An Improvement of ComiR Algorithm for MicroRNA Target Prediction by Exploiting Coding Region Sequences of mRNAs

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Abstract : MicroRNAs are small non-coding RNAs that post-transcriptionally regulate the expression levels of messenger RNAs. MicroRNA regulation activity depends on the recognition of binding sites located on mRNA molecules. ComiR (Combinatorial miRNA targeting) is a user friendly web tool realized to predict the targets of a set of microRNAs, starting from their expression profile. ComiR incorporates miRNA expression in a thermodynamic binding model, and it associates each gene with the probability of being a target of a set of miRNAs. ComiR algorithms were trained with the information regarding binding sites in the 3'UTR region, by using a reliable dataset containing the targets of endogenously expressed microRNA in D. melanogaster S2 cells. This dataset was obtained by comparing the results from two different experimental approaches, i.e., inhibition, and immunoprecipitation of the AGO1 protein; this protein is a component of the microRNA induced silencing complex. In this work, we tested whether including coding region binding sites in the ComiR algorithm improves the performance of the tool in predicting microRNA targets. We focused the analysis on the D. melanogaster species and updated the ComiR underlying database with the currently available releases of mRNA and microRNA sequences. As a result, we find that the ComiR algorithm trained with the information related to the coding regions is more efficient in predicting the microRNA targets, with respect to the algorithm trained with 3'utr information. On the other hand, we show that 3'utr based predictions can be seen as complementary to the coding region based predictions, which suggests that both predictions, from 3'UTR and coding regions, should be considered in a comprehensive analysis. Furthermore, we observed that the lists of targets obtained by analyzing data from one experimental approach only, that is, inhibition or immunoprecipitation of AGO1, are not reliable enough to test the performance of our microRNA target prediction algorithm. Further analysis will be conducted to investigate the effectiveness of the tool with data from other species, provided that validated datasets, as obtained from the comparison of RISC proteins inhibition and immunoprecipitation experiments, will be available for the same samples. Finally, we propose to upgrade the existing ComiR web-tool by including the coding region based trained model, available together with the 3'UTR based one.

Keywords : AGO1, coding region, Drosophila melanogaster, microRNA target prediction