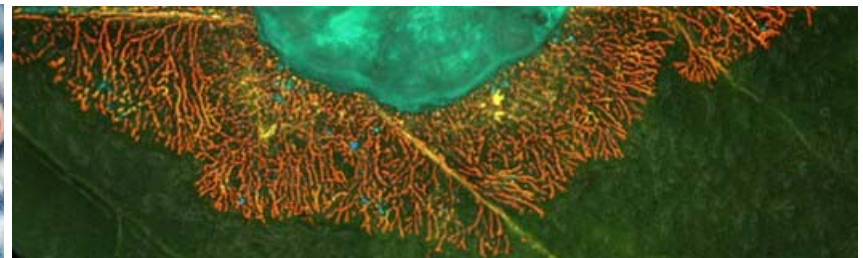
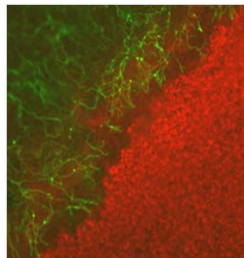


Adaptations to diffuse co-evolution in plant pathogenic fungi

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Lab. Interactions Plant-Microbes (LIPM) – INRA Occitanie Toulouse (FR)



Outline

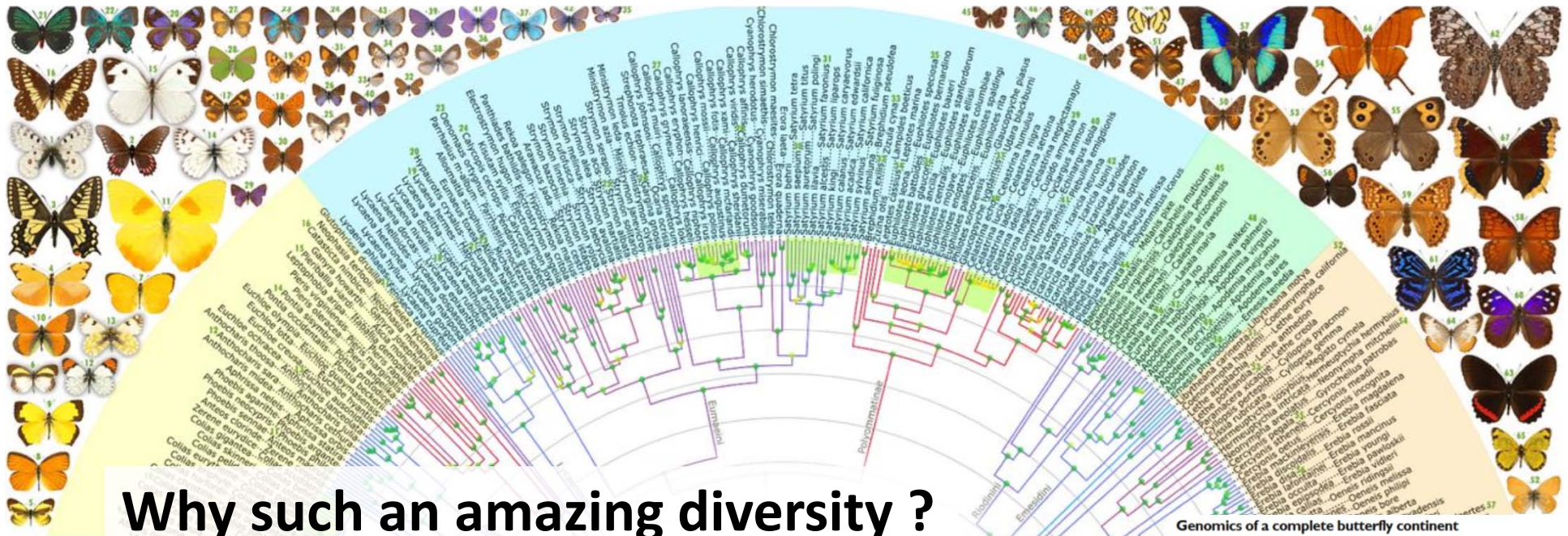
Intro – pairwise coevolution and beyond

- . Key concepts: Co-evolution, selection, adaptation [3-8]
- . Theory of pairwise co-evolution [9-10]
- . Case study: *Phytophthora infestans* (potato late blight) [11-16]
- . What is happening under diffuse co-evolution? [17-21]

Diffuse coevolution: the fungal pathogen *Sclerotinia sclerotiorum* (white mold)

- . 1/ Signatures of adaptive translation in the genome of polyphagous pathogens [22-35]
- . 2/ Transcriptional plasticity and host range expansion [36-47]
- . 3/ Division of labor supports the colonization of resistant plants [48-58]

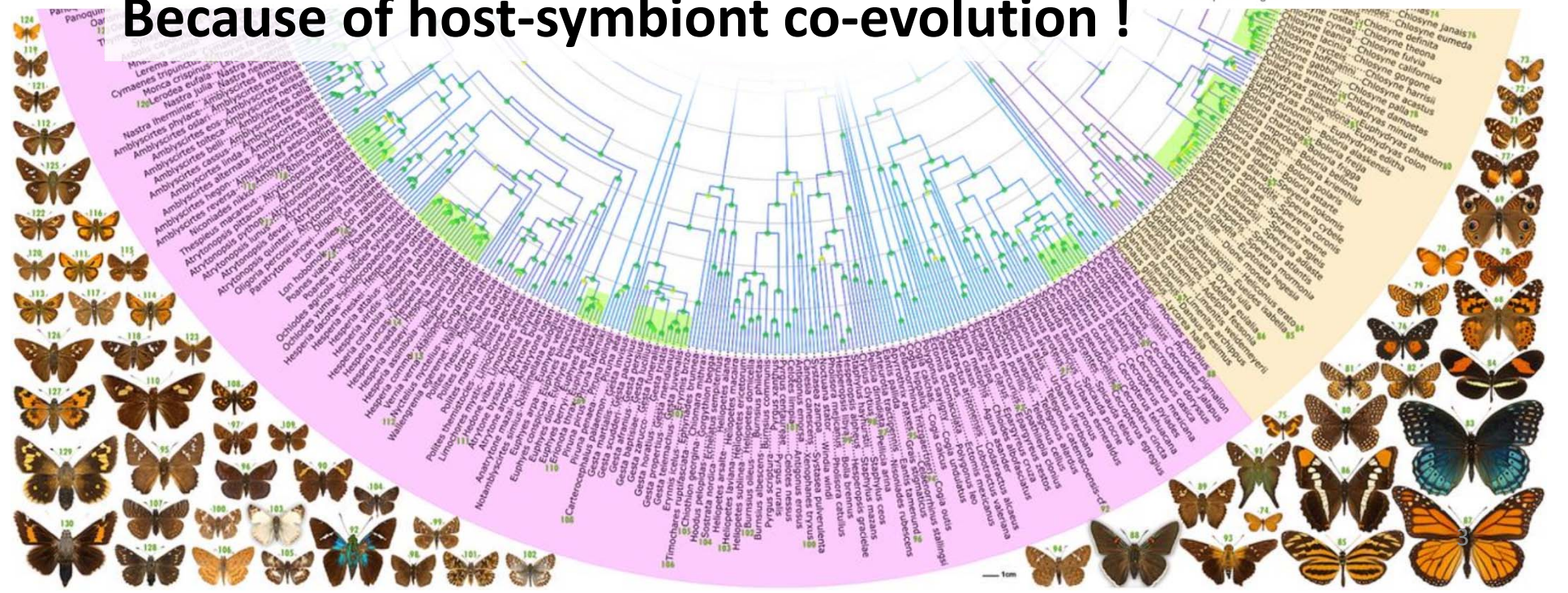
Conclusions: summary and a few last words [59-62]



Why such an amazing diversity ?

Genomics of a complete butterfly continent
 ● Jing Zhang, ● Qian Cong, ● Jinhui Shen, Paul A. Opler, ● Nick V. Grishin
 doi: <https://doi.org/10.1101/829887>

Because of host-symbiont co-evolution !

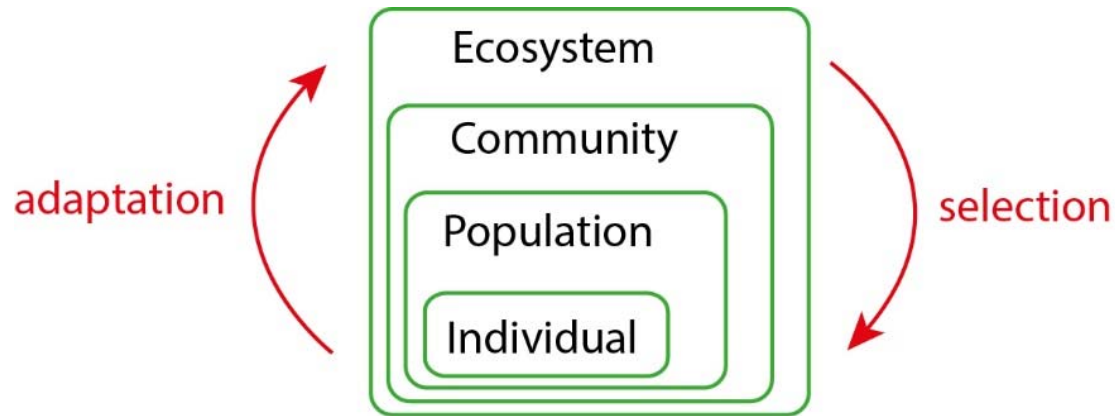


Co-evolution= a change in the traits of one species acts as a selection pressure on the other species

Seen in pair of species that **interact frequently or closely**

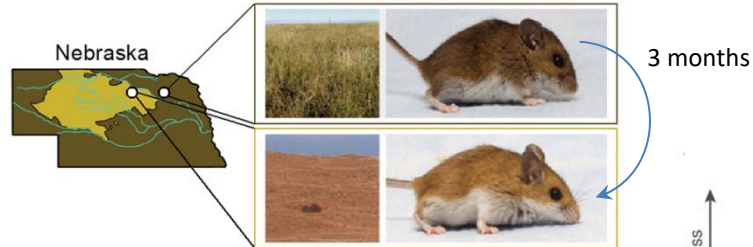


Basics in evolutionary studies

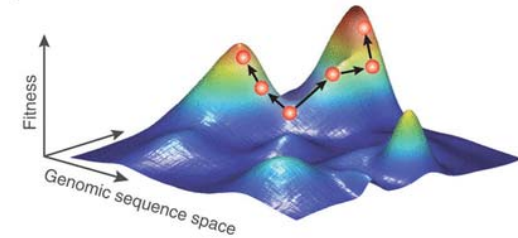


Fake news:

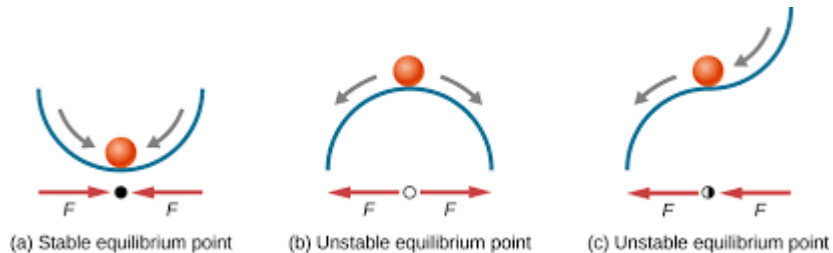
. Evolution is slow



. Evolution leads to optimization
(population level features are rarely optimized, optima vary)

