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Ref: Manuscript entitled: “**Meta-Analysis of RNA Binding Protein Interaction profiles using the RBPInper tool**”

**Dear Prof. Alfonso Valencia**

Please find our manuscript entitled “**Meta-Analysis of RNA Binding Protein Interaction profiles using the RBPInper tool**” for your consideration of publication in Bioinformatics as an Application Note.

RNA-binding proteins (RBPs) ubiquitously regulate the fate and function of transcripts across all cellular processes, and their dysregulations are emerging as key players in major chronic diseases. Characterizing RBP regulatory networks in different cellular contexts is of great interest to many research groups, such as ours. However, experimentally performing this task for every single context and RBP is prohibitively expensive. Mining existing RBP-RNA interaction datasets has become a popular approach to remedy this issue. However, the analytical process poses challenges, including limited transferability of sample-specific interactions to unseen contexts and a lack of specific computational tools that account for the unique features of RBP-RNA interactions. Interpreting multiple gene lists has been addressed by various algorithms and web-based methods. However, these approaches primarily focus on visualization rather than empirical data integration suitable for the above RBP interaction analysis. These issues hinder the complete and accurate characterisation of RBP interactions. Thus, we developed RBPInper to generate robust global RBP interactomes. It would invariably enhance the mining of existing omics datasets for cost-effective generation of new biological insights and hypotheses for RBP functions and roles in diseases.

RBPInper generates global RBP interactomes by using a twostep meta-analysis to combine statistical evidence from multiple omics datasets. Use case analysis demonstrates the utility of RBPInper in generating global RBP interactomes that transfer to unseen cellular contexts. We demonstrate that RBPInper outperforms using single interaction profiles. The RBPInper software offers the cell and molecular biologist a simple tool with minimal dependencies and

straightforward input requirements to incorporate into their research. Researchers can use the 'rbpinper.run()' function to process and retrieve RBP interactomes. We also provide the 'prebed()' function to allow researchers to easily prepare bed files for the RBPInper input format.

Combined, we feel that RBPInper can:

1. Expedite the discovery of RBP functions in health and disease.
2. Enhance the integration of multiple RBP-RNA interaction profiles.
3. Be of interest to your readership and biologists across a wide range of fields.

I can confirm that the material is original research, has not been previously published, and has not been submitted for publication elsewhere. The authors declare no competing interests.

Yours sincerely

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