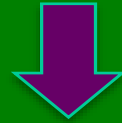


CollaborativeNet (originally called TF-Cluster): Identification of collaborative regulatory genes that govern a biological process or a complex trait

NETWORK CONSTRUCTION

Gene	T1	T2	T3	T4	T5	T6	T7	T8	T9	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	890	1250	99	450
...
G n-1	550	225	388	650	470	559	899	250	590	460
G n	150	260	950	750	470	585	865	125	99	450

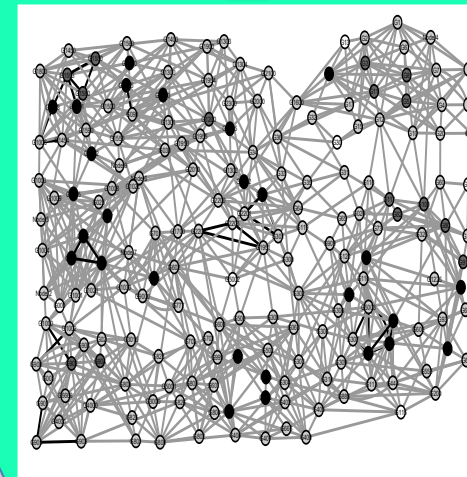
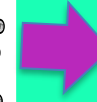
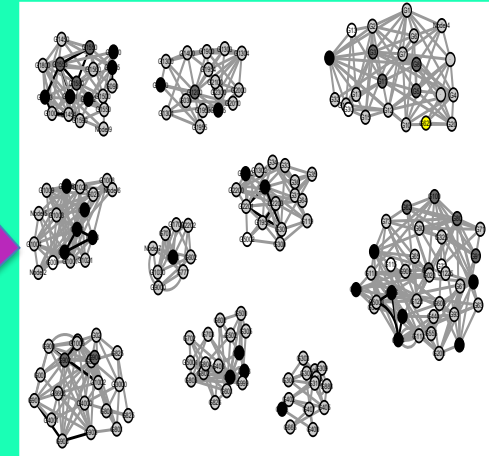
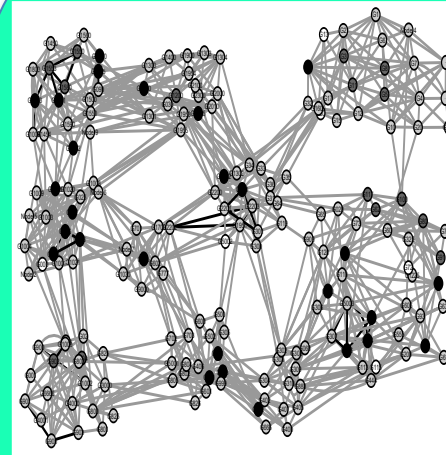
Expression data



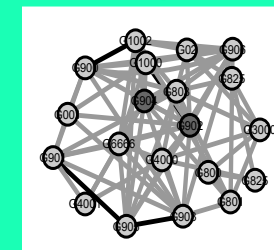
	TF1	TF2	TF3	TF4	TF5	TF6	TF7	TF8	TF9	TF10	TF11	TF12
TF1	00	50	00	00	00	30	00	00	40	00	00	00
TF2	50	00	00	00	32	00	00	00	00	00	00	55
TF3	00	00	00	00	00	00	39	00	00	00	00	00
TF4	00	00	00	00	00	00	00	00	60	00	00	00
TF5	00	32	00	00	00	00	00	00	00	36	00	00
TF6	30	00	00	00	00	00	00	38	00	00	00	00
TF7	00	00	39	00	00	00	00	00	00	00	00	40
TF8	00	00	00	00	00	00	00	00	00	00	50	00
TF9	40	00	00	00	00	38	00	00	00	00	00	00
TF10	00	00	00	00	36	00	00	00	00	00	00	00
TF11	00	00	00	00	00	00	50	00	00	00	00	00
TF12	00	55	00	00	00	40	00	00	00	00	00	00

SCCM--Shared Coexpression Connectivity Matrix

NETWORK DECOMPOSITION



Collaborative Network

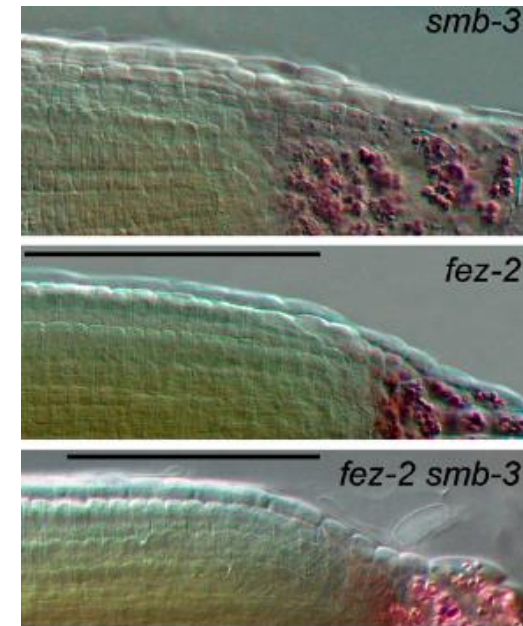
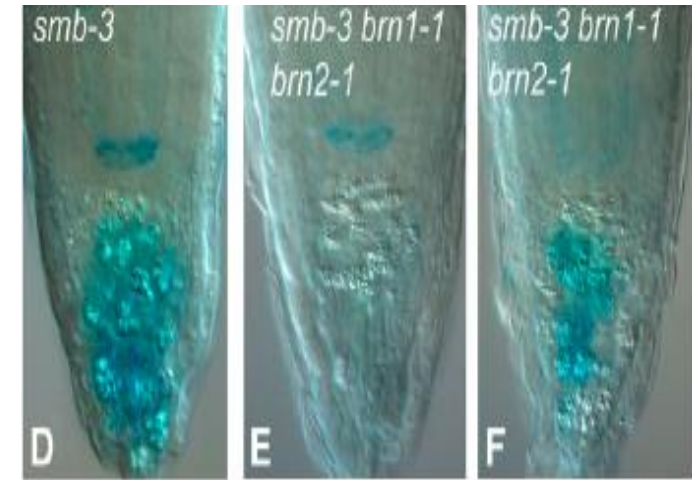


Each subnetwork contains TFs that control a complex trait or a biological process

