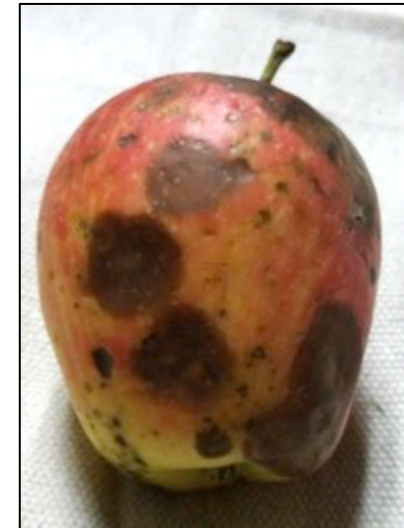


Resisting resistance: Incorporation and preservation of SDHI fungicides for disease management



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SDHI Fungicides: A Brief History

Target site/code	Group name	Chemical Group	Common Name	Comments	FRAC Code
C2: complex II: succinate-dehydrogenase	SDHI (Succinate dehydrogenase inhibitors)	phenyl-benzamides	benodanil flutolanil mepronil	Resistance known for several fungal species in field populations and lab mutants. Target site mutations in sdh gene, e.g. H/Y (or H/L) at 257, 267, 272 or P225L, dependent on fungal species. Resistance management required. Medium to high risk. See FRAC SDHI Guidelines for resistance management.	7
		phenyl-oxo-ethyl thiophene amide	isofetamid		
		pyridinyl-ethyl-benzamides	fluopyram		
		furan- carboxamides	fenfuram		
		oxathiin-carboxamides	carboxin oxycarboxin		
		triazole carboxamides	thifluzamide		
		pyrazole-4-carboxamides	benzovindiflupyr bixafen fluxapyroxad furametpyr isopyrazam penflufen penthioapyrad sedaxane		
		N-methoxy-(phenyl-ethyl)-pyrazole-carboxamides	pydiflumetofen		
		pyridine-carboxamides	boscalid		

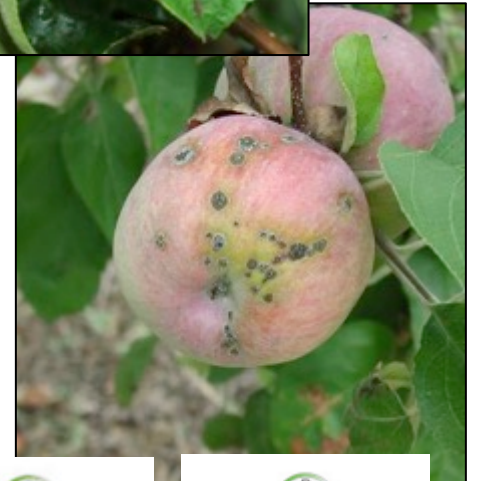
SDHI Fungicides: A Brief History

- 50 years ago: First SDHI product (carboxin) released for seed treatments
 - Very limited m.o.a (mushrooms and smuts)
- 1971-1997: 6 additional SDHI fungicides
 - Still very narrow spectrum
- 2003: Boscalid hits the market
 - Endura, Pristine (+ pyraclostrobin)
 - Broad spectrum, foliar disease



SDHI Fungicide Overview

- “Next generation” **S**uccinate **D**ehydrogenase **I**nhibitor fungicides
 - New spin on an old chemistry
- FRAC 7
 - 9 chemical groups
 - Standalone and pre-mix products for tree fruit disease control
 - Extremely broad spectrum (no oomycetes yet)