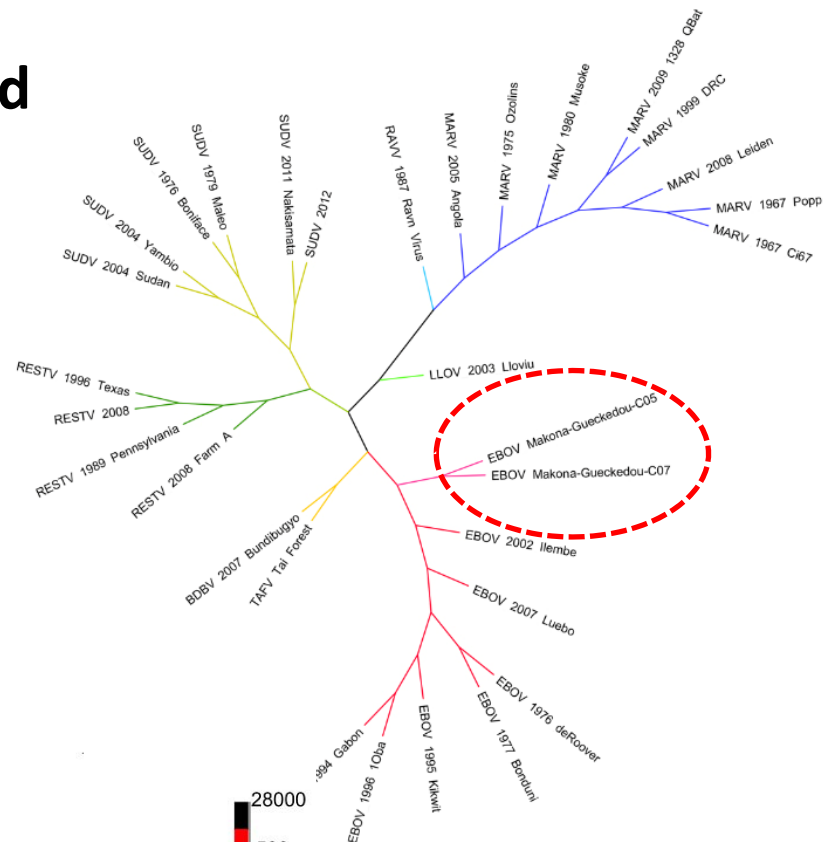
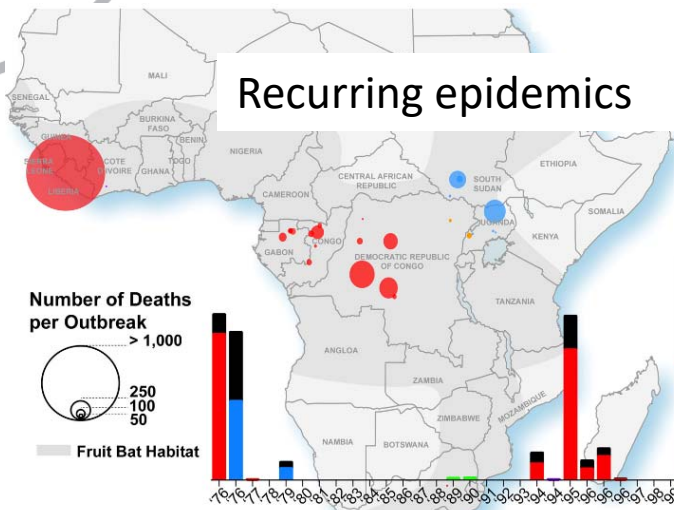
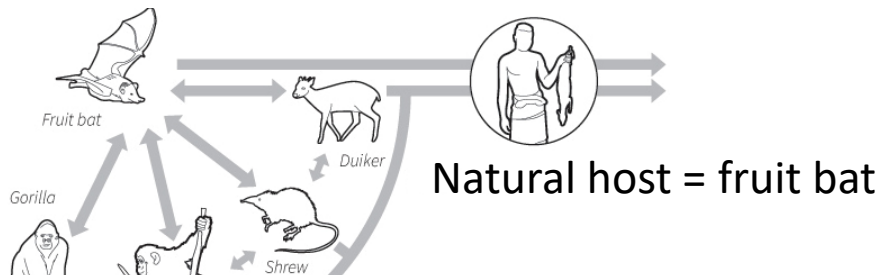


. Evolution leads to stable equilibrium



Host-parasite co-evolution governs the emergence and spread of disease

2014 Ebola virus outbreak in West Africa



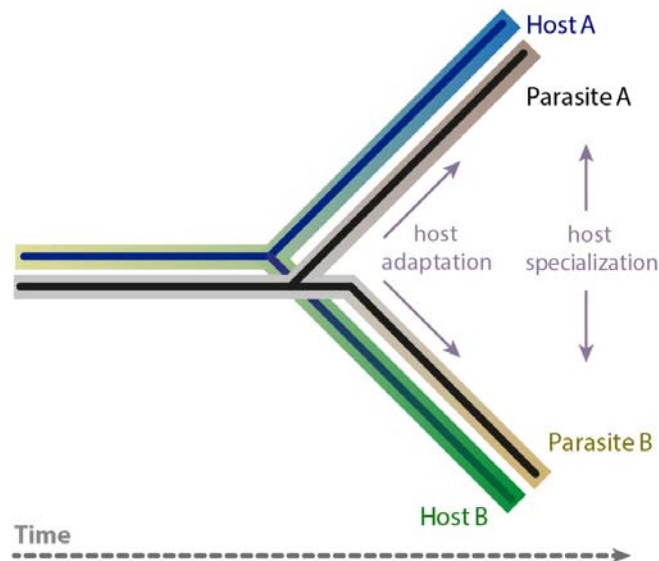
Genomics: emergence of new viral lineage
Direct human-to-human transmission

De la Vega et al. Plos Patho. 2015

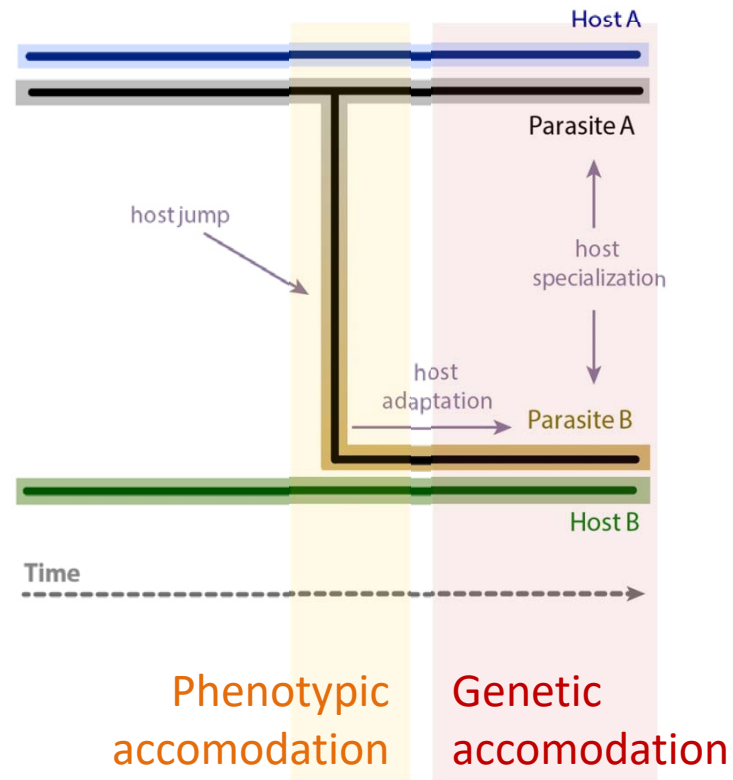
How do pathogens adapt to their hosts ?

Plasticity and adaptation

Co-speciation



Host jump / host shift



Phenotypic plasticity: capacity of a genotype to produce different phenotypes in response to environmental variation

Causes and consequences ?

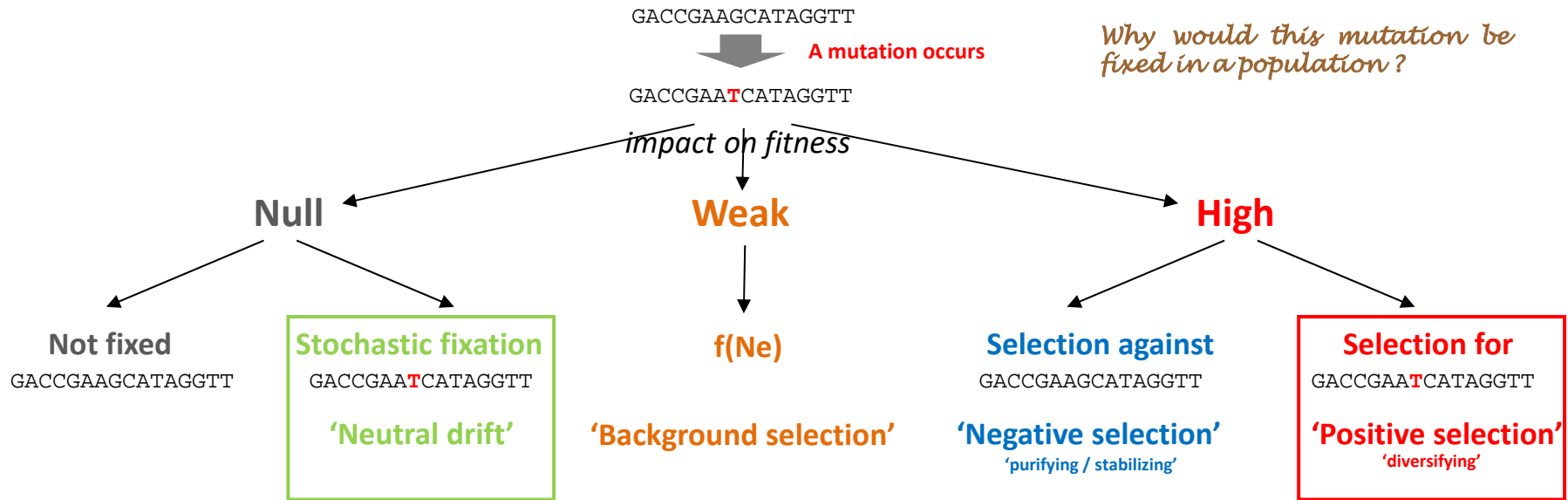
Plasticity lost or retained

Roy, *Evolution* 2001

West-Eberhard 2003

Dong *et al.*, *Curr. Opin. Genet.* 2015

The (nearly) neutral theory of sequence evolution



Kimura, Nature 1968
King and Jules, Science 1969
Ohta, Nature 1973

Selectionist: either advantageous or deleterious

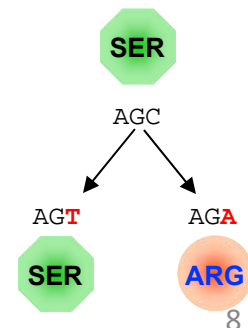
Neutral: neutral more frequent than advantageous