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	

These genes were identified by other researchers

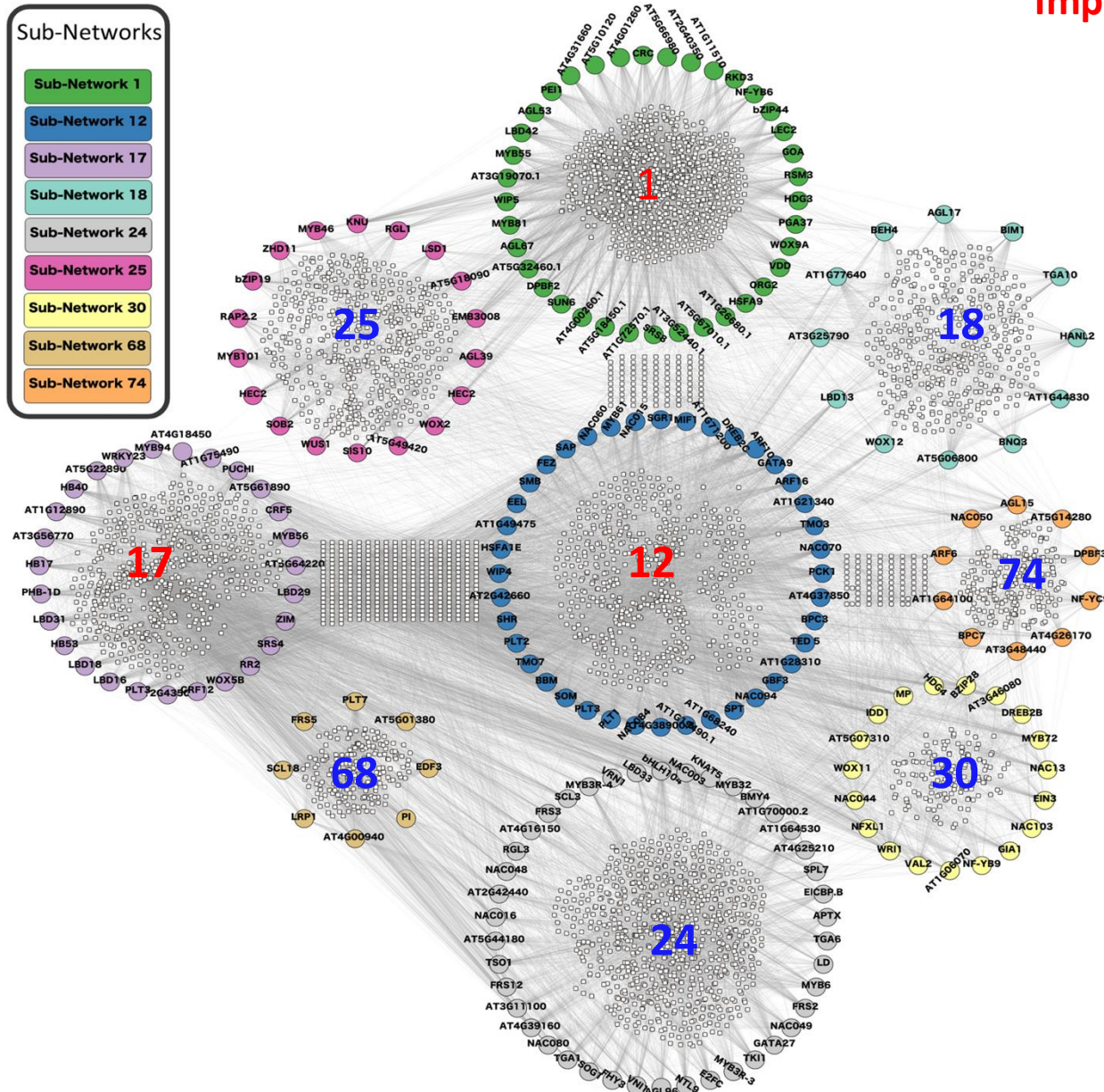


BRN1
BRN2
SMB
FEZ

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>

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

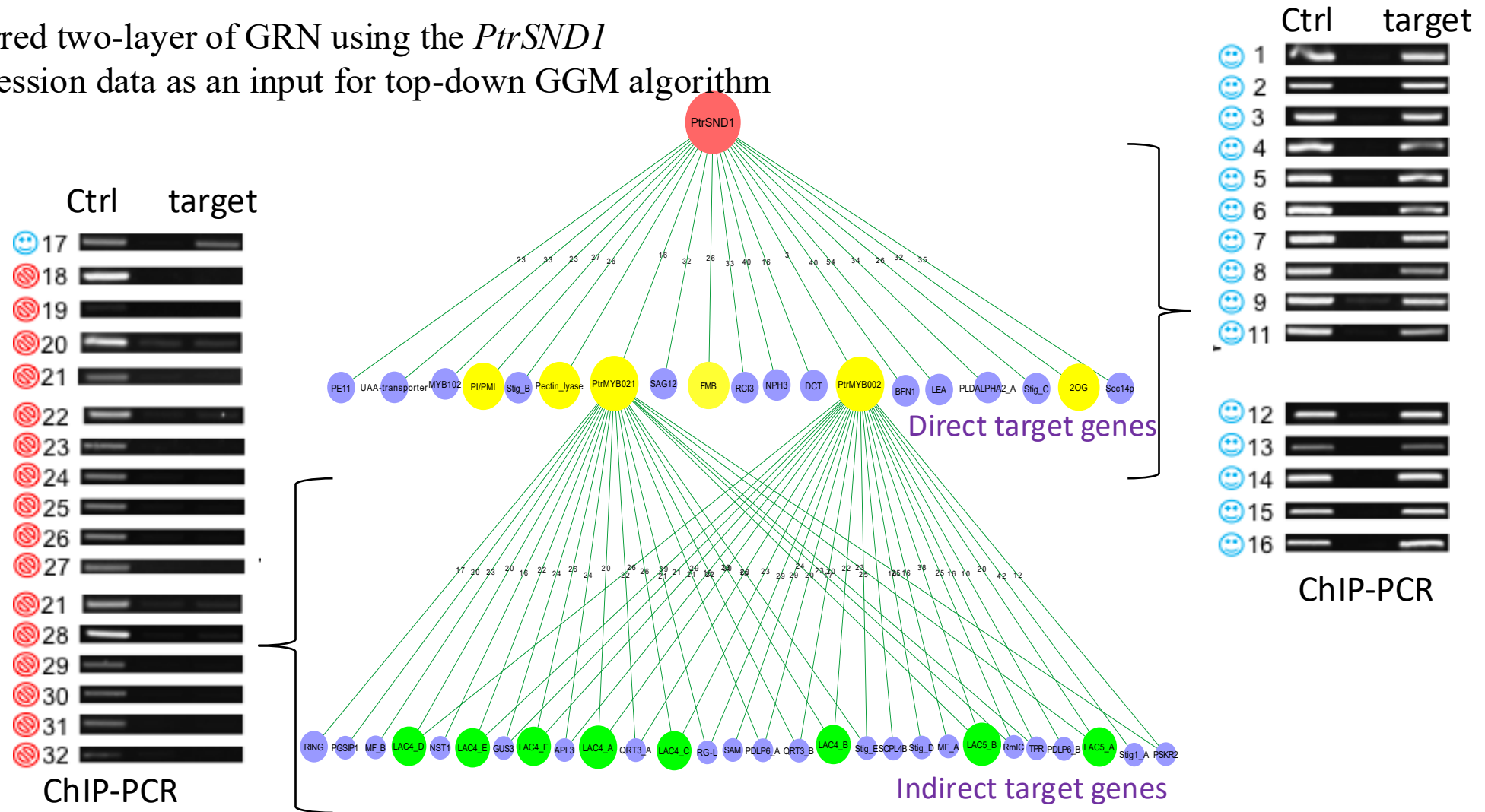
Implementation of CollaborativeNET



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

