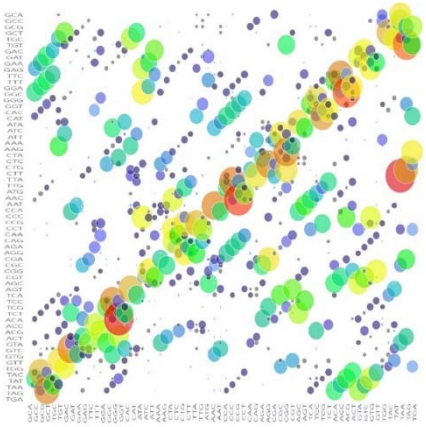
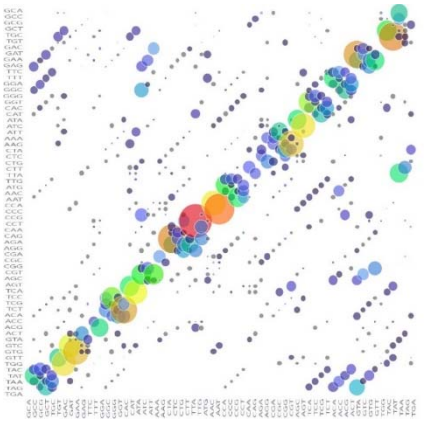
Evidence for adaptive translation in *S. sclerotiorum*

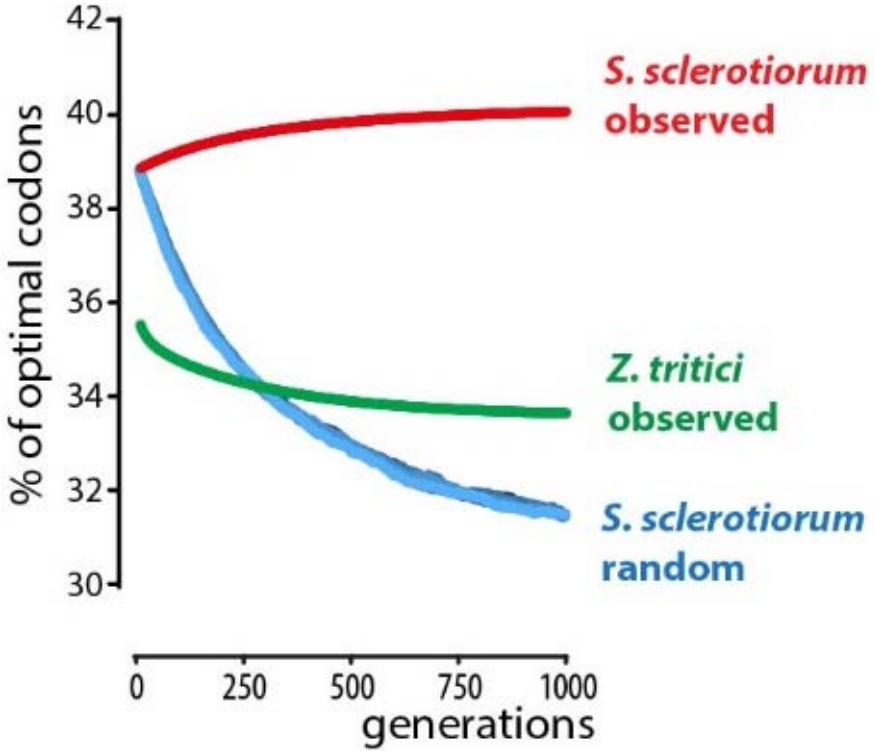
- Codon substitution matrix



Zymoseptoria tritici

Hosts: Wheat (1 species)
9 Swiss isolates
14 571 coding SNP/isolate
Source: Croll *et al*. Plos Patho. 2013



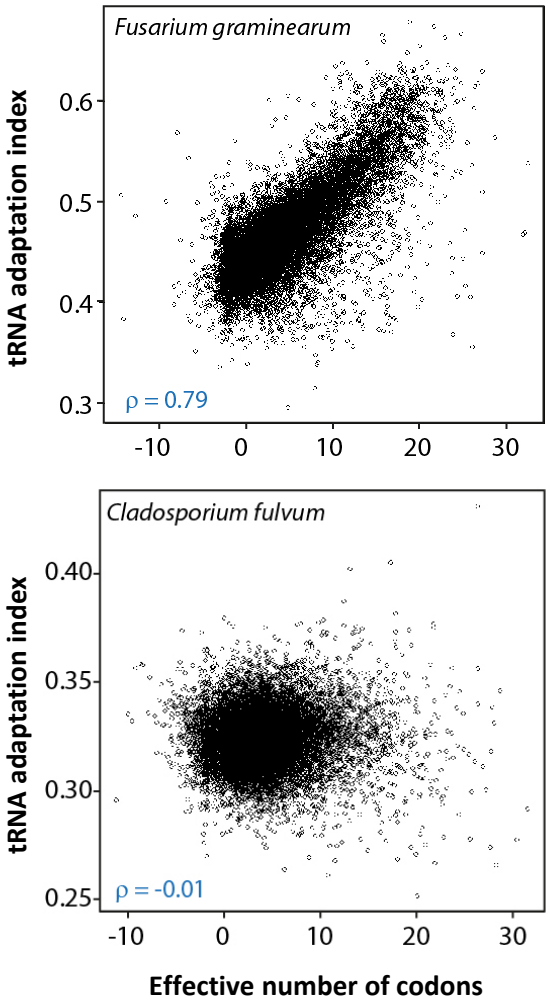


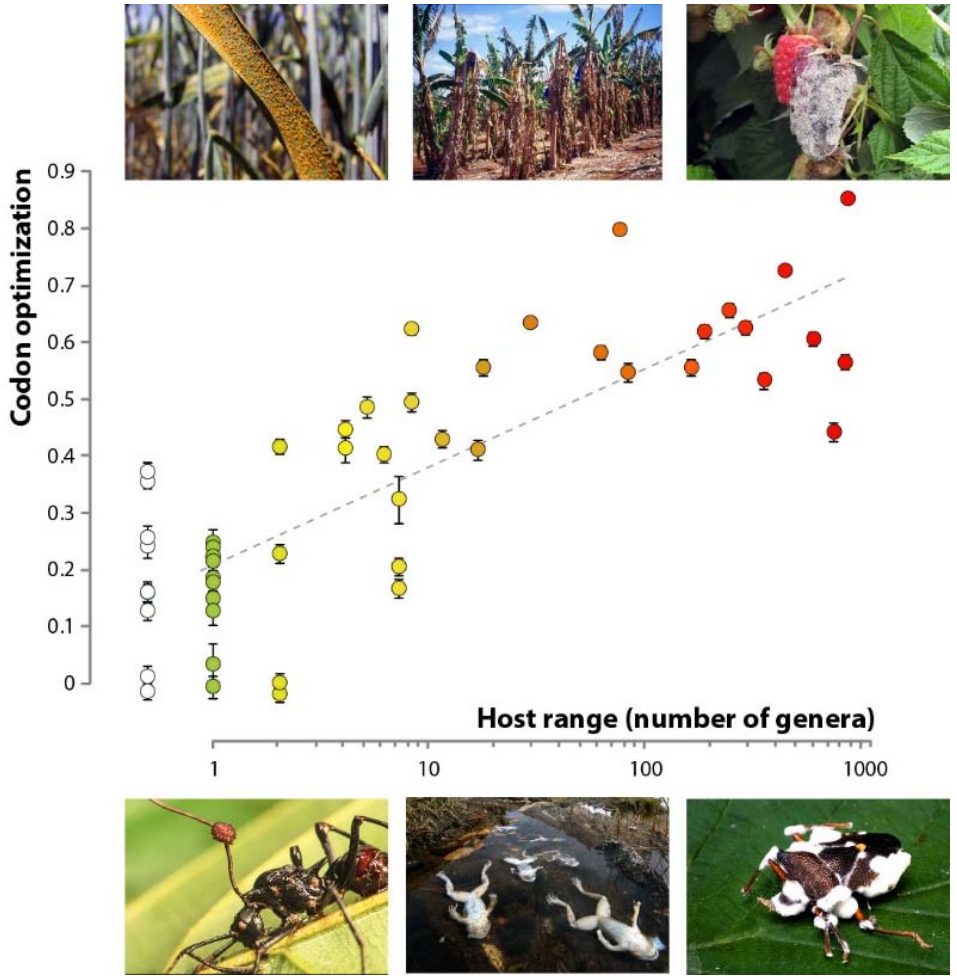
- SNP patterns in *S. sclerotiorum* supports increased translation efficiency

Is this evolutionary pattern related with Sclerotinia lifestyle?

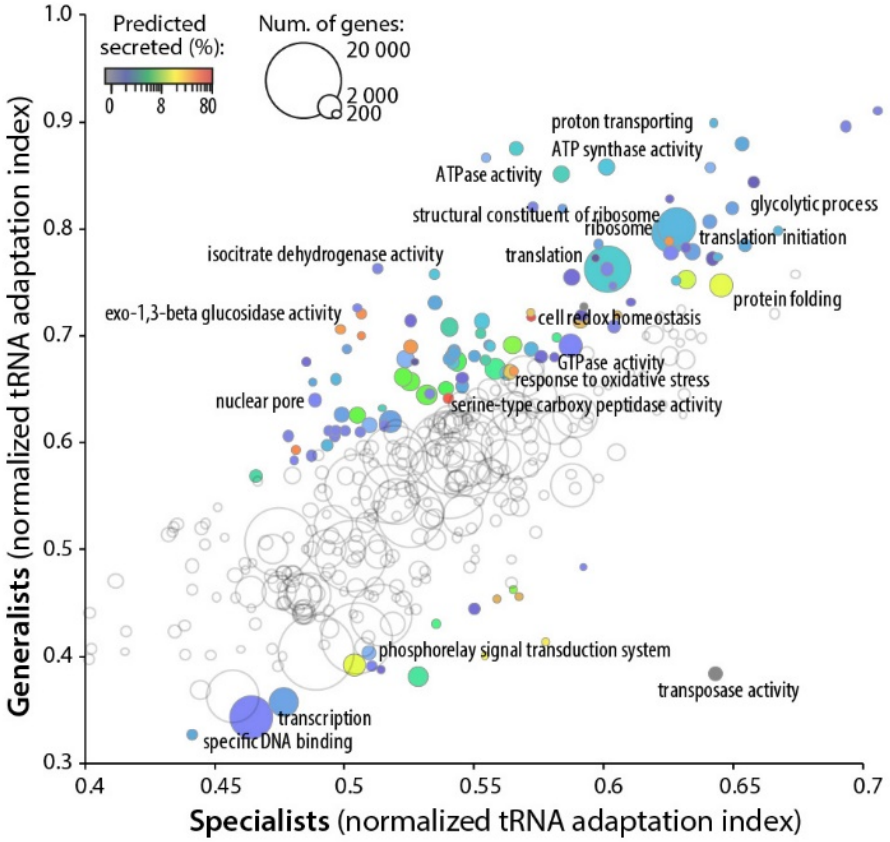
Codon adaptation correlates with host range in Fungi

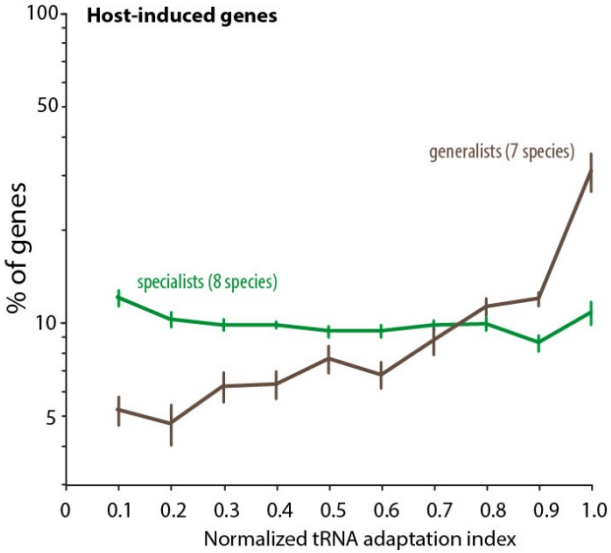
Adaptive translation at
the genome scale

