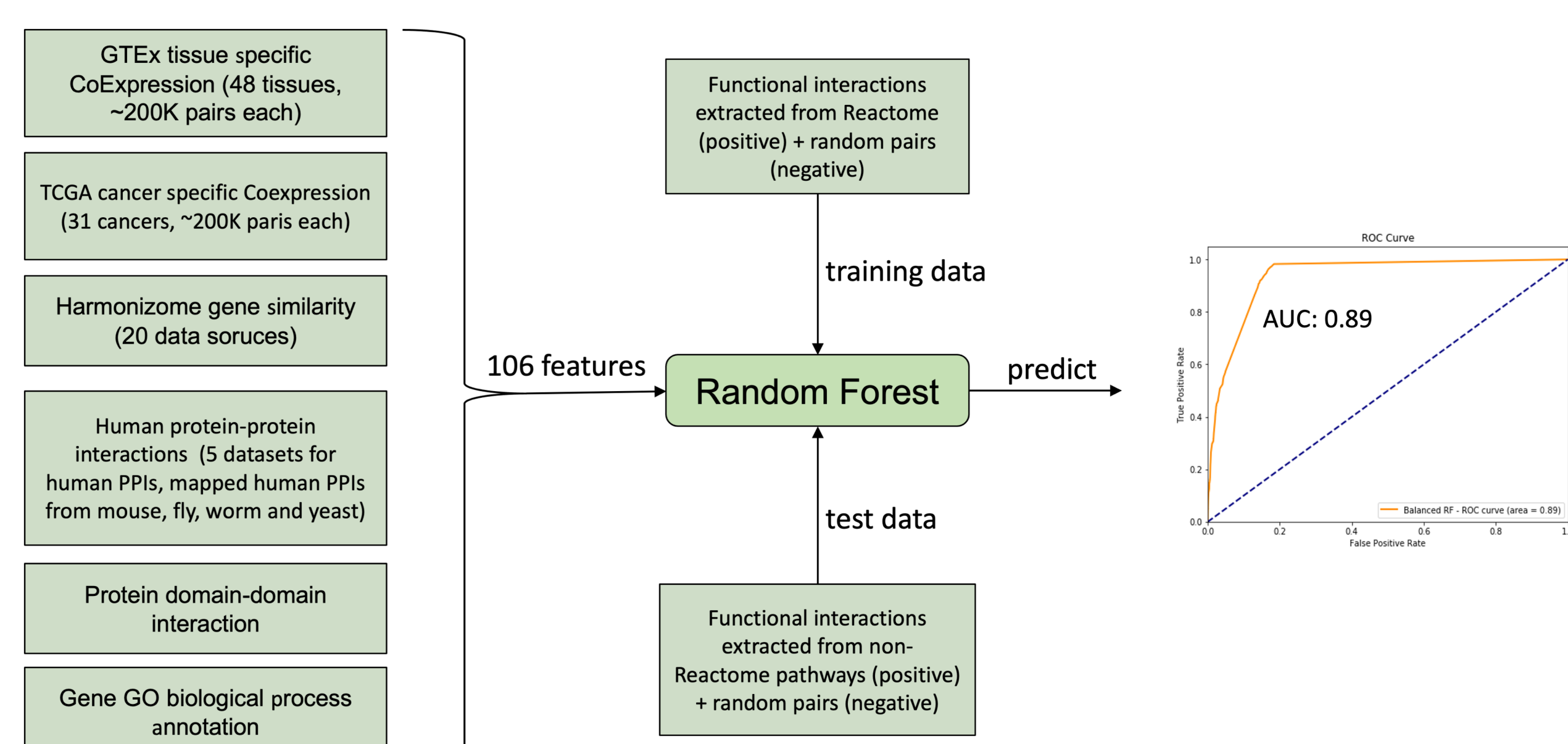
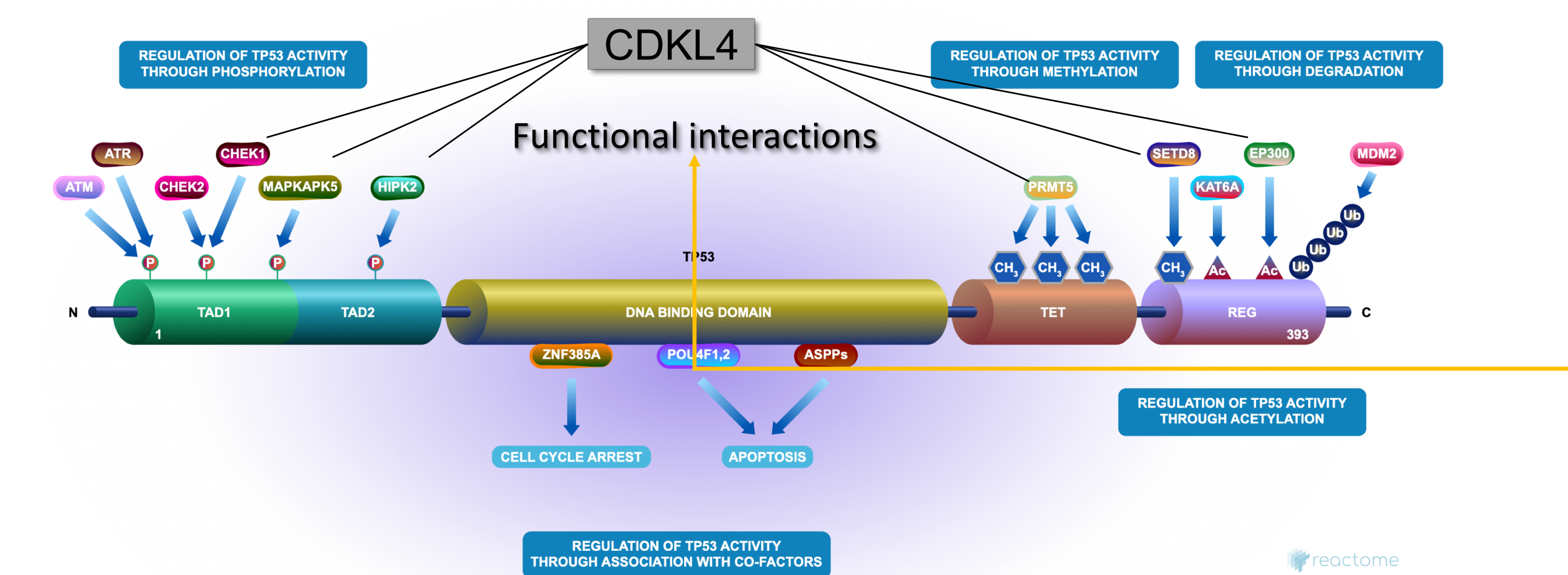


Lisa Matthews¹, Guanming Wu², Robin Haw³, Timothy Brunson², Nasim Sanati², Solomon Shorser³, Deidre Beavers², Patrick Conley², Lincoln Stein³, Peter D'Eustachio¹

