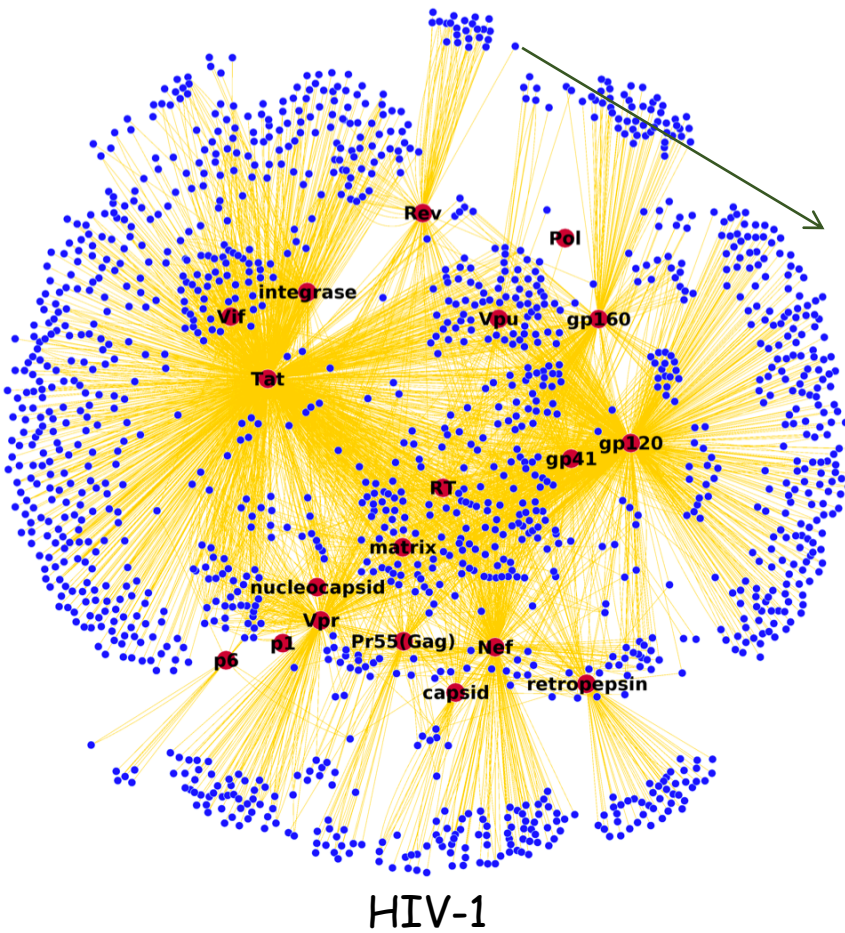


A Systems Biology Perspective to the Evolution of Virus-Plant Interactions

Santiago F. Elena

Evolutionary Systems Virology Group

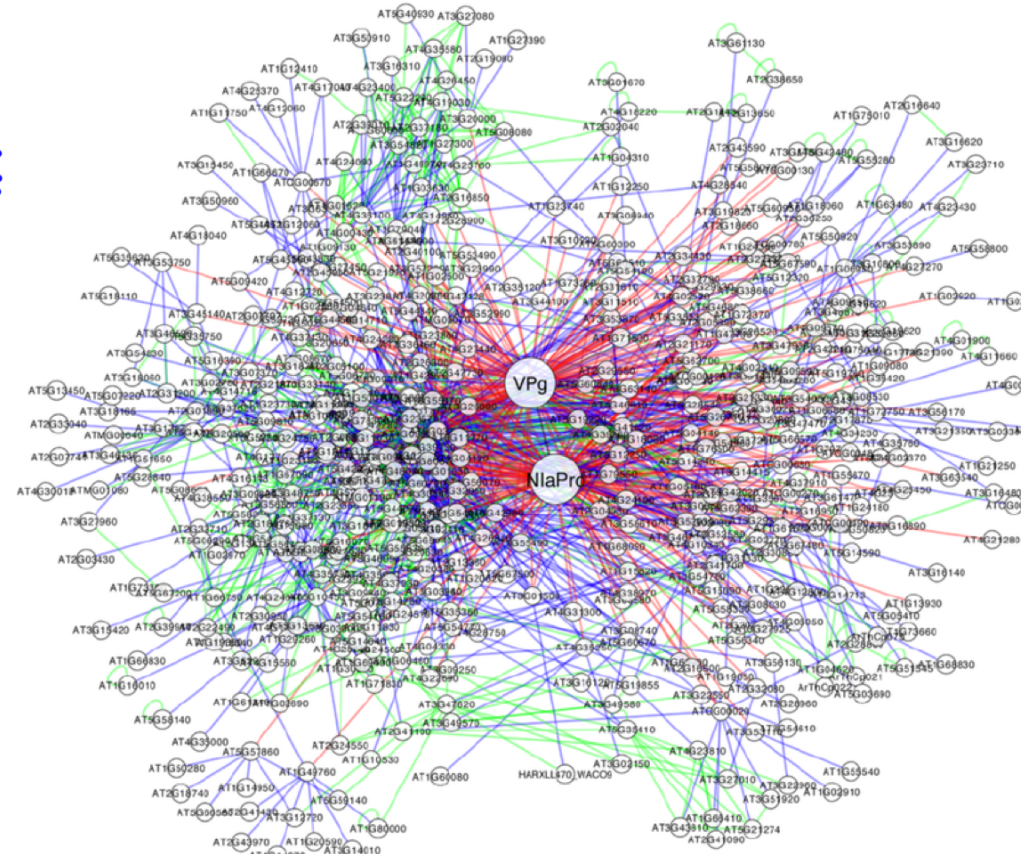
Virus-host interaction networks



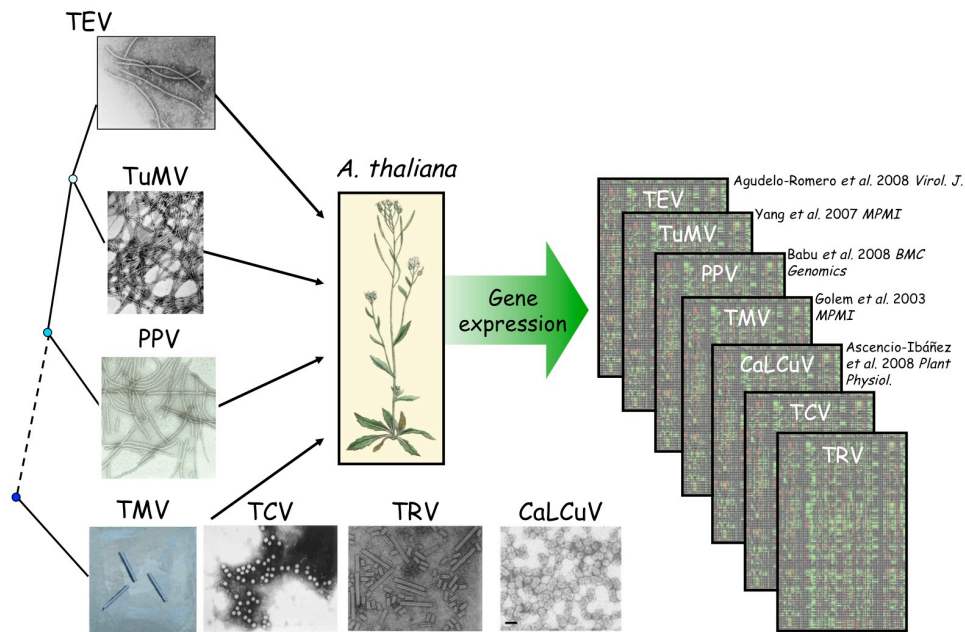
HIV-1

VRGs

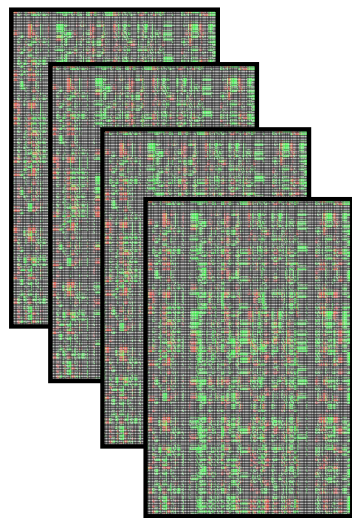
TEV



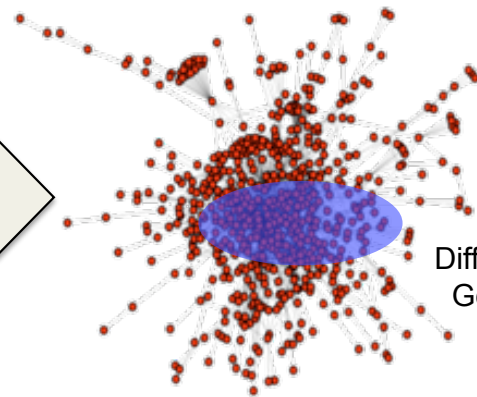
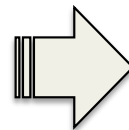
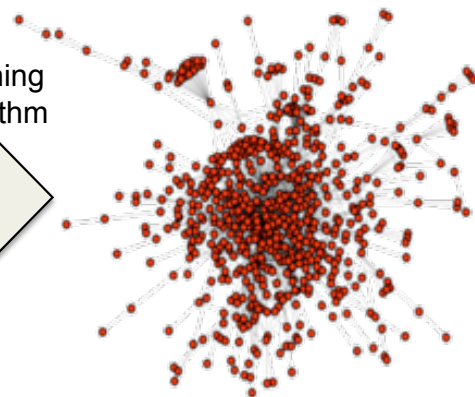
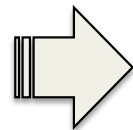
1. Characterizing *Arabidopsis*-virus interactome: a meta-analysis



