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PREDICTION FOR TARGETING EFFICIENCY OF GUIDE RNA FOR A GENE OF INTEREST IN BACTERIA

Keywords: gene silencing, guide efficiency, Cas9, CRISPRi, software, predictive model, machine learning, AI

INVENTION NOVELTY

Provided is a machine learning-based tool that improves reliable prediction of targeting efficiency of guide RNA for gene silencing in bacteria.

VALUE PROPOSITION

CRISPR interference (CRISPRi) technology is used to block gene expression with a catalytically inactive mutant of Cas9 (dCas9). This requires a short guide-RNA to target dCas9 to the gene of interest, where it binds and blocks transcription, thus leading to gene silencing. In general, gene silencing is not complete, and silencing efficiency is affected by several factors, such as basal gene expression. Available machine learning-based tools for prediction fail to account for gene-specific factors that could influence guide depletion during training, such as their transcriptional activity or operon structures. In contrast, the offered innovative and robust methods to produce predictive models for guide efficiency represents an important tool to increase efficacy in a cost-effective way.

Workflow of prediction of guide efficiency
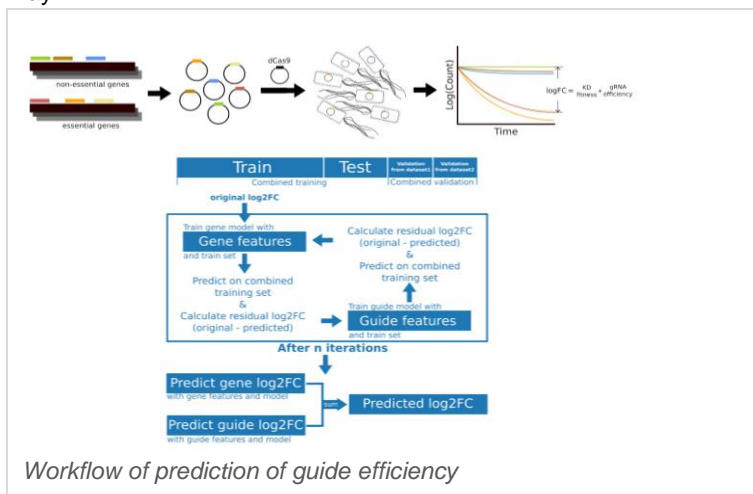
TECHNOLOGY DESCRIPTION

The invention relates to a method for prediction of the targeting efficiency of guide RNA (gRNA) for gene targeting by evaluating data obtained in genome-wide screens. , which provide levels of targeting characteristics efficiency of guides including levels of targeting efficiency confounded with gene specific effects. The method is based on a mixed-effect random forest regression model that can learn from multiple datasets and isolates effects manipulable in guide design, combined with methods from explainable AI to infer interpretable design rules.

COMMERCIAL OPPORTUNITY

Enabling technology for basic research as well as for applied biotechnology by enabling precision modification of the bacterial transcriptome. The technology is offered for licensing.

DEVELOPMENT STATUS

The workflow is provided as a software implementation that can be applied to any bacterium for which a genome wide CRISPRi screen is available. In addition, a model to predict the guide efficiency of dCas9 has been implemented in *E. coli*, including a webserver, and a command-line tool is available.

PATENT SITUATION

Priority application was filed in July 2020, the international (PCT-)application was published in 2022 (WO2022013186), national/regional applications are pending in Europe and the US.

FURTHER READING

Yu et al. 2022. bioRxiv preprint: https://doi.org/10.1101/2022.05.27.493707