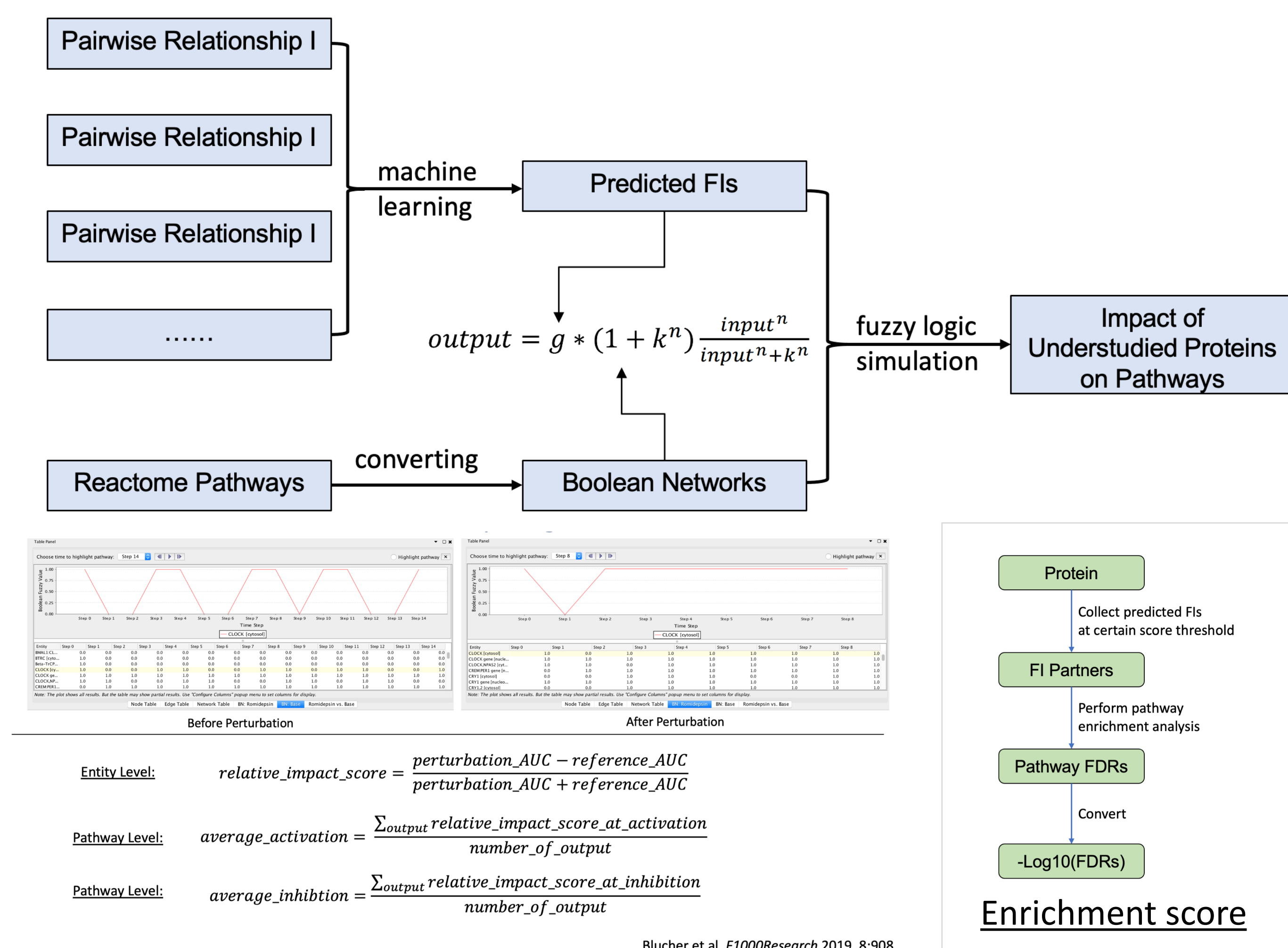
¹NYU School of Medicine, New York, NY 10016, USA, ²Oregon Health & Science University, Portland, OR 97239, USA, ³Ontario Institute for Cancer Research, Toronto, ON M5G0A3, Canada,

