

Open Community Challenge Reveals Molecular Network Modules With Key Roles in Diseases

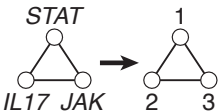
Sarvenaz Choobdar, Mehmet E. Ahsen, Jake Crawford, Mattia Tomasoni, David Lamparter, Junyuan Lin, Benjamin Hescott, Xiaozhe Hu, Johnathan Mercer, Ted Natoli, Rajiv Narayan, The DREAM Module Identification Challenge Consortium, Aravind Subramanian, Gustavo Stolovitzky, Zoltán Kutalik, Kasper Lage, Donna K. Slonim, Julio Saez-Rodriguez, Lenore J. Cowen, Sven Bergmann, and Daniel Marbach

The Networks

The community contributed a collection of diverse human molecular networks for the challenge:

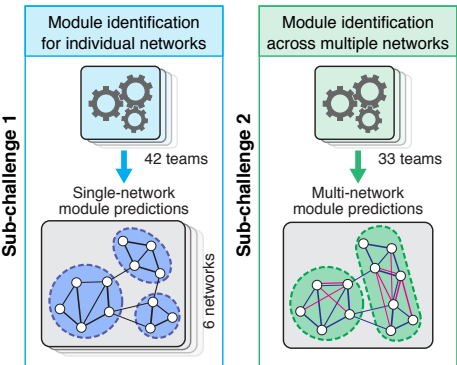
| | Network type | #Genes | #Edges |
|---|---------------------|--------|-----------|
| 1 | Protein interaction | 17,397 | 2,232,405 |
| 2 | Protein interaction | 12,420 | 397,309 |
| 3 | Signaling | 5,254 | 21,826 |
| 4 | Co-expression | 12,588 | 1,000,000 |
| 5 | Cancer dependency | 14,679 | 1,000,000 |
| 6 | Homology | 10,405 | 4,223,606 |

They were anonymized, mapping each gene to a unique ID:



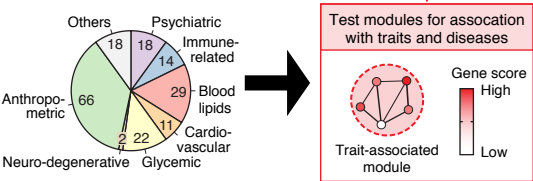
Challenges

Teams were given two separate “subchallenges”:



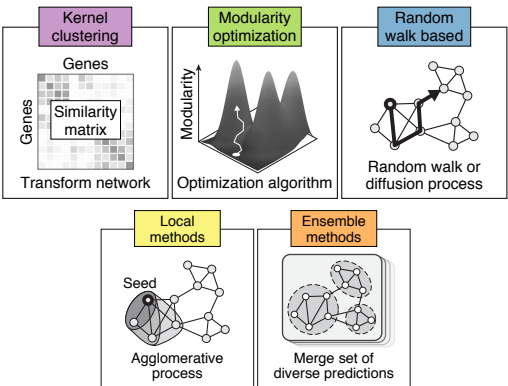
Evaluation

We evaluated module predictions for trait associations using a compendium of 180 GWAS datasets.¹



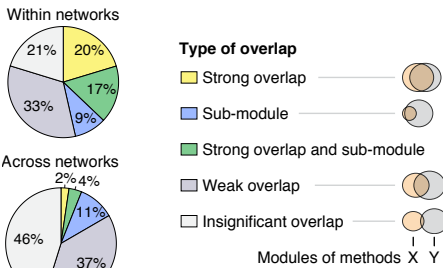
Results

Competing teams submitted 42 single-network methods (SC1) and 33 multi-network methods (SC2), including methods from many different categories.

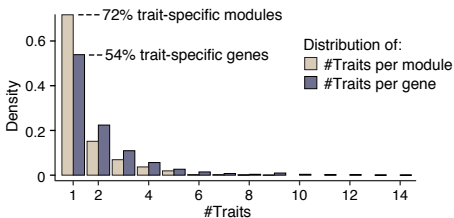


Trait-associated modules were largely dissimilar between methods, even within the same network.

Overlap of trait-associated modules between methods

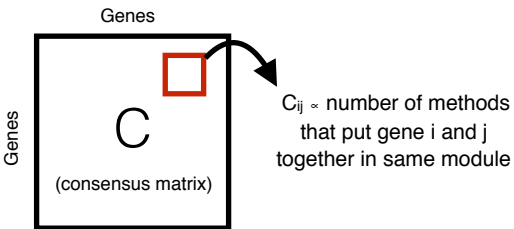


Most trait-associated modules and genes were only enriched for a small number of traits.

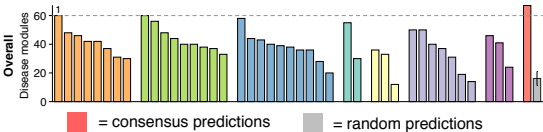


Consensus Predictions

We compared individual submissions with predictions based on a “consensus matrix”, constructed for each network by aggregating predictions from multiple teams.

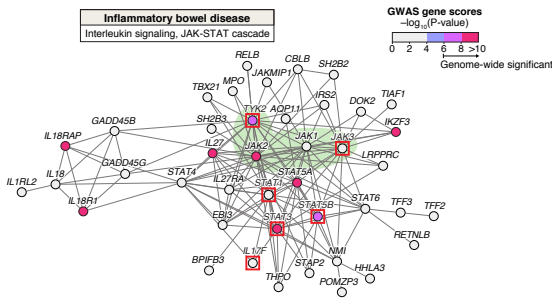


Using the top 50% of submissions and clustering C with the top-performing method, this outperformed all individual submissions (overall results for SC1 shown):



Interesting Modules

Many trait-associated modules comprise biologically significant pathways. Example from consensus method predictions:



JAK-STAT inhibitors are currently in clinical trials for Crohn's/UC. (Green shading above represents a therapeutic target pathway)

¹ Lamparter, D., Marbach, D., Rueedi, R., Kutalik, Z., & Bergmann, S. Fast and rigorous computation of gene and pathway scores from SNP-based summary statistics. PLoS computational biology 12(1) (2016).