Nearly neutral: population size modifies selection on weak effect mutations

dS : rate of synonymous substitution (neutral)

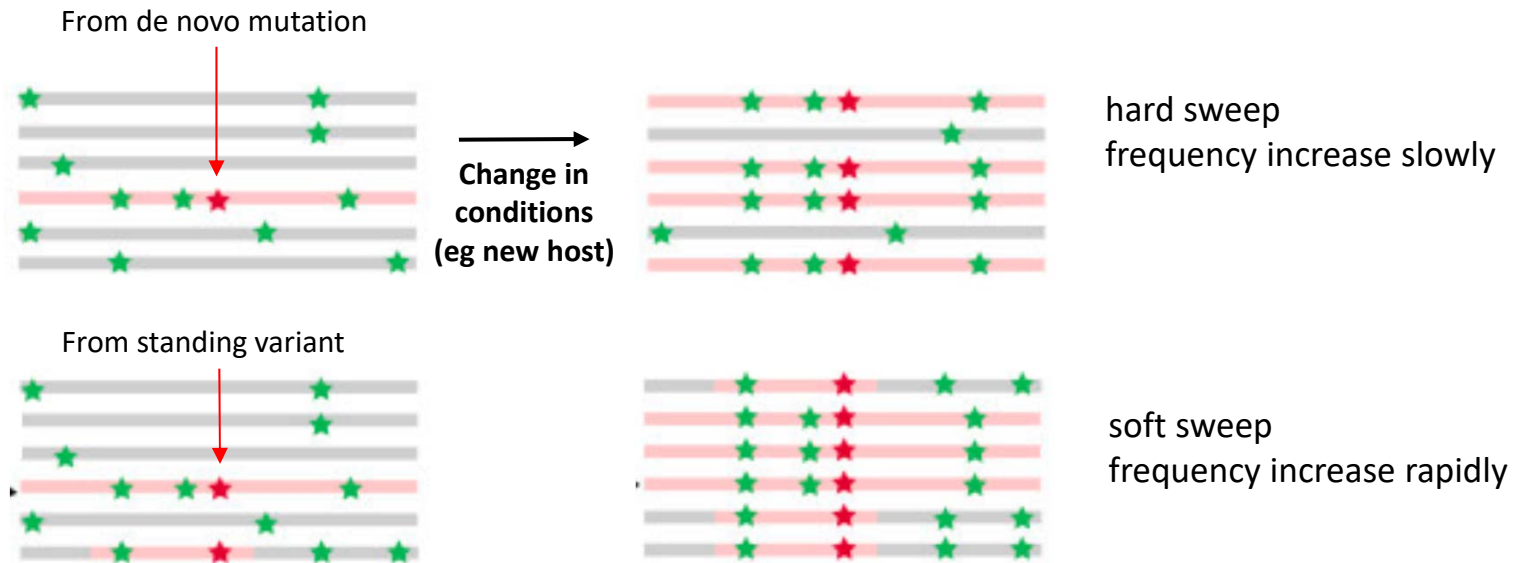
dN : " non synonymous "

Selection outweigh drift if $dN/dS > 1$

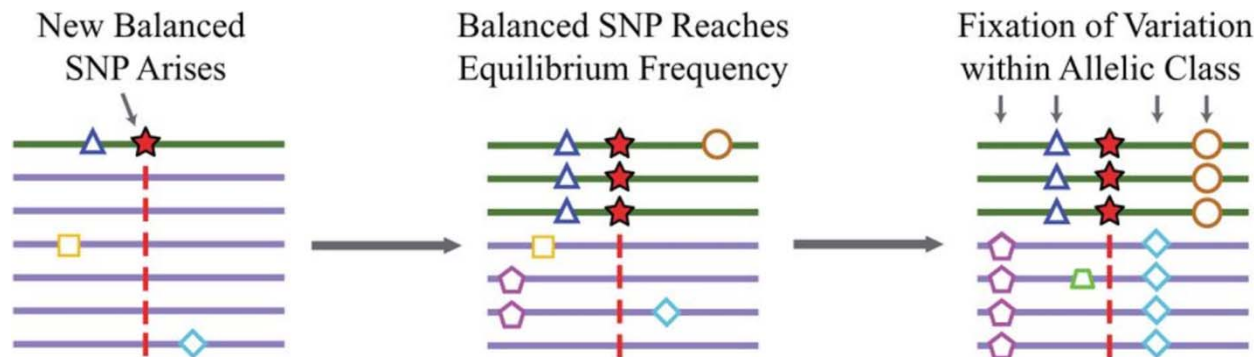


Theoretical models of pairwise co-evolution

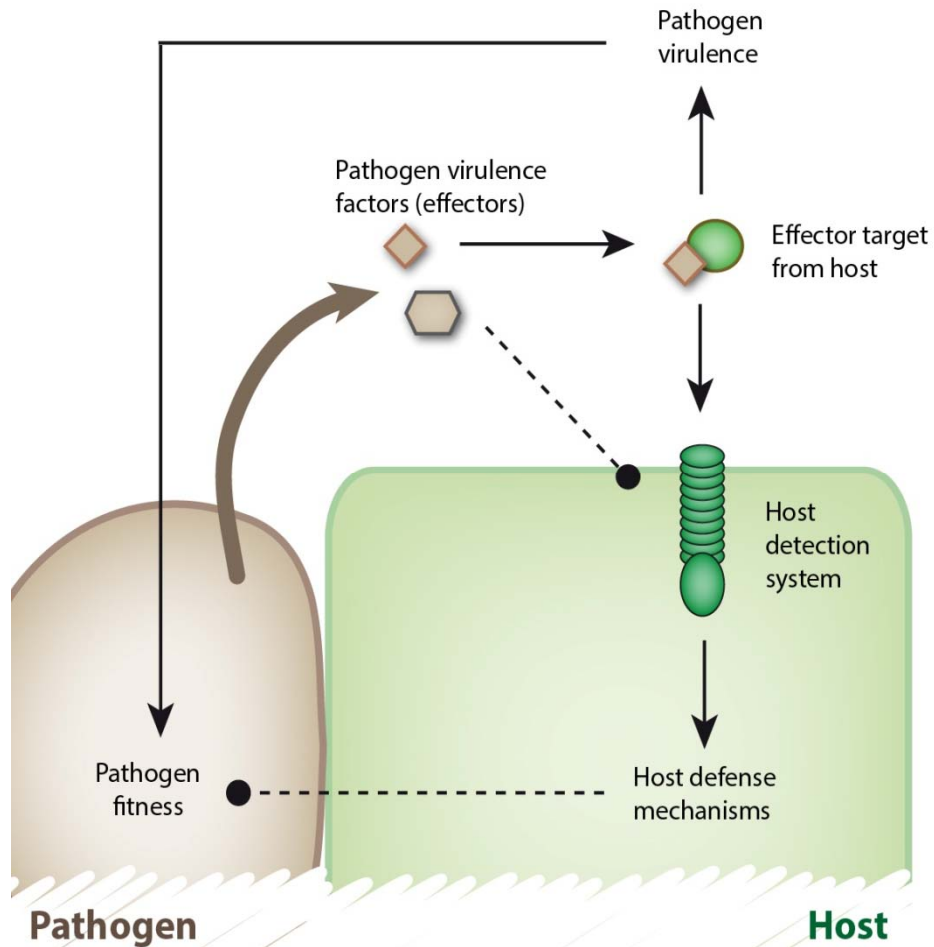
Selective sweep: rapid increase in frequency of a beneficial genetic variant



Balancing selection: Natural selection maintains 2 or more phenotypic forms



Host-pathogen arms race at the molecular level



.Antagonistic activity of pathogen effectors:

- Modify host target molecules efficiently and specifically

- Recognized as non-self by host



.Tradeoff :

Improved activity in Host A =
reduced activity in Host B

Phytophthora infestans, the plant destroyer



Causal agent of late blight,
#1 disease of potato

Irish potato famine of
1845-1849



Without agrochemicals, late
blight is highly destructive

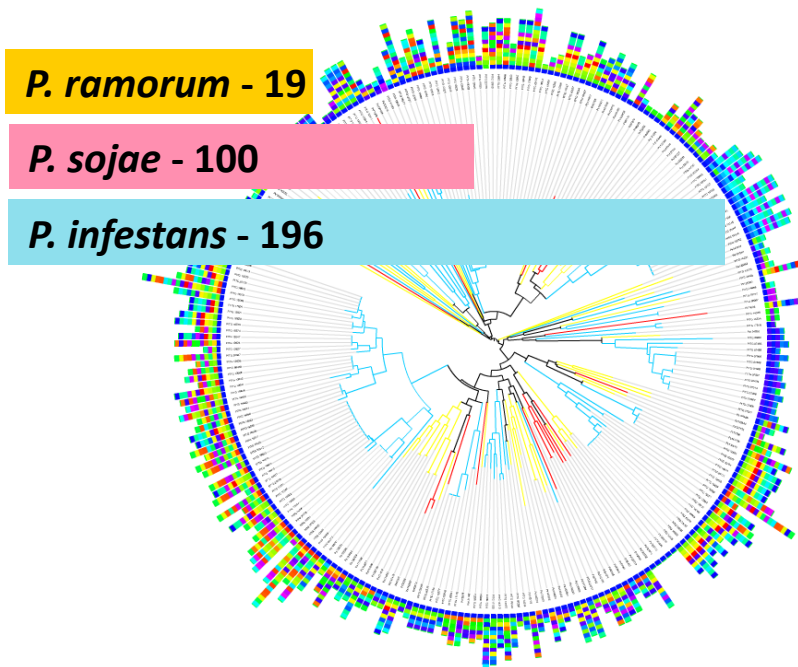


P. infestans genome sequence: diversification of effector families

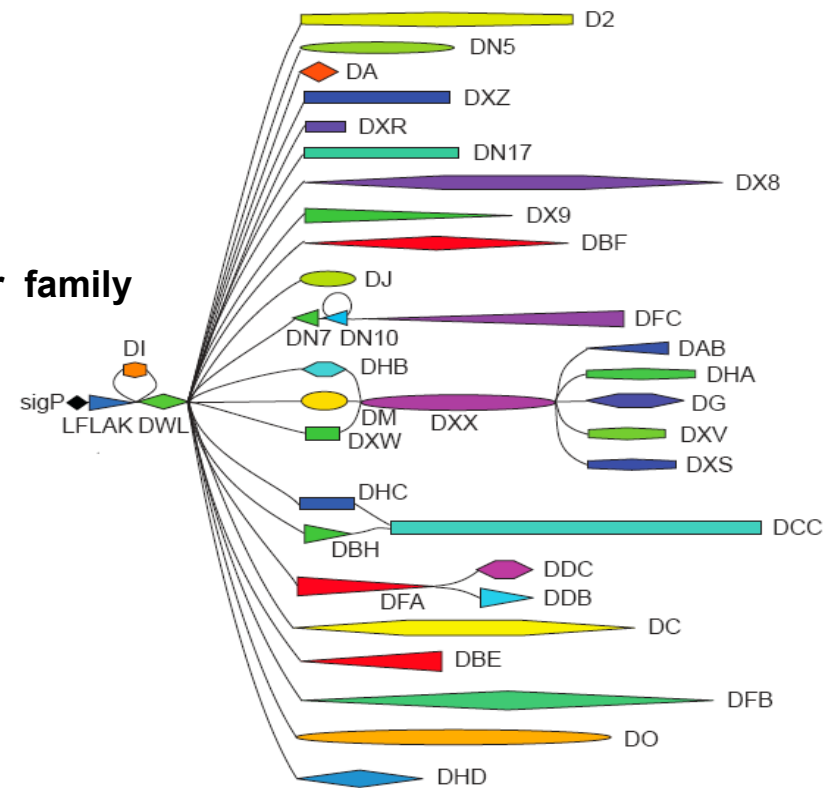


Sequencing *P. infestans* T30-4 genome (Haas *et al.* Nature 2009)