Define Interacting Pathways for Dark Proteins



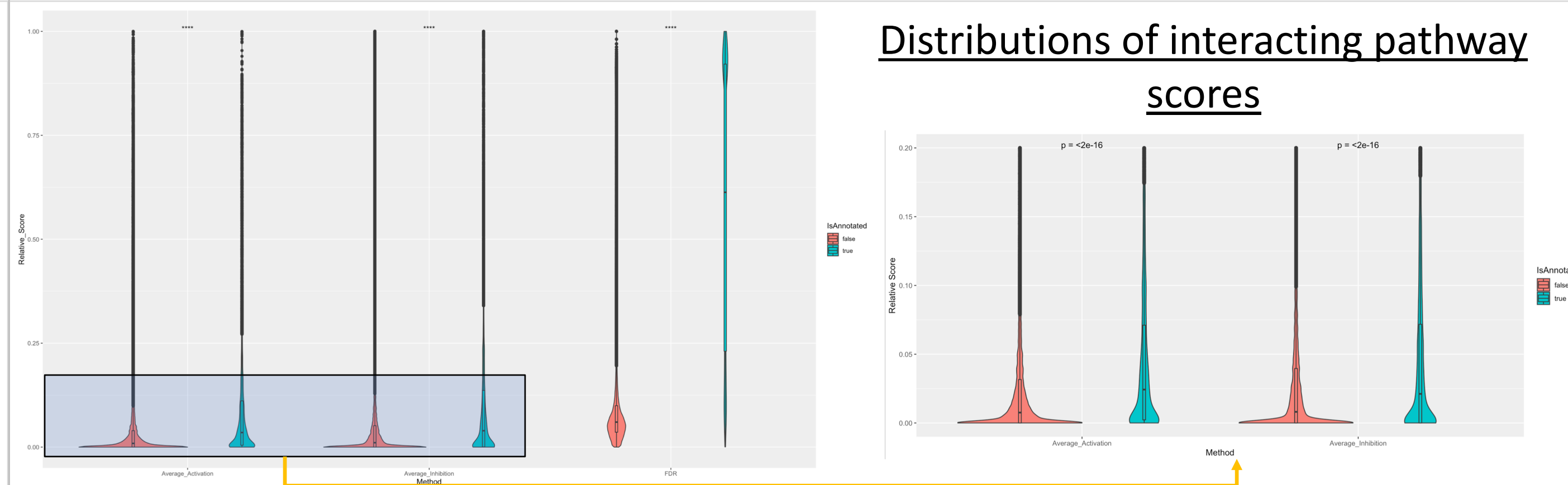
- **Interacting pathways:** Reactome pathways annotated with proteins that may functionally interact with dark proteins.
- **Functional interactions (FIs):** Predicted