequences
- Validated fine-tuning of gene expression *in vitro*

Duke File (IDF) Number

IDF #:T-007927

Meet the Inventors

Reddy, Timothy
Gersbach, Charles
Melore, Schuyler

Contact For More Info

Thomas, Dennis
919-681-7580
dennis.thomas@duke.edu

Department

Biostatistics and Bioinformatics

Publication(s)

•