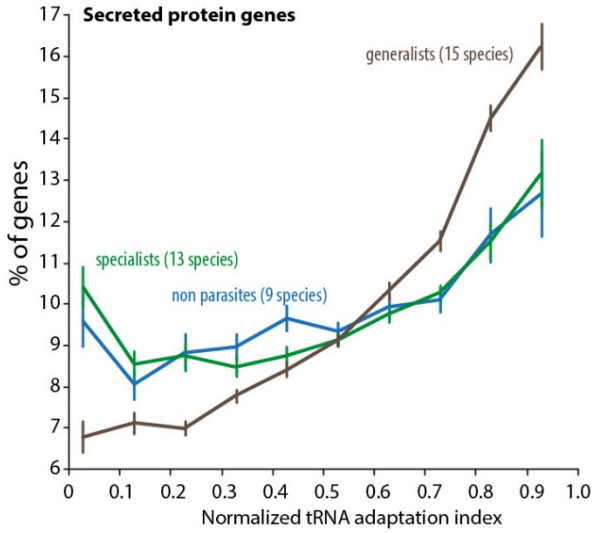




Codon adaptation is stronger in infection-related genes

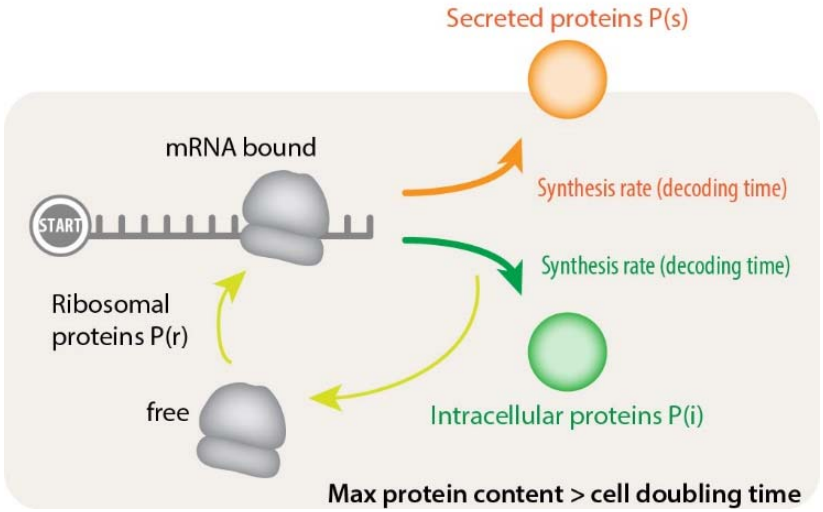


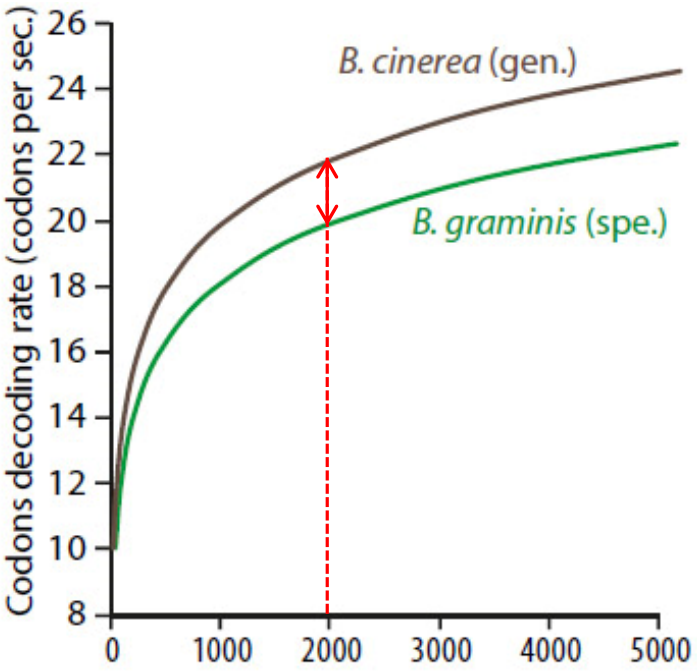


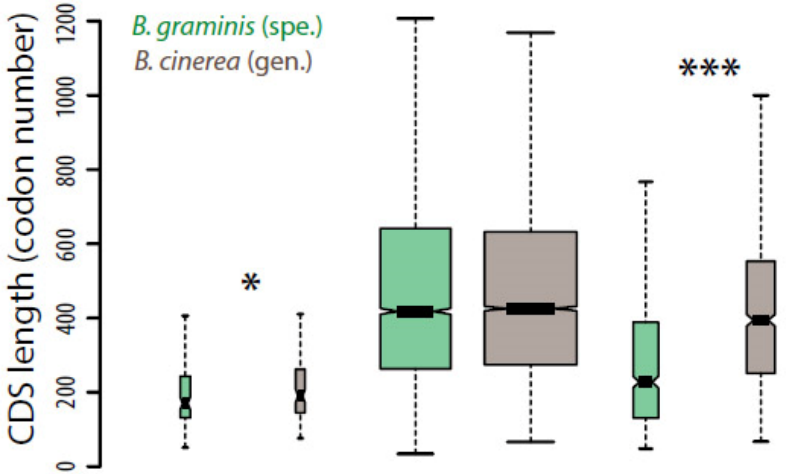


- Codon optimization reduces the 'cost of production' of all effectors simultaneously

Why is adaptive translation stronger in generalist fungi?

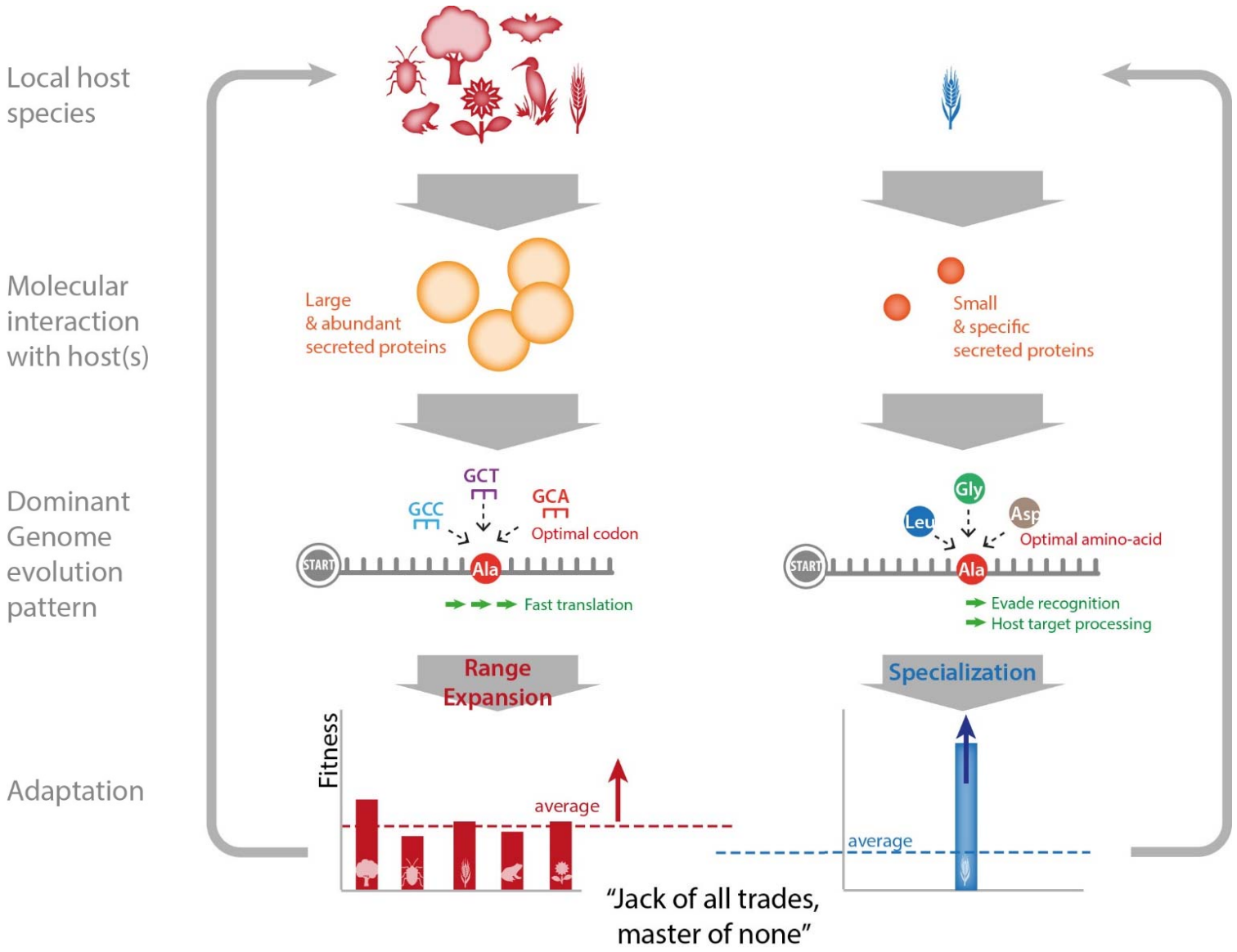






- *B. cinerea* must decode codons faster to reach the same growth rate as *B. graminis*

Conclusion: Adaptation to multiple hosts at the codon level

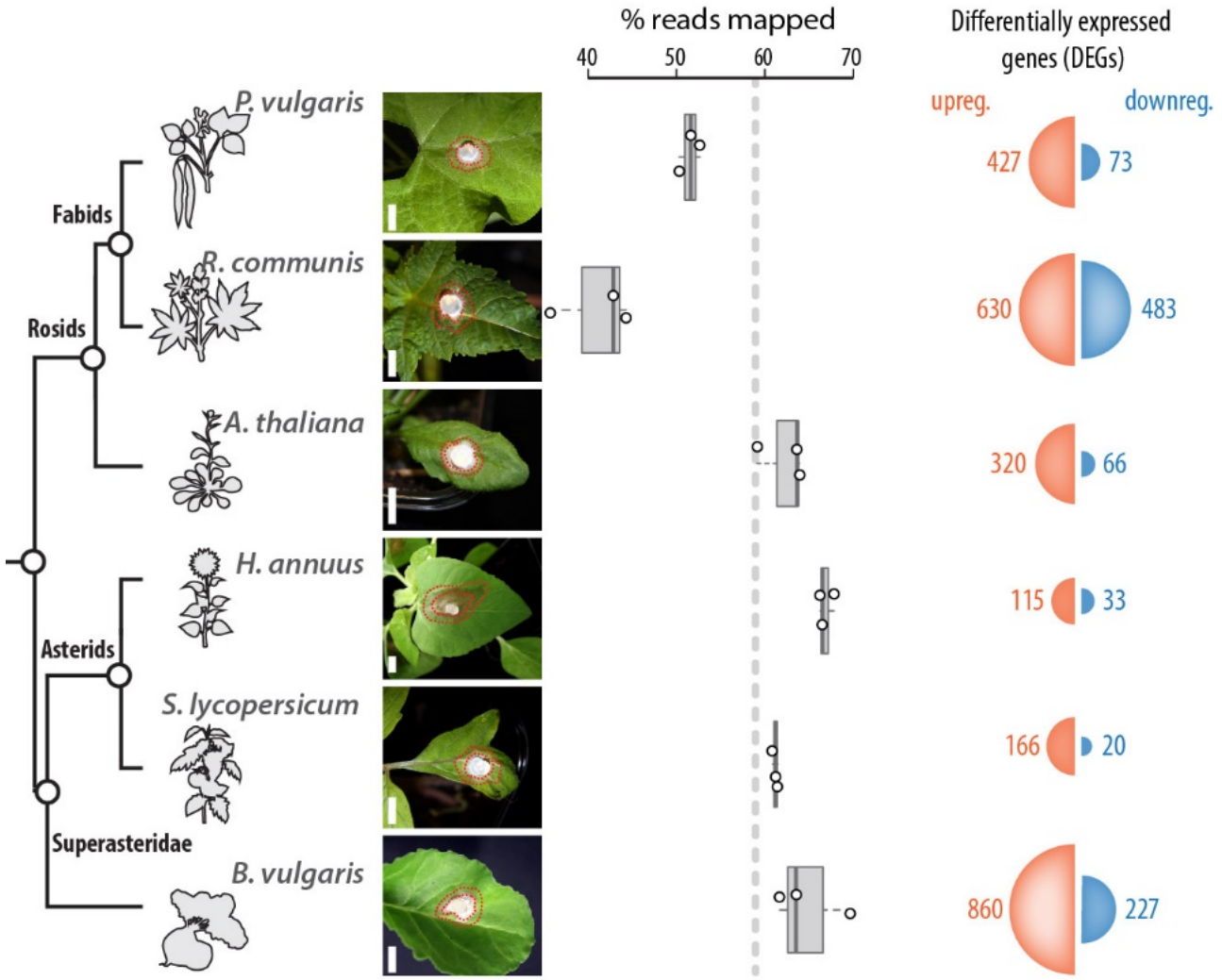


Badet, Peyraud, Mbengue *et al.*, eLife. **2017**

Transcriptional plasticity and host range expansion

Ingredients:
Transcriptomics (RNAseq), comparative genomics

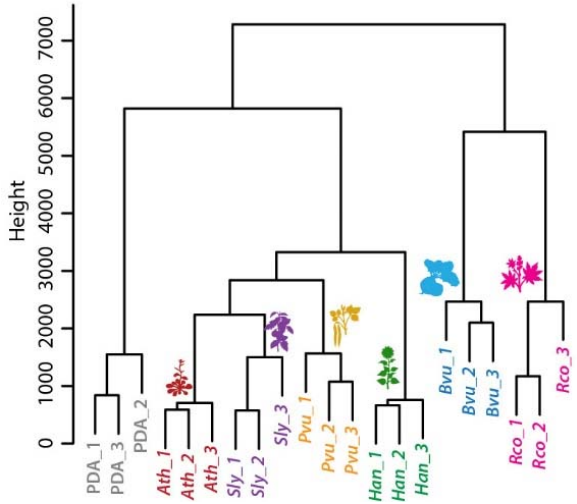
S. sclerotiorum transcriptome: one pattern fits all hosts?