by a trained random forest using 106 pairwise protein/gene features.

Measure Interacting Pathways

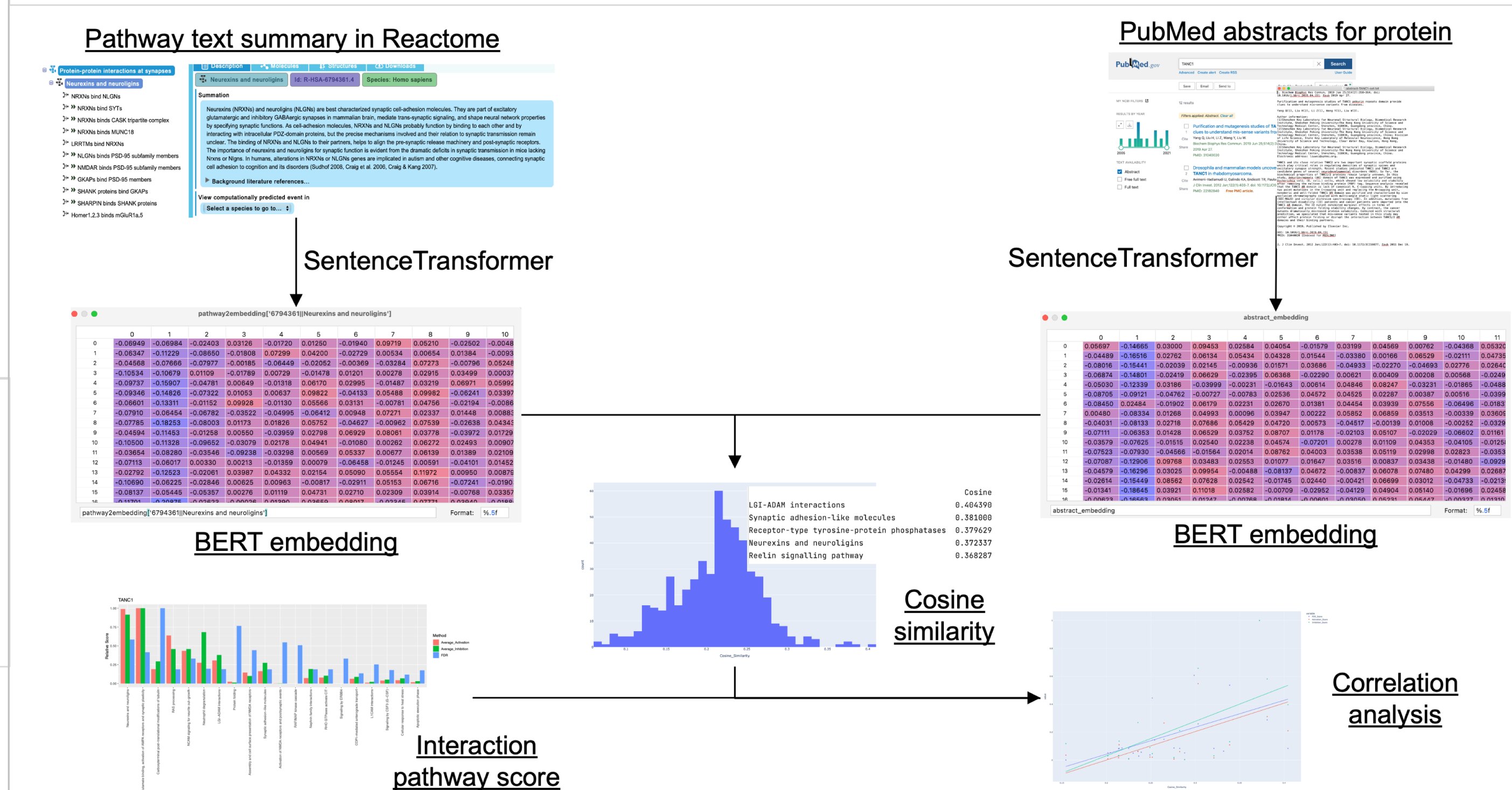


- **Simulation scores** (left): Average relative_impact_scores calculated via fuzzy logic simulation using Boolean networks converted from Reactome pathways.
- **Enrichment score** (right): Results from pathway enrichment analysis for functionally interacting partners. FIs with score > 0.80 were collected for this analysis.