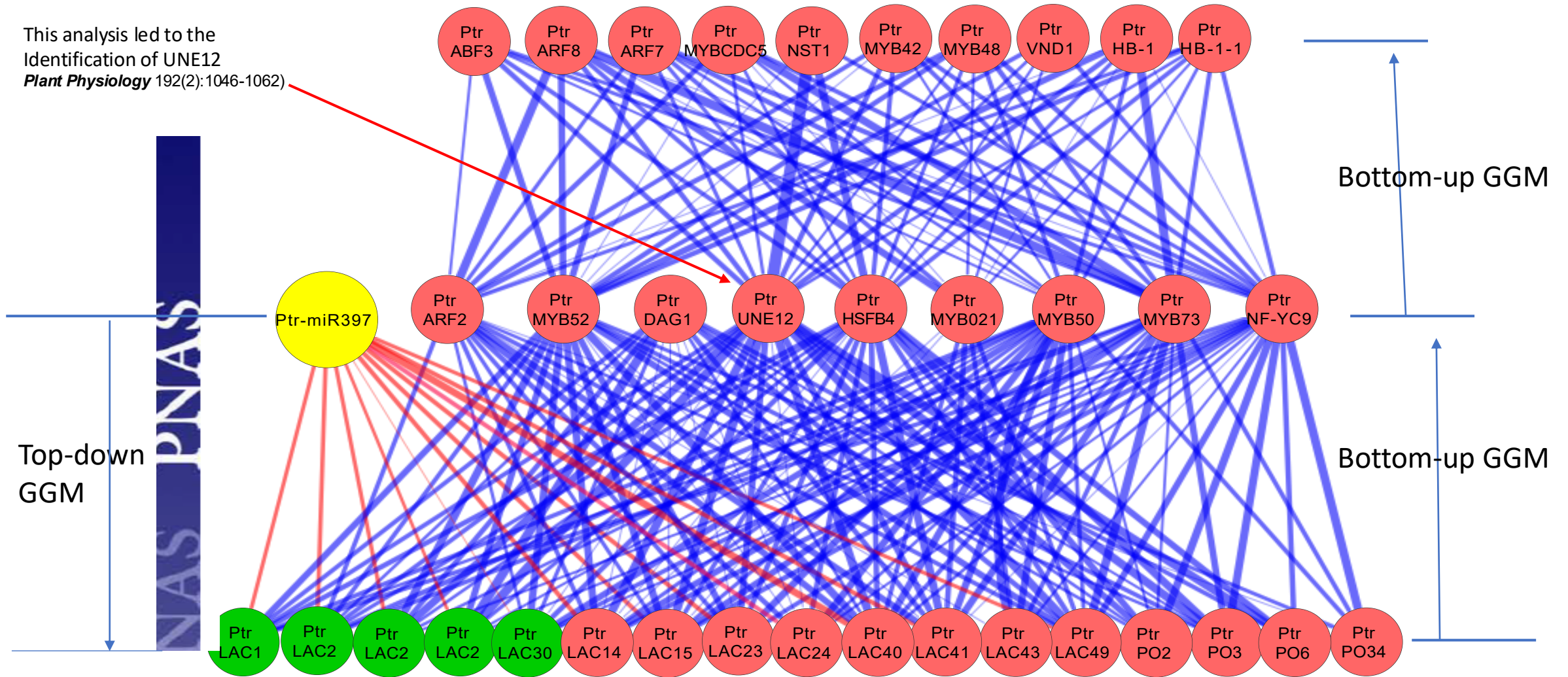
Top-down GGM Algorithm: Identification of SND1-mediated hierarchical network

The inferred two-layer of GRN using the *PtrSND1* overexpression data as an input for top-down GGM algorithm



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

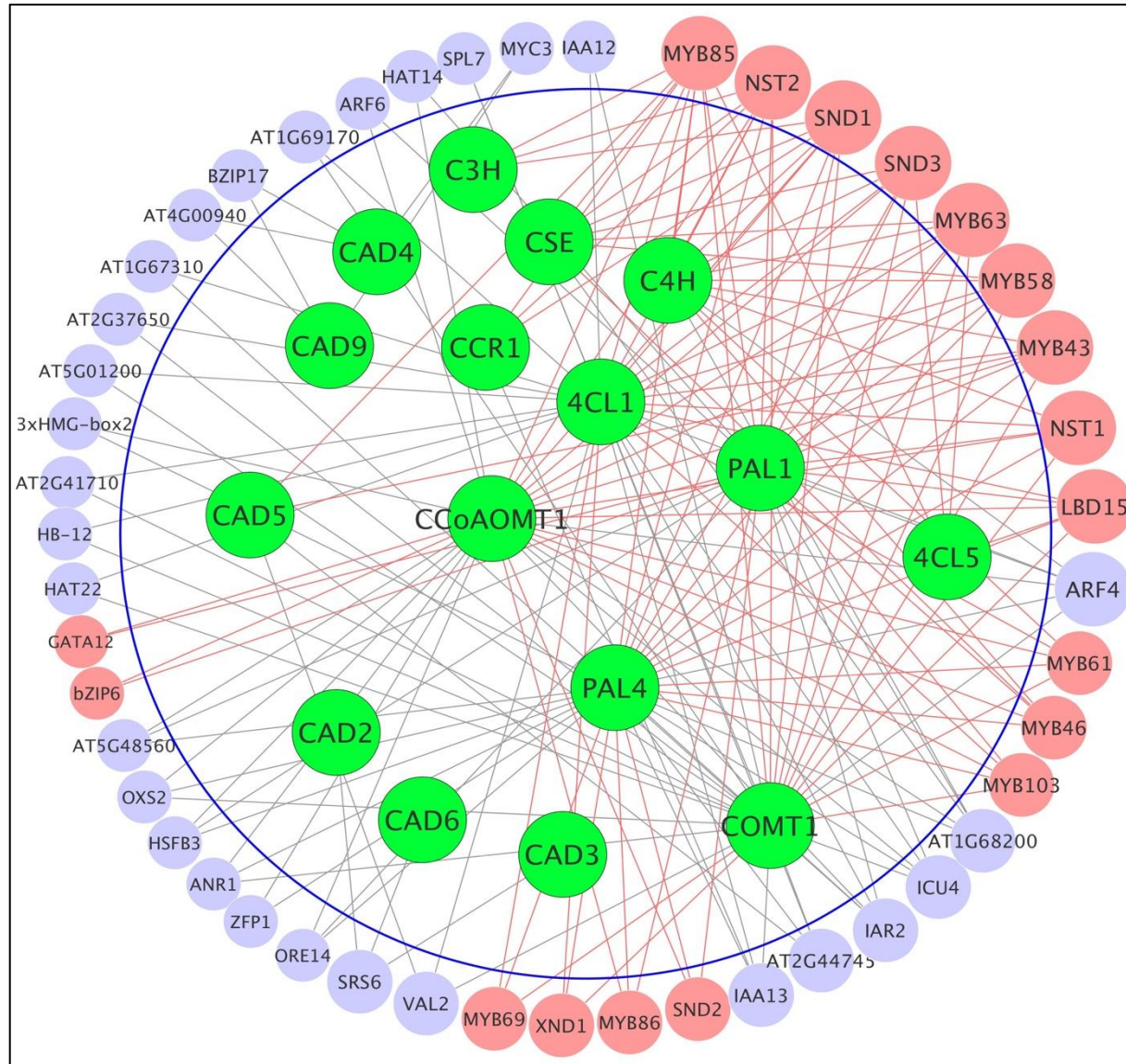
The three layered GRN constructed with **Top-down GGM** and **Bottom-up GGM** Algorithms