Comparison to *P. sojae* and *P. ramorum* genomes (Tyler *et al.* Science 2006)

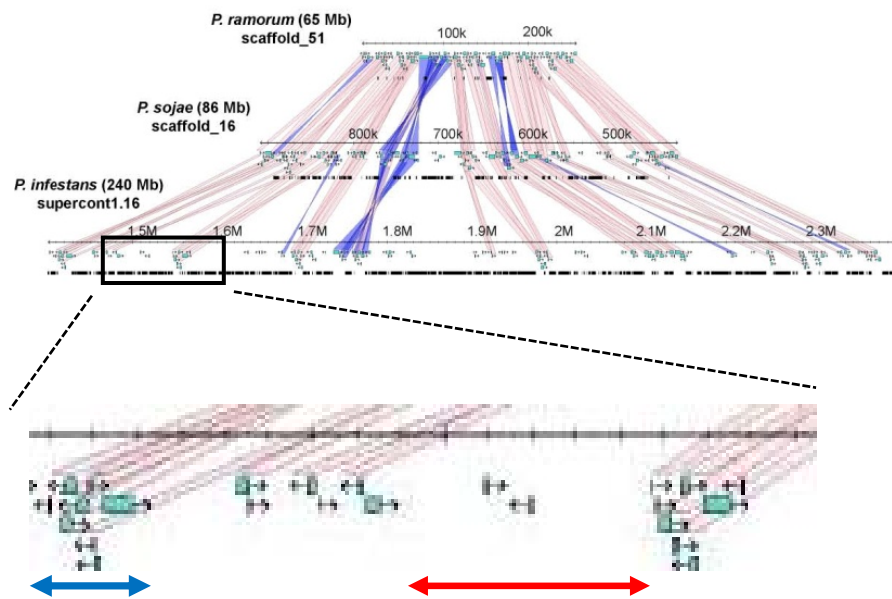


Crinkler effector family

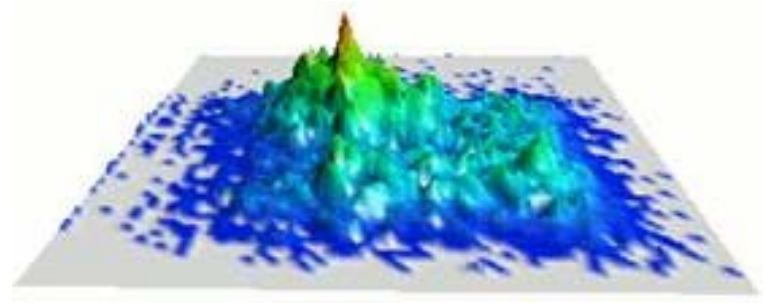
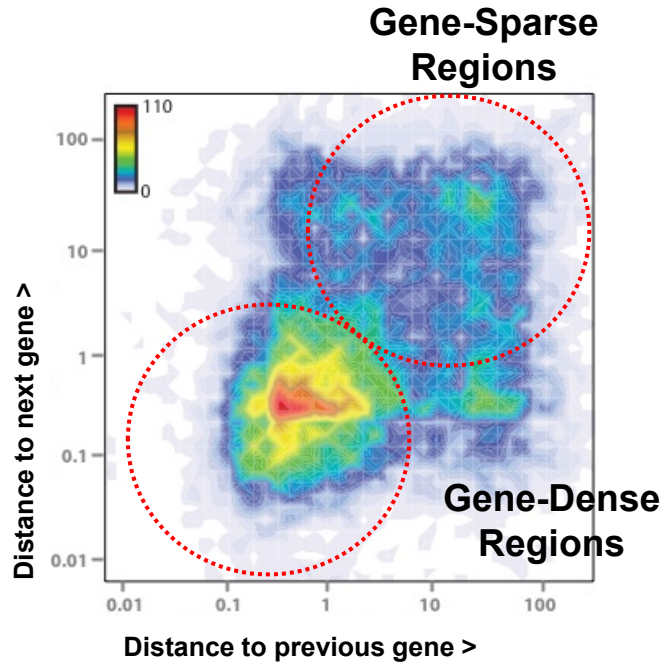


Duplications = reduced selective constraints
+ high standing variation

Transposon-driven local genome inflation

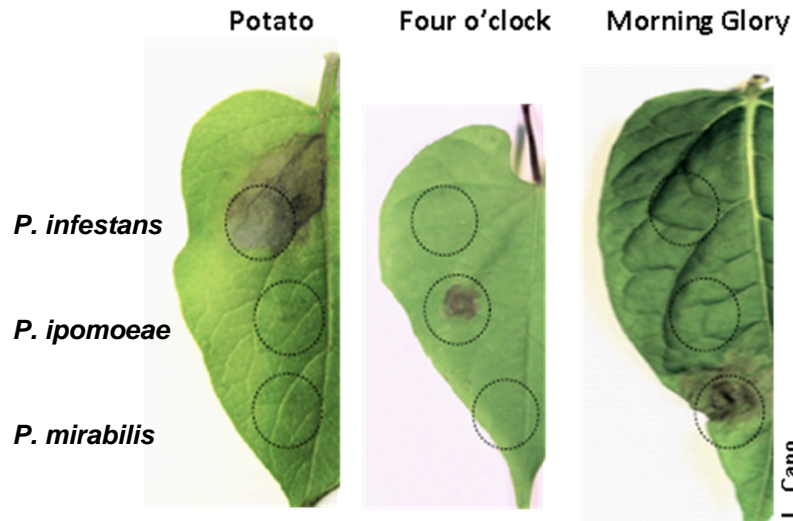
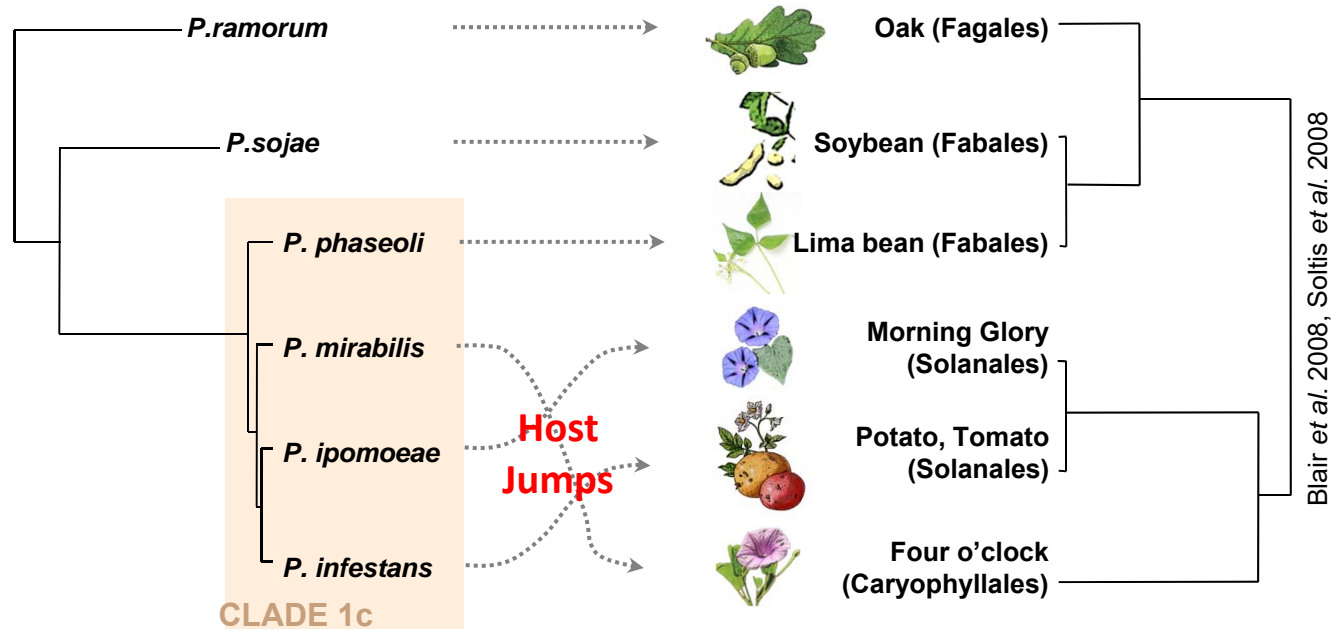


<p>Gene-dense</p> <p>Conserved synteny <i>Phytophthora</i> 'core' genes</p>	<p>Gene-sparse</p> <p>No synteny Species-specific genes</p>
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Haas et al., Nature 2009

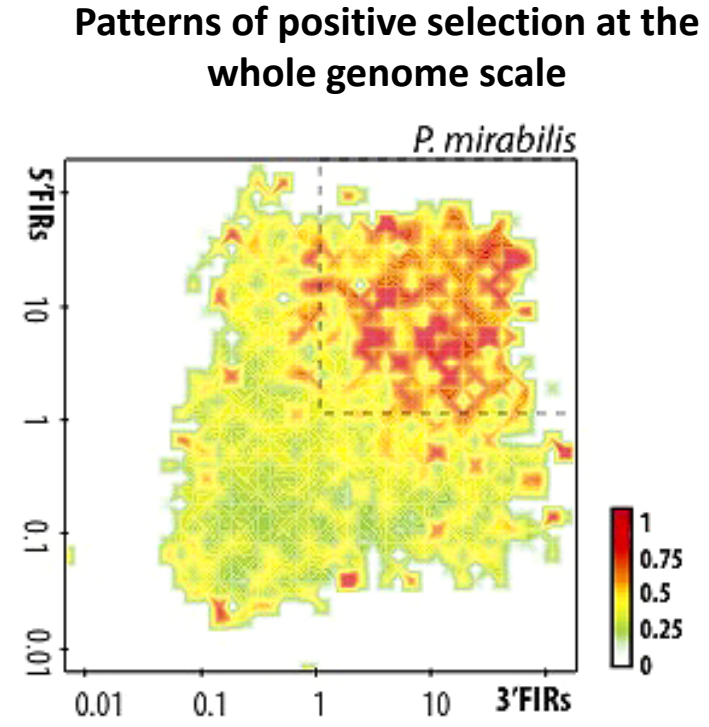
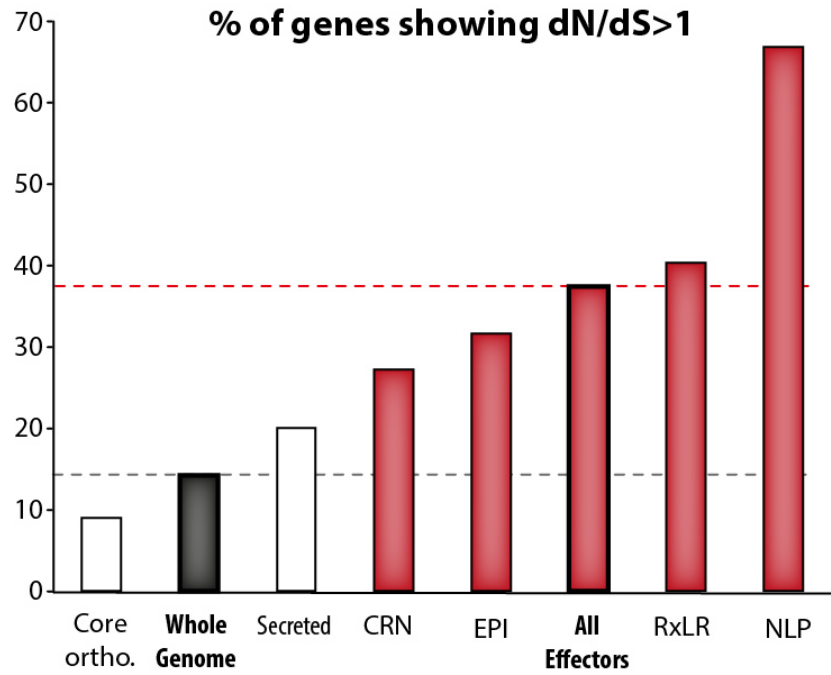
How does *P. infestans* genome adapt after host jumps ?



