


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

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**Disease Module Identification
DREAM Challenge**

Discover disease pathways in genomic networks

DREAM CHALLENGES
powered by Sage Bionetworks

Unil
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SIB
Swiss Institute of Bioinformatics

Joint Research Center for Computational Biomedicine

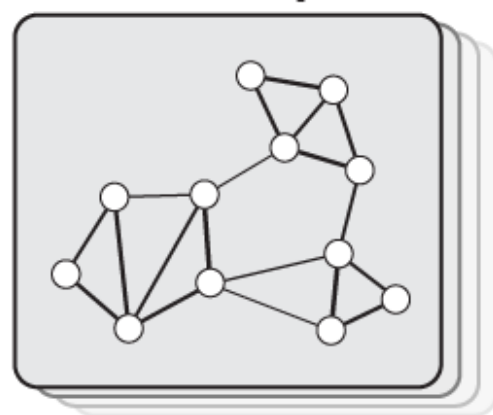
RWTH AACHEN UNIVERSITY

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Sage BIONETWORKS

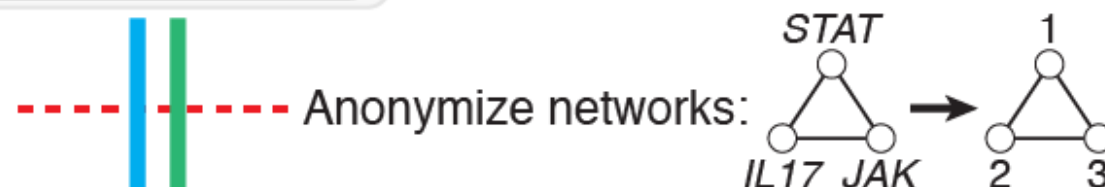
Cell

A Network compendium



6 networks

	Network type	#Genes	#Edges	Degree distribution
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	