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

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

TGMI: Identified the TFs that regulate lignin biosynthesis pathway

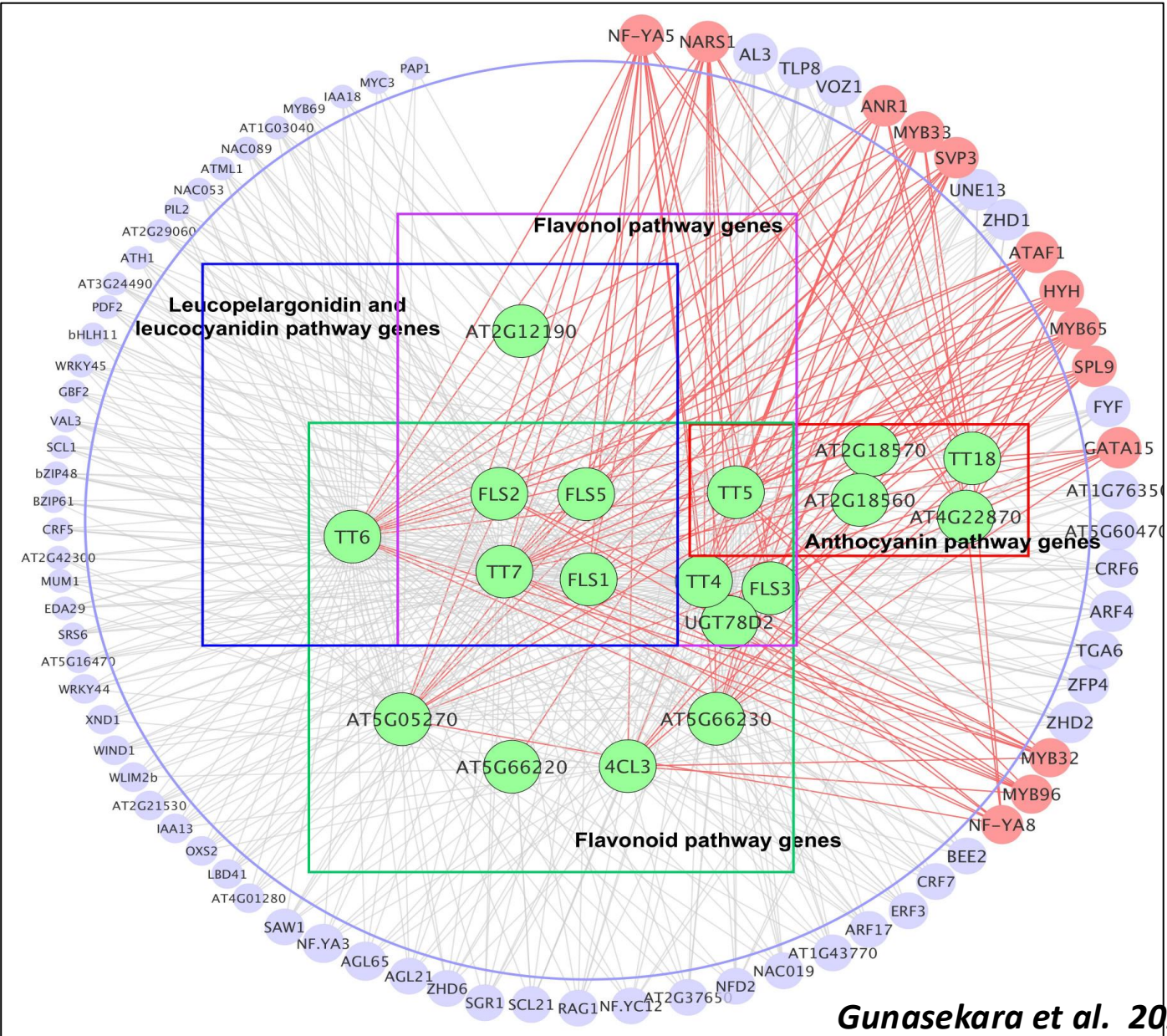


Rank	TF	Frequency	References
1	MYB85	11	(Zhou, Lee, Zhong, & Ye, 2009)
2	NST2	9	(Zhong & Ye, 2015)
3	SND1	9	(Zhong & Ye, 2015)
4	MYB63	8	(Zhou et al., 2009)
5	SND3	8	(Zhong, Lee, Zhou, McCarthy, & Ye, 2008)
6	MYB43	7	(Yoon, Choi, & An, 2015)
7	MYB58	7	(Zhou et al., 2009)
8	ARF4	6	-
9	LBD15	6	(Shuai, Reynaga-Pena, & Springer, 2002)
10	NST1	6	(Mitsuda et al., 2007)
11	AT1G68200	5	-
12	IAR2	5	-
13	ICU4	5	-
14	MYB103	5	(Ohman et al., 2013)
15	MYB46	5	(Kim, Kim, Ko, Kang, & Han, 2014)
16	MYB61	5	(Zhong & Ye, 2009)
17	AT2G44745	4	-
18	IAA13	4	-
19	ANR1	3	-
20	AT5G48560	3	-
21	HSFB3	3	-
22	MYB69	3	(Zhong et al., 2008)
23	MYB86	3	(Zhong et al., 2008)
24	ORE14	3	-
25	OXS2	3	-
26	SND2	3	(Hussey et al., 2011)
27	SRS6	3	-
28	VAL2	3	-
29	XND1	3	(Zhao, Avci, Grant, Haigler, & Beers, 2008)
30	3xHMG-box2	2	-
31	ARF6	2	-
32	AT1G67310	2	-
33	AT1G69170	2	-
34	AT2G37650	2	-
35	AT2G41710	2	-
36	AT4G00940	2	-
37	AT5G01200	2	-
38	BZIP17	2	-
39	bZIP6	2	(Zhong & Ye, 2012)
40	GATA12	2	(Nishitani & Demura, 2015)

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

Gunasekara, Zhang, Deng, Brown and Wei*. 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 re-discovered by TGMI algorithm.

