CollaborativeNet (originally called TF-Cluster): How to identify collaborative regulatory genes that govern a biological process or a complex trait?

NETWORK CONSTRUCTION

Gene	т1	Т2	тз	т4	Т5	т6	Т7	т8	Т9	T10
G1	123	790	2300	1597	655	530	321	229	234	354
G2	400	750	790	996	213	350	1504	340	250	1780
G3	250	250	380	150	470	559	9 890	1250	99	450
G n-1	550	225	388	650	470	559	899	250	590	460
Gn	150	260	950	750	470	585	865	125	99	450

Expression data



SCCM--Shared Coexpression Connectivity Matrix

NETWORK DECOMPOSITION







Collaborative Network



Each subnetwork contains TFs that control a complex trait or a biological process

A sample **Collaborative Subnetwork** identified by **CollaborativeNET**

Cluster 2: A cluster of TFs control root cap development (stem cells of roots)							
AT1G33280	BRN1	BRN1, SMB control root cap maturation	[66]				
AT4G10350	BRN2	BRN2, SMB control root cap maturation	[66]				
AT1G79580	SMB	FEZ and SMB control root stem cells	[67]				
AT5G39820	ANAC094	Apical meristem protein, function unknown	[59]				
AT1G26870	FEZ	FEZ and SMB control root stem cells in cap	[67]				
AT1G74500	TOM7	Embryonic root initiation	[68]				
AT3G27010	TCP20	Postembryonic cell division in root	[70]				
AT2G30340	LBD13	Expressed in cells at the adaxial base of lateral roots	[104]				
AT2G40470	LBD15	Expressed in cells at the adaxial base of lateral roots	[104]				
AT1G51190	PLT2	Control root stem cell activity near cap	[69]				
AT1G66350	RGL1	Root epidermal differentiation	[105]				
AT2G37260	TTG2	Differentiation of trichomes and root hairless cells	[106]				
AT5G57420	IAA33	IAA is involved in root development	[107, 108]				
AT2G29060		scarecrow transcription factor family protein					

Nie, J., Stewart, R., Zhang, H., Thomson, Ruan, F. Cui, X. and Wei. H et al. TF-Cluster: A pipeline for identifying functionally coordinated transcription factors via network decomposition of the shared coexpression connectivity matrix (SCCM). BMC Syst Biol 5, 53 (2011). https://doi.org/10.1186/1752-0509-5-53





BRN1 BRN2 SMB FEZ

Bennett T et al. SOMBRERO, BEARSKIN1, and BEARSKIN2 regulate root cap maturation in Arabidopsis. Plant Cell. 2010 Mar;22(3):640-54. doi: 10.1105/tpc.109.072272



Subnetwork 1, 12 and 17, which regulate the regeneration potential in Arabidopsis, were identified by CollaborativeNet (Islam et al. 2023).

Top-down GGM Algorithm: Identification of SND1-mediated network



The **ChIP-PCR** validation (Lin et al. 2013. Plant Cell)

The three layers of GRN constructed built by Top--down and Bottom-up GGM Algorithms



The width of each edge represents the frequency of interference or regulatory strength.

Lu et al., 2013. Proc Natl Acad Sci U S A. 25;110(26):10848-53. doi: 10.1073/pnas.1308936110.

TGMI: Identified TFs which regulate lignin biosynthesis pathway



Coral nodes contain the known regulators regulating lignin pathway that are re-discovered by TGMI algorithm.

Gunasekara et al. 2018 Nucleic Acids Res. 46(11):e67.

TGMI: Regulatory network regulates pigment biosynthesis pathways



Coral nodes contain the known regulators regulating lignin pathway that are rediscovered by TGMI algorithm.

Gunasekara et al. 2018 Nucleic Acids Res. 46(11):e67.



Α

Identification of **40 TFs** were found to potentially regulate 62 anthocyanin biosynthesis pathway genes. Wang et al BMC Plant Biology (<u>https://doi.org/10.1186/s12870-025-06053-4</u>)

TGMI

Joint Construction of multiple gene networks (JRmGRN)



Deng et al. 2018, *Bioinformatics* 5;34(20):3470-3478

How does BWERF (<u>Backward Elimination Random Forest</u>) work?



Multilayered gene regulatory network (ML-hGRN) built with BWERF algorithm



Tree Physiol, Volume 39, Issue 7, July 2019, Pages 1159–1172, <u>https://doi.org/10.1093/treephys/tpz025</u>



The content of this slide may be subject to copyright: please see the slide notes for details.

Multilayered hierarchical gene regulatory network (ML-hGRN) built with BWERF algorithm



The transcriptional landscape of Populus pattern/effector-triggered immunity and how PagWRKY18 involved in it Plant Cell & Environment, First published: 26 February 2024, DOI: (10.1111/pce.14860)

https://onlinelibrary.wiley.com/doi/10.1111/pce.14860

TGPred Package: six methods of predicting target genes of a TF



Cao, X., L. Zhang, M. K. Islam, M. Zhao, C. He, K. Zhang, S. Liu, Q. Sha, H. Wei, TGPred: efficient methods for predicting target genes of a transcription factor by integrating statistics, machine learning and optimization, NAR Genomics and Bioinformatics, Volume 5, Issue 3, September 2023, Iqad083, https://doi.org/10.1093/nargab/Iqad083



Thank you!