 **Pristine**
FUNGICIDE
boscalid


isofetamid

Merivon
Xemium® Brand Fungicide
fluxapyroxad

 **Aprovia**[®]
benzovindiflupyr

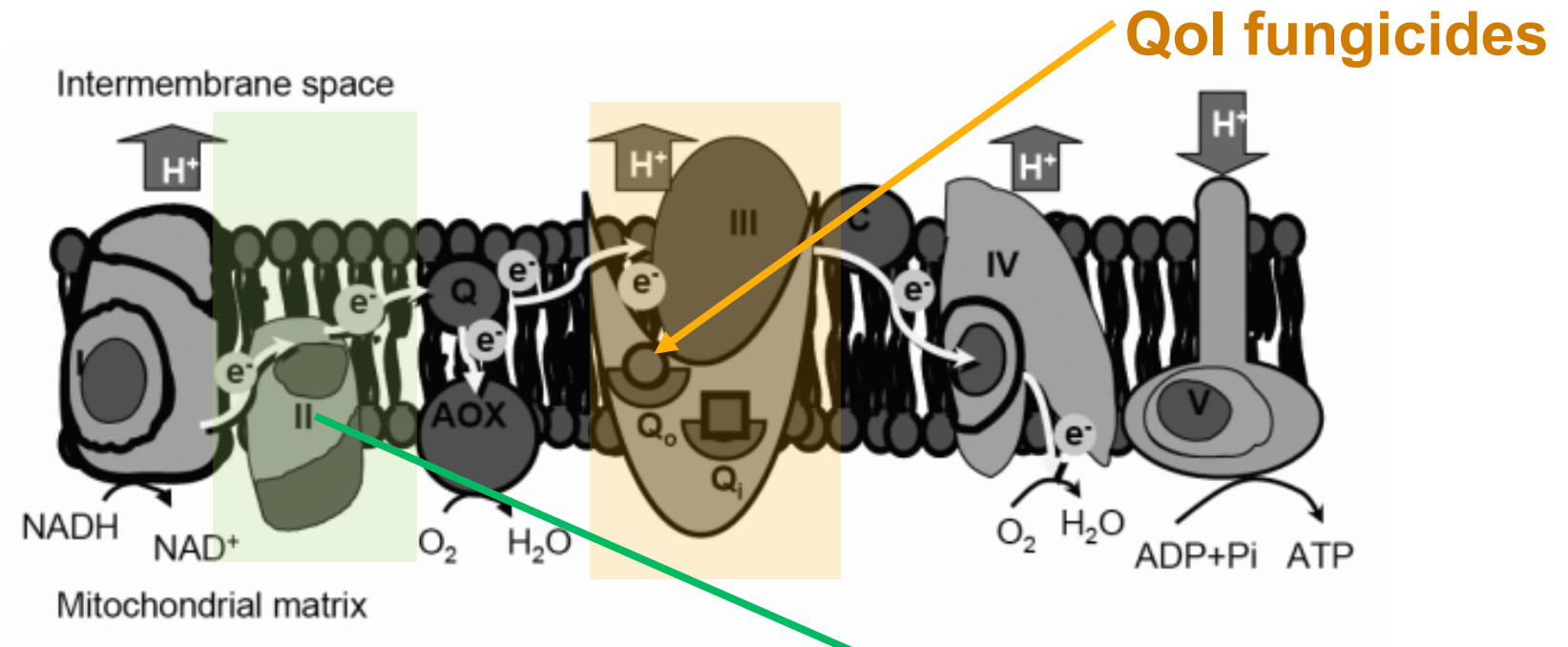
 **DuPont**
Fontelis[™]
angitola
penthioopyrad

