The Networks

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

<table>
<thead>
<tr>
<th>Network type</th>
<th>#Genes</th>
<th>#Edges</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Protein interaction</td>
<td>17,397</td>
<td>2,232,405</td>
</tr>
<tr>
<td>2 Protein interaction</td>
<td>12,420</td>
<td>397,309</td>
</tr>
<tr>
<td>3 Signaling</td>
<td>5,254</td>
<td>21,826</td>
</tr>
<tr>
<td>4 Co-expression</td>
<td>12,588</td>
<td>1,000,000</td>
</tr>
<tr>
<td>5 Cancer dependency</td>
<td>14,679</td>
<td>1,000,000</td>
</tr>
<tr>
<td>6 Homology</td>
<td>10,405</td>
<td>4,223,606</td>
</tr>
</tbody>
</table>

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

STAT

IL17

JAK

33 teams

Single-network module predictions

Multi-network module predictions

Sub-challenge 1

Sub-challenge 2

Module identification for individual networks

Module identification across multiple networks

Evaluation

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

Challenges

Teams were given two separate “subchallenges”:

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

KNN clustering

Modularity optimization

Random walk based

Genes

Similarity matrix

Optimization algorithm

Random walk or diffusion process

Local methods

Agglomerative process

Ensemble methods

Merge set of diverse predictions

Overlap of trait-associated modules between methods

Within networks

Type of overlap

Strong overlap

Sub-module

Overlapping and sub-module

Weak overlap

Insignificant overlap

Modules of methods X Y

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

Results

Consensus Predictions

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

C_i - number of methods that put gene i and j together in same module

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)

Poster PDF and link to preprint at jjc2718.github.io