Joint construction of multiple gene regulatory networks with data from multiple conditions or tissues (*JRmGRN*)

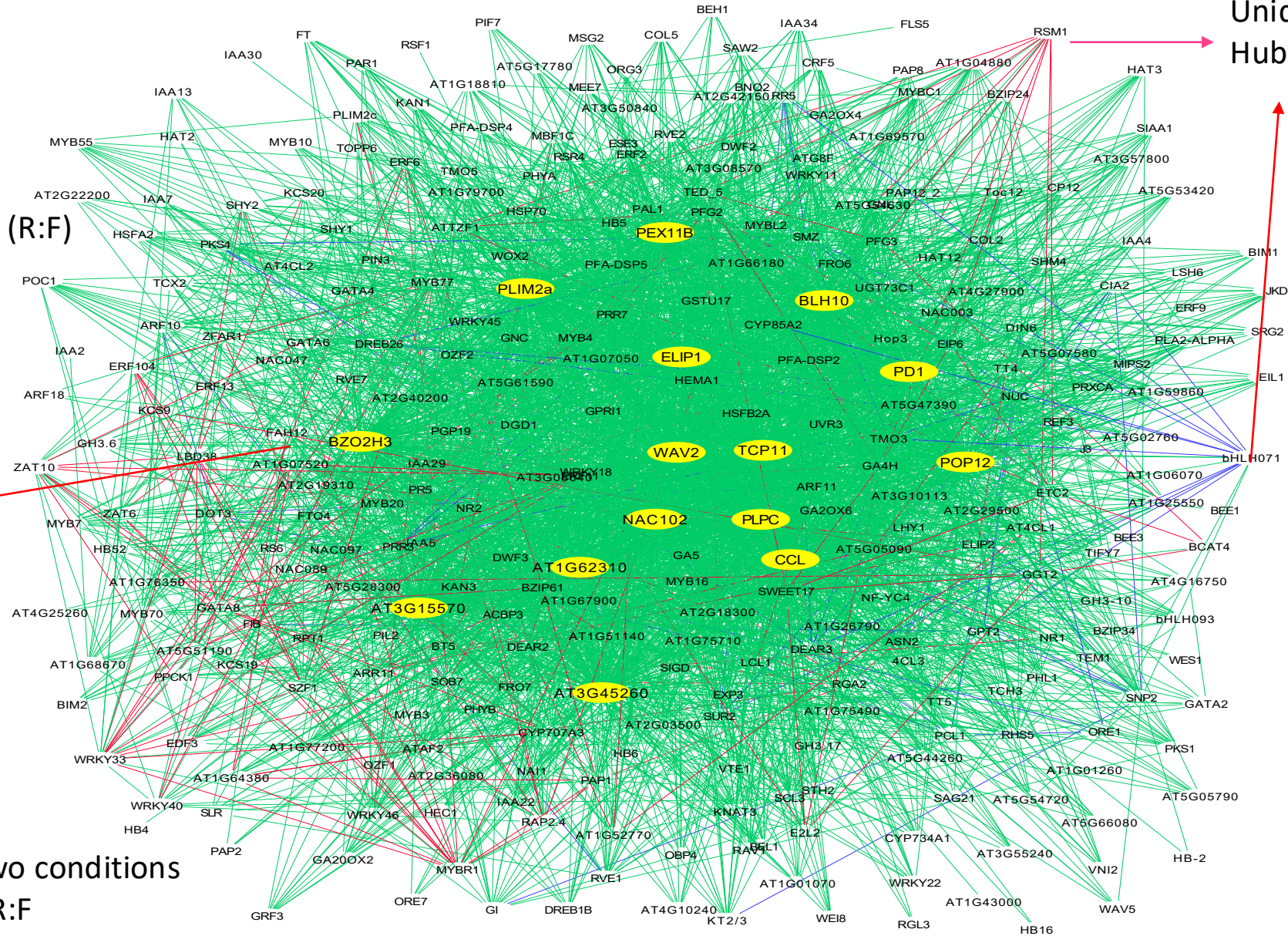
Unique Hub

Arabidopsis data

Conditions:

1. High Red : Far-red (R:F)
2. Low Red : Far-red

Common hub
In two networks
(yellow nodes)