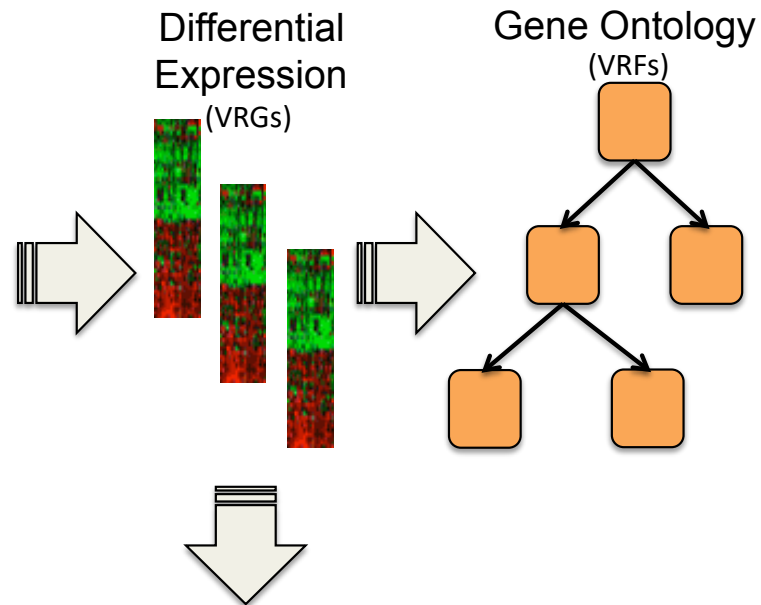
Collected Microarrays



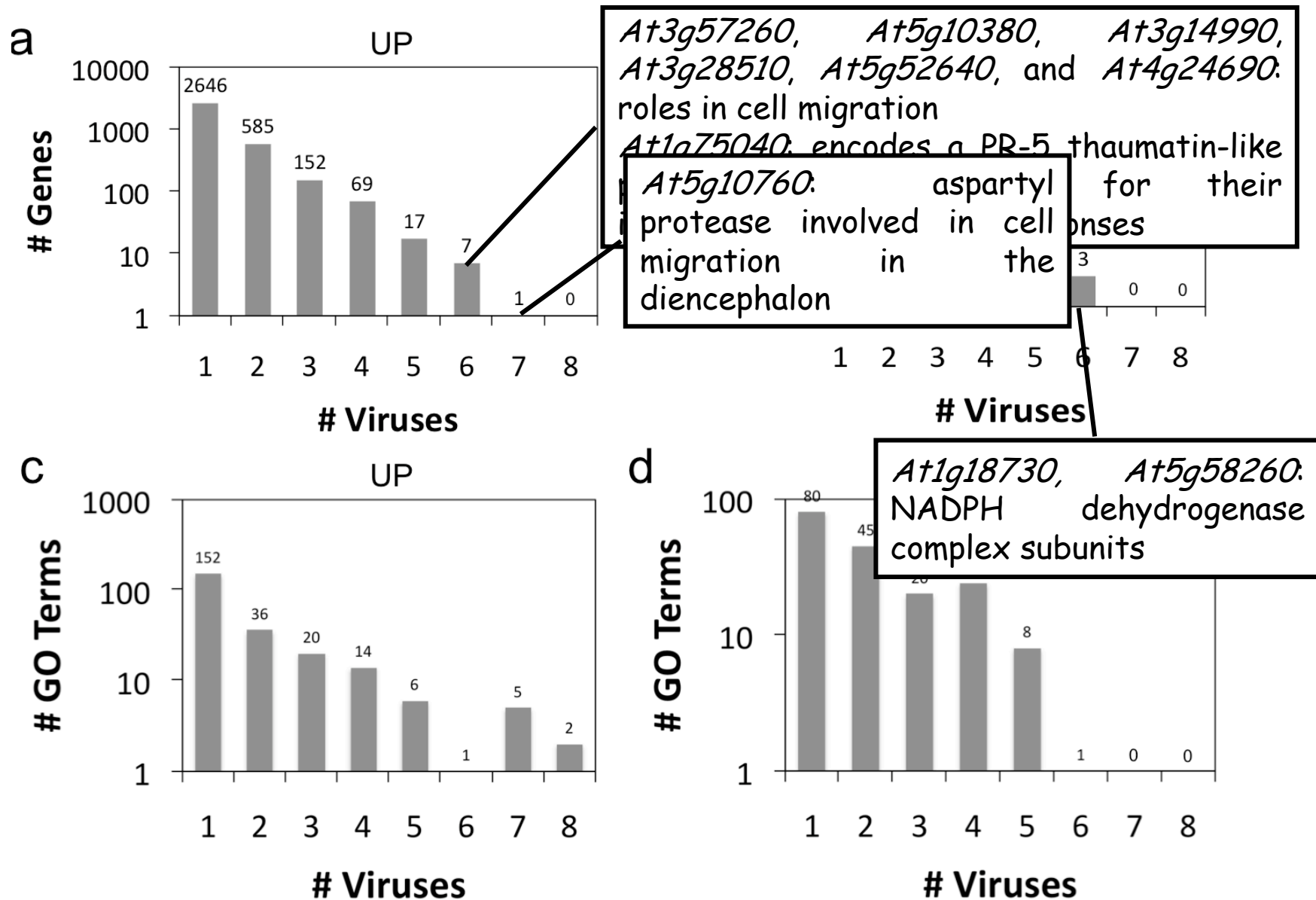
Learning Algorithm



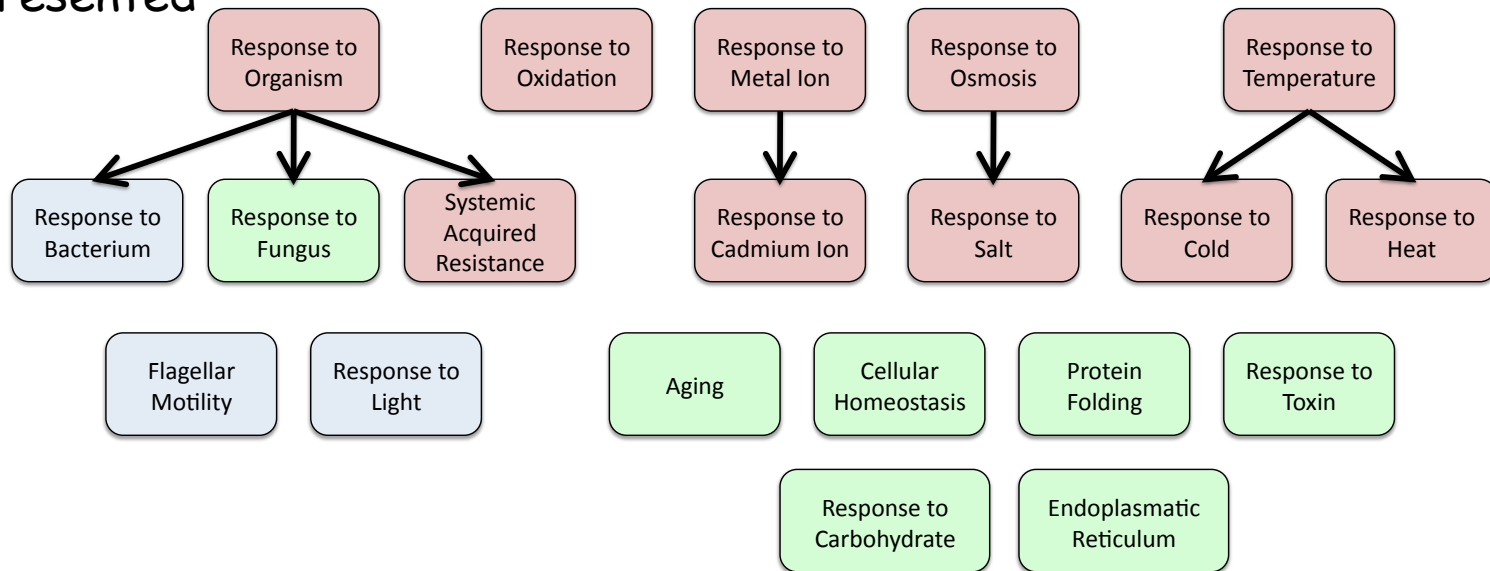
Diff. Exp. Genes



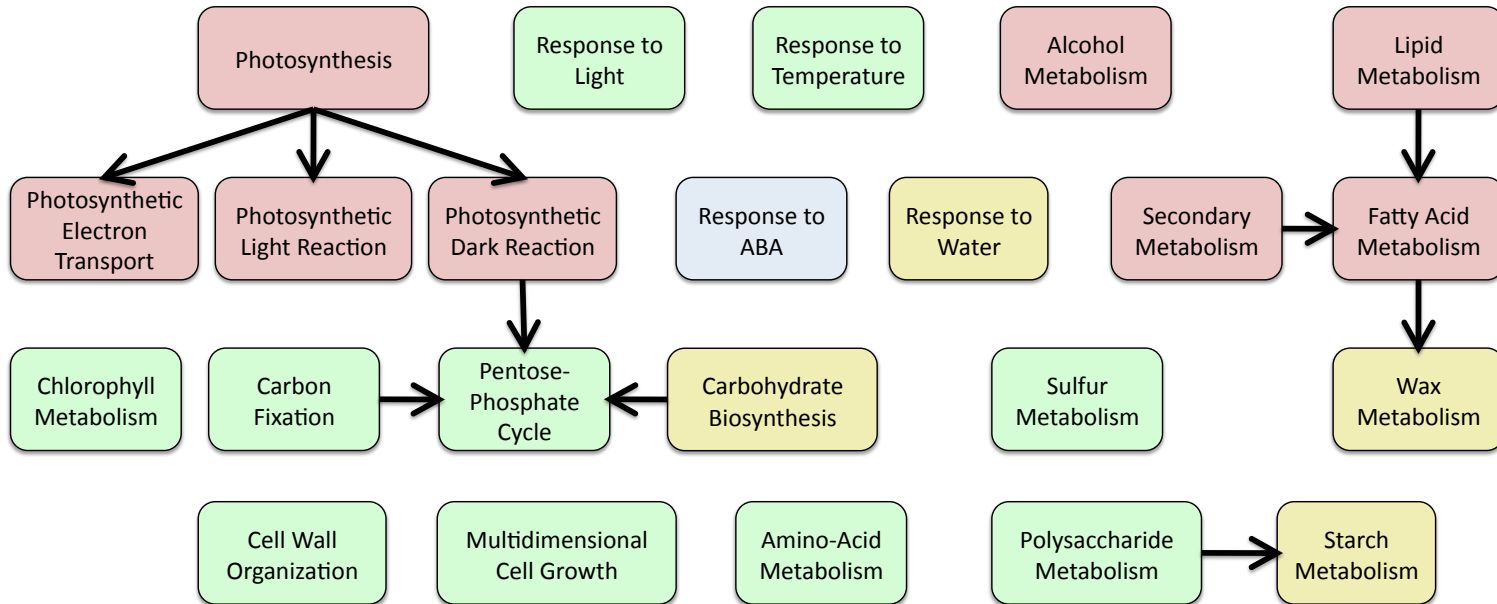
1.1. Identification and functional analyses of common VRGs



Over-represented



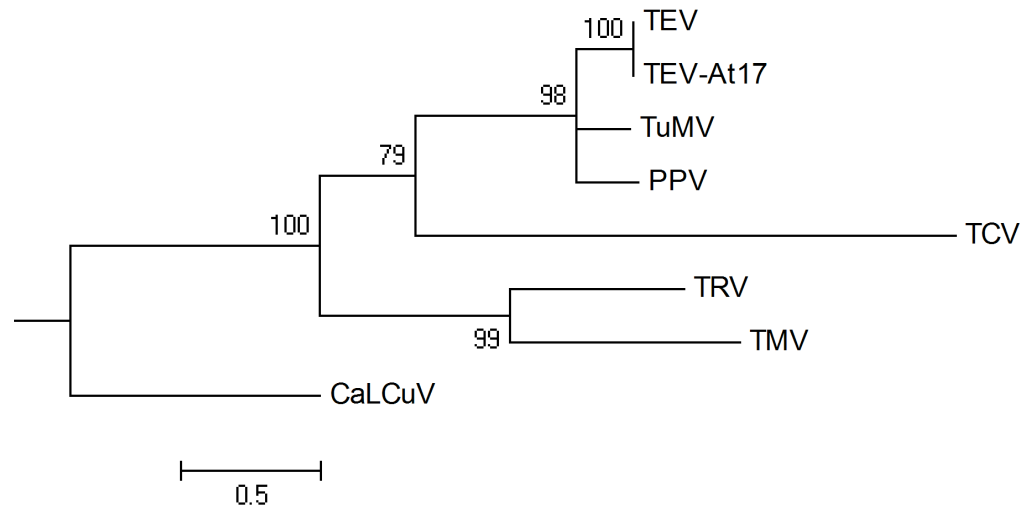
Under-represented



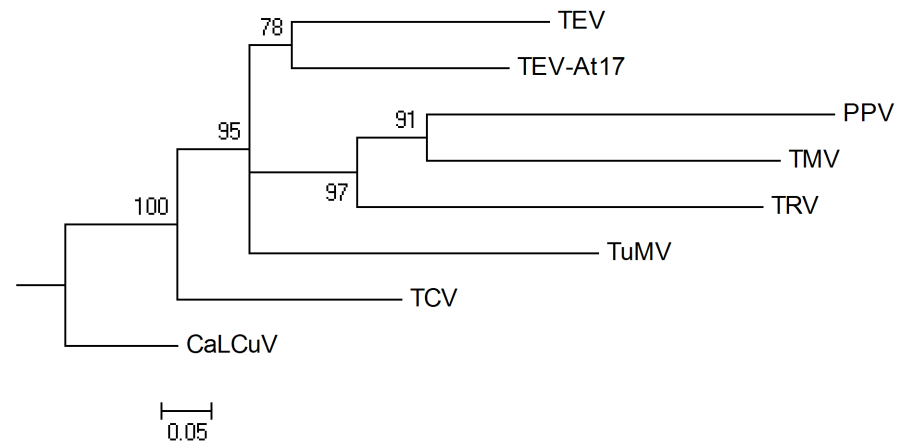
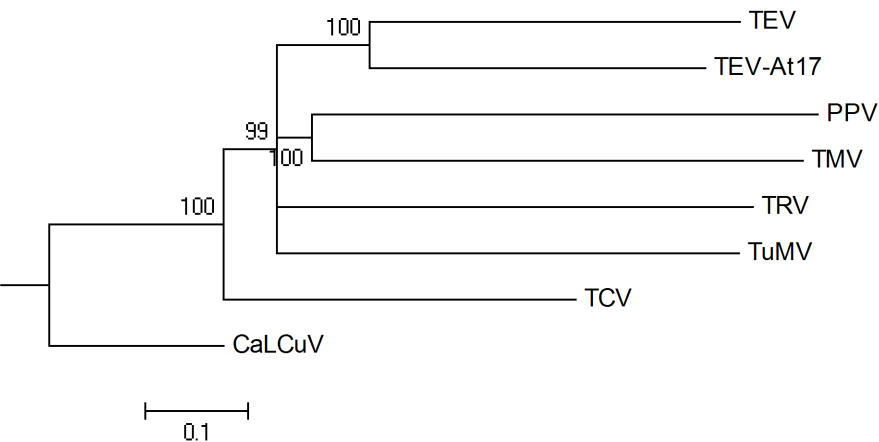
Metabolic alterations

- ✓ Unspecific **up-regulations**:
 - Cellulose biosynthesis -required for cell wall integrity.
 - Nitrogen fixation.
- ✓ *Brassica*-infecting viruses specific **up-regulations**:
 - Induction of cytokins biosynthesis -central to plant development, growth, and idetoxification.
 - Rubisco shunt -a more efficient converter of carbohydrates into acetyl-CoA than glycolysis.
- ✓ Unspecific **down-regulations**:
 - Reprogramming of Calvin cycle and glycolysis.
- ✓ *Brassica*-infecting viruses specific **down-regulations**:
 - Biosynthesis of starch photorespiration, and fatty acid biosynthesis.
- ✓ These observations are consistent with the idea that viruses impel the plant to redirect resources towards immune systems and other biotic stress responses, to the detriment of developmental processes. As a result, increased tolerance to viral infections might be achieved.

