Accurate transcriptome-wide prediction of microRNA targets and small interfering RNA off-targets with MIRZA-G

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Small interfering RNA (siRNA)-mediated knock-down is a widely used experimental approach to characterizing gene function. Although siRNAs are designed to guide the cleavage of perfectly complementary mRNA targets, acting similarly to microRNAs (miRNAs), siRNAs down-regulate the expression of hundreds of genes to which they have only partial complementarity. Prediction of these siRNA 'off-targets' remains difficult, due to the incomplete understanding of siRNA/miRNA-target interactions. Combining a biophysical model of miRNA-target interaction with structure and sequence features of putative target sites we developed a suite of algorithms, MIRZA-G, for the prediction of miRNA targets and siRNA off-targets on a genome-wide scale. The MIRZA-G variant that uses evolutionary conservation performs better than currently available methods in predicting canonical miRNA target sites and in addition, it predicts non-canonical miRNA target sites with similarly high accuracy. Furthermore, MIRZA-G variants predict siRNA off-target sites with an accuracy unmatched by currently available programs. Thus, MIRZA-G may prove instrumental in the analysis of data resulting from large-scale siRNA screens.
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