“Recently” diverged:
99.9% identity in ITS sequence

Naturally co-occur in Mexico

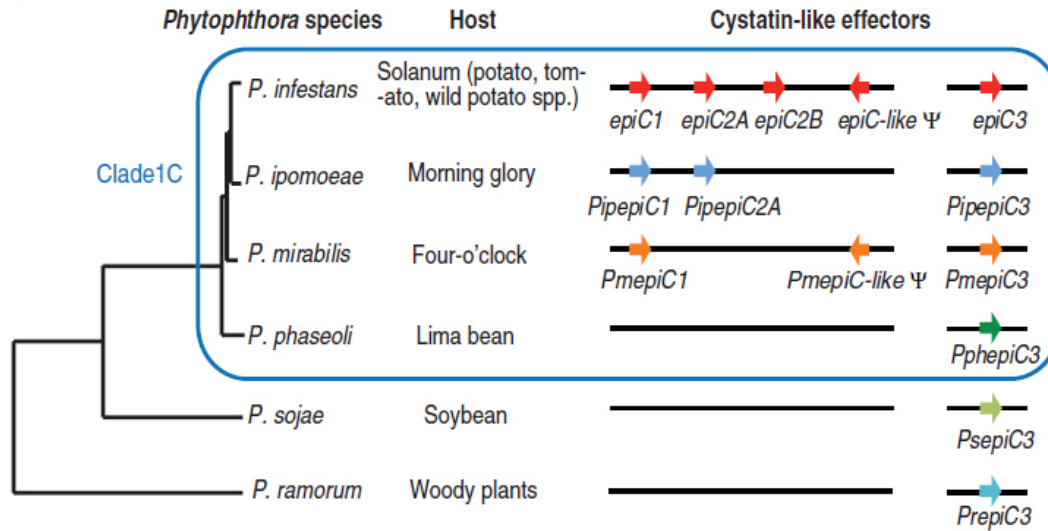
Gene-sparse regions are “niches” containing fast-evolving genes



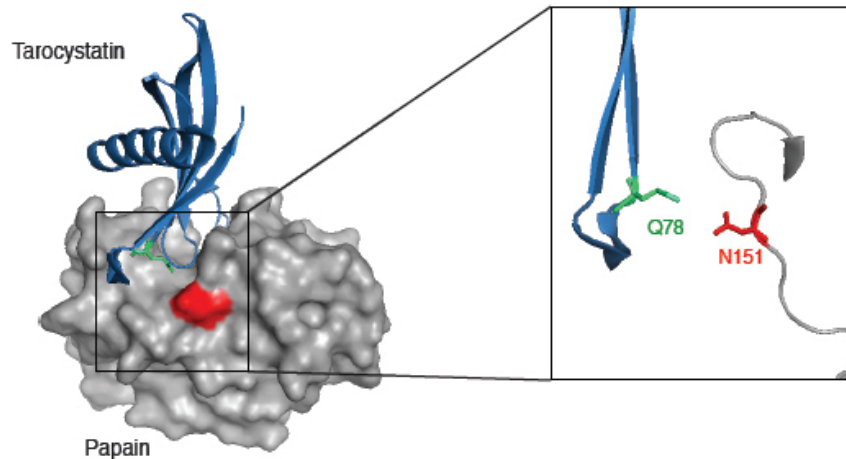
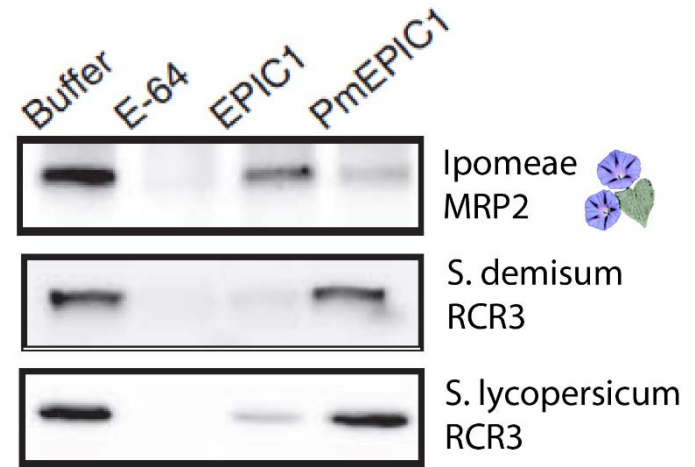
Signatures of positive selection are frequent in genes related to host adaptation

High standing genetic variation + reduced deleterious linkage = fast sweeps

Tradeoff for EPIC1 effector function on different hosts



Co-evolution of host protease and its *Phytophthora* inhibitor



. A tradeoff governs the evolution of EPIC1 virulence factor activity in different hosts

Molecular plant-microbe interactions in context

Current theories : specialization 1 host – 1 pathogen



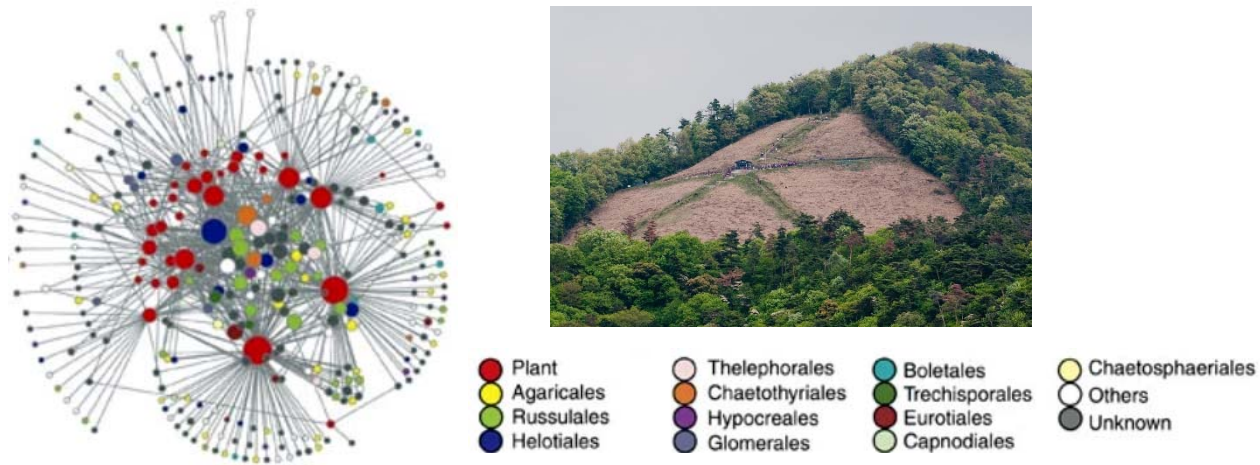
Pairwise interactions



Diffuse interactions
Multiple hosts / competitors / environments

Diffuse co-evolution

Interactions include multiple parasites and/or multiple hosts



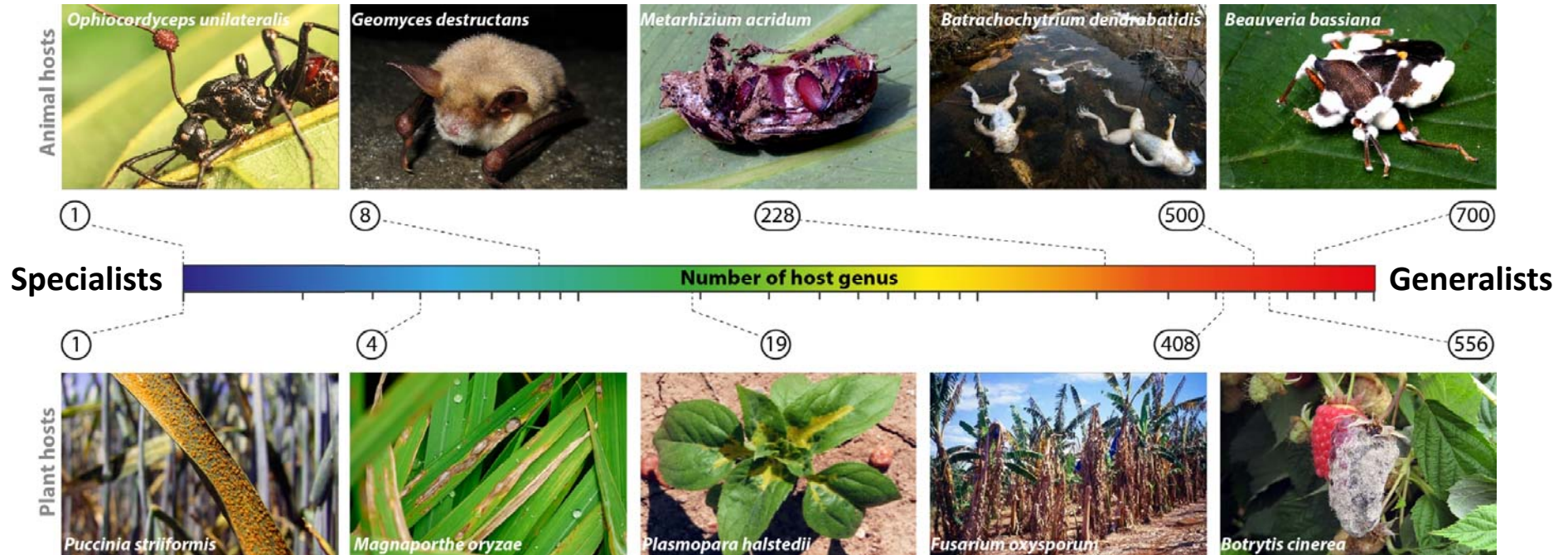
Toju *et al.* Nature Comm 2014

Host traits and the underlying genes evolve in response to >1 parasites,
a parasite trait evolves in response to selection by >1 host

Host range and the species barrier

Host range : the list of host species actually used by a parasite in Nature.