B Challenge

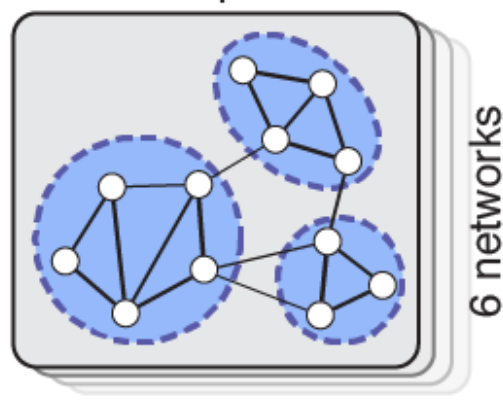
Sub-challenge 1

Module identification for individual networks



42 teams

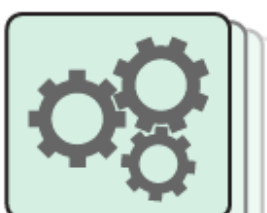
Single-network module predictions



6 networks

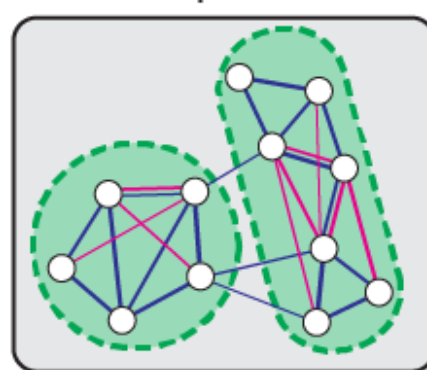
Sub-challenge 2

Module identification across multiple networks

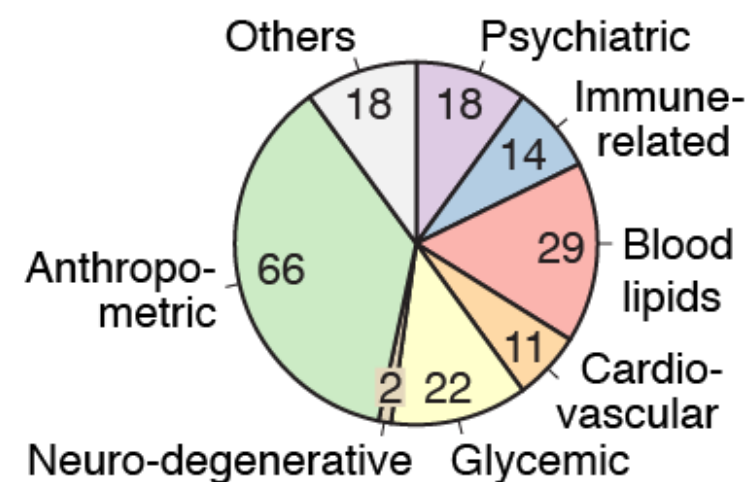


33 teams

Multi-network module predictions

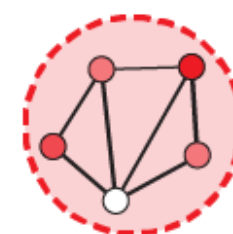