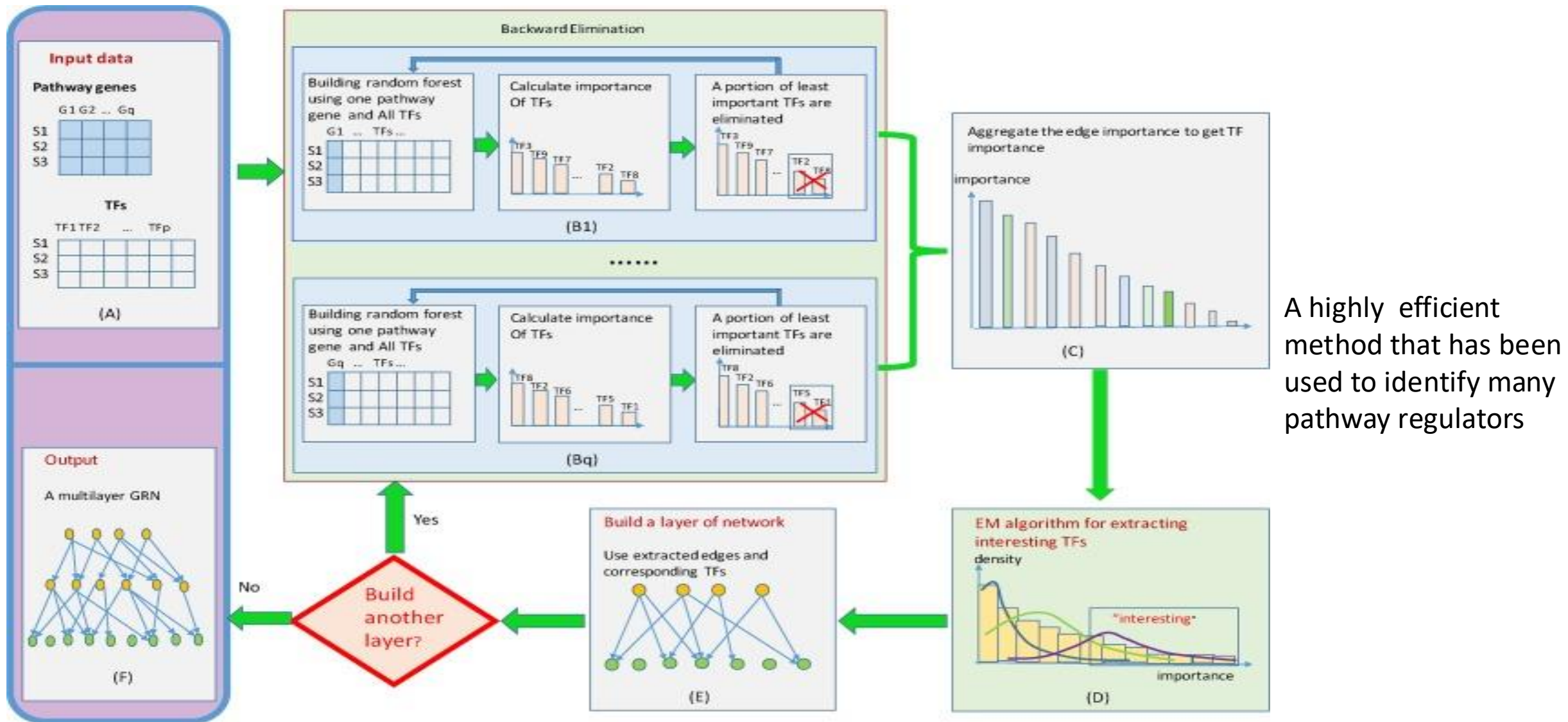


Two networks

1. Green edges: common to two conditions
2. Red edges: specific to high R:F
3. Blue edges: specific to low R:F

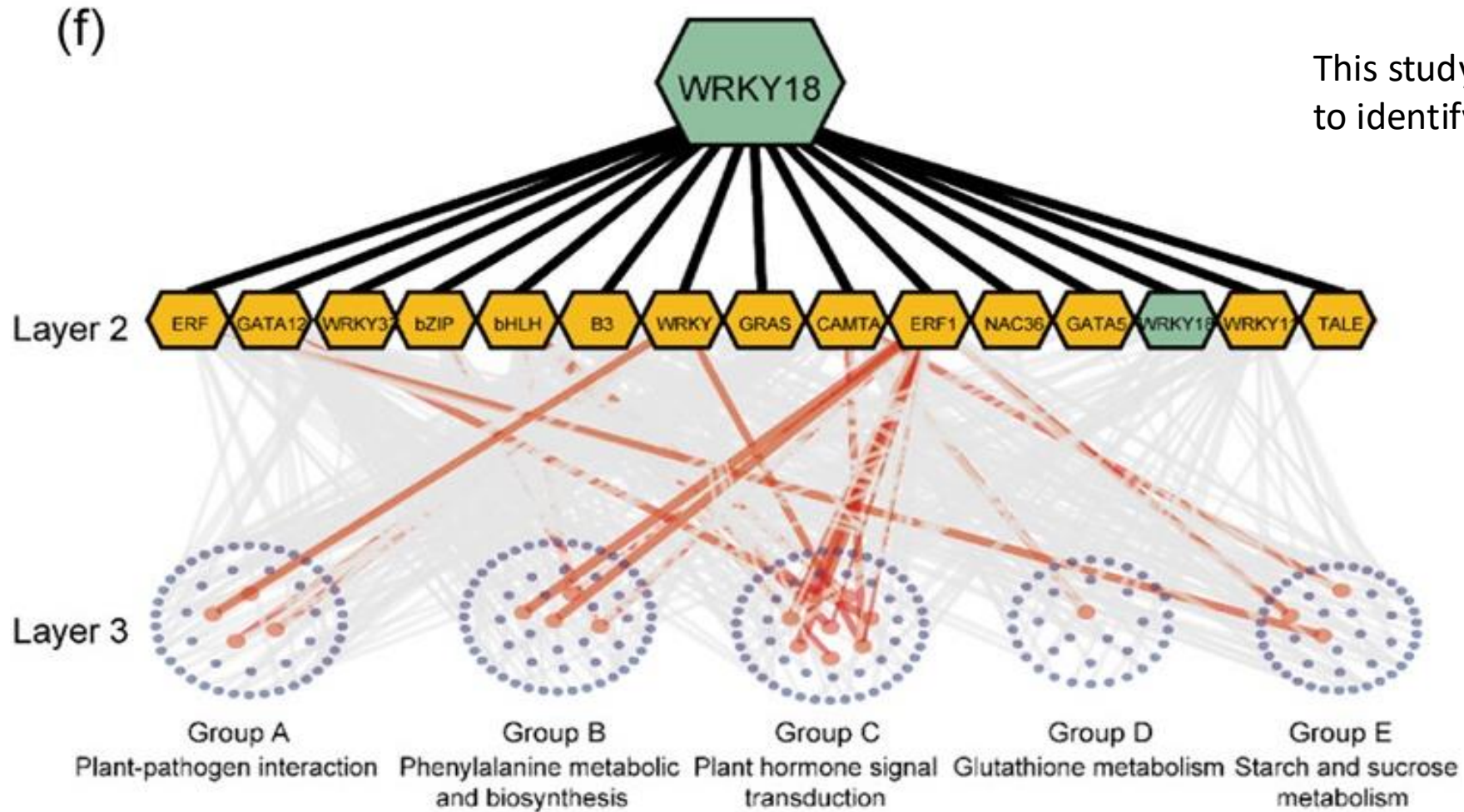
How does BWERF (Backward Elimination Random Forest) work?

---An algorithm for building hierarchical gene regulatory networks governing a biological processes or pathways



A highly efficient method that has been used to identify many pathway regulators

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



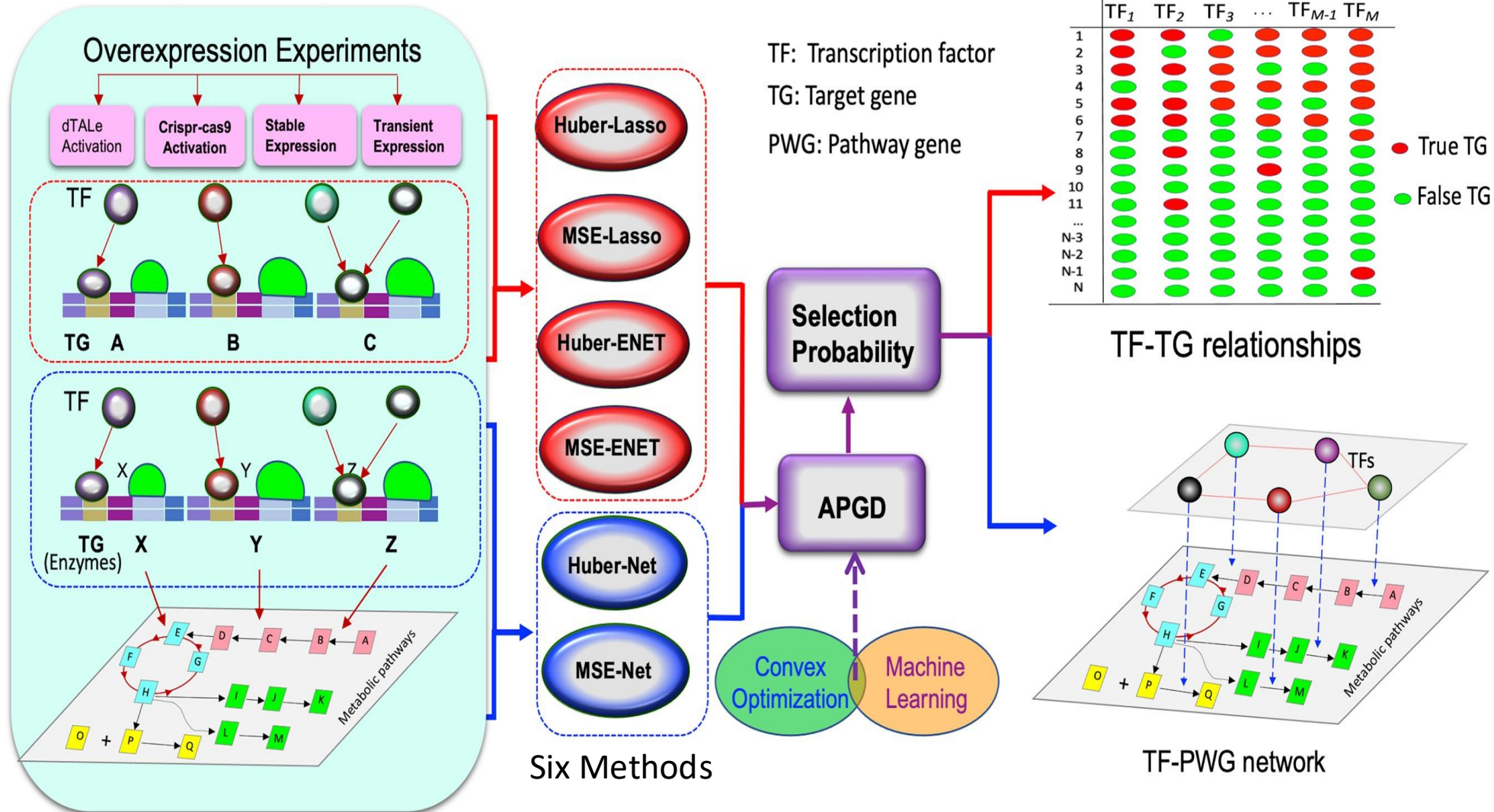
This study used BWERF to identify WRKY18