 **Luna**
SENSATION

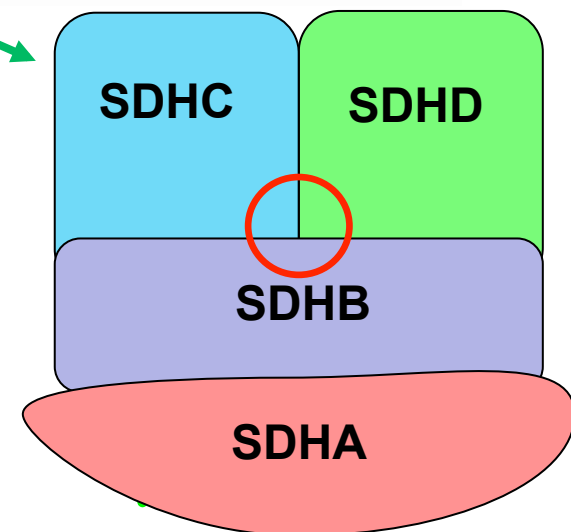
 **Luna**
TRANQUILITY

fluopyram

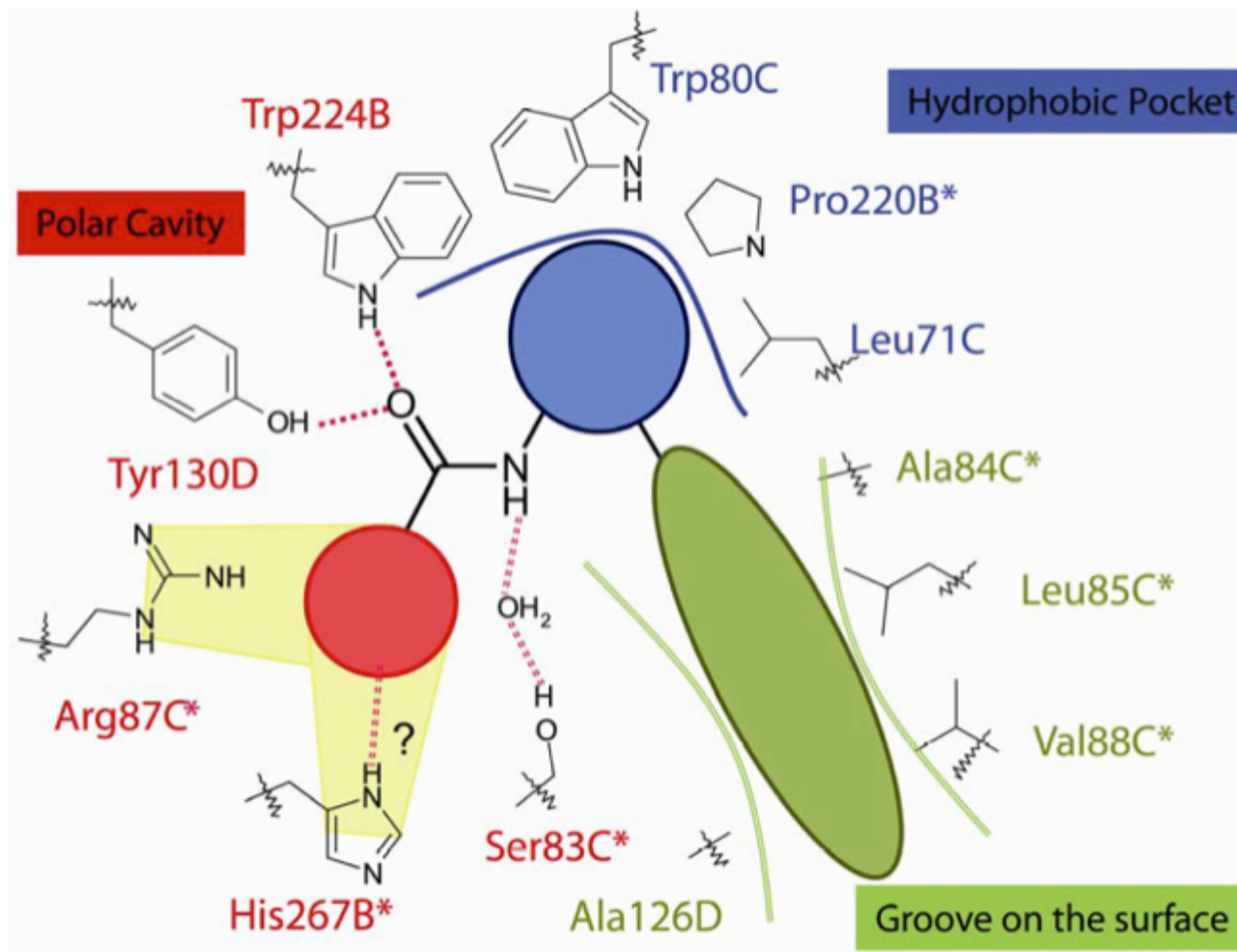
SDHI Fungicide Overview



- **SDHI fungicides:** Respiration inhibitors: Target succinate dehydrogenase reductase enzyme
 - 4 subunits