Phylogenetic similarity

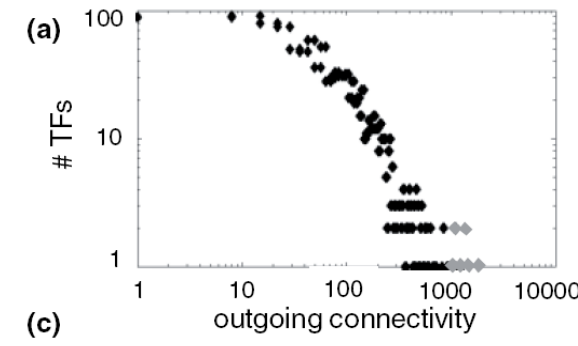
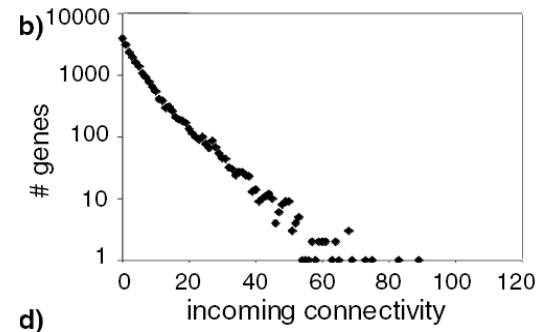
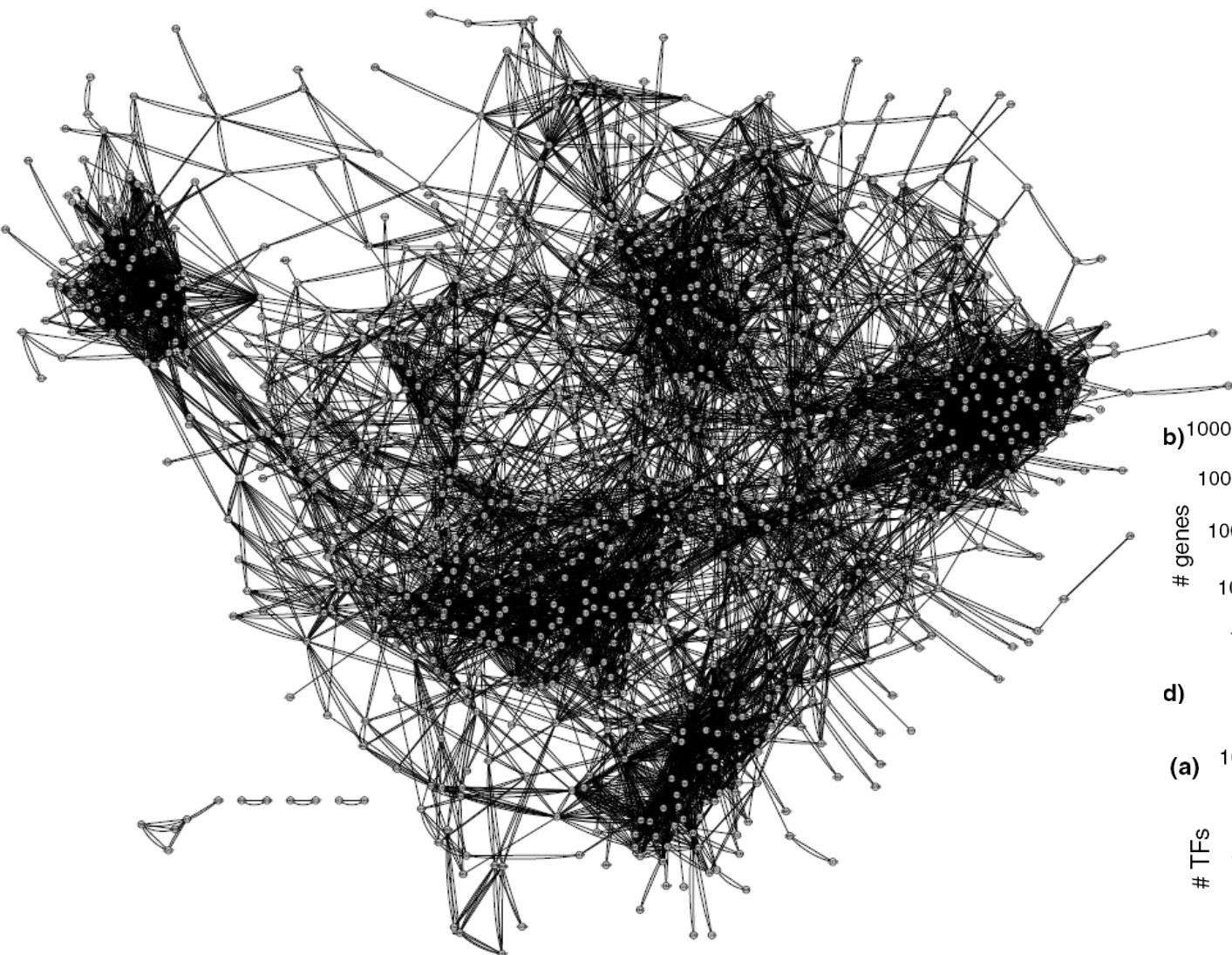


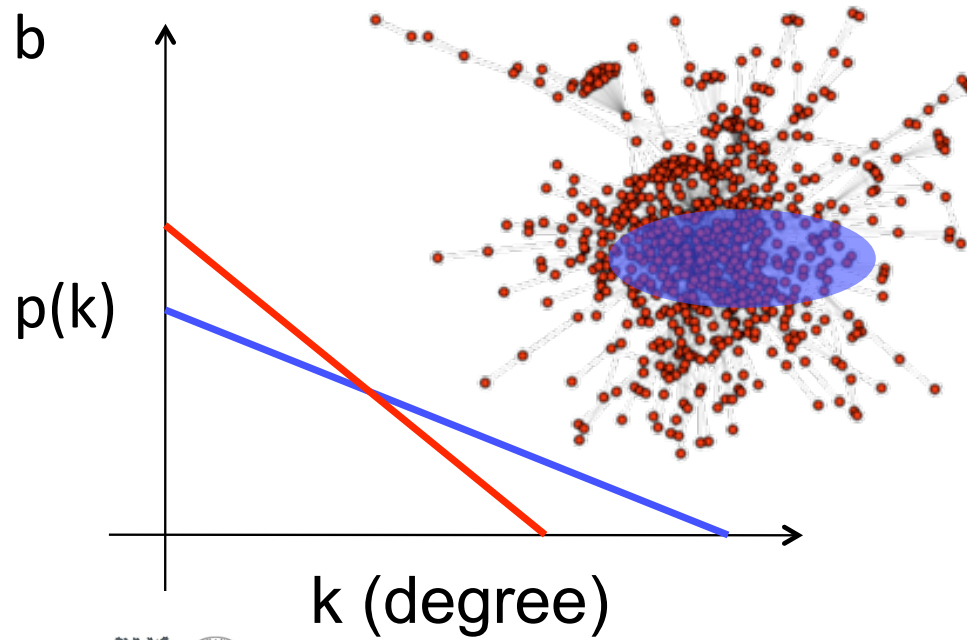
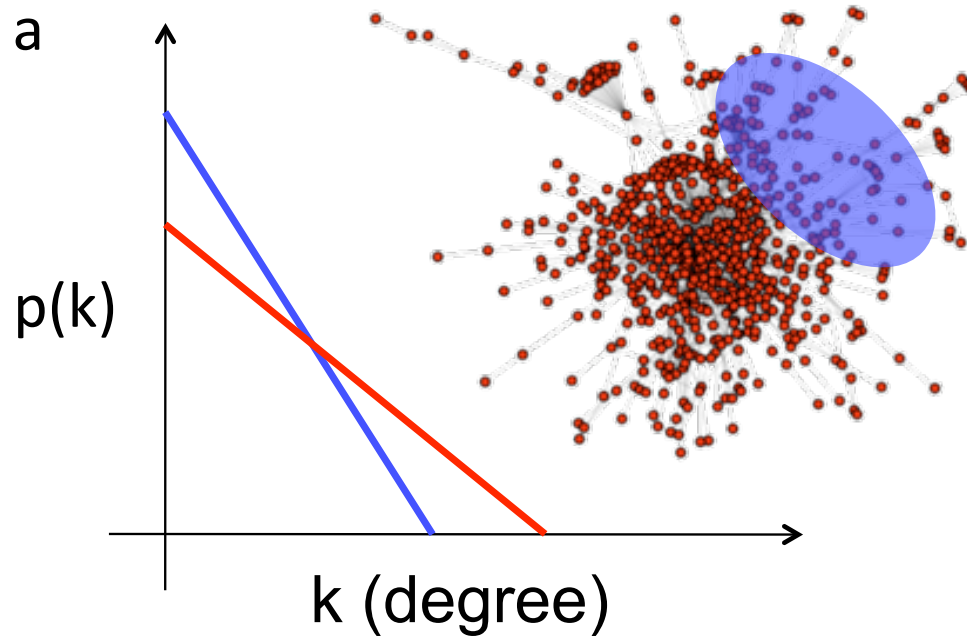
ML phylogenetic tree obtained for the replicase gene