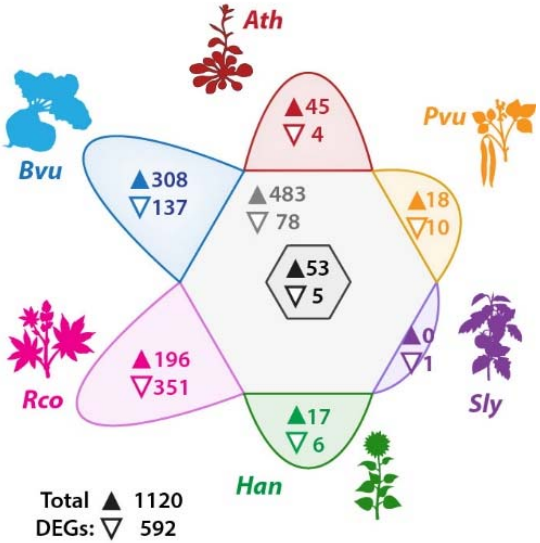


RNAseq on hosts from 6 botanical families

Strong variation in DEG number according to host

S. sclerotiorum host-specific transcriptome

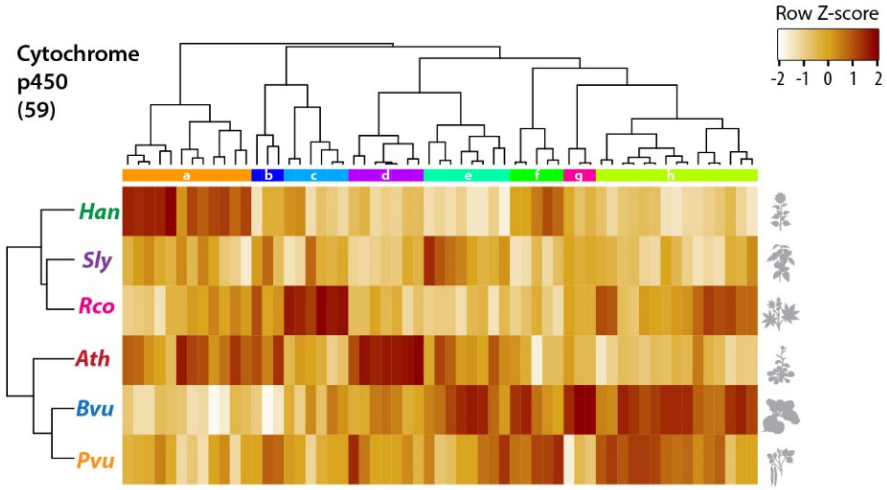


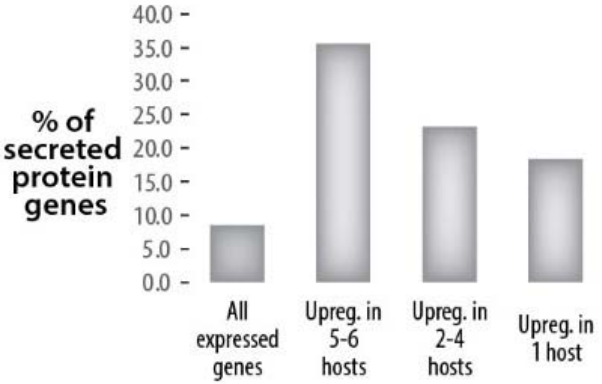


4.7% of DEGs up on all hosts

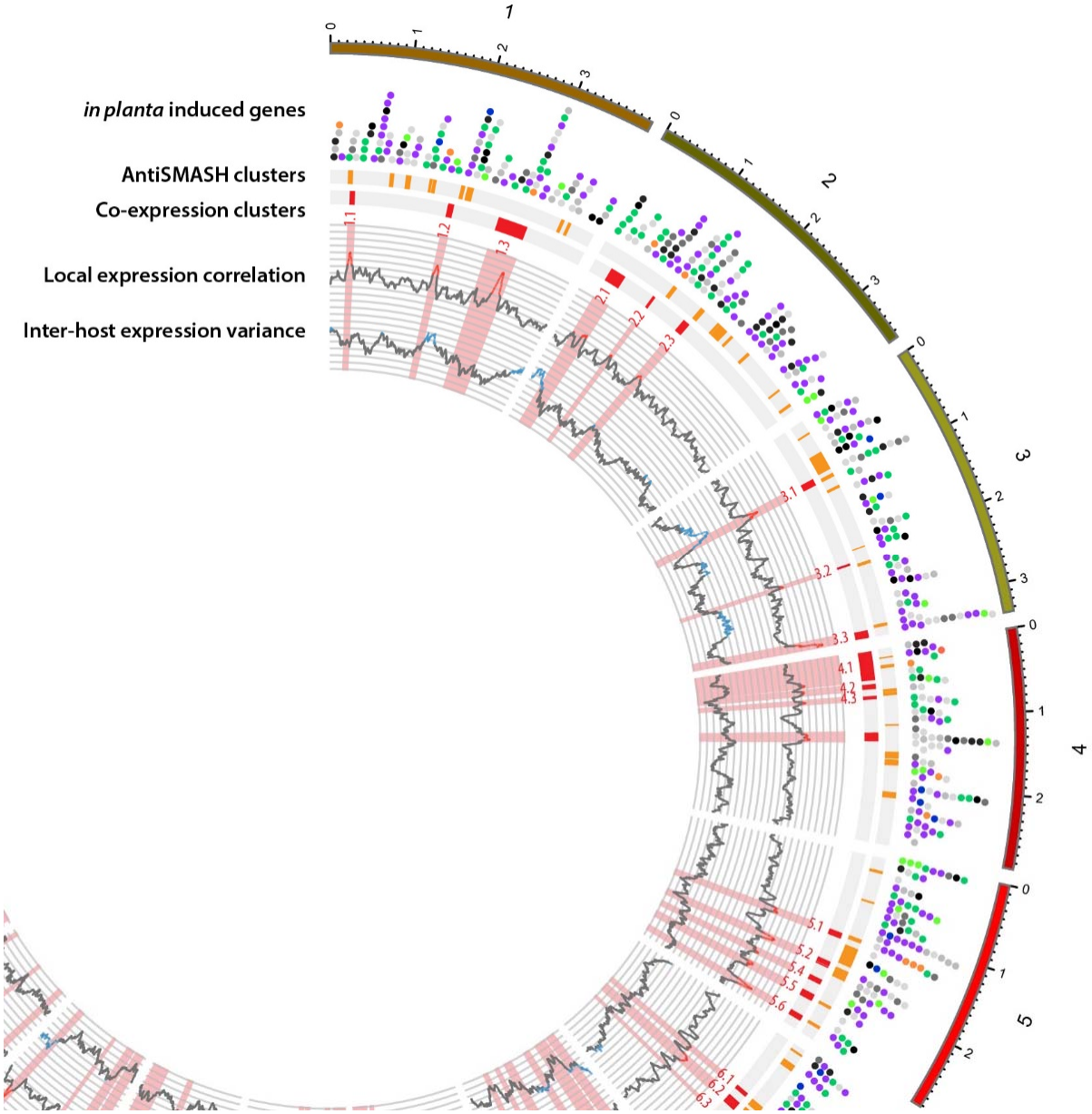
Some hosts trigger specific reprogramming

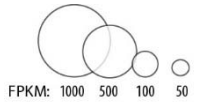
Host specific signatures of gene family regulation



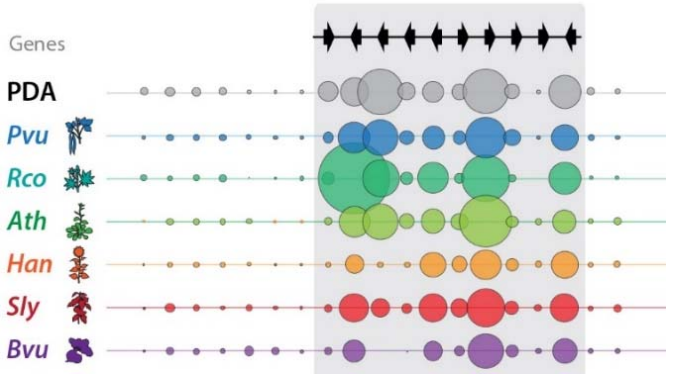


Generalist and host-specialized genomic clusters

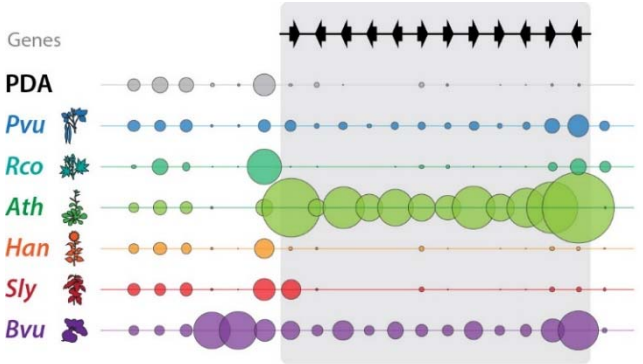




~17% of host-induced genes occur in 58 clusters

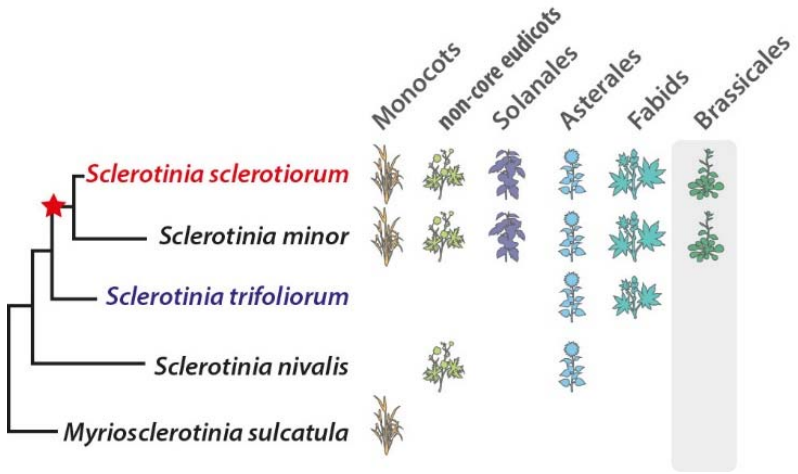


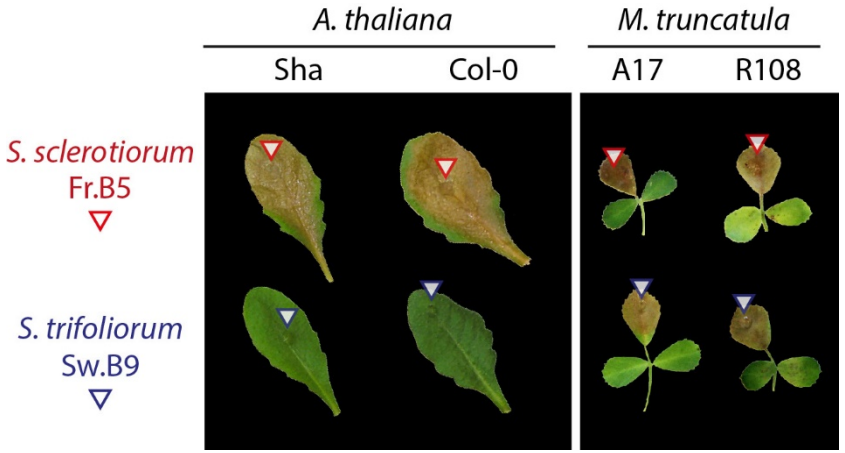
Some are host-specialized



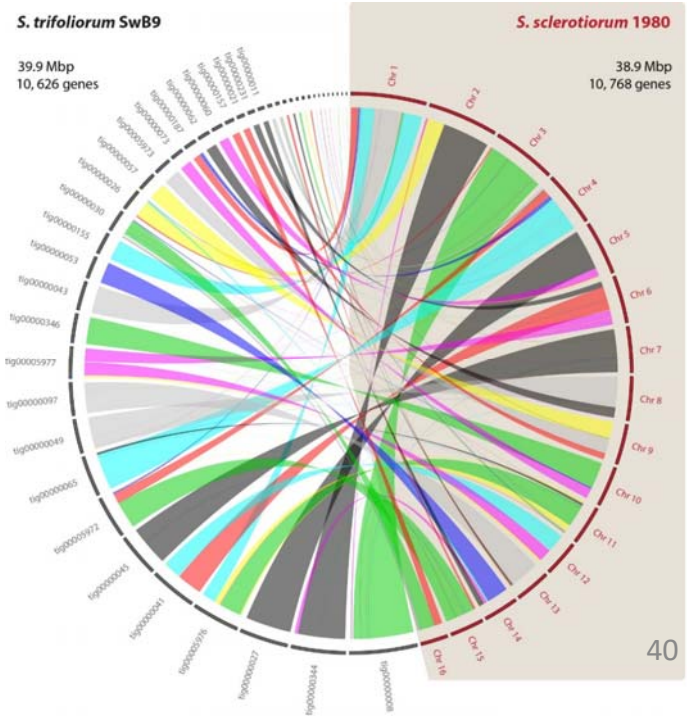
S. trifoliorum genome assembly

- *S. trifoliorum* is non pathogenic on Brassicales





Evolution of *A. thaliana*-specific upregulated genes in the *Sclerotinia* lineage ?

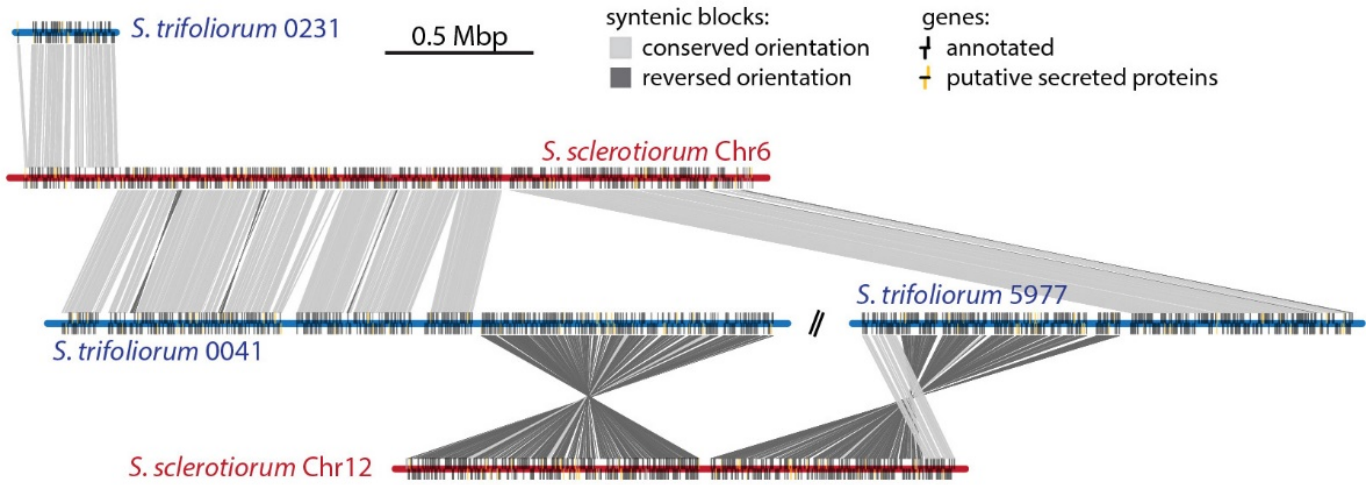


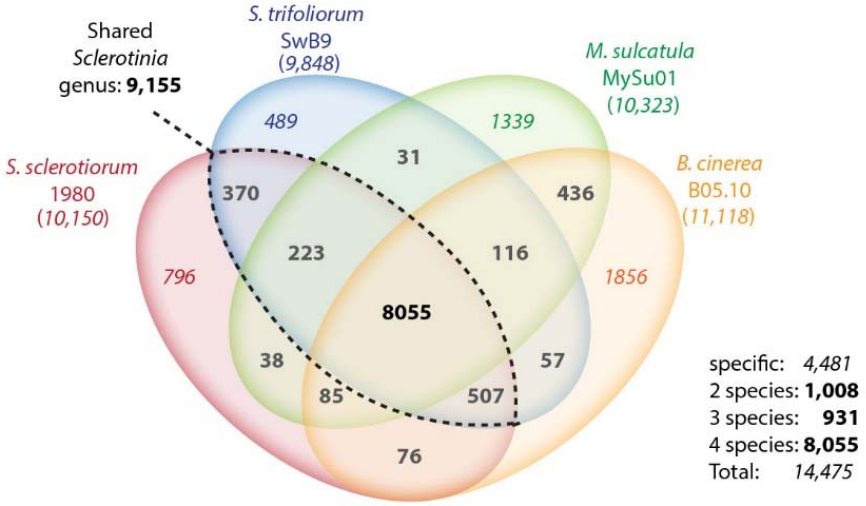
Nanopore sequencing of *S. trifoliorum* SwB9