Filamentous pathogens host range:



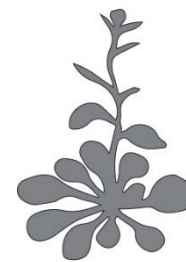
Determined by genetic and environmental factors

Changes through the course of host and pathogen evolution:
specialization, shift, expansion

How does host range evolve in fungal plant pathogens ?

Sclerotinia sclerotiorum

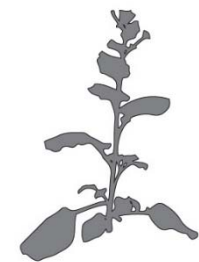
- White Mold on >600 plant species
- Major threat to oil production in EU
- Limited genetic sources of resistance – only QDR observed



Arabidopsis thaliana



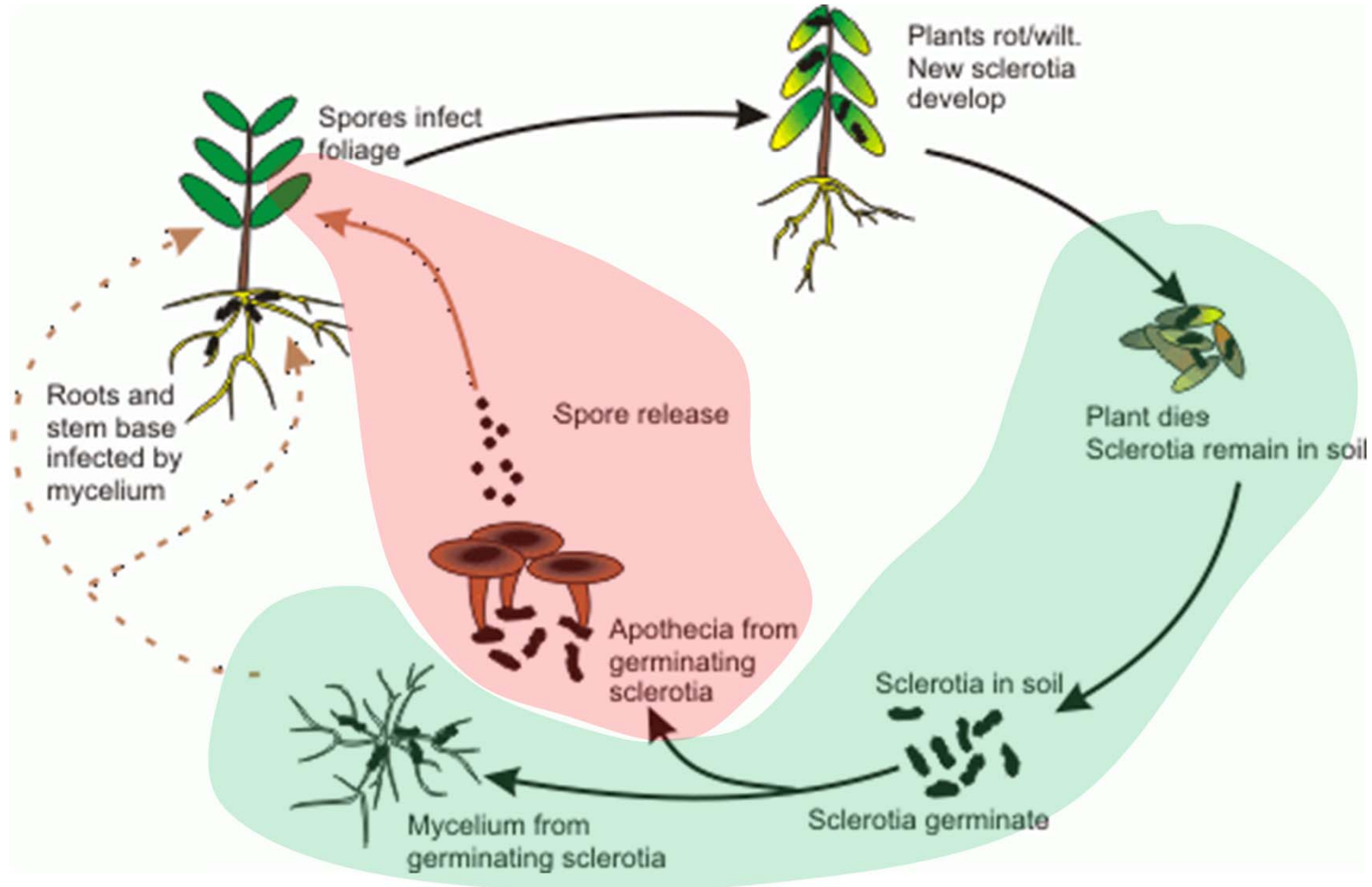
Tomato



Nicotiana benthamiana

Sclerotinia sclerotiorum

Sclerotinia sclerotiorum is a fungal **necrotroph** of the **Ascomycetes** phylum
It kills and feeds on dead tissues of a **broad spectrum** of host plants (≈ 400 known)



Not required in the lab

Report of this mode of infection in the field



Signatures of adaptive translation in the genome of polyphagous pathogens

Ingredients:

Population genomics, comparative genomics, modelling

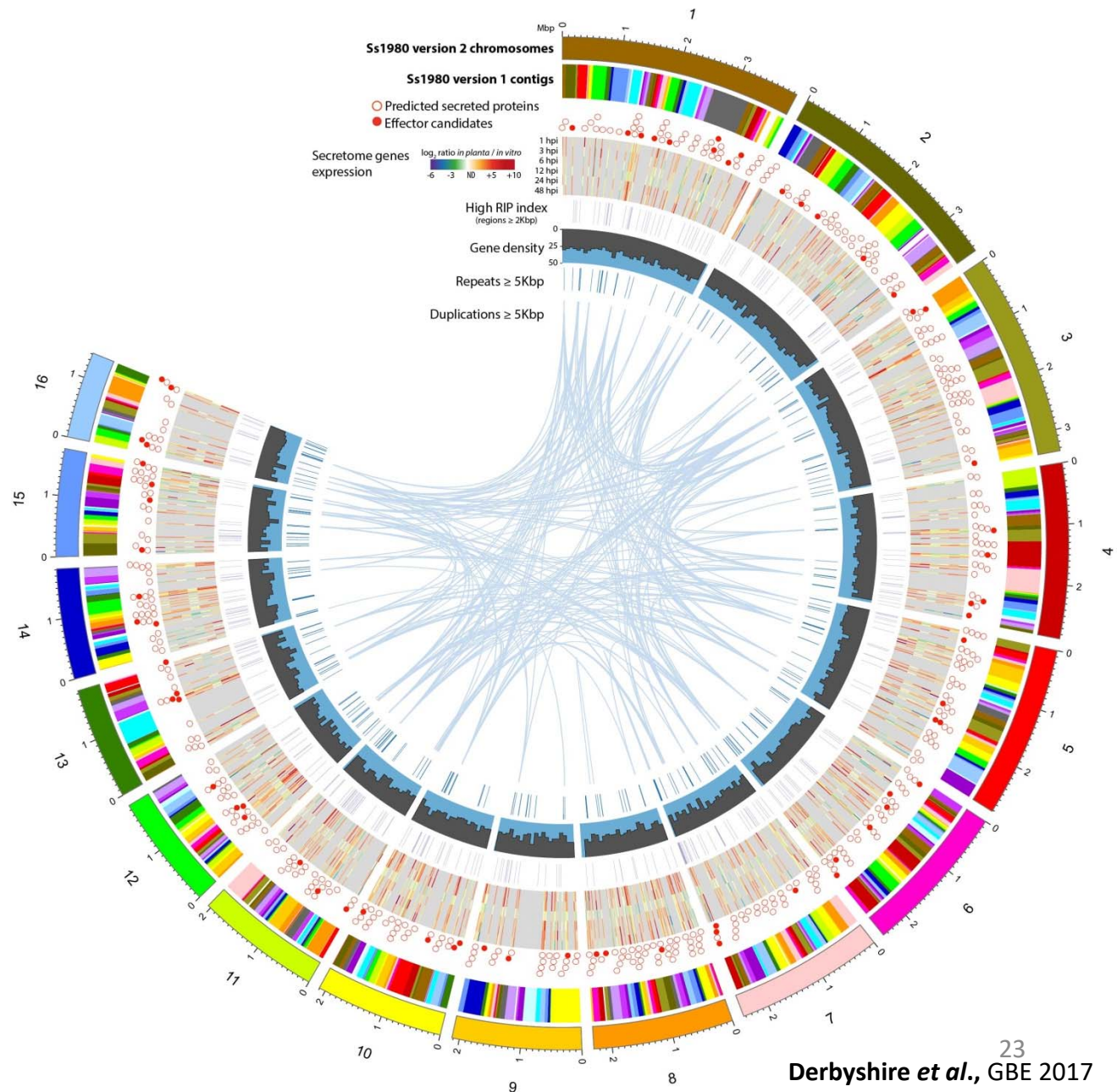
A finished genome for *S. sclerotiorum* 1980



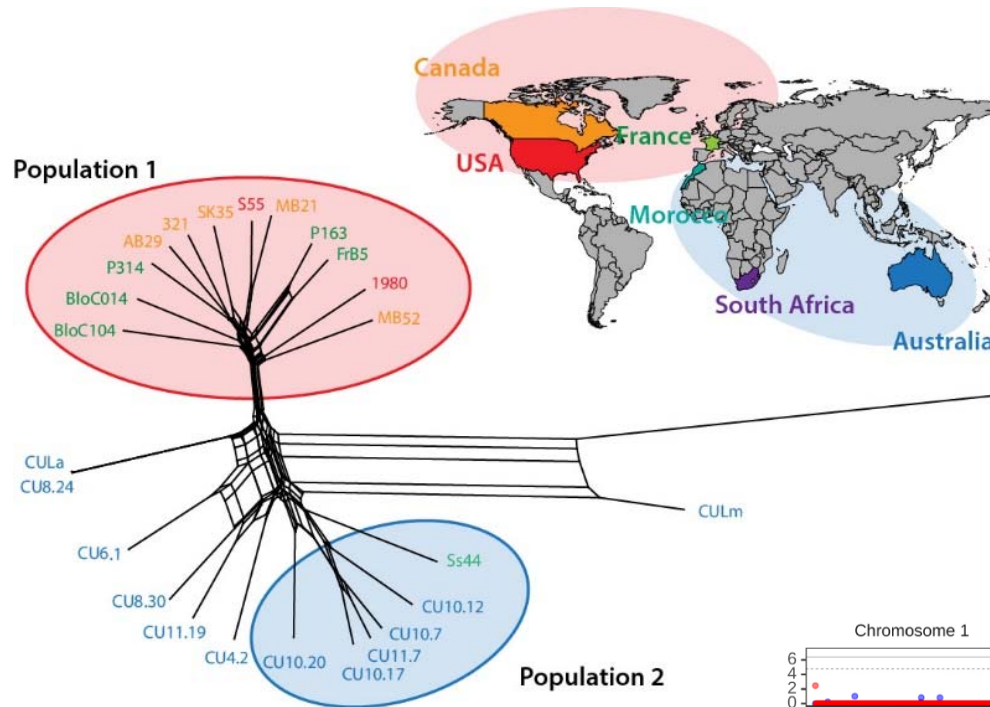
- **Genomic sequencing:**
PacBio + Illumina
36x coverage

