miRabel: A web tool for an effective prediction of microRNA targets and their related biological pathways.

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1. Biological background

- miRNAs (miRs) are small (21-23 nt) non-coding RNAs.
- They regulate gene expression by binding to target miRNAs in the 3'UTR region.
- They act by either degradation of the mRNA or inhibition of its translation.

2. miR :: mRNA interactions network

- miRNAs can interact with hundreds of target mRNAs and one miRNA can be targeted by several miRNAs.
- Through this mechanism, miRNAs can potentially modulate every cellular processes.

3. miR :: mRNA interactions predictions

- Simple Watson-Crick pairing is not sufficient to recognize miRNA target sites.
- Indeed, when studying a miR :: mRNA interaction, several characteristics are to be considered:
  - Seed complementarity
  - Free energy
  - Site accessibility
  - Site conservation
- Several algorithms such as miRanda, PITA and SVMicro, take some or all of the above characteristics into consideration to predict these interactions.
- However, these algorithms have limited success with a low accuracy and high discrepancy.

How to improve miRNAs' targets predictions and to define their potential biological pathways context?

1. Our method: aggregating prediction ranks and integrating biological pathways

2. Interface and content of miRabel

A. Example of miRabel’s user interface and result table after a search for miR’s potential targets.

B. miRabel’s content

- 275 biological pathways
- 267 human miRs
- 15 million predicted interactions

- miRabel is a new efficient tool for miR’s mRNA targets prediction and their associated biological functions.
- miRabel aggregates the predictions of 7 major algorithms (miRanda, PITA and SVMicro)
- The mRNA targets predicted by miRabel are linked to metabolic and cellular pathways retrieved from KEGG.
- miRabel shows better performances than miRanda, PITA and is comparable to SVMicro.
- miRabel has a higher number of experimentally validated targets in its top ranking predictions when compared to ComiR and miRmap.

3. Performance of miRabel

- How many experimentally validated targets are ranked within the top predictions?

A. Receiver Operating Characteristic (ROC) analysis of miRabel vs miRanda, PITA and SVMicro: Computing 42 miRs with at least 10 validated interactions predicted (Wilcoxon statistical test).

- miRabel’s predicted target miRNAs

- Experimentally validated target miRNAs

B. miRabel vs others miRNA’s targets prediction software (ComiR, miRmap): example of hsa-mir-155-5p (170 targets validated by luciferase assay).

Conclusion

- miRabel performs better than miRanda and PITA and equally well to SVMicro.
- miRabel has a higher number of experimentally validated targets in its top ranking predictions when compared to ComiR and miRmap.