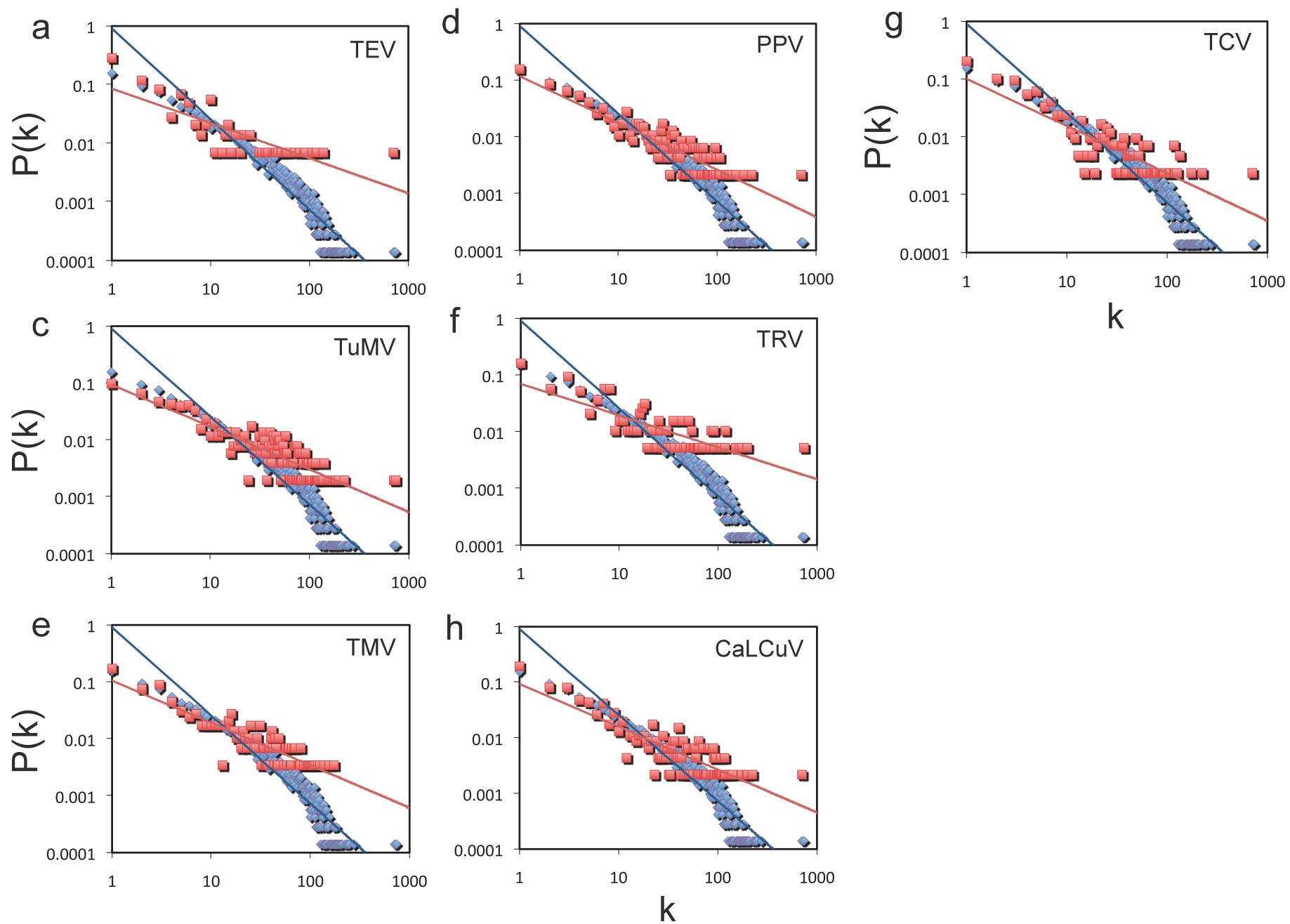


NJ similarity dendrogram for VRFs:
 $I_{cong} = 1.227$, $P = 0.101$

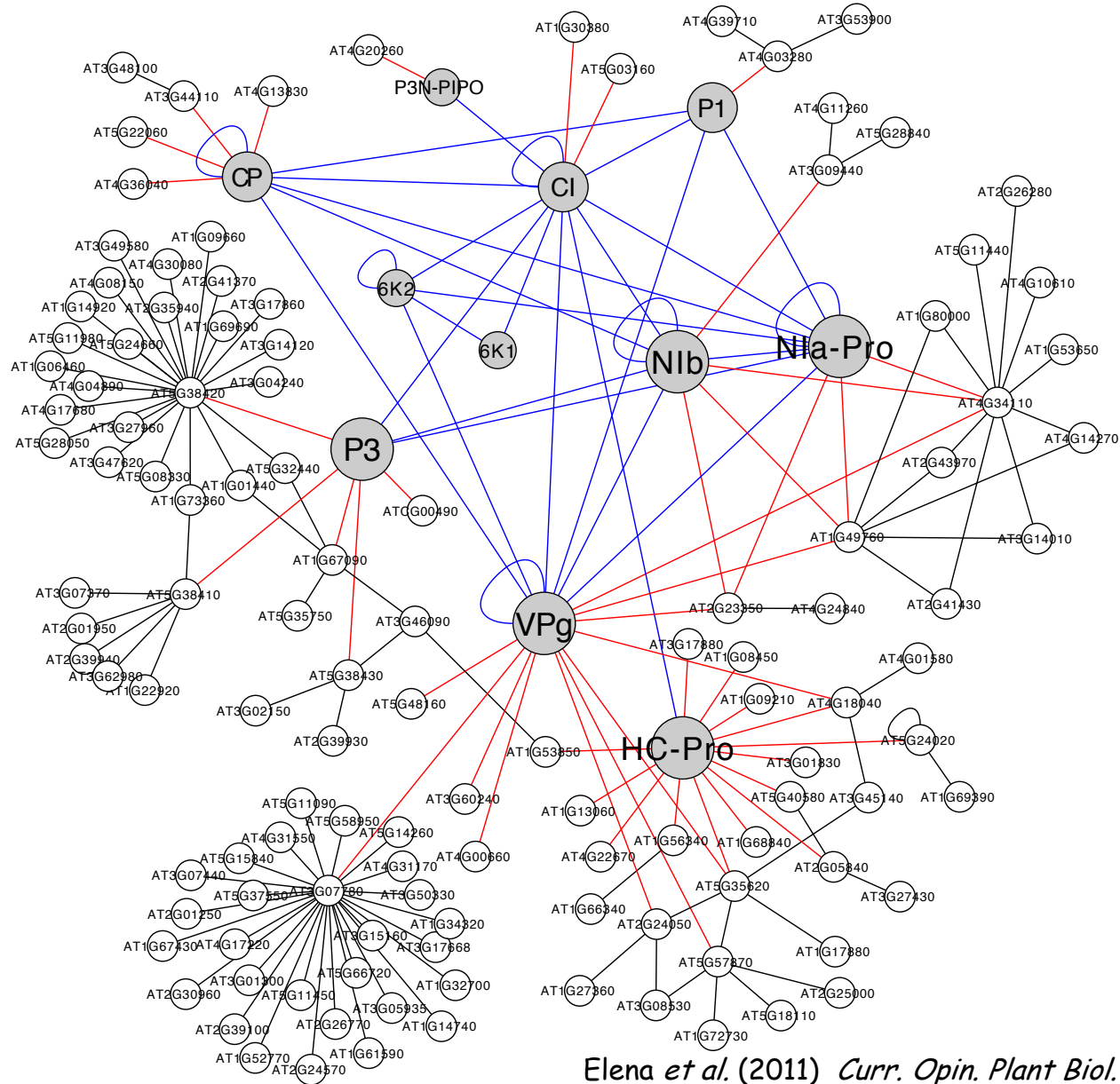
1.2. Mapping VRGs into *A. thaliana* TRN and PPIN







The potyvirus-host PPIN



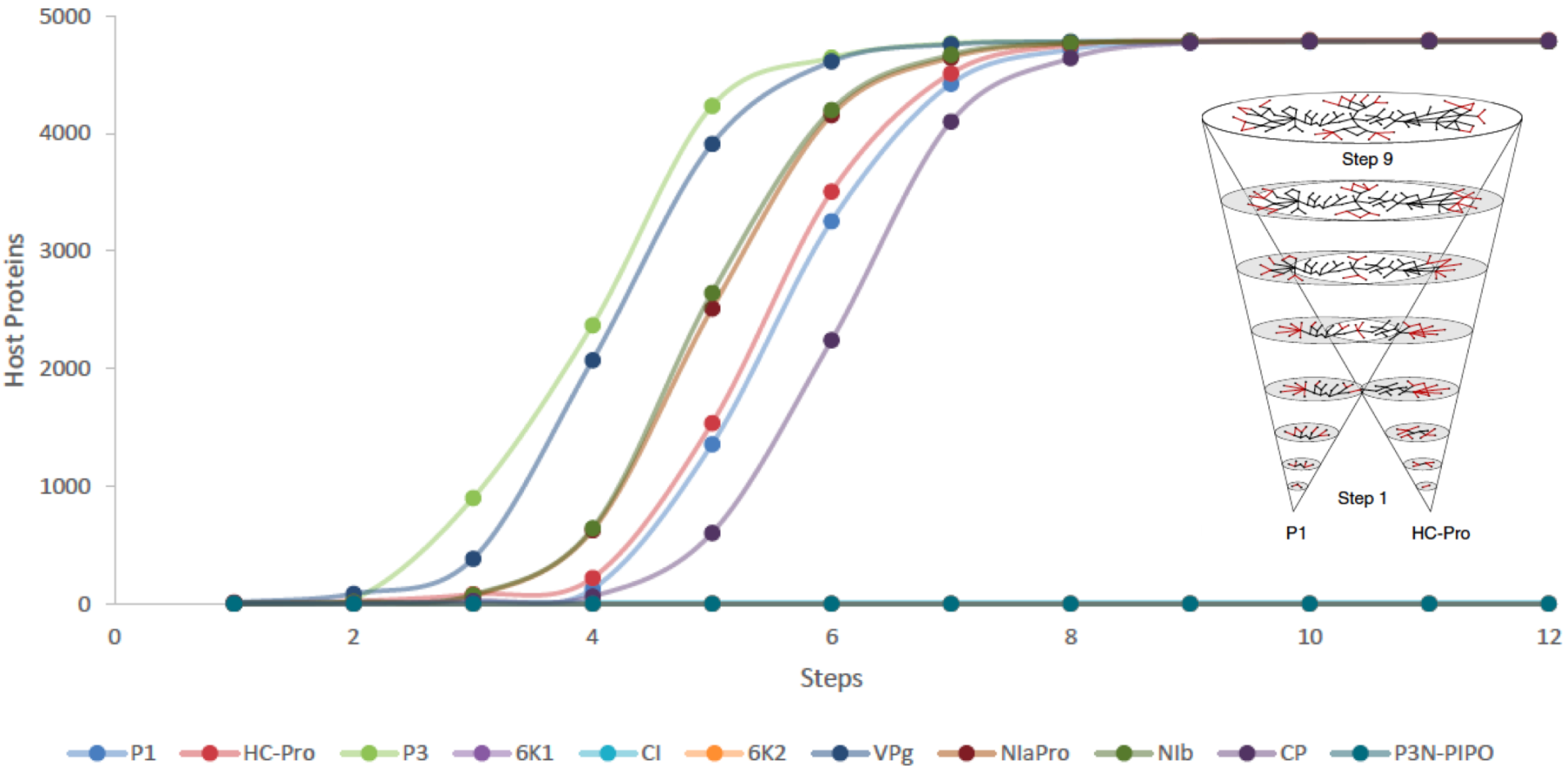
Elena *et al.* (2011) *Curr. Opin. Plant Biol.* **14**, 372

Bosque *et al.* (2014) *BMC Syst. Biol.* **8**, 129

Folch-Vidal *et al.* (2016) *Mol. BioSys.* **12**, 253

Martínez *et al.* (2016) *BMC Genomics* **17**, 87

The potyvirus-host PPIN



Number of VRGs, interactions and degree of connectivity for different viruses for the *A. thaliana* TRN and PPIN.