C GWAS compendium

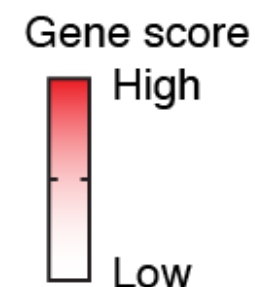


Scoring

Test modules for association with traits and diseases

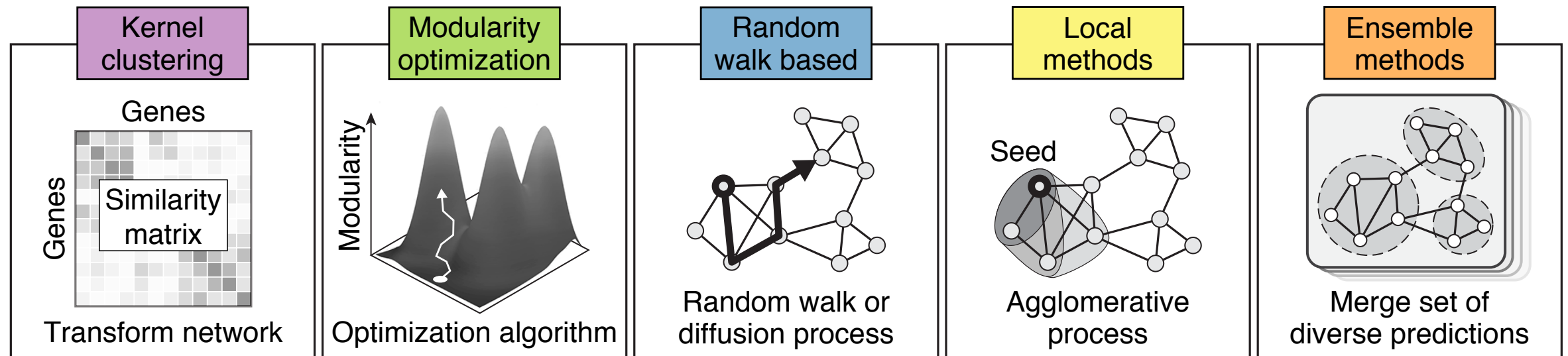


Trait-associated module



Results

- 42 teams submitted single-network methods
- Diversity of methods

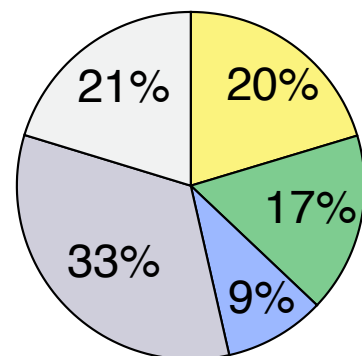


Results

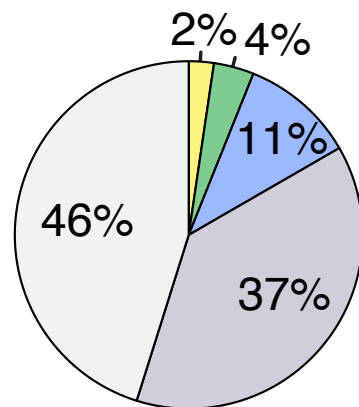
- Methods often find unique trait-associated modules