Annotation: 10 626 protein-coding genes

S. trifoliorum genome assembly

Synteny with *S. sclerotiorum*

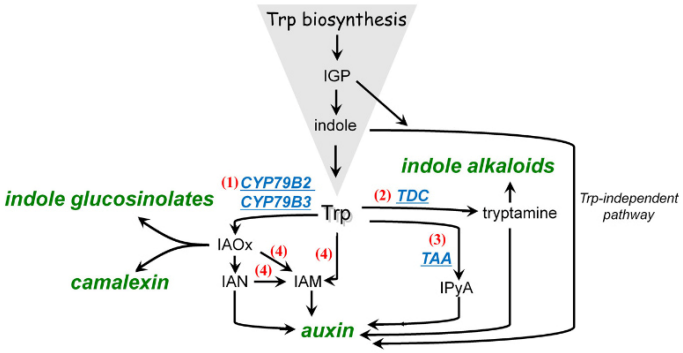


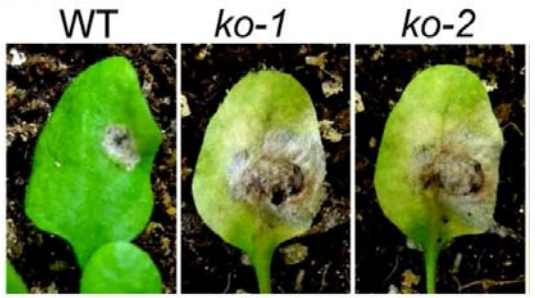


42/45 *S. sclerotiorum* genes upregulated specifically on *A. thaliana* have orthologs in *S. trifoliorum*

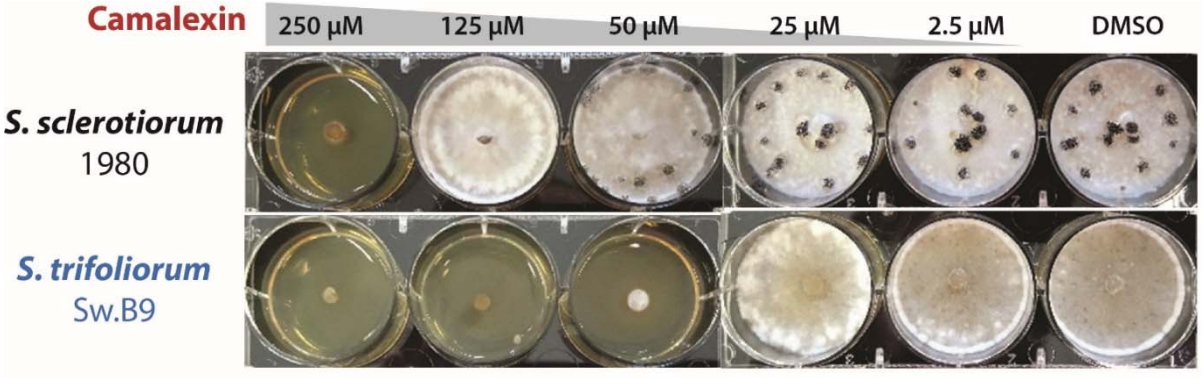
Importance of genes acquired prior to the divergence between *S. sclerotiorum* and *S. trifoliorum*

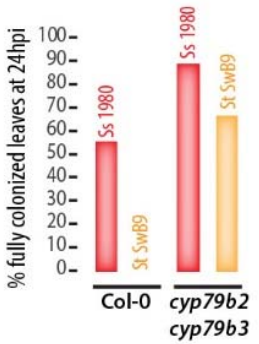
How does *S. trifoliorum* respond to Brassicales phytoalexins ?



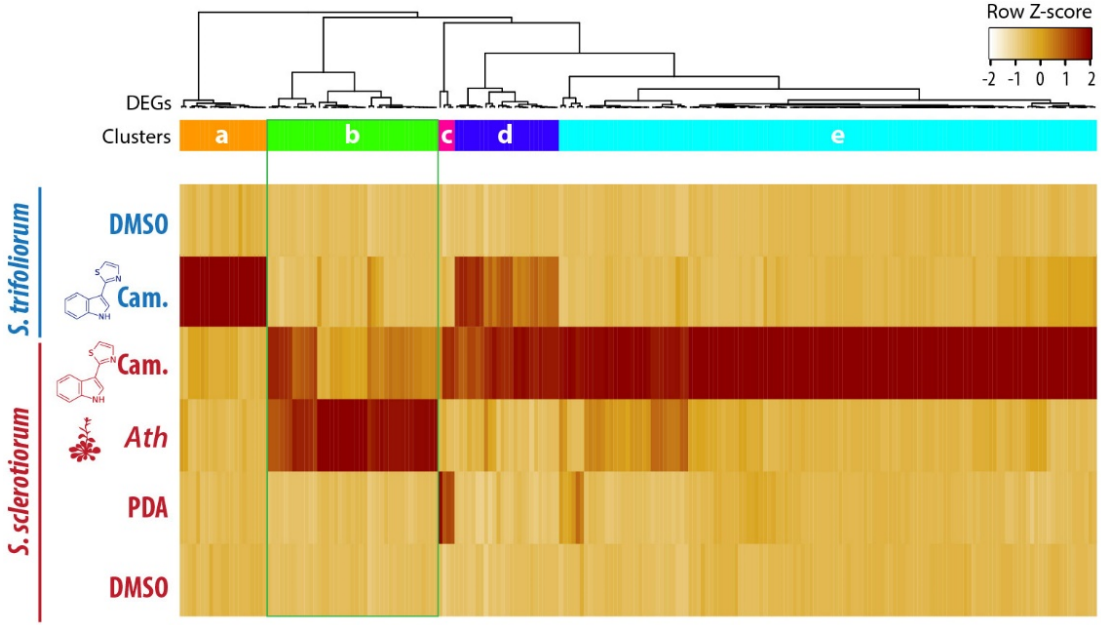


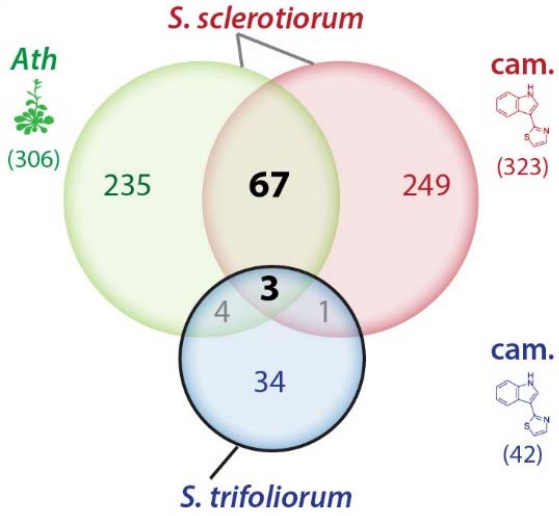
- *S. trifoliorum* shows enhanced susceptibility to camalexin

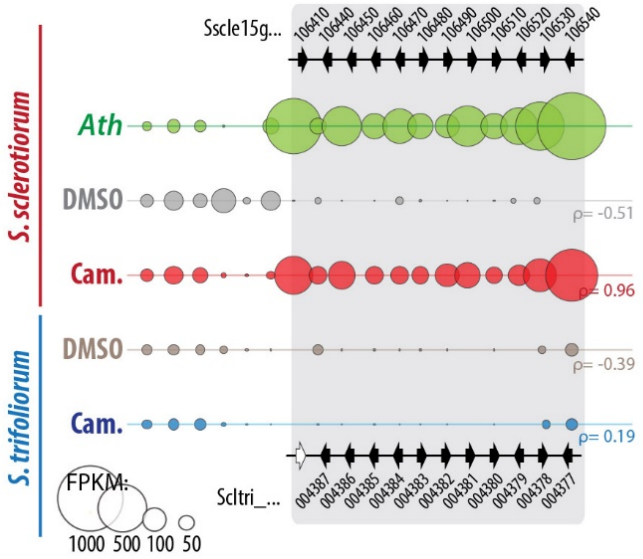




S. trifoliorum transcriptome is « blind » to camalexin



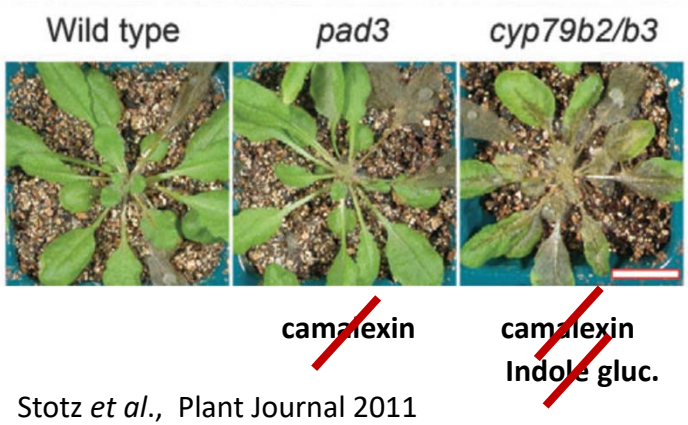




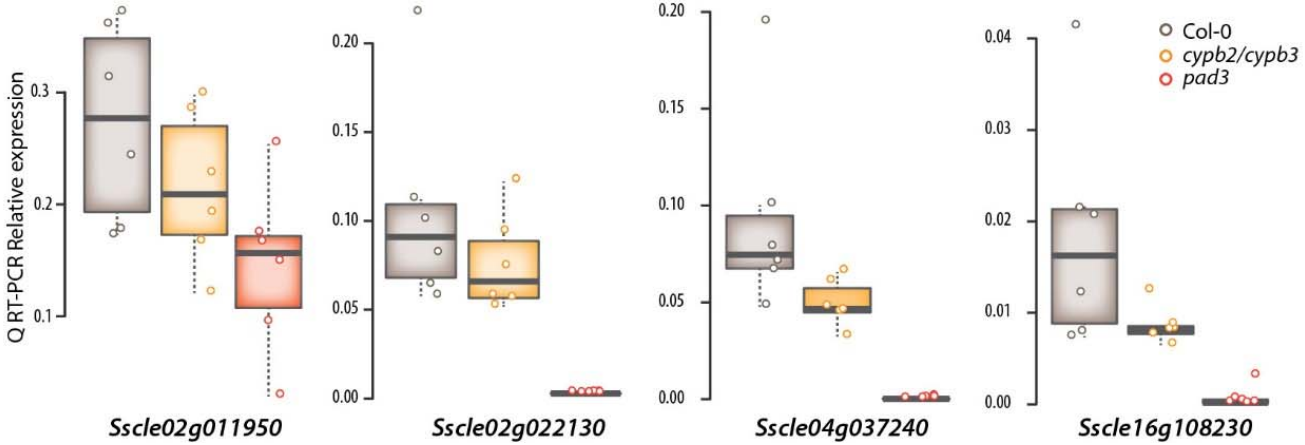
70 *S. sclerotiorum* genes induced during *Arabidopsis* infection and by camalexin

Responsiveness to camalexin associated with expansion of *Sclerotinia* host range

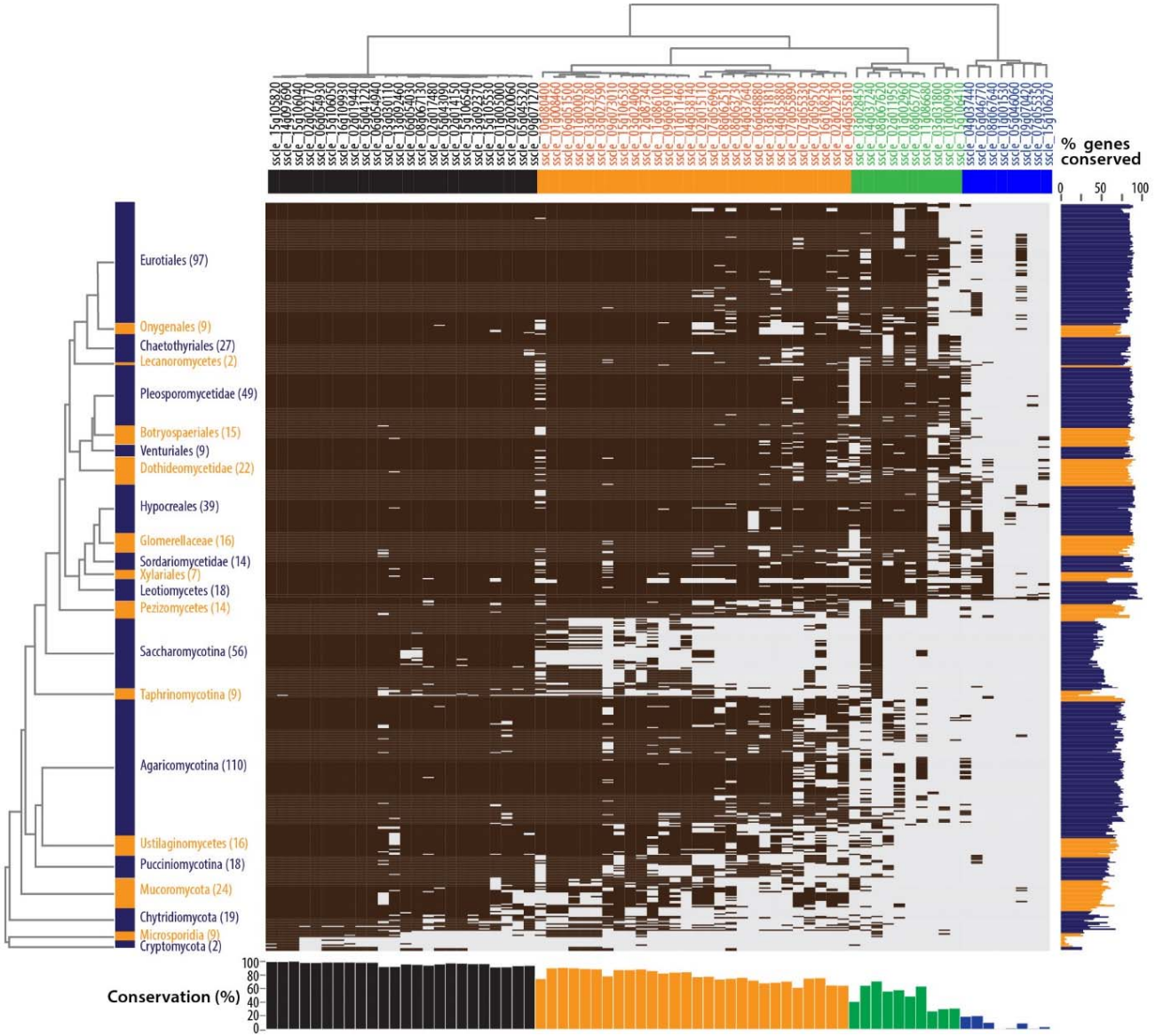
host-specific cues activate plant responsive genes in *S. sclerotiorum*