- **Annotation:**
>20 RNAseq conditions

- 11 130 gene models
- 12.96% repetitive
- 63 novel effector candidates

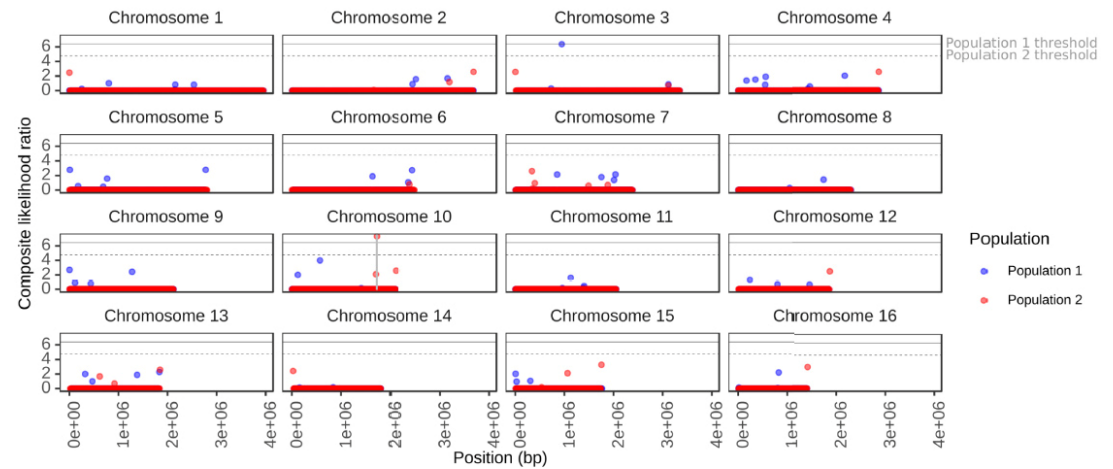


Population genomics of 25 strains – selective sweep scan



- Population substructure:
 - 1) Europe + North America
 - 2) Africa + Australia

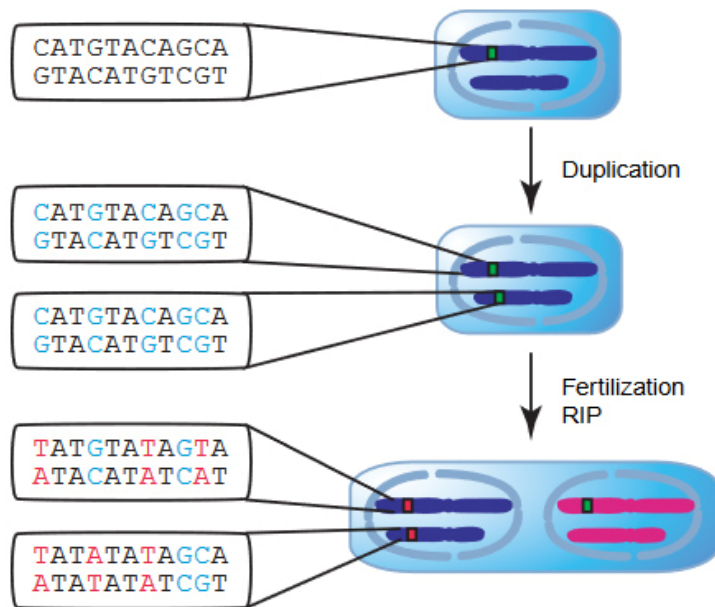
South America & Asia?



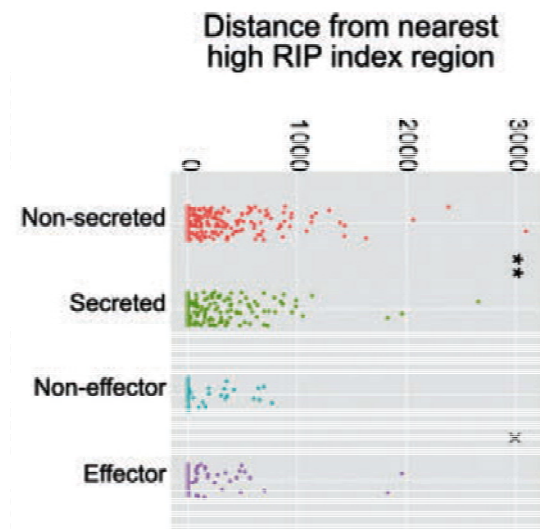
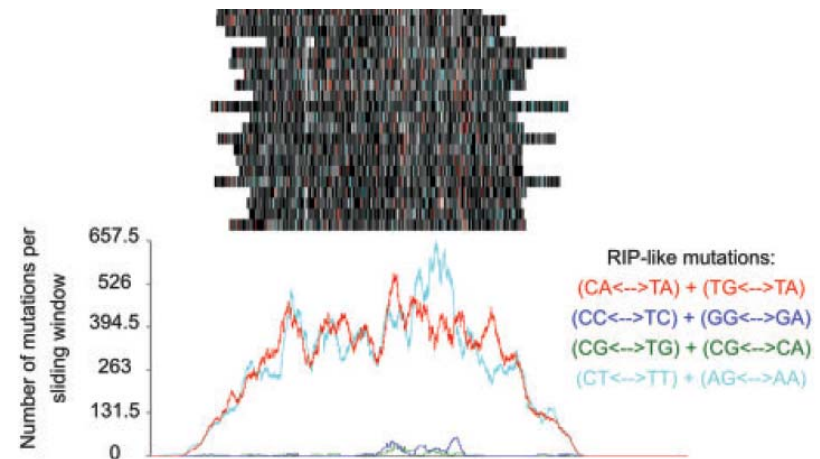
- A single clear selective sweep in pop 2

Signatures of Repeat Induced Point mutations (RIP)

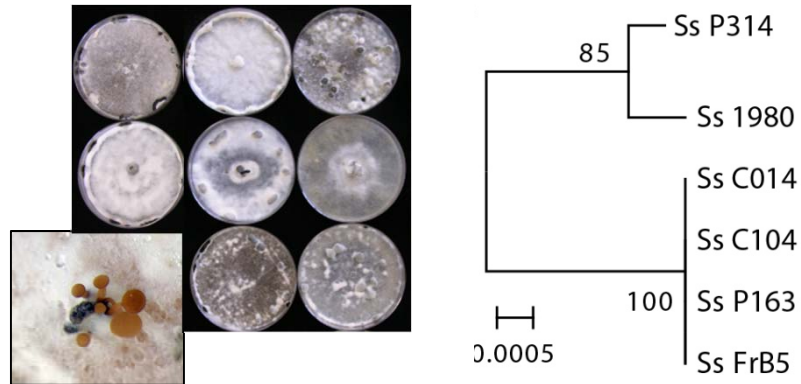
homology-based process that mutates repetitive DNA and frequently leads to epigenetic silencing of the mutated sequences



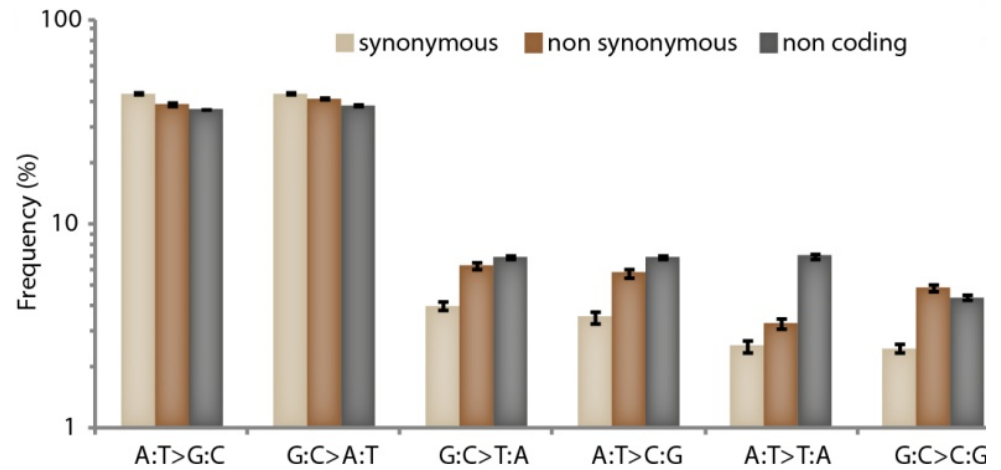
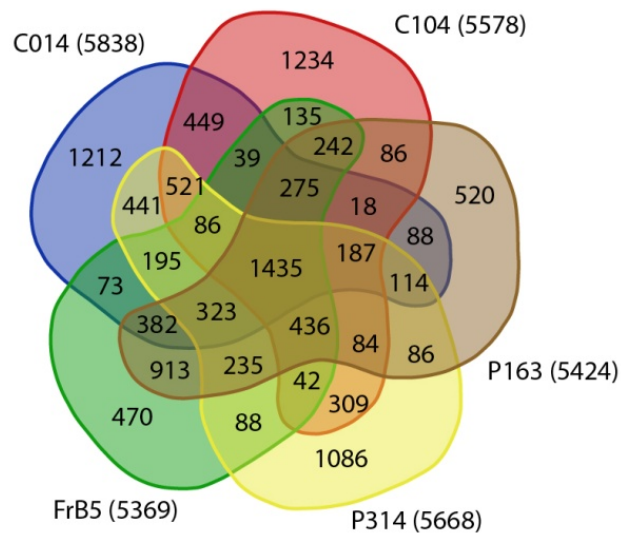
Galagan & Selker, Trends Genet. 2004



SNP patterns in a French population of *S. sclerotiorum* isolates

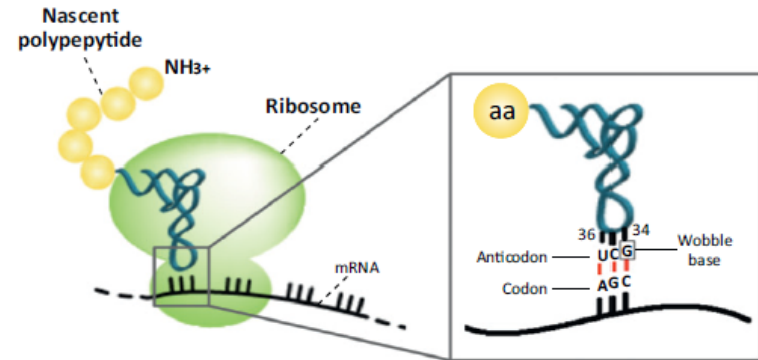
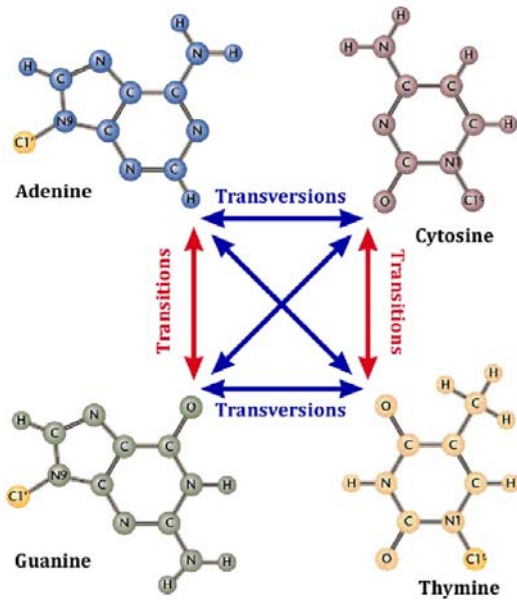


- 5 isolates collected in 2010 reads aligned to Ss1980_v2
- Non redundant SNPs: 11 804 synonymous; 12 540 non-syn.



