

A tool for CRISPR-Cas9 gRNA evaluation based on computational models of gene expression

Shai Cohen¹†, Shaked Bergman¹†, Nicolas Lynn¹ and Tamir Tuller^{1,2,*}

¹Department of Biomedical Engineering, Tel Aviv University, Tel-Aviv, 69978, Israel

²Sagol School of Neuroscience, Tel Aviv University, Tel-Aviv, 69978, Israel

*To whom correspondence should be addressed. Tel +972 507 601260; Fax: +972 3-6405836; Email: tamirtul@post.tau.ac.il

† Equal contribution

CRISPR is often used to silence genes by inducing mutations that are expected to nullify its expression. To this end, dozens of computational tools have been developed to design gRNAs with high cutting efficacy and no off-target effect. However, these tools do not consider the induced mutation's effect on the gene's expression, which is the actual objective that should be optimized. This fact can often lead to failures in the design, as an efficient cutting of the DNA does not ensure the desired effect in protein production.

Therefore, we developed EXPosition, a computational tool for gRNA design, which for the first time is based on the true objective of using CRISPR: affecting gene expression. To this end we used predictive deep-learning-based models of the central gene expression steps: transcription, splicing and translation initiation. We validated our tool by demonstrating it can classify sites into "silencing" and "non-silencing" better than models that consider only the cutting efficiency. We believe that this tool will significantly improve the efficiency and accuracy of genome editing endeavors. EXPosition can be found at <http://www.cs.tau.ac.il/~tamirtul/EXPosition>.