EVALUATING PREDICTORS OF SpCas9 GUIDE RNA PERFORMANCE

Mark Dunne[1], Neil Humphryes-Kirilov[1], Søren Hough[1], **Riley Doyle**[1]

[1]Desktop Genetics, London, UK || Contact: **crispr@deskgen.com**

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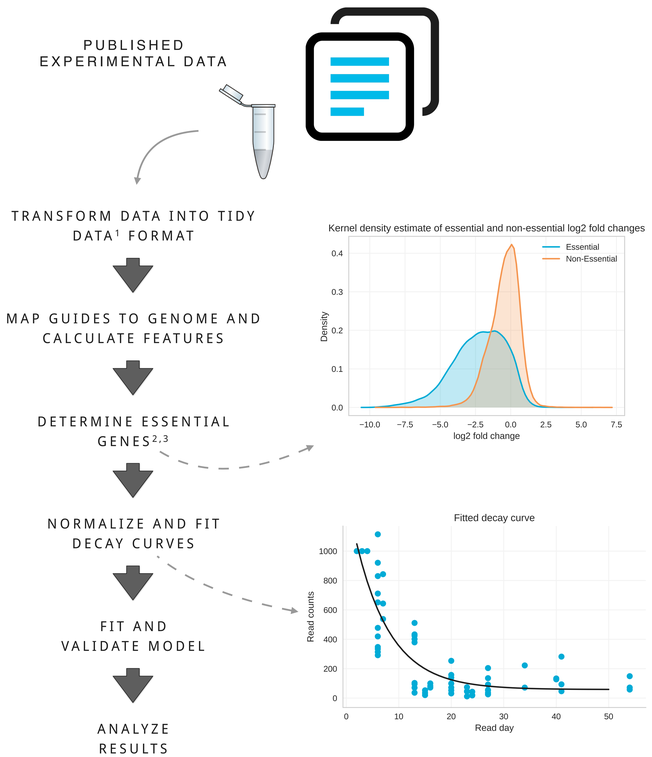
1. INTRODUCTION

- Understanding the features which dictate CRISPR guide behavior remains an outstanding problem in the field of genome editing
- We combined data from multiple sources and built a novel CRISPR guide scoring function, **Dunne 2017**
- We compared **Dunne 2017** to others using Spearman's Correlation Coefficient to test the quality of the ranking, and Coefficient of Determination to test the accuracy of the predicted log2 fold change
- With a better understanding of what factors affect the performance of a guide, we can design smaller but more effective libraries, ultimately reducing costs

2. ANALYSIS OVERVIEW

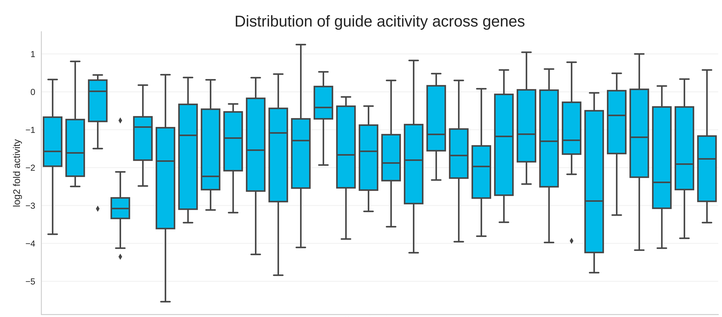


3. SEQUENCE FEATURES

- Our model found different weights for nucleotide identity and position as compared with older algorithms
- Guide performance is determined primarily by nucleotides in the seed region of the protospacer (position 15–20)
- G in the seed region is a positive predictor of guide performance
- T in the seed region is a negative predictor of guide performance

4. GENOME-WIDE TARGETING

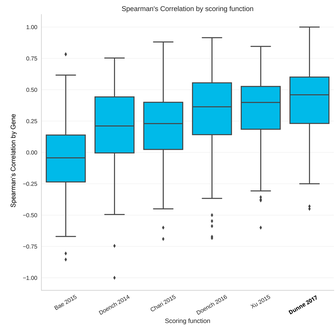
- Some genes require fewer guides to knock out, while others require more
- More guides are required when there are fewer high-quality guides to choose from
- Ranking guides within a gene is therefore insufficient; a small number of high performance guides can do the work of many low performers



5. COMPARING SCORING FUNCTIONS

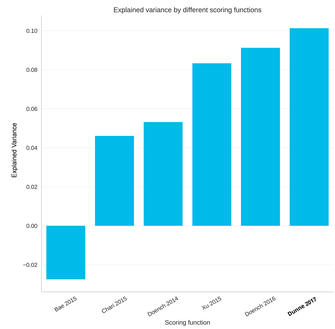
SPEARMAN'S CORRELATION COEFFICIENT

- The quality of guide ranking within genes is not the only important metric
- Spearman's measures how well the features predict guide performance based on *ranked* guide activity
- Predicting *actual* guide activity is key to designing more efficient libraries



COEFFICIENT OF DETERMINATION

- Coefficient of Determination explains how much of the variance can be explained by the model
- With better prediction of *actual* guide activity, we can reduce the minimum necessary number of guides for successful gene knockout



6. CONCLUSIONS

- By incorporating more features in our algorithm, we can build a better model (**Dunne 2017**) for predicting the behavior of guide RNAs
- Ranking guides within a gene is insufficient; a small number of high performance guides can do the work of many low performers
- It is important that scoring functions can predict the absolute activity of a guide
- **Dunne 2017** outperforms older algorithms measured both by Spearman's Correlation Coefficient and Coefficient of Determination

7. REFERENCES

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