Comprehensive modular epigenome editing platform

gRNA



Challenge

- Various human disorders and disease susceptibilities are triggered by aberrant changes in gene activity and/or the epigenome.
- Precision therapeutics could restore appropriate epigenetic marks and gene activity, it therefore represents a potentially powerful strategy to ameliorate disease.

Technology

- Precise programming of nine specific chromatin modifications at target loci to quantitatively tune target gene activity with high ON-target efficiency and low OFF-target activity.
- Design: dCas9 engineered with an optimised tail-array of five GCN4 motifs (dCas9GCN4), which tethers up to five epigenetic 'effectors' to genomic targets. The effectors can be selected from a comprehensive and validated library of catalytic domains of a DNA- or histonemodifying enzyme linked with scFV (CDscFv).

Intellectual Property

Priority application filed in 2022.

Commercial Opportunity

The technology is comprehensively evaluated ex vivo and available for outlicensing or co-development. We also offer a technology evaluation program.

Further Reading

Policarpi et al., bioRxiv 2022, Epigenome Editing & Function of Chromatin Modifications



Cas9^{GCN4} +DOX sfGFP SCF Catalytic domain 'effectors' (CDscFV H3K4me3 H3K27ac (p300-CDscFV (Prdm9-CDsof H3K79me2 H3K36me3 (Dot1L-CDscFV (Setd2-CDscFV) H2AK119ub H3K27me3 (Ring1b-CDscFV) (Ezh2-FLscFV) H3K9me2 H4K20me3 (G9a-CDsoF) (Kmt5C-CDscF **DNAme** Control (Dnmt3a3L-CDsc (GEPscFV

Schematic of the epigenetic editing platform. Upon DOX-induction, dCas9GCN4 recruits five copies of chromatin-modifying effector(s) or control GFPscFV to target loci via a specific gRNA. https://doi.org/10.1101/2022.09.04.506519

Internal Reference

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