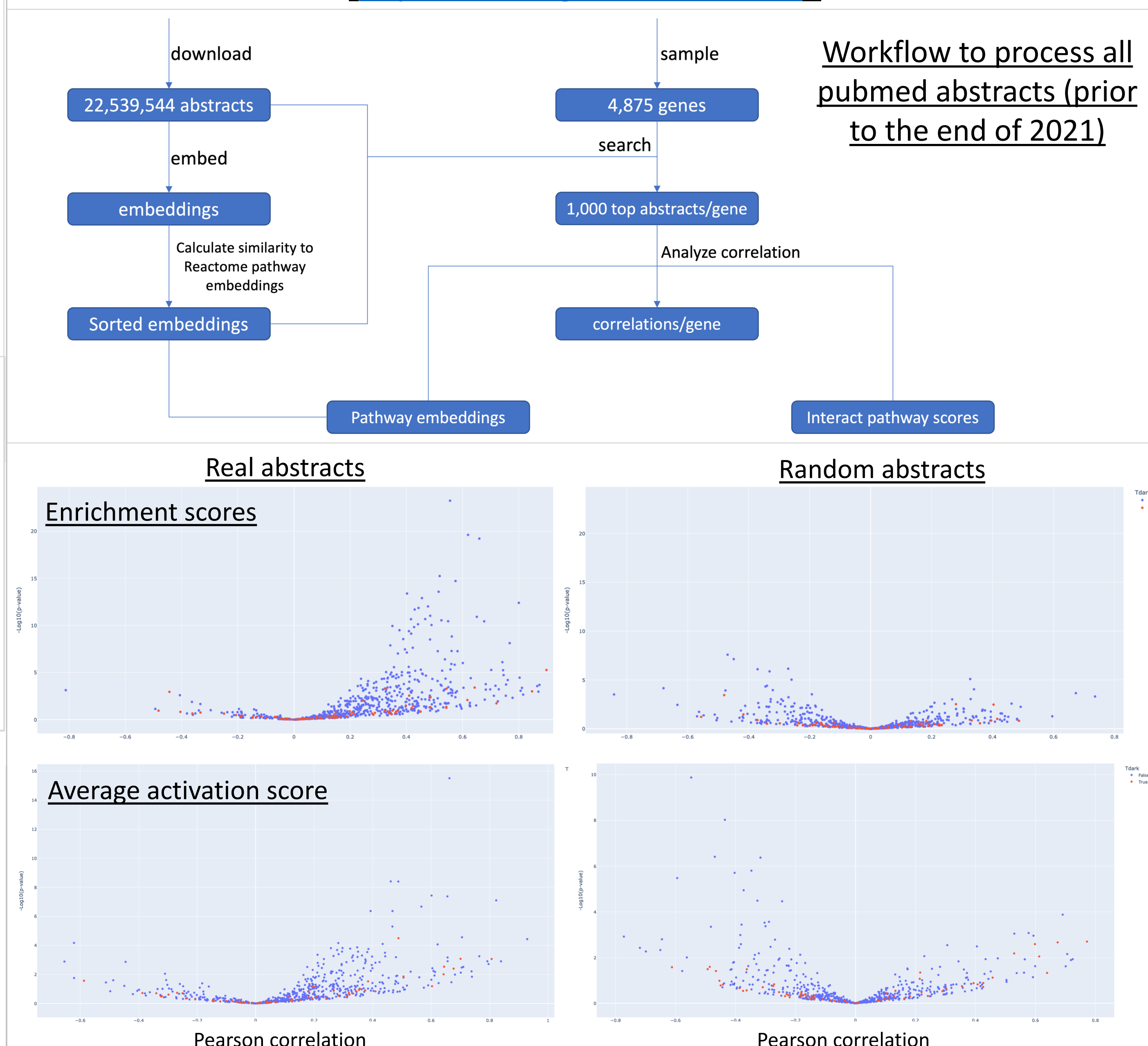
Literature Validation of Interacting Pathways



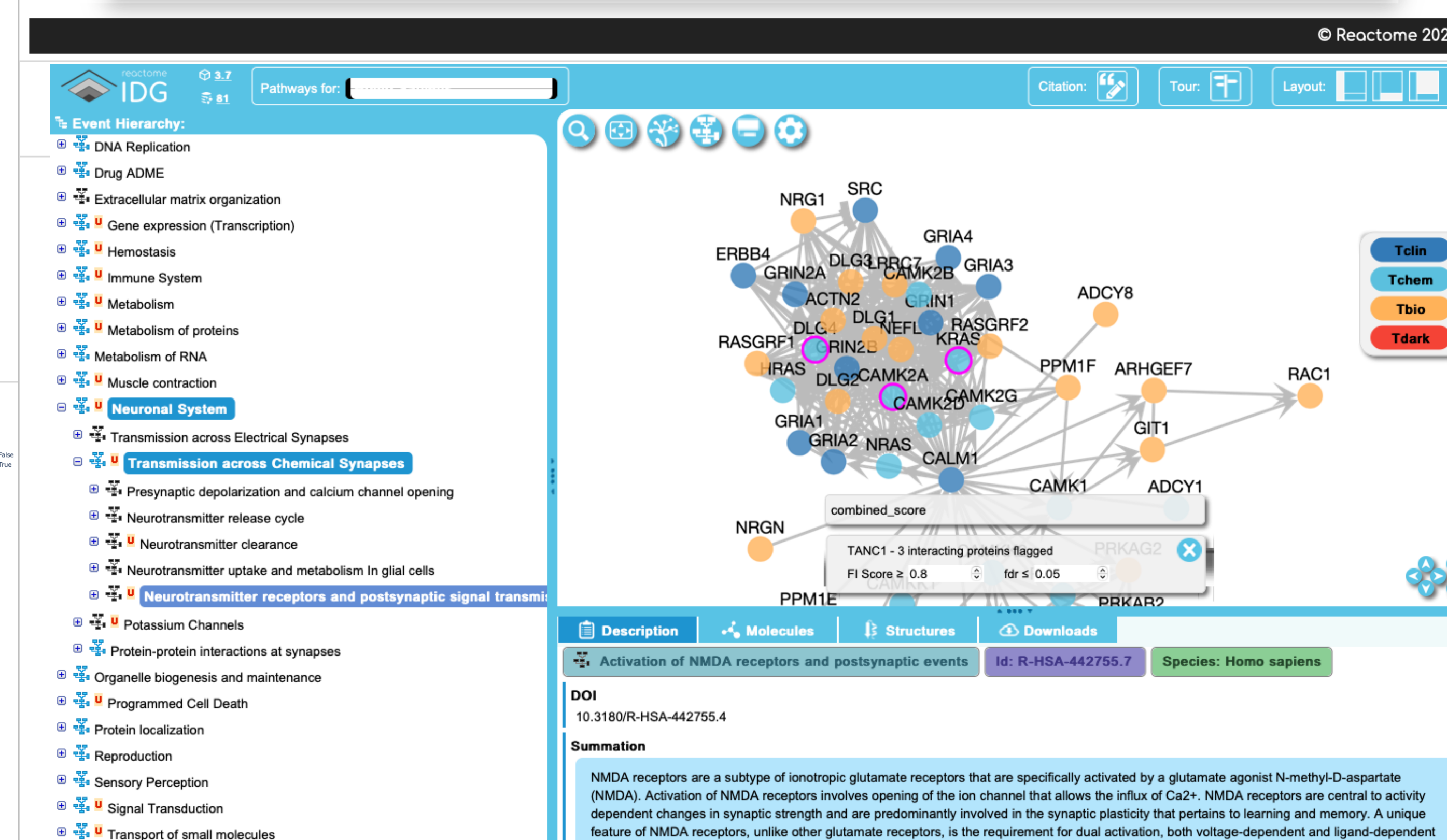
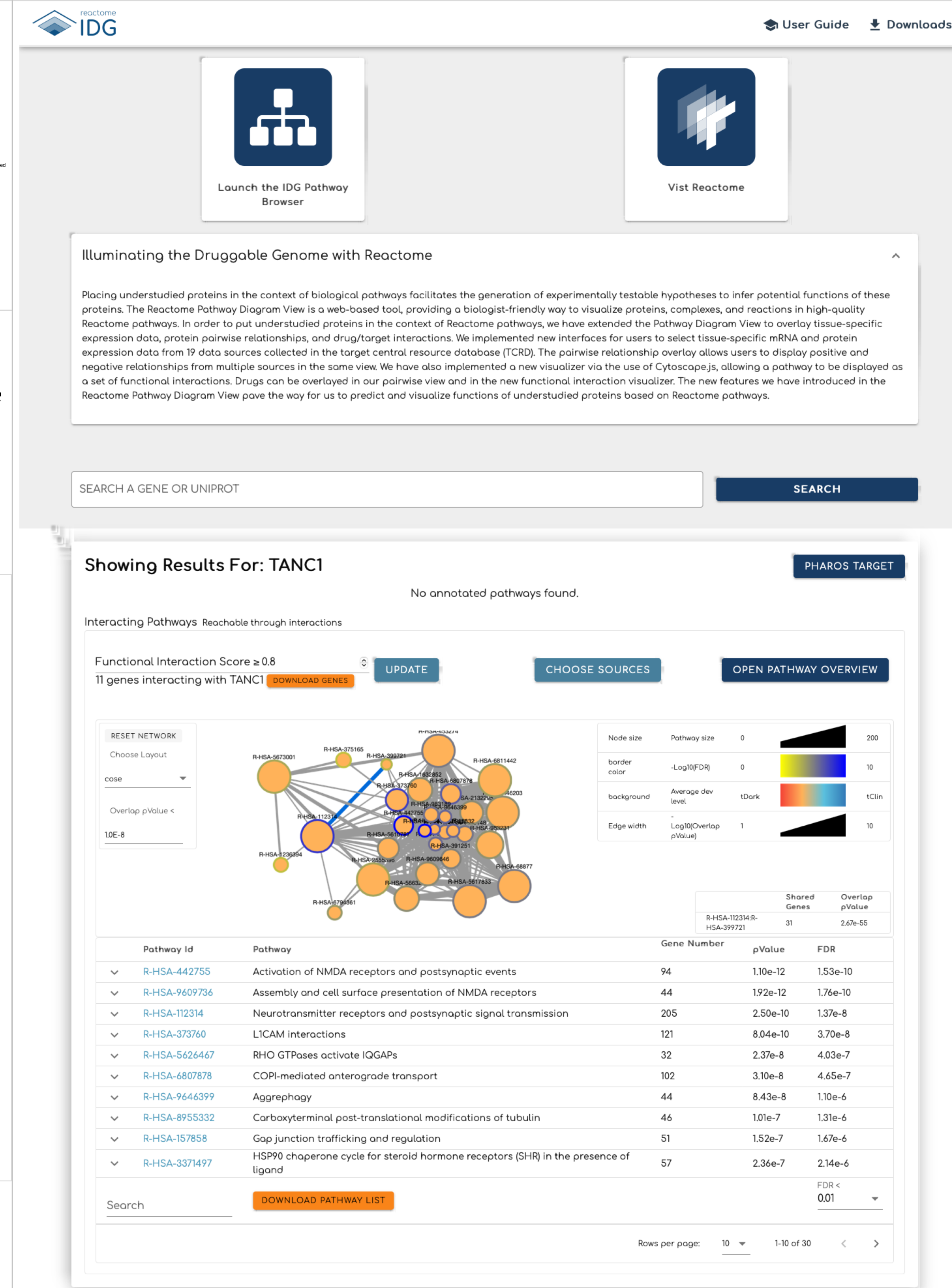
- **524 Reactome pathways** having reactions drawn out in their diagrams were subject to the systematic analysis.
- **Two simulations** were run for each pathway and each dark protein: One assuming the dark protein has an activation role (**average_activation_score**) and another an inhibition role (**average_inhibition_score**).
- Reactome annotated proteins have **significantly higher** interacting pathway scores, **recapitulating** the functional relationships between proteins and pathways in Reactome and **supporting** interacting pathways for dark proteins.



Literature correlation analysis via NLP using SentenceTransformer
(<https://www.sbert.net>) for text embedding based on BERT
(<https://arxiv.org/abs/1810.04805>).



Reactome IDG Portal: <https://idg.reactome.org>



Summary

- **Interacting pathways for dark proteins:** developed on the top of Reactome and supported by comprehensive NLP analysis.
- <https://idg.reactome.org>: Reactome's web portal for NIH IDG

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