Stotz *et al*., Plant Journal 2011



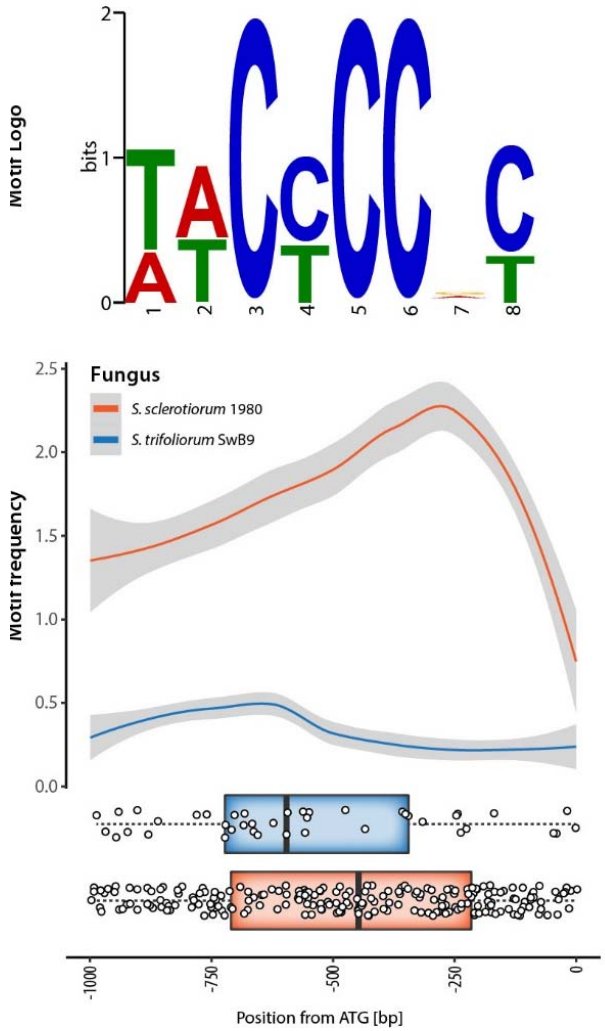
S. Sclerotiorum host-specific genes are well conserved



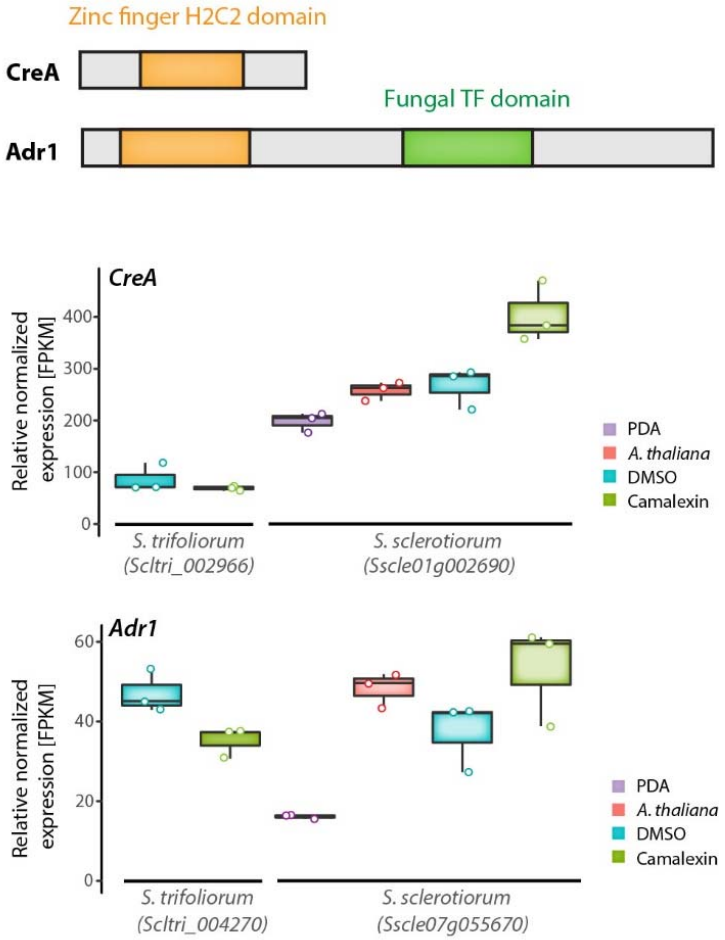
649 fungal species

Cis-regulatory variation & host range expansion

Motif in promoter of *S. sclerotiorum* host-specific genes

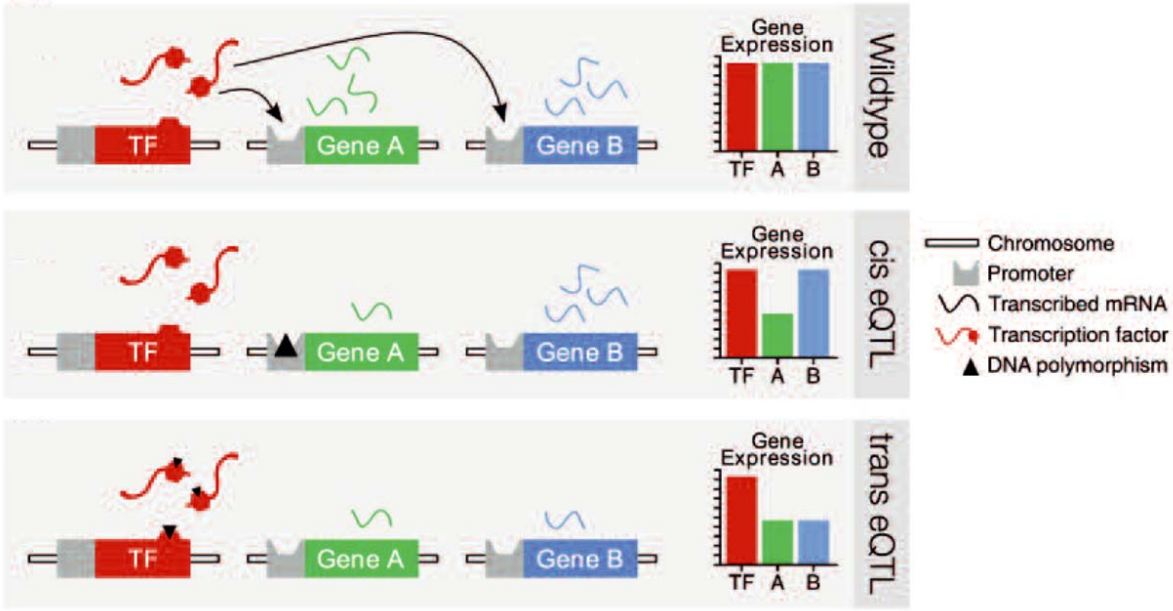


Predicted binding transcription factors



Kusch *et al.*, bioRxiv **2020**

Host adaptation through regulatory variation



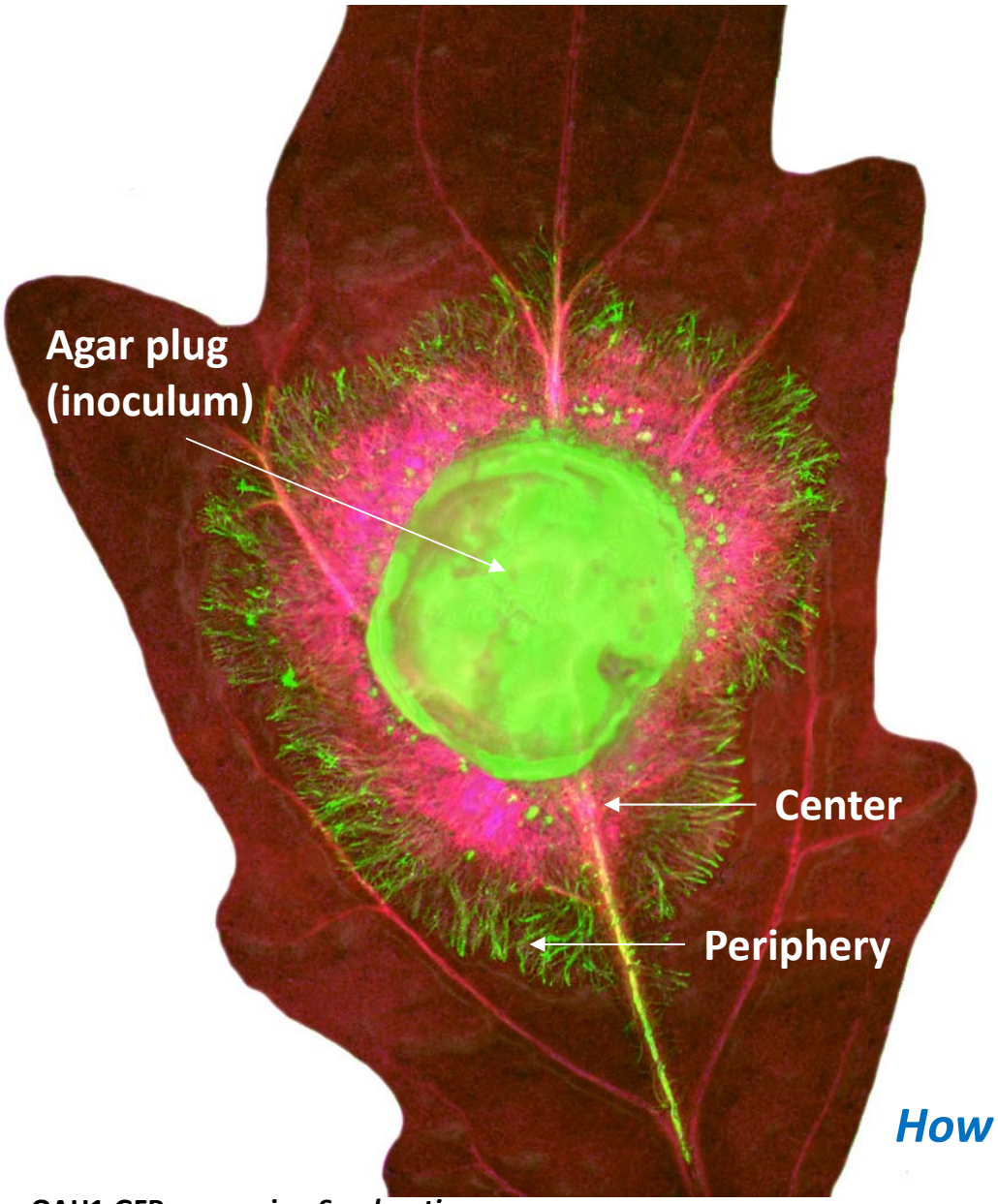
Reduced deleterious pleotropic effect

Evolvable with limited gene flow

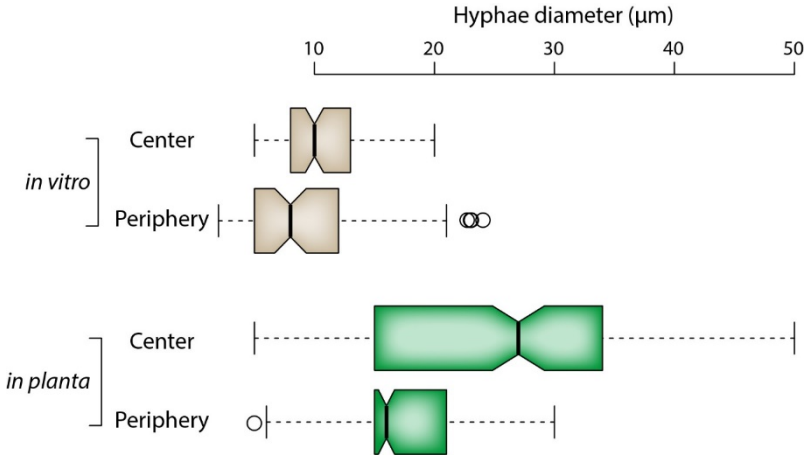
Division of labor supports the colonization of resistant plants

Ingredients:
Transcriptomics (RNAseq), modelling

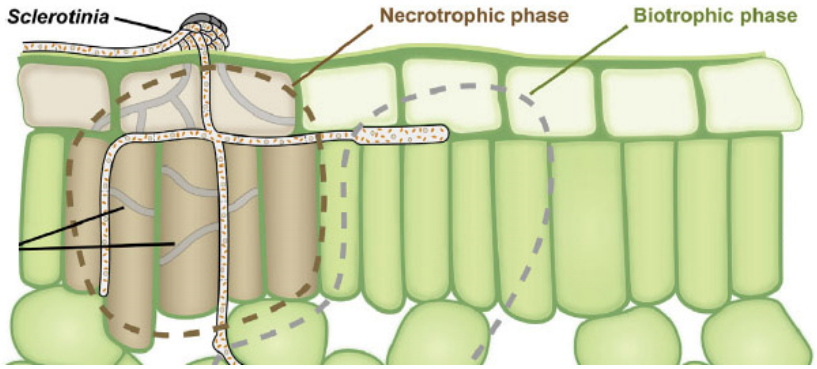
S. sclerotiorum forms heterotypic colonies *in planta*



OAH1:GFP-expressing *S. sclerotiorum*



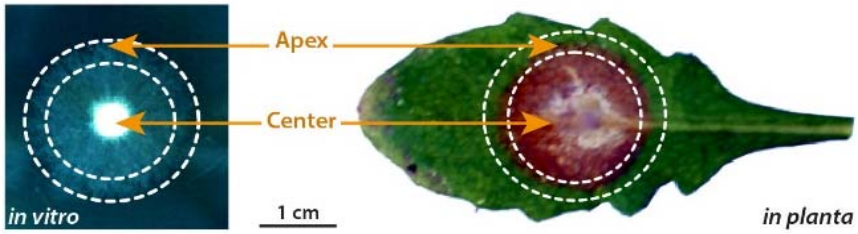
Adapted from **Lumsden & Low 1973**

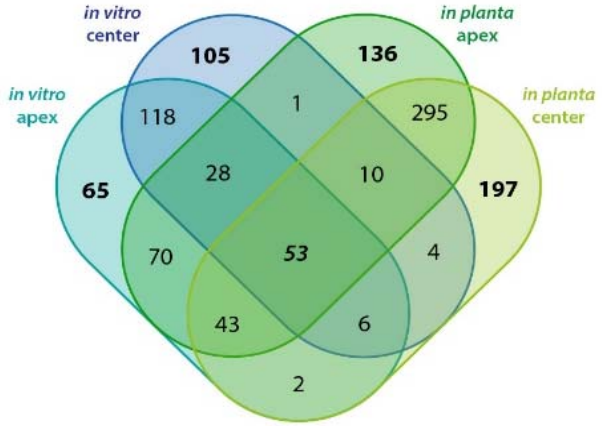


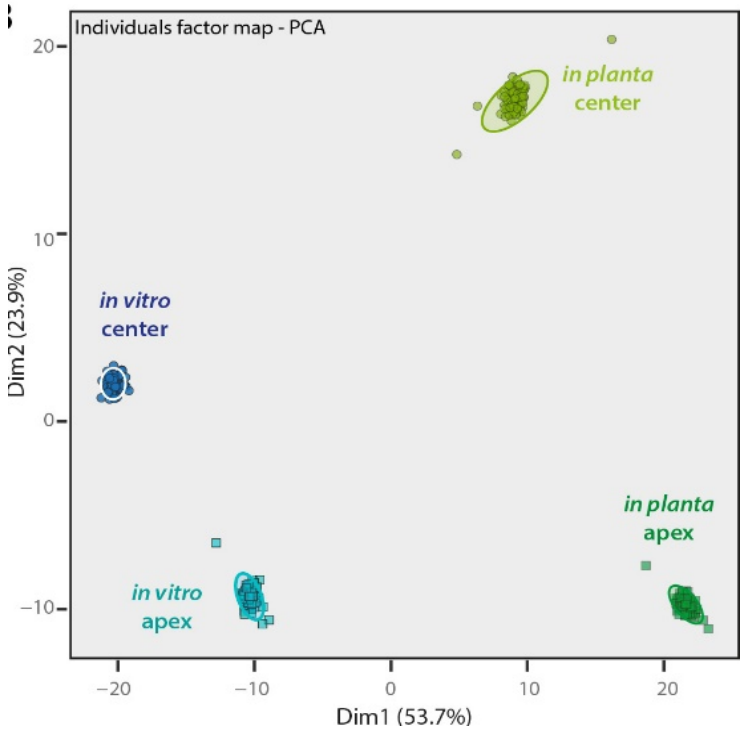
Kabbage *et al*. 2015

How is this reflected at the molecular level ?