Virus	VRGs ^a	Interactions ^{TRN}	$\langle k \rangle^{TRN}$	Interactions ^{PPIN}	$\langle k \rangle^{PPIN}$
Viruses naturally infecting Brassicaceae					
CaLCV	1186	2108	255	664	24
TCV	1554	4326	188	364	19
TEV- <i>At17</i>	2391	2840	115	881	22
TuMV	1144	1026	172	1665	34
Average	1568.75	2575.00	182.50	893.50	24.75
Viruses not naturally infecting Brassicaceae					
PPV	1487	939	153	535	24
TEV	678	1269	162	64	18
TMV	723	67	76	214	22
TRV	499	82	111	154	26
Average	846.75	589.25	125.50	241.75	22.50
<i>P</i> ^b	0.047	0.020	0.077	0.035	0.282

^a Virus-regulated genes identified by differential expression in microarray data comparing mock-inoculated plants and plants infected by the corresponding virus.

^b Statistical significance assessed by one-tailed *t*-tests.

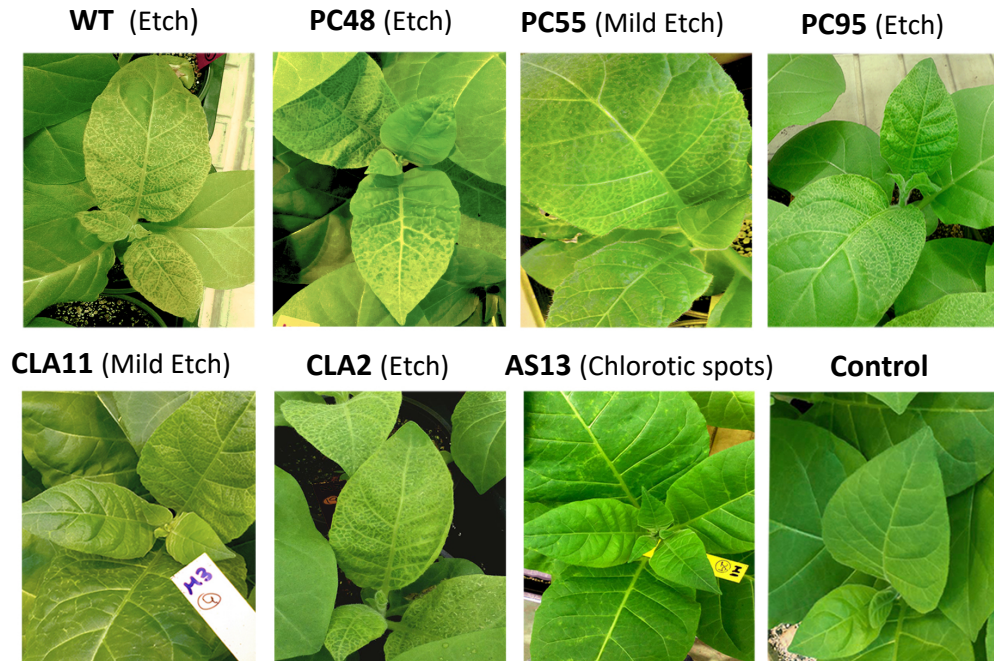
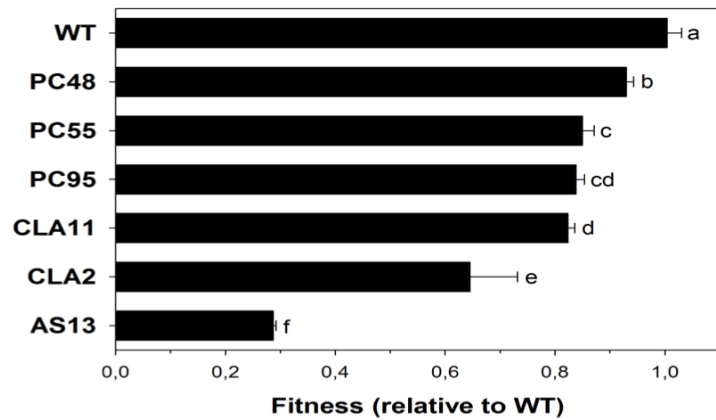
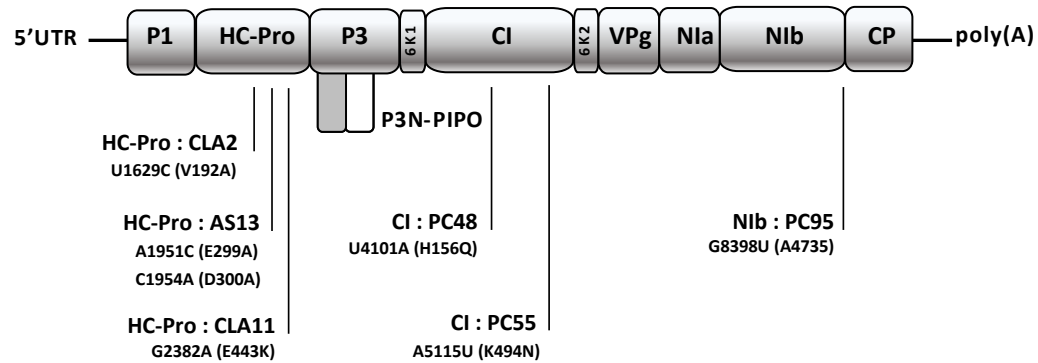
Yes... but *A. thaliana* is NOT a natural host for all these viruses

- ✓ Only TuMV is prevalent in wild *A. thaliana* populations.
- ✓ Infections of wild *A. thaliana* populations have not been described for CaLCuV, PPV, TEV, and TMV.
- ✓ CaLCuV naturally infect other plants of the *Brassicaceae* family.

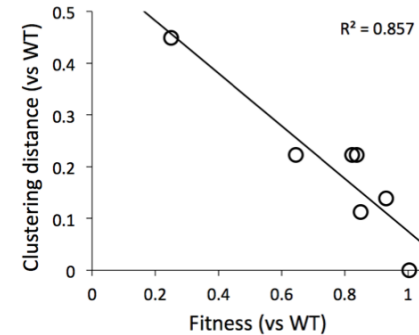
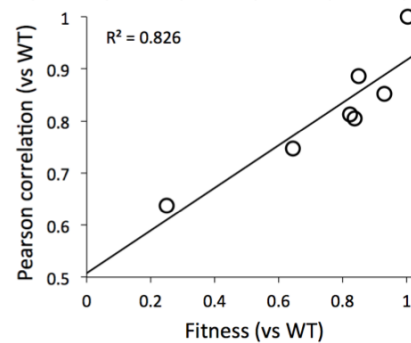
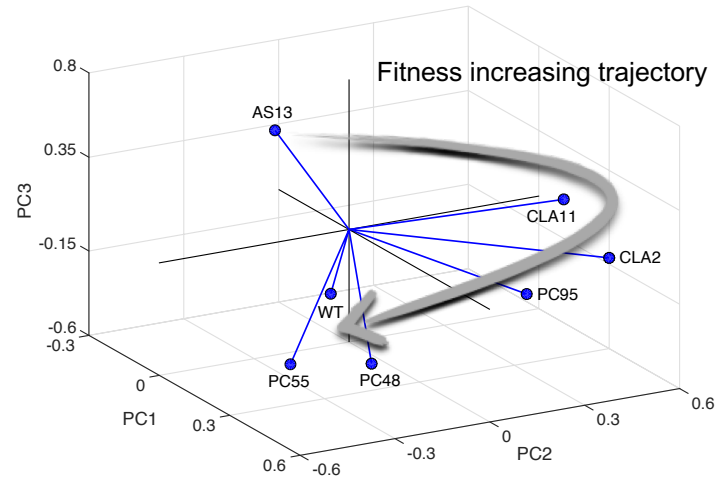
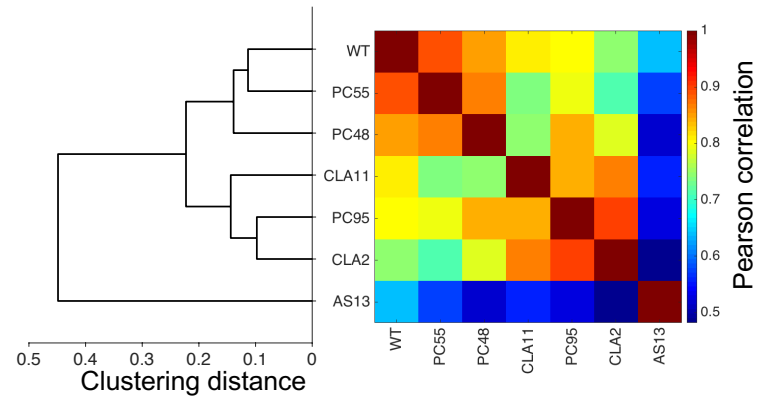
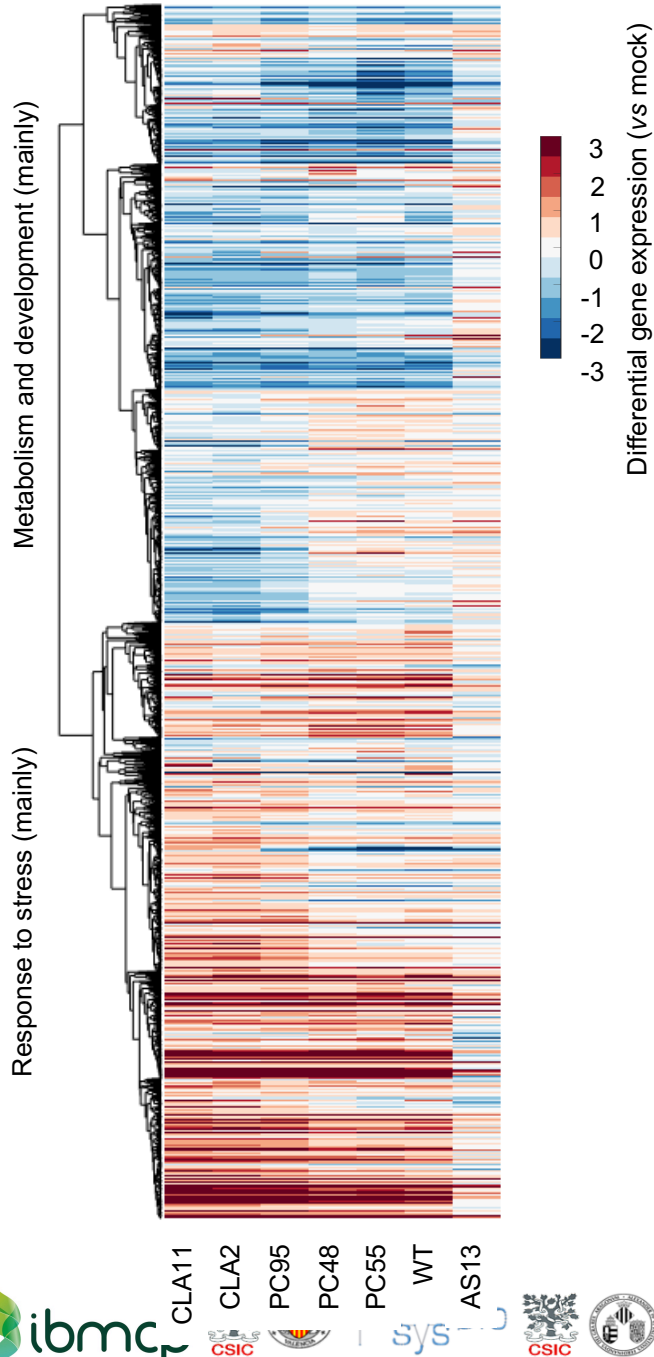
2. Relationship between virus adaptation to a host and the magnitude of the perturbation induced in the plant transcriptome