The transcriptional landscape of Populus pattern/effector-triggered immunity and how PagWRKY18 involved in it

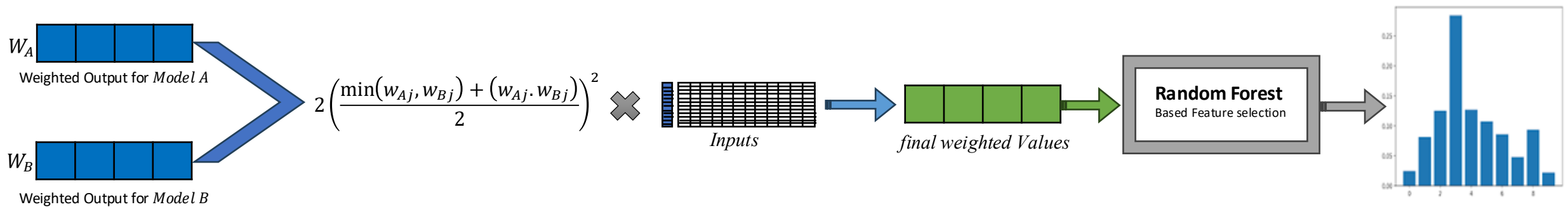
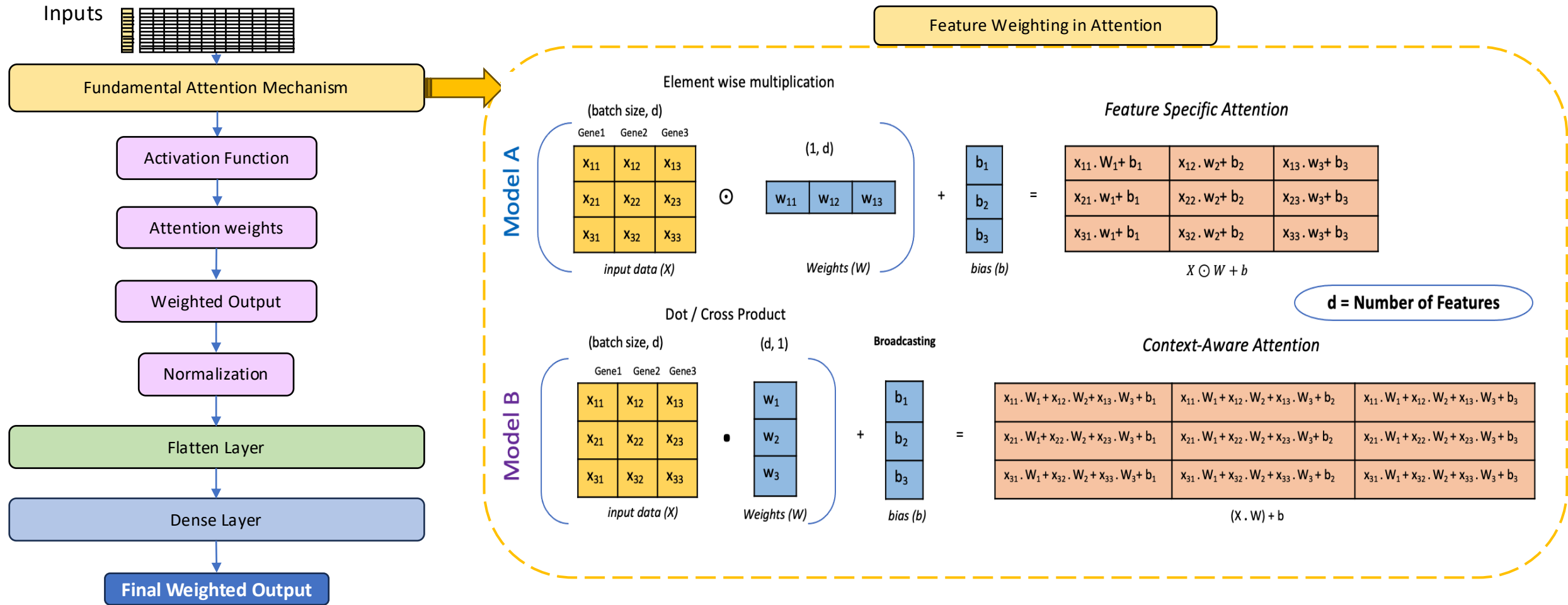
Plant Cell & Environment, First published: 26 February 2024, DOI: (10.1111/pce.14860)

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

TGPred package: four methods for predicting transcription factor target genes and two methods for predicting pathway regulators



DyGAF: a deep learning-based dynamic attention model for identifying disease-associated biomarkers in infectious diseases



The efficiency and output of DyGAF

Table 1. Classification report comparing dynamic gene attention focus (DyGAF), random forest (RF), differential expression analysis (DEA-RF), support vector machines (DyGAF-SVM), and K-nearest neighbors (DyGAF-KNN) models based on the gene expression profiles from human nasopharyngeal swabs.

Models	Accuracy				
	Training	Testing	F1-score	Specificity	Sensitivity
DyGAF	100	94.23	96	91.9	100
DyGAF (Model A)	100	88.46	92	100	66.67
DyGAF (Model B)	100	90.38	93	100	72.23
RF	100	88.46	80	85	100
DyGAF-SVM	100	86.53	90	86.5	86.7
DyGAF-KNN	90.82	76.29	84	97	80
DEA-RF	100	92	94	77.78	100