S. sclerotiorum transcriptome reprogramming during plant colonization







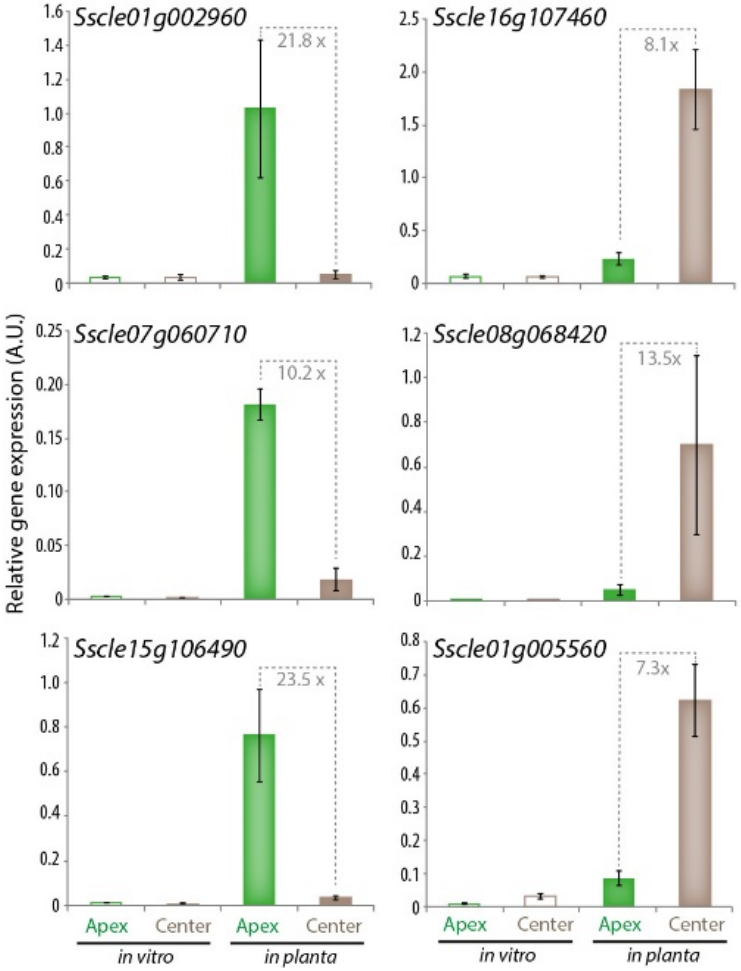
580 (51.2%) genes are area-specific

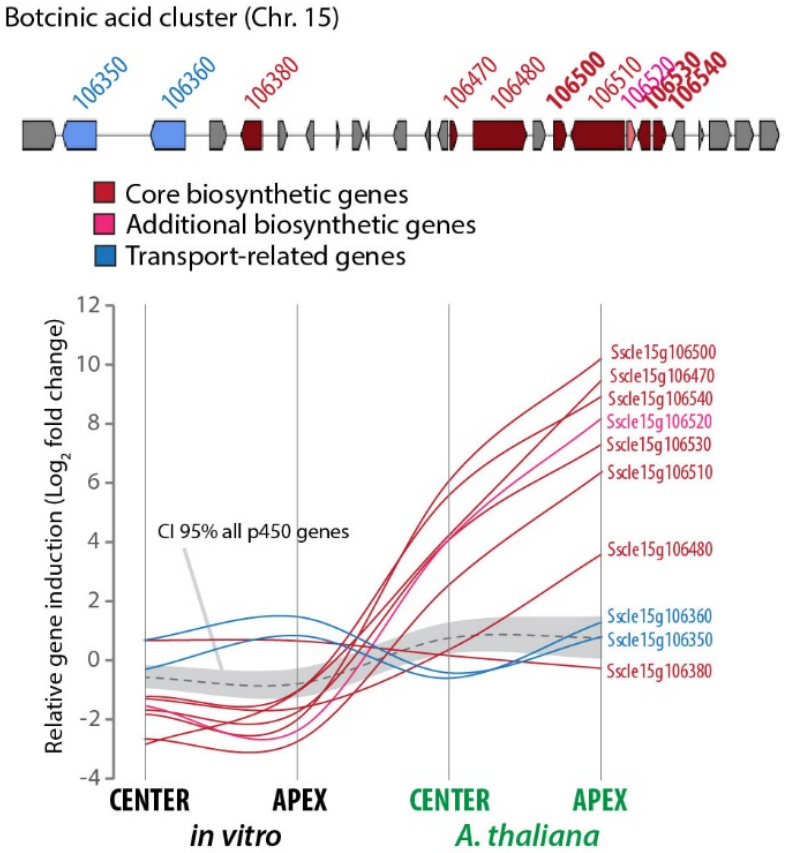
627 (55.4%) were induced *in planta* only

- Co-existence of 2 distinct transcriptional states *in planta*
- Host colonization triggers highly divergent reprogramming of fungal cells

Local reprogramming of *S. sclerotiorum* colonies *in planta*

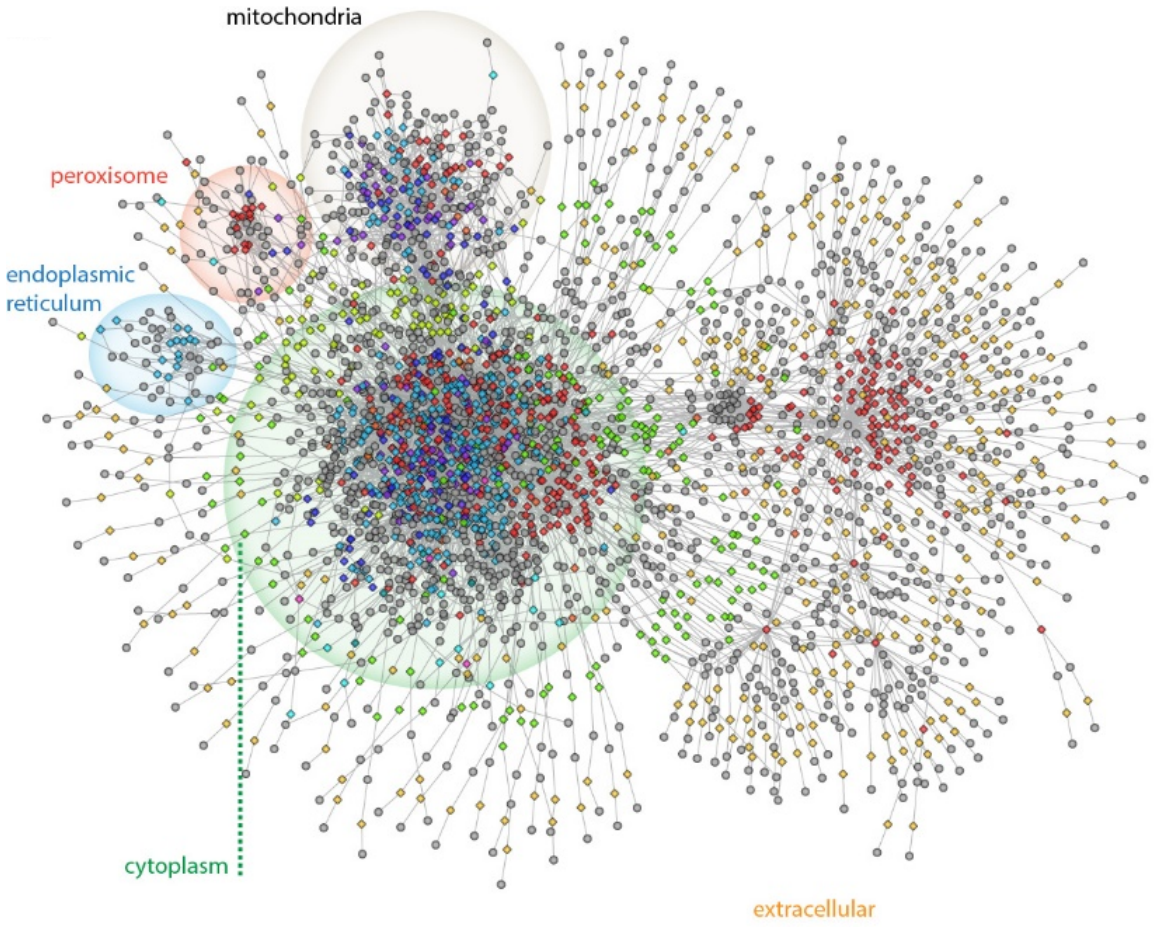
- The expression of some fungal genes is restricted to specialized cells





How (much) does local reprogramming affect hyphal cells functions?

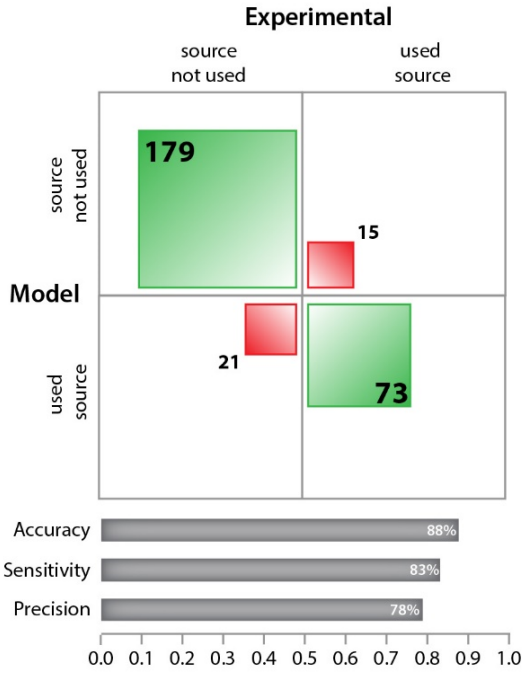
Analysis of major cell functions performed locally with a genome-scale metabolic model



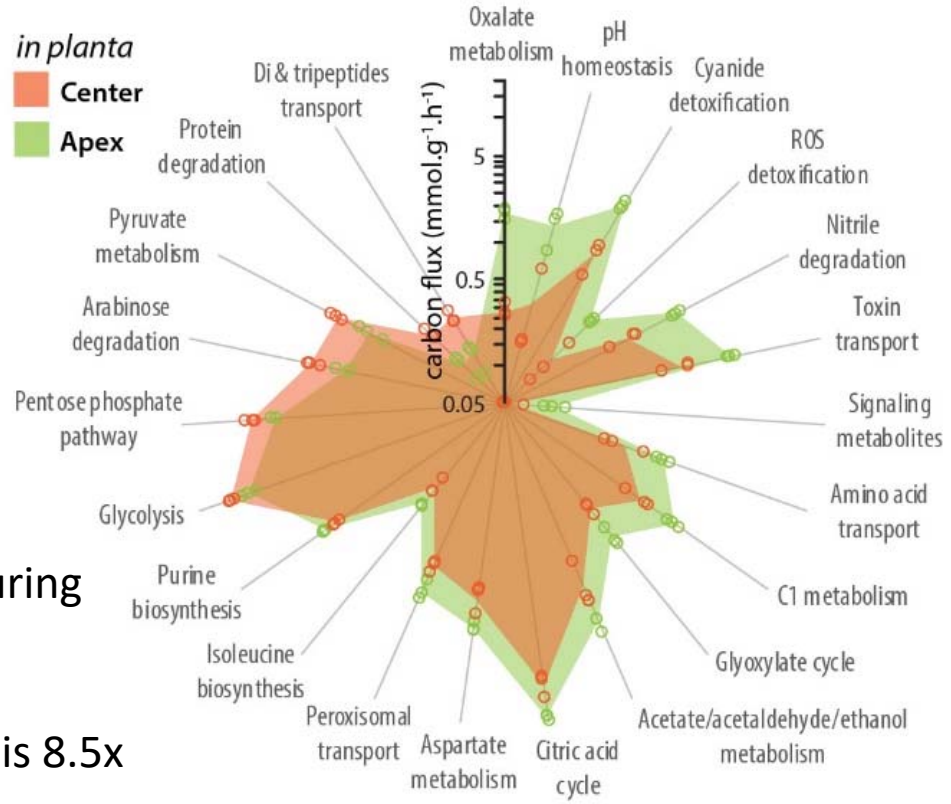
Model features	Metabolic module	PCW deg. module
Reactions		
Biomass biosynthesis	291	0
Central metabolism	89	0
Cofactor biosynthesis	77	0
Degradation pathway	280	83
Exchange	213	135
Regulation	6	0
Salvage pathway	9	0
Secondary metabolism	33	0
Sink	14	0
Transport, external	183	0
Transport, internal	82	0
Total	**1277**	**218**
Metabolites		
Genes	919	120