- ✓ Transcriptomic profiles of infected and control *Nicotiana tabacum* plants with a collection of TEV mutants that differ in the fitness and symptomatology.
- ✓ Agilent *N. tabacum* Gene Expression 4x44K Microarray.

Different mutants induce different symptoms

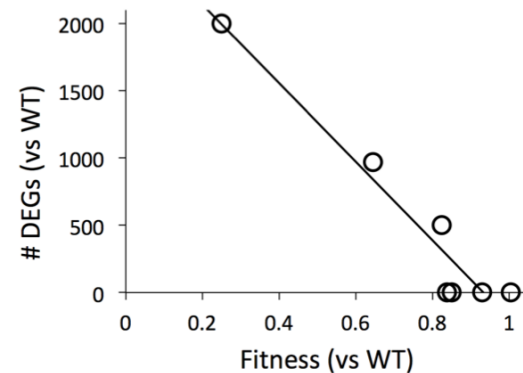
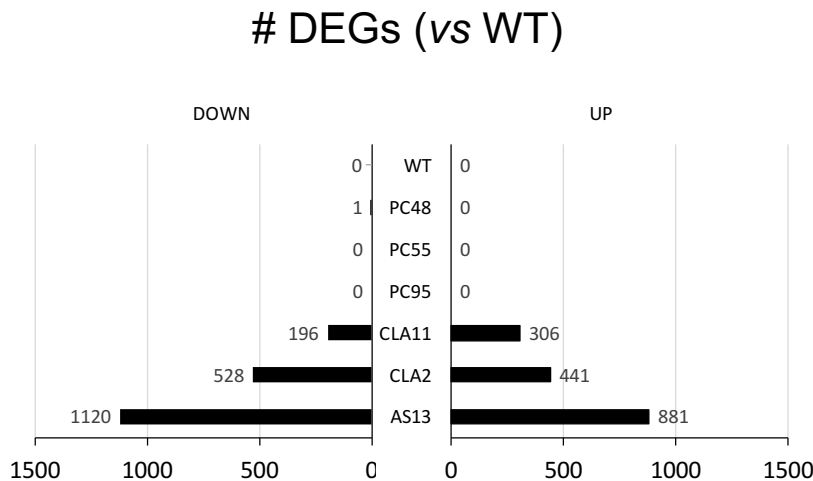
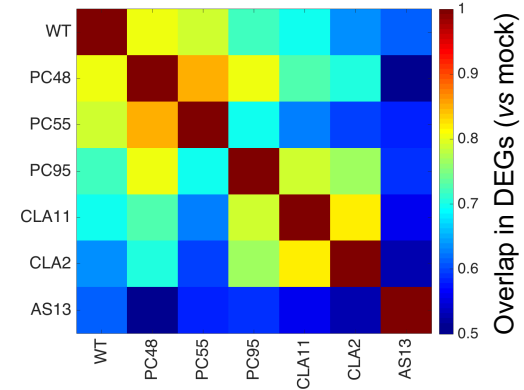
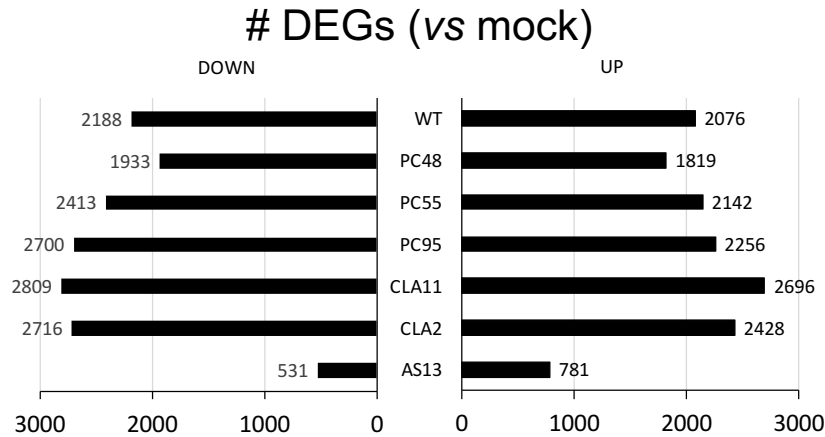


Host's gene expression correlates with TEV fitness



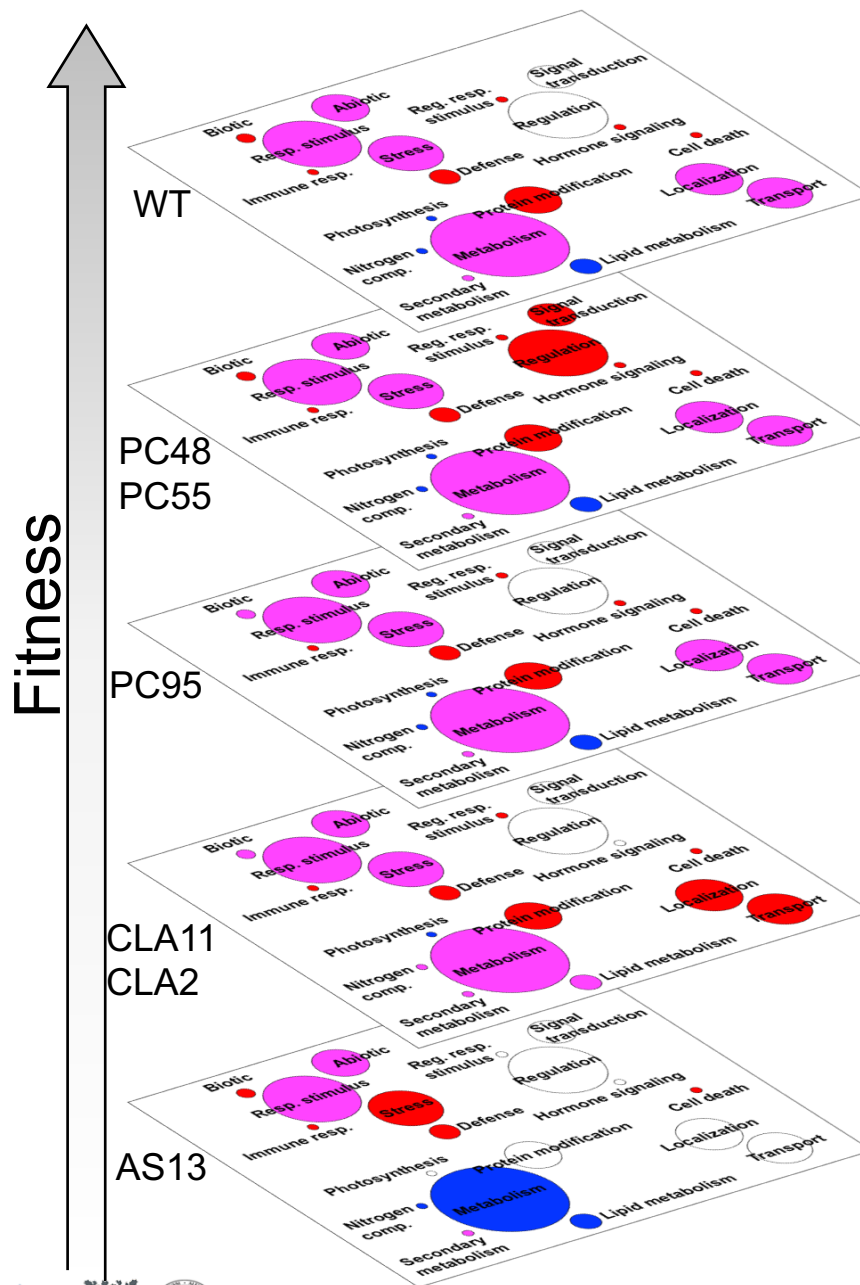
Cervera et al. (2018) *Mol. Biol. Evol.* In press

Altered functional categories and TEV fitness

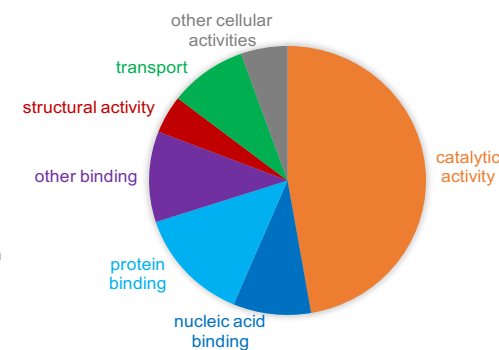
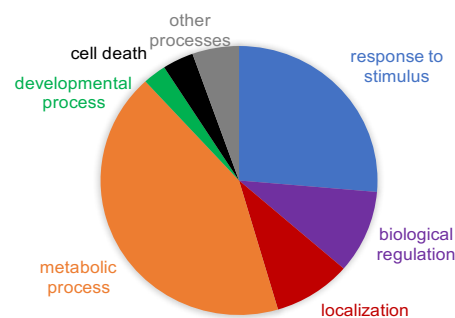
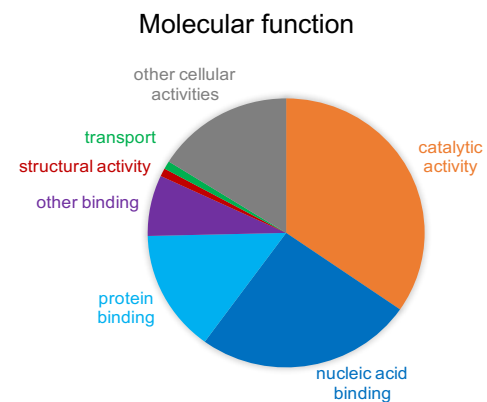
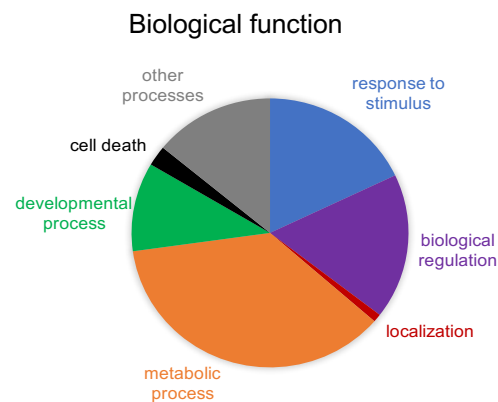
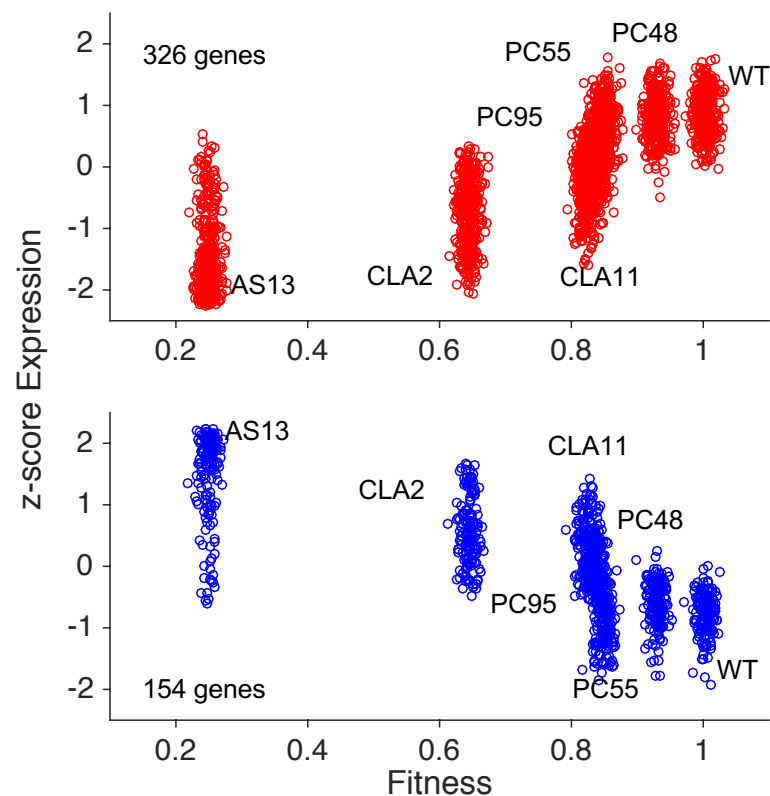


Over-represented relative to mock

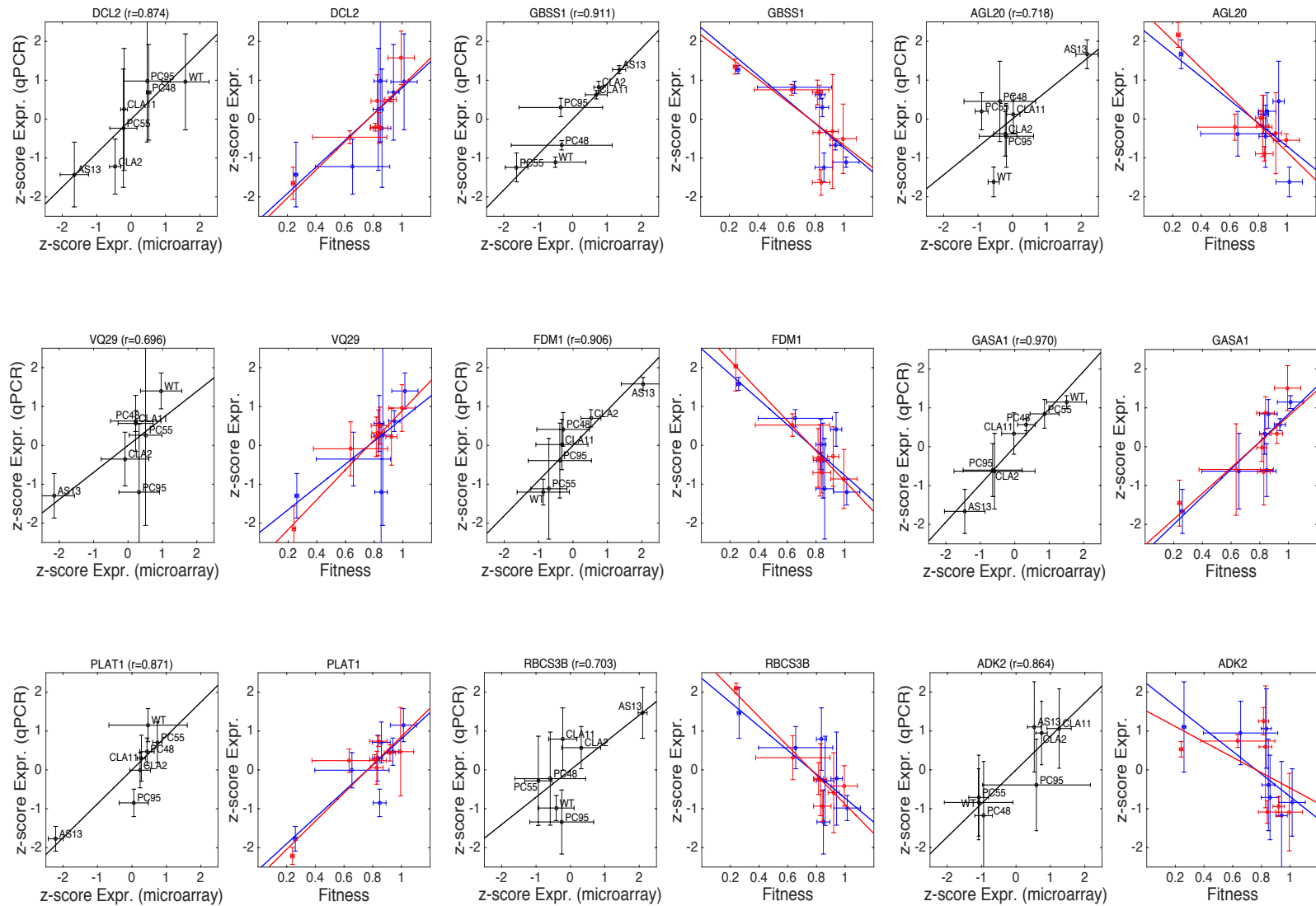
- DEGs UP
- DEGs DOWN
- DEGs UP & DOWN



Identifying genes and processes whose expression varies with TEV fitness



Validating data



Microarray quantification of gene expression —
RT-qPCR quantification of gene expression —