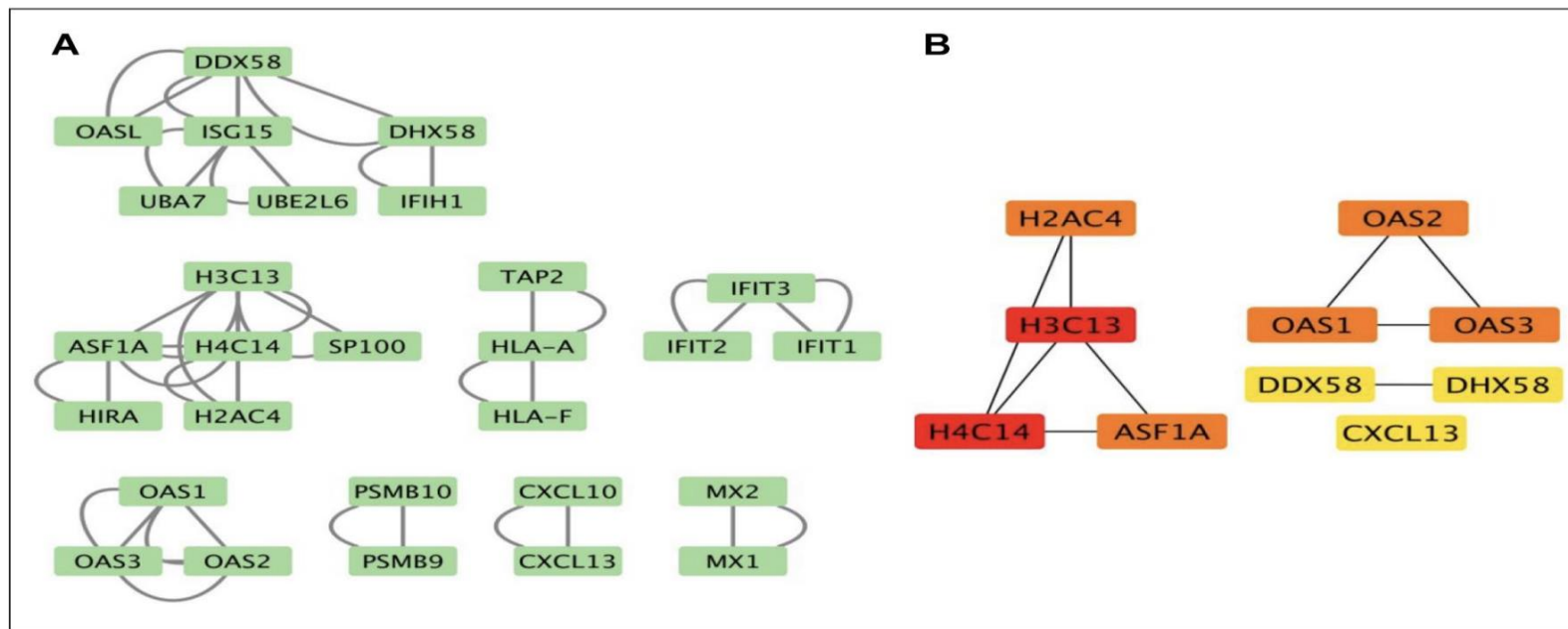
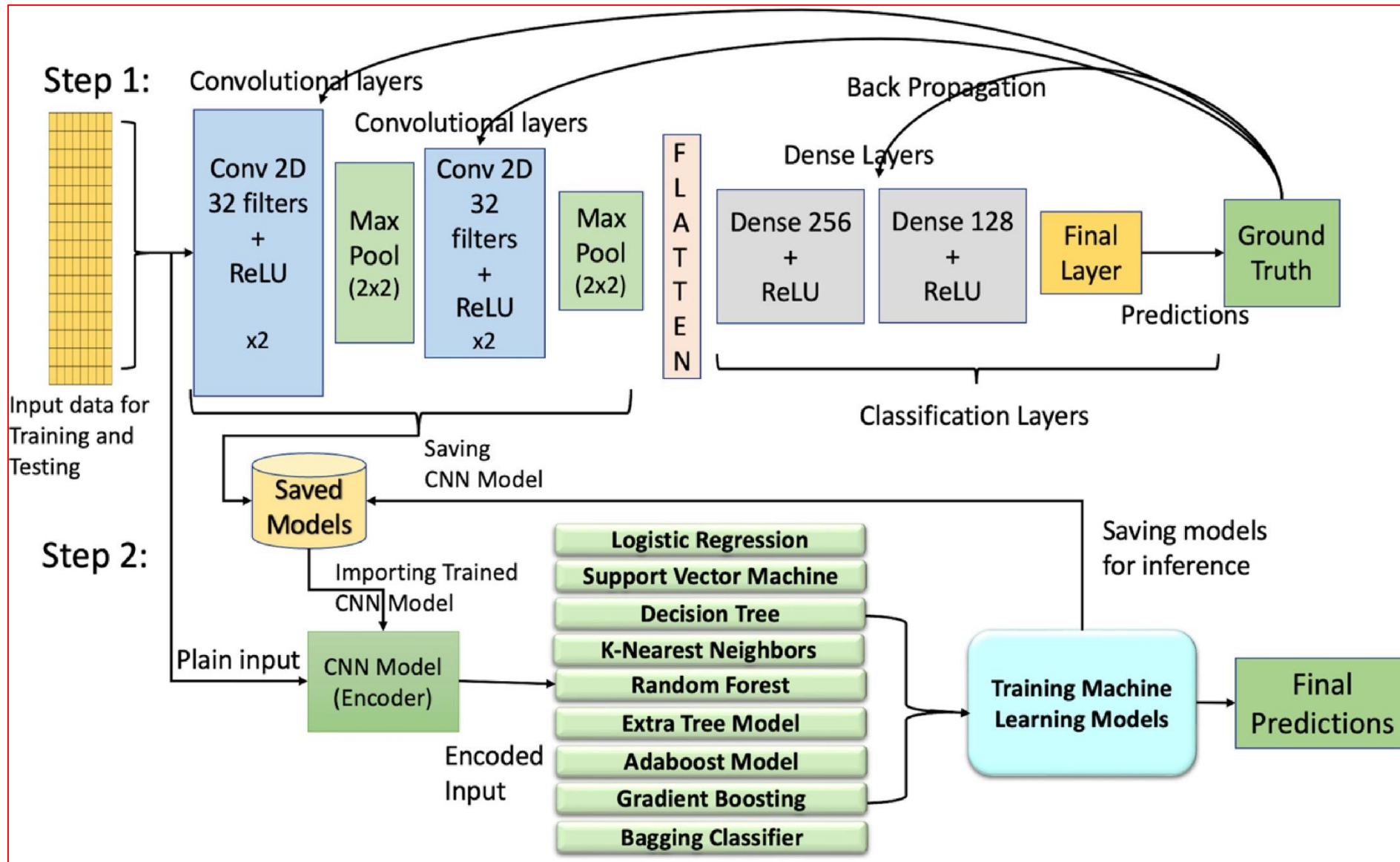


Figure 7. Key protein-protein interactions (PPI) and hub proteins with COVID-19. (A) PPI retrieve from STRING database using the top 100 significant genes. (B) Hub-proteins found out using different algorithms available in cytoHubba.

IntegraGRN: A machine learning and deep learning combined approach for identifying pathway regulators



The package identified the high hierarchical regulators, MYB26 and E2FC, and the central hub regulators, MYB83 and MYB46, of the lignin pathway.

A close-up photograph of several small, pink, succulent-like flowers with a spiky, rosette-like structure. The flowers are set against a blurred green background. The text "Thank you!" is overlaid in the center in a bold, yellow, sans-serif font with a black outline.

Thank you !