- Reconstruction of *S. sclerotiorum* Genome-scale Metabolic model
- Cell-scale analysis, quantify metabolic 'cost', make simulations

Metabolic heterogeneity in *S. sclerotiorum*



Experimental growth on 288 metabolites using Biolog - compared to model predictions



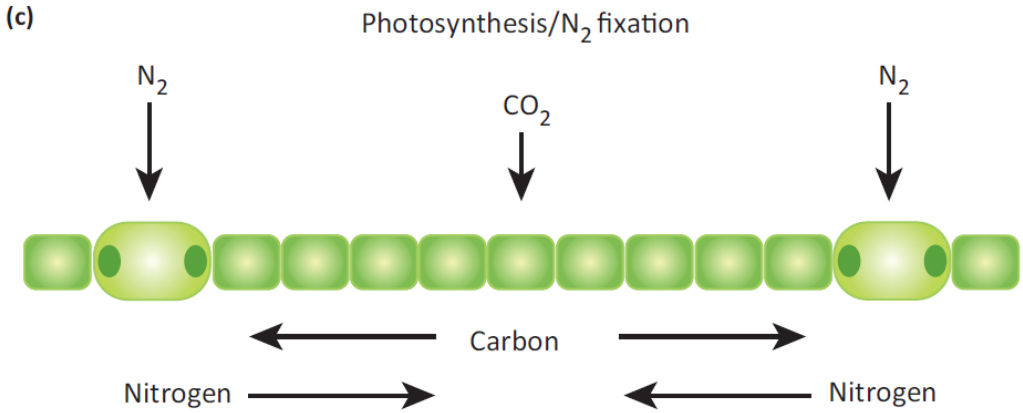
16 pathways with fluxes apex > center during *A. thaliana* colonization

C flux towards major virulence functions is 8.5x higher in apex cells

Division of labor (DOL): a solution to optimization problems

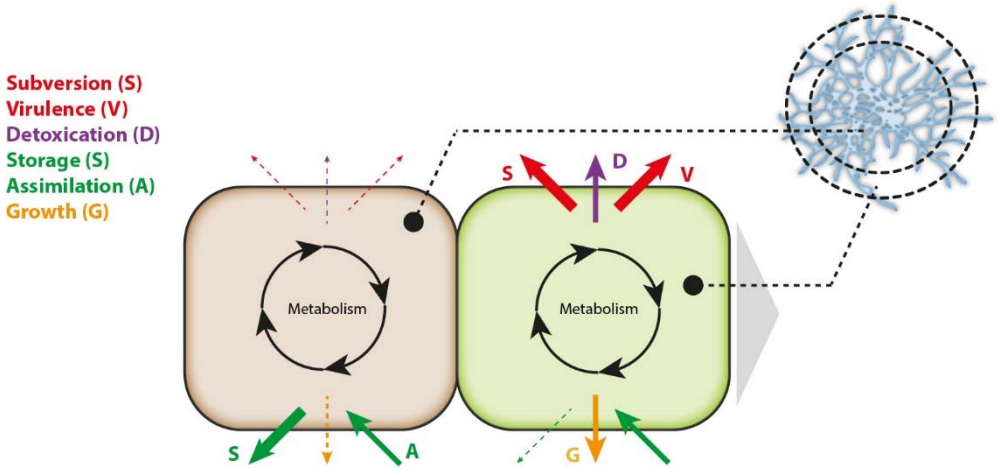
DOL = different tasks are executed by specific and specialized modules

Heterocysts in cyanobacteria



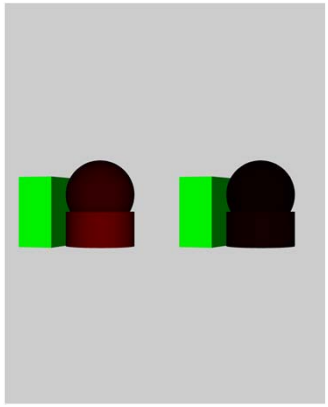
Muro-Pastor and Hess, Trends Micro. 2012

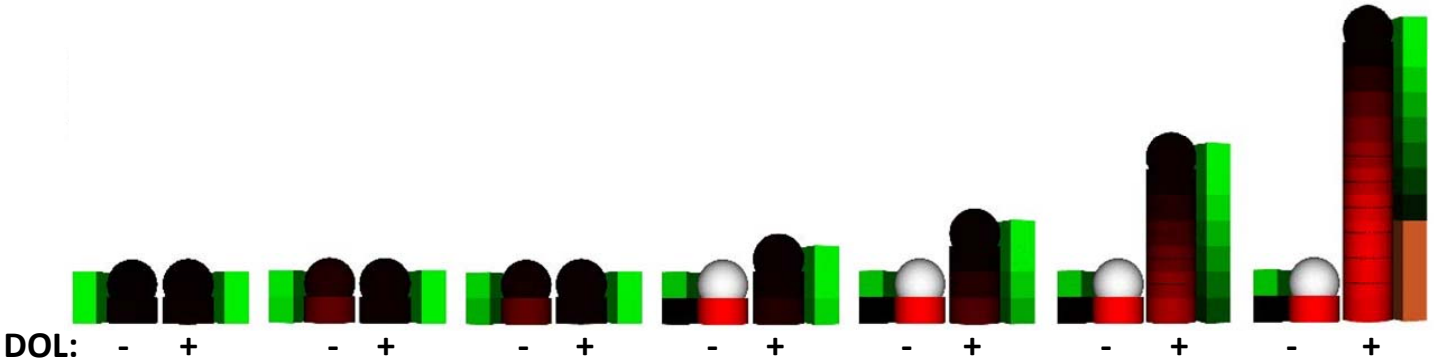
- Center cells 'feed' apex cells to afford the cost of effectors production

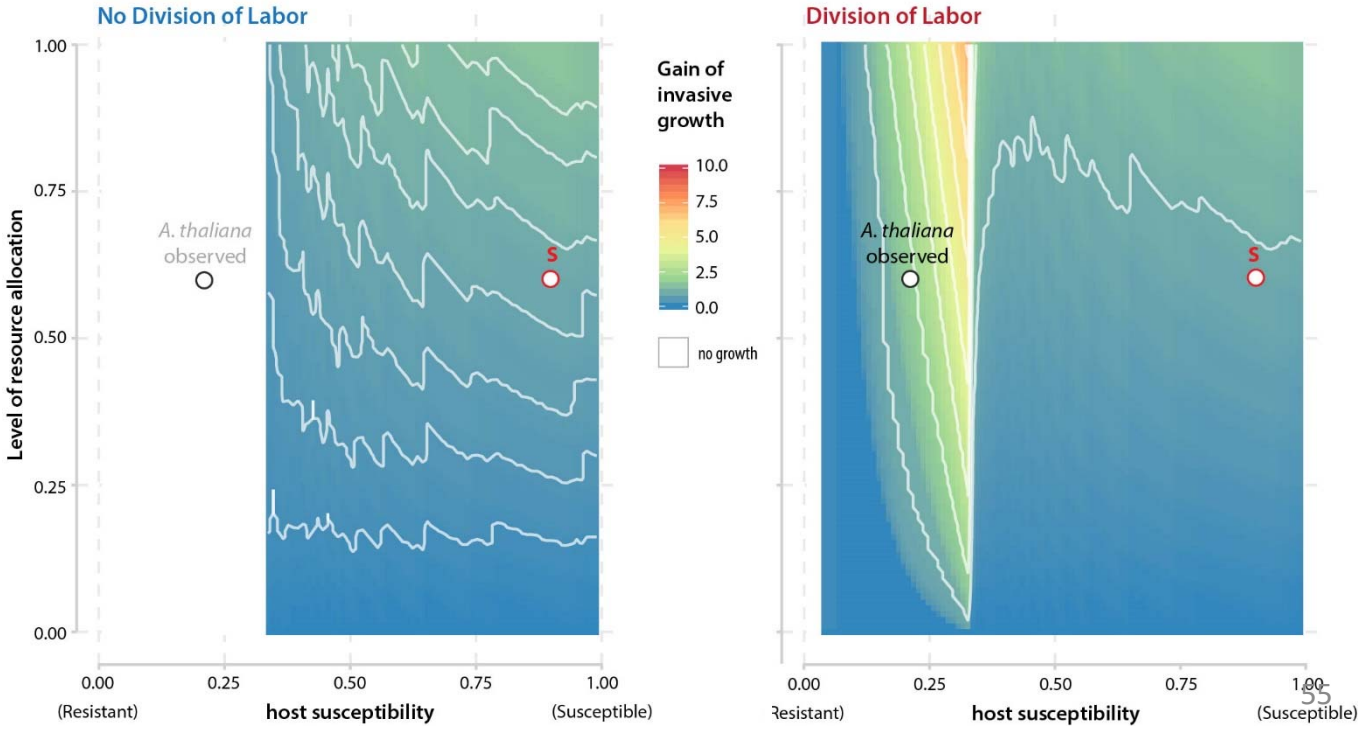


Is there a selective advantage of DOL in S. sclerotiorum?

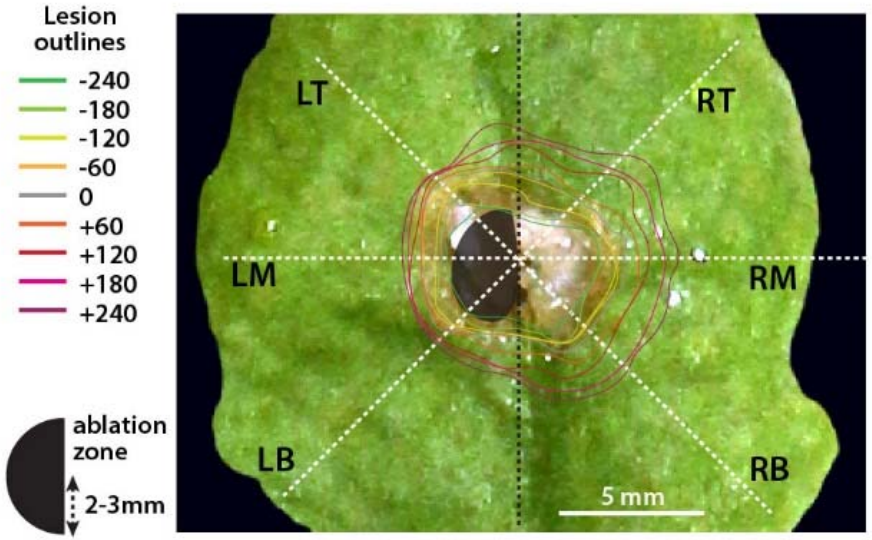
DOL enables the colonization of resistant hosts