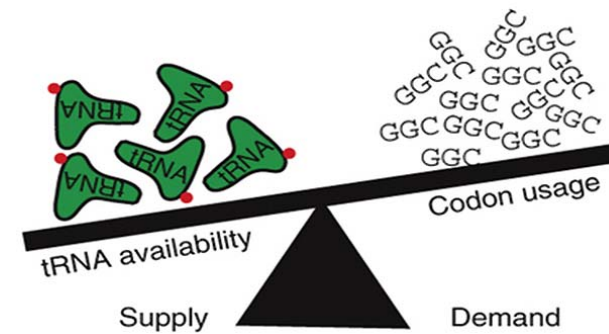
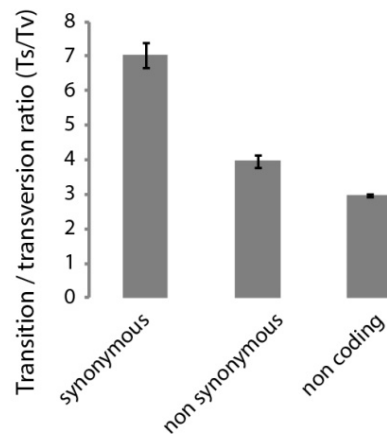
SNP patterns in a French population of *S. sclerotiorum* isolates

- Extreme Ts/Tv ratio for synonymous SNPs



Synonymous substitutions can alter:

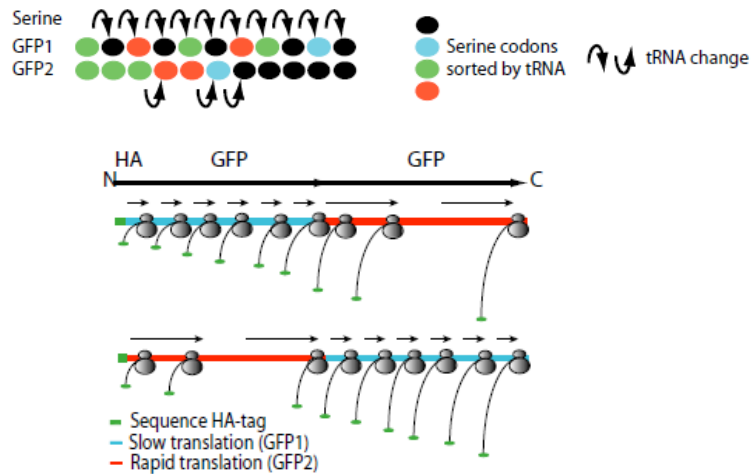
- . Translation speed and accuracy
- . Protein folding
- . Robustness to deleterious mutations



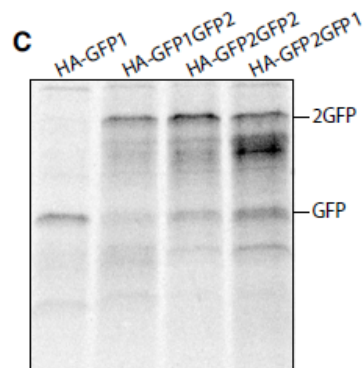
Lauring *et al.* Nat. Rev. Micro. 2013
 Gingold and Pipel, Mol. Sys. Biol. 2011

Are synonymous substitutions always neutral ?

Codon order influences the speed of translation

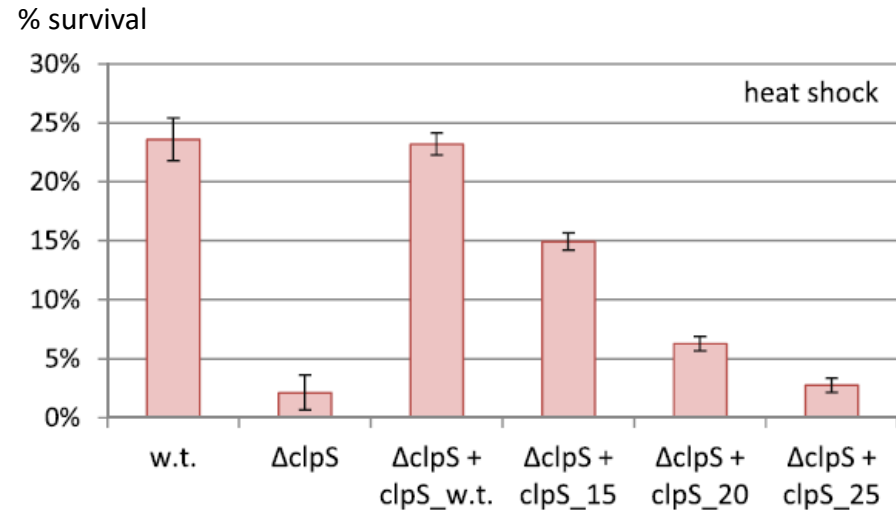


3 min labelling pulse



Cannarozzi *et al.* Cell 2010

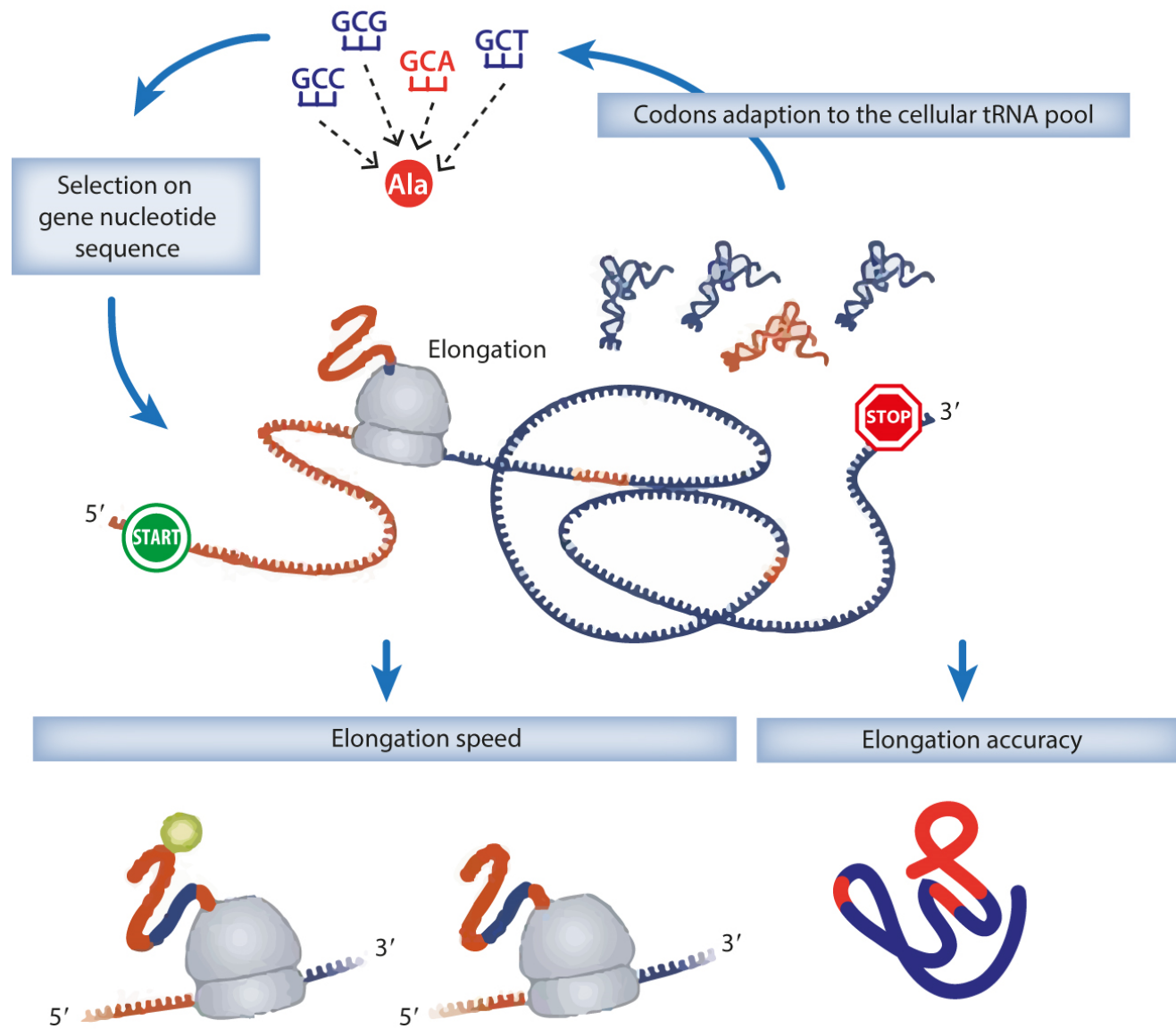
Phenotypic effects of designed gene variants with reduced translation efficiency



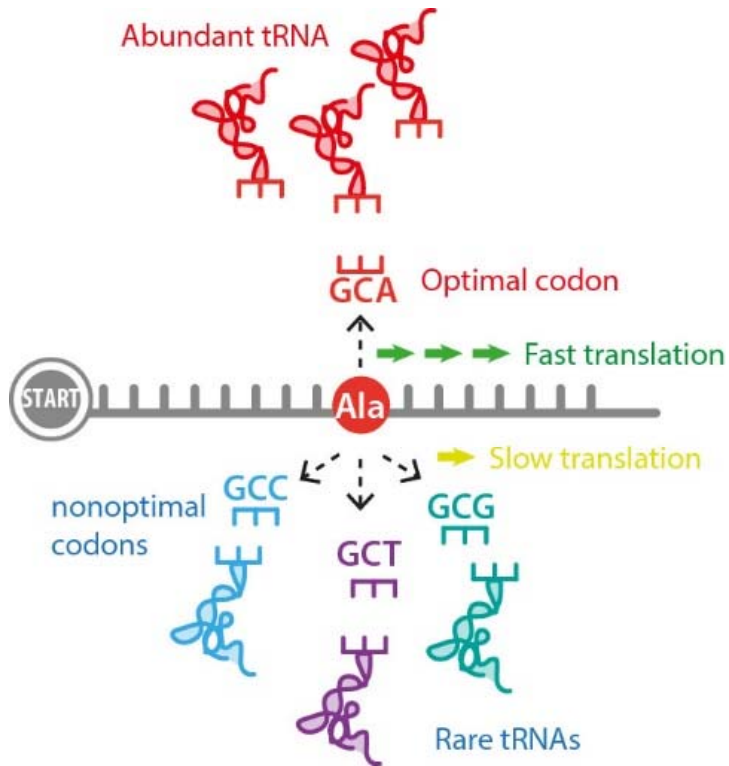
Same protein sequence
Reduced proportion of optimal codons

Krisko *et al.* Genome Biol. 2014

Selection on synonymous substitutions and adaptive translation



Codon variation in a natural population of *S. sclerotiorum*



- SNPs are less frequent in optimal codons

*Long term effect on translation?
Signature of selection?*

