A multi-parametric vector approach for target prioritization of CRISPR screens

Merve Mutlu [1], Isabel Schmidt [1], David Estoppey [1], Florian Nigsch [1], Dominic Hoepfner [1], Christian Parker [1]

Affiliations: [1]Novartis Institutes for BioMedical Research, Novartis Pharma AG, Forum 1 Novartis Campus, 4056 Basel, Switzerland

Efficient gene editing by CRISPR/Cas9 technology has significantly enhanced field of drug discovery. Pooled genome-wide CRISPR/Cas9 genetic screens allows the identification of drug targets and suggests their underlying mechanism of action. However, subjectivity of the selection parameters, such as cell line model, library and the method of hit calling may alter the results, even obstructing the identification of true hits. This is especially pronounced when libraries of multiple guides produce various magnitude and significance of effect for each guide for any given gene.

Thus, it is essential to exploit all available information to prioritize targets. Described here is a multi-parametric, vector-based approach designed to guide target prioritization by constructing a condensed screening score from independent CRISPR screens. This approach aims to identify frequent hitters at a given CRISPR library, detect the library or cell line biases, and eventually rank the true hits.