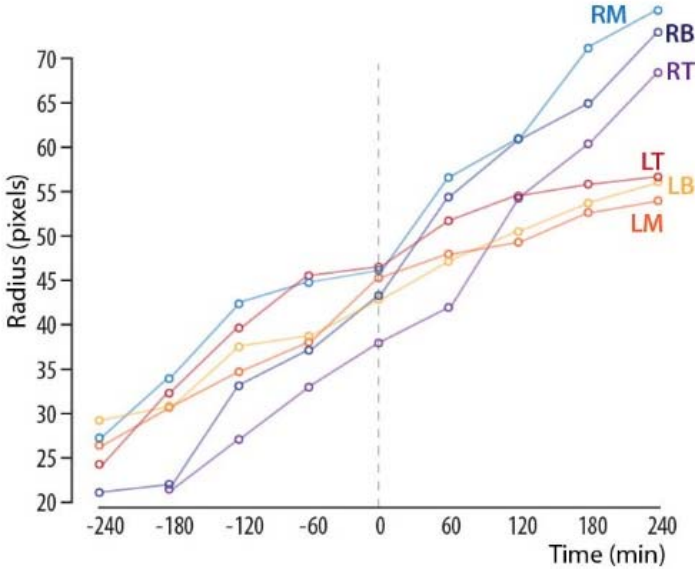


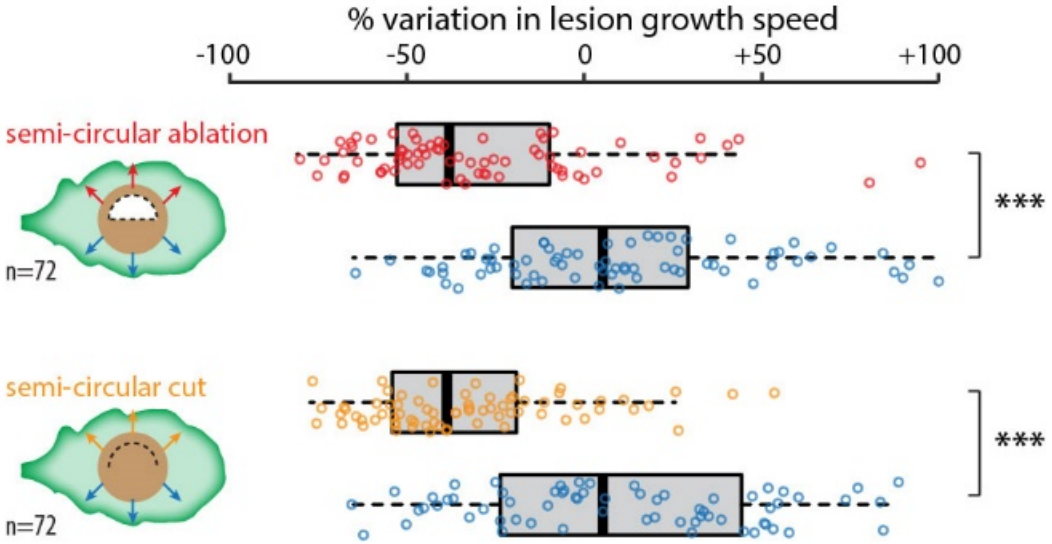




Cooperation promotes host colonization



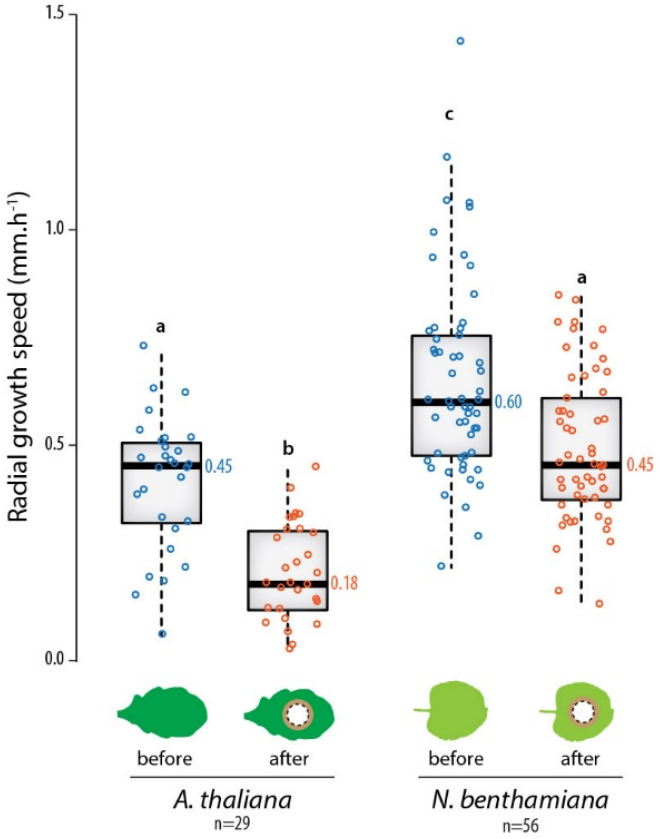




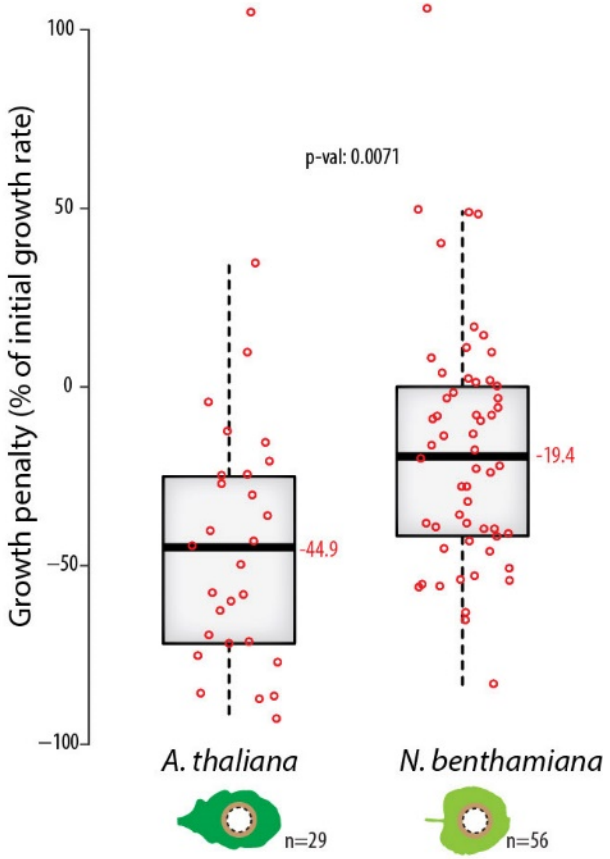
- Growth penalty to hyphae downstream of cut center cells only

The gain from cooperation is higher on resistant hosts

- Disconnection from center reduces the colonization of *A. thaliana* and *N. benthamiana*



- Plant more resistant (eg At vs Nb) = Higher gain from cooperation



Cooperation promotes host colonization

Peyraud *et al.*, PNAS 2019

Conclusions

Take home: both generalist and polyspecialist

Generalist

Adapted to a wide niche

- **Adaptive protein translation**
- **Division of labor and cooperation**

Molecular bases?

more…?

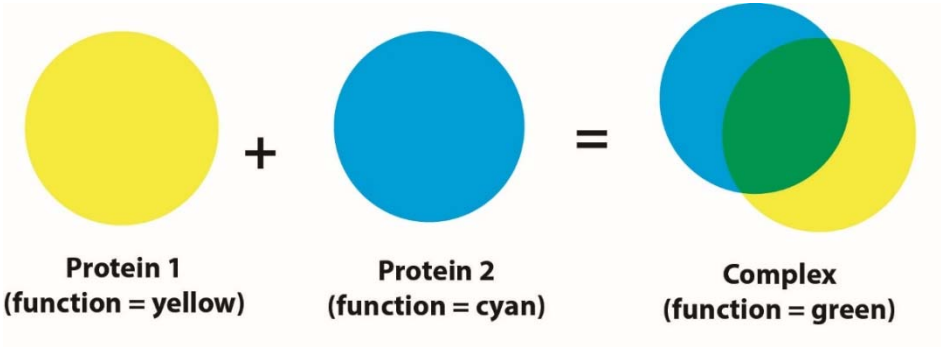
Polyspecialist

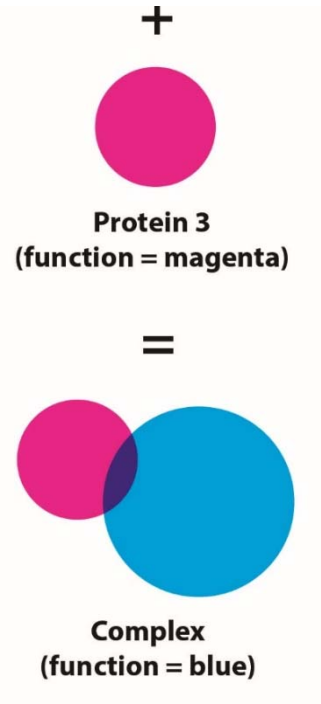
Adapted to multiple niches

- **Host-specialized gene clusters**

The whole is more than the sum of its parts

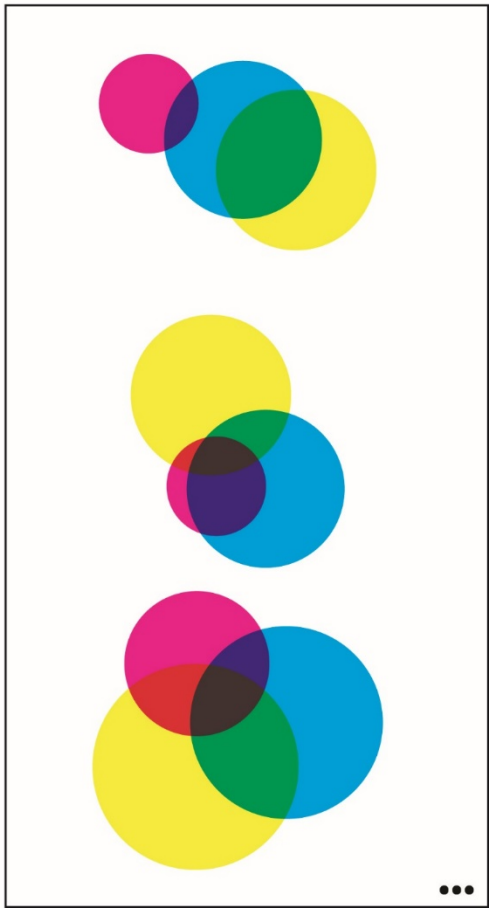
- A 3-component system





Green=
Emergent property

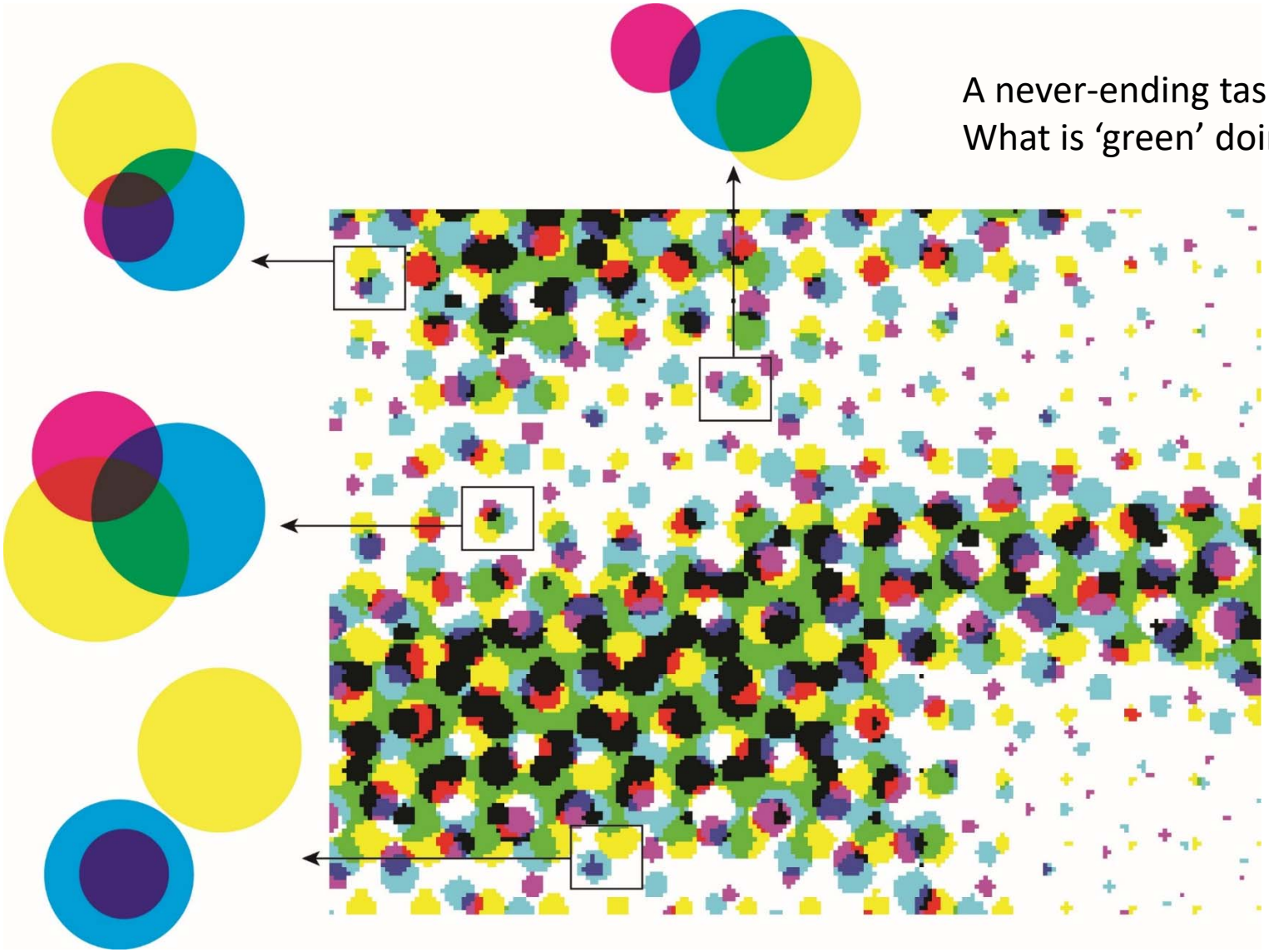
- >>3 outcomes



Sometimes yellow + cyan ≠ green

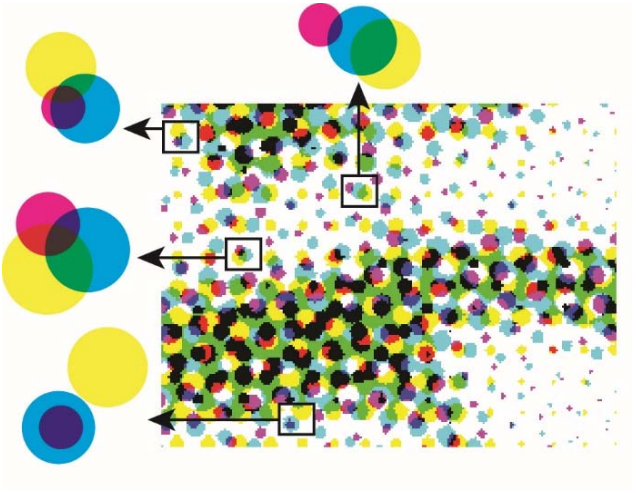
The whole is more than the sum of its parts

- Mapping the multiple states of the system

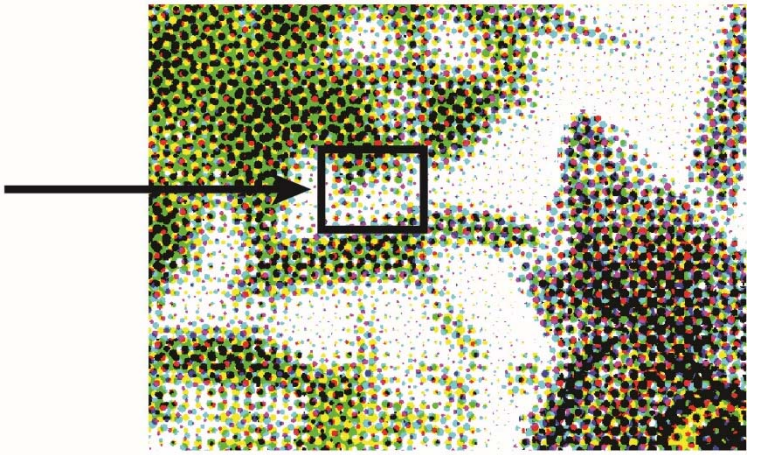


A never-ending task ?
What is ‘green’ doing ?

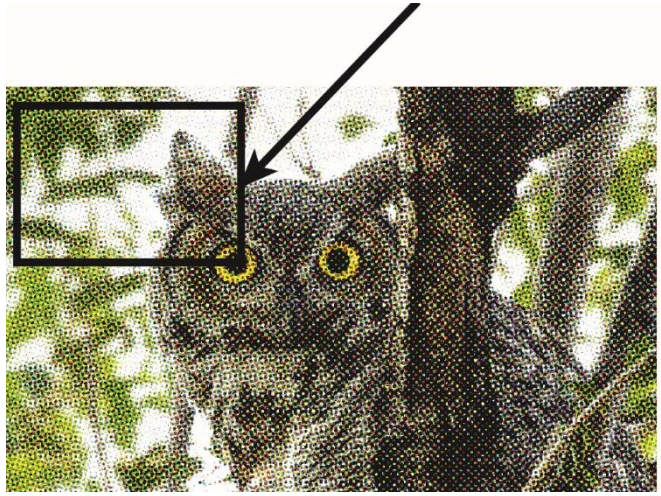
The whole is more than the sum of its parts



• Inferring global patterns from incomplete local information (modeling)



• Testing for un-anticipated Molecular functions



• Emerging property at high-order

> Effect on organism physiology/fitness

Maths models reveal phenotypes emerging from molecular events

Science is teamwork!

www.qiplab.weebly.com @QIPlab

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Ludovic Cottret
Benjamin Gourion

Mark Derbyshire

Frederick Garcia
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Thank you !

Questions?

Get the slides here: http://qiplab.weebly.com/tools

Late questions: sylvain.raffaele@inrae.fr