Overlap of trait-associated modules between methods

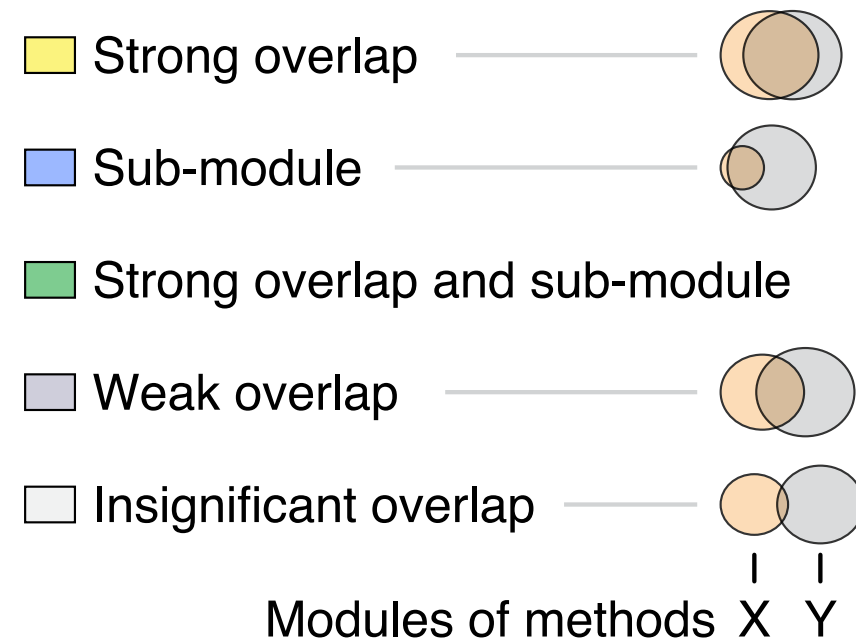
Within networks



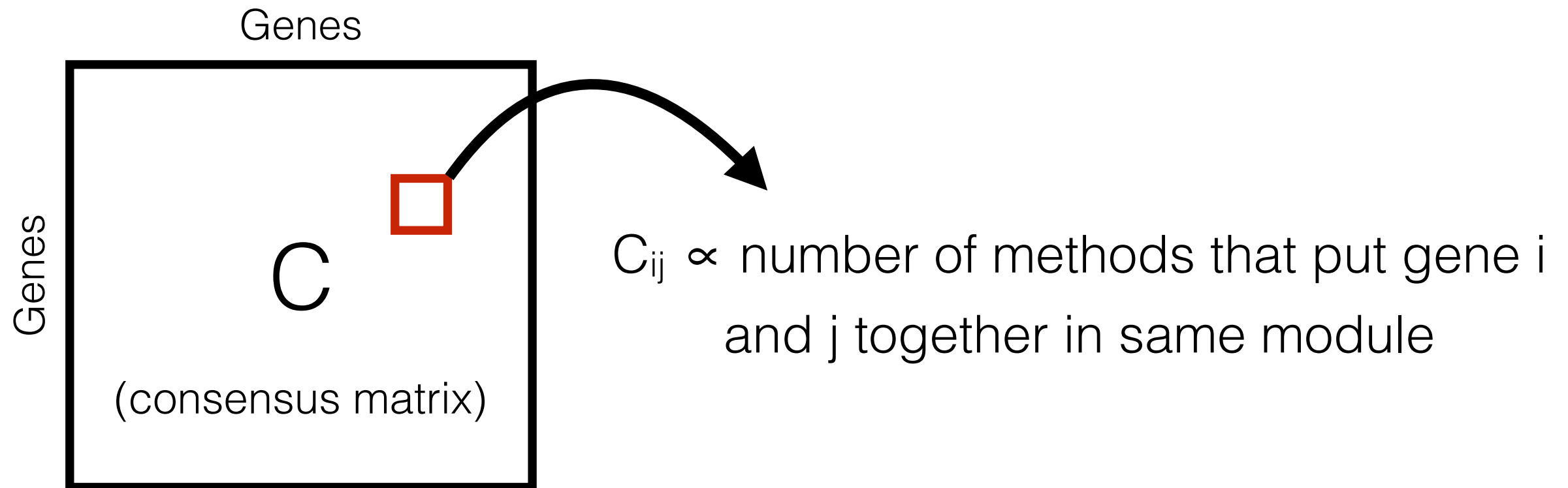
Across networks



Type of overlap



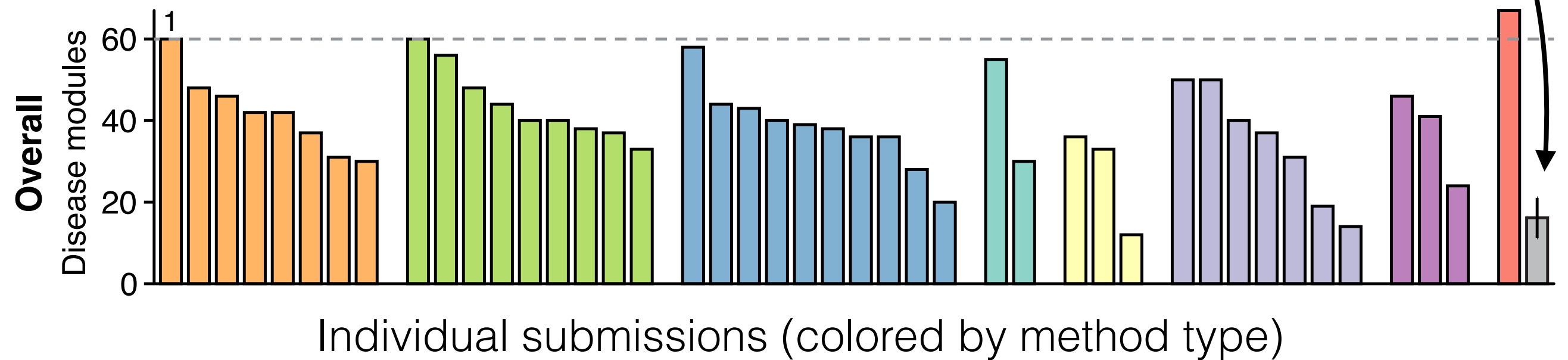
Consensus predictions



Then, clustered using top-performing method.

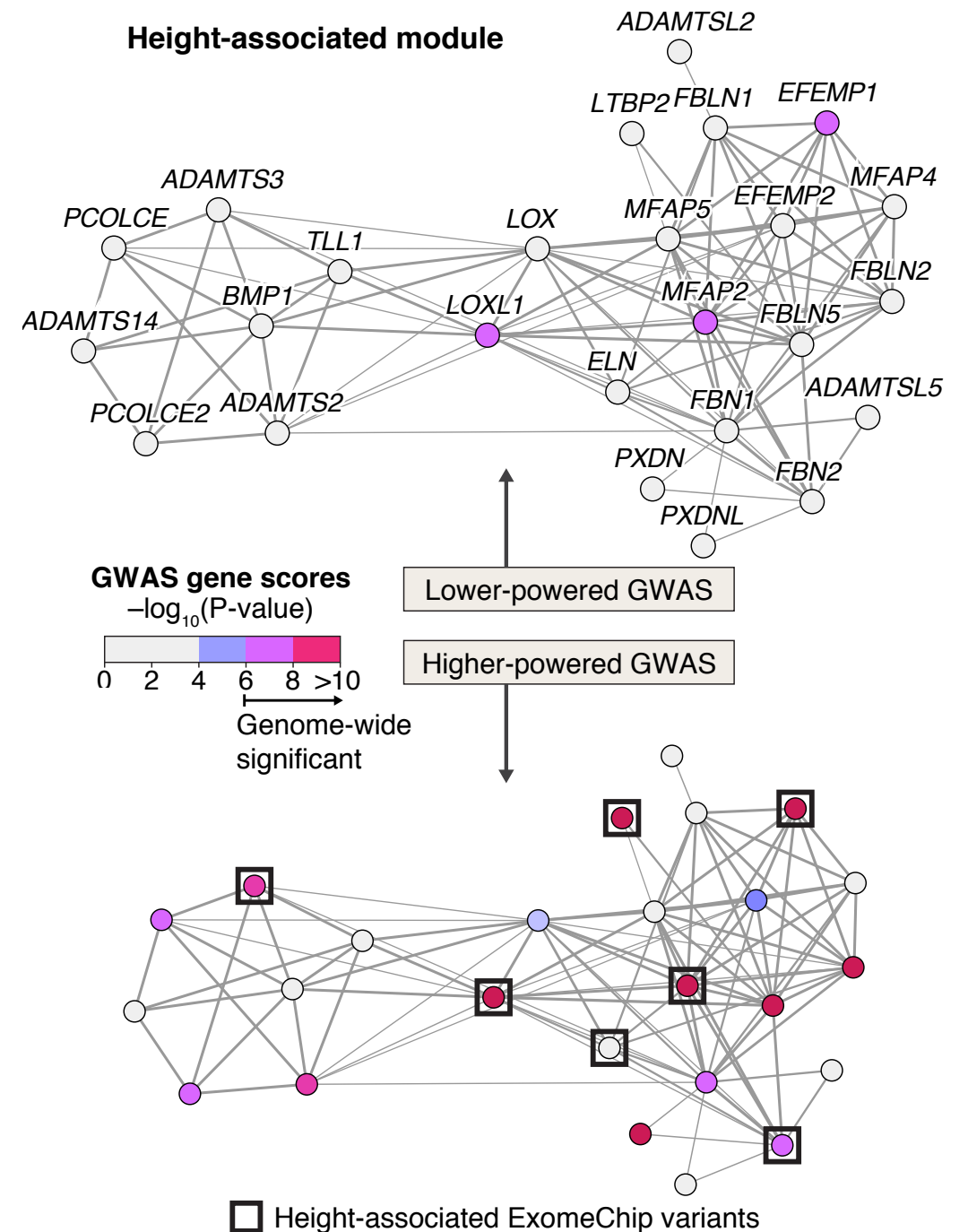
Random predictions

Consensus predictions
(using top 50% of methods)



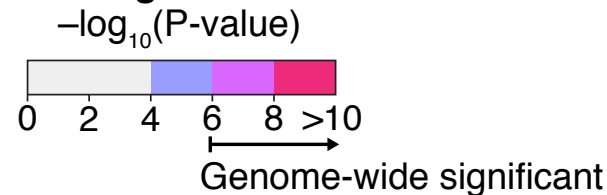
Validating modules

A height-associated module predicted by a lower-powered GWAS is confirmed by a higher-powered GWAS



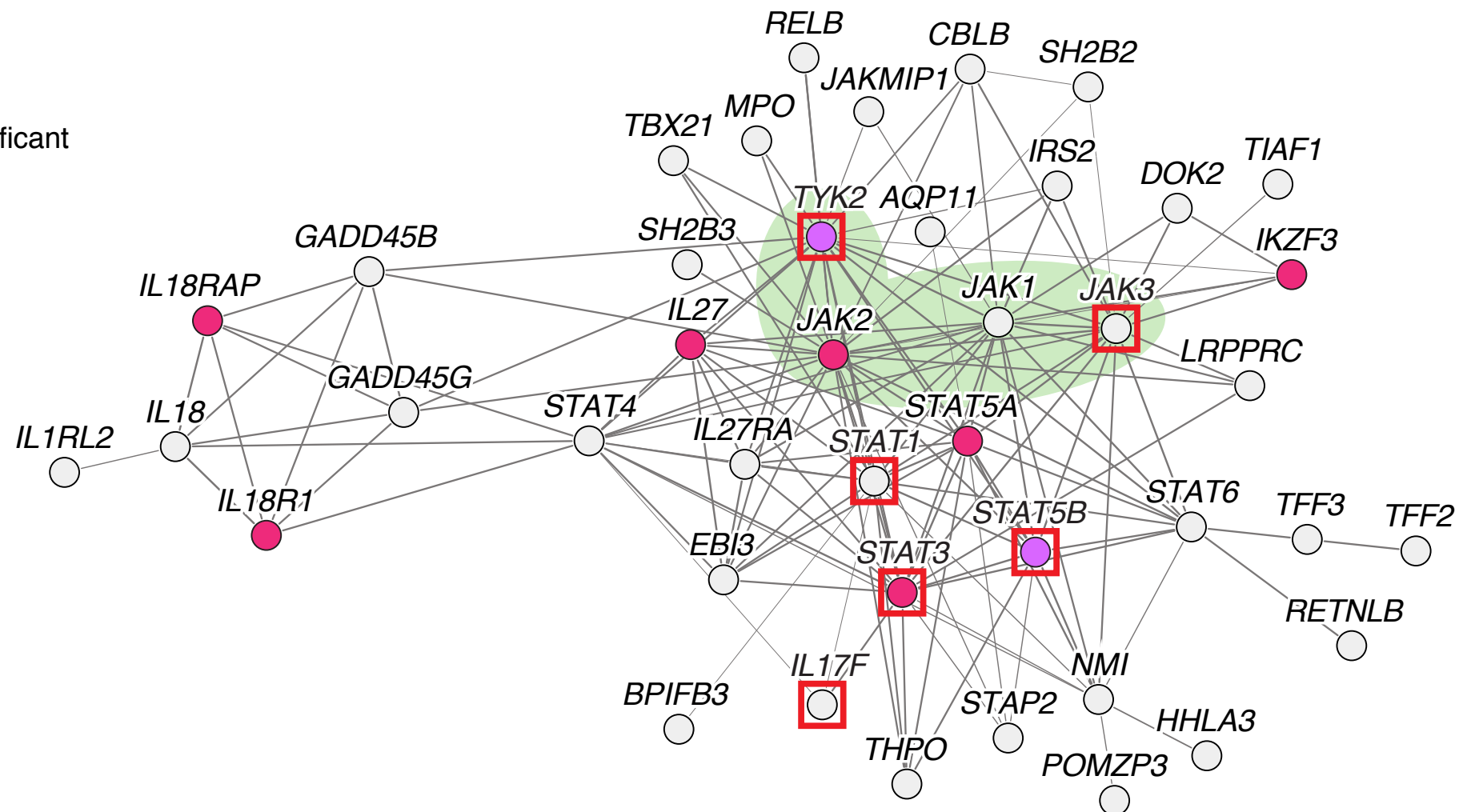
Example interesting module

GWAS gene scores



Inflammatory bowel disease

Interleukin signaling, JAK-STAT cascade



- JAK-STAT inhibitors are in clinical trials for Crohn's/UC

Link to preprint at jjc2718.github.io; poster A-200

Most code/data is available at <https://synapse.org/modulechallenge>, more to come

Thanks to all my collaborators!

Sarvenaz Choobdar (UNIL)

Eren Ahsen (Mt. Sinai)

Daniel Marbach (UNIL, Roche)



Sven Bergmann



Gustavo Stolovitzky



David Lamparter

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Mattia Tomasoni

Kasper Lage

Johnathan Mercer

Ted Natoli

Rajiv Narayan

Aravind Subramanian

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Xiaozhe Hu
Joanne Lin
Lenore Cowen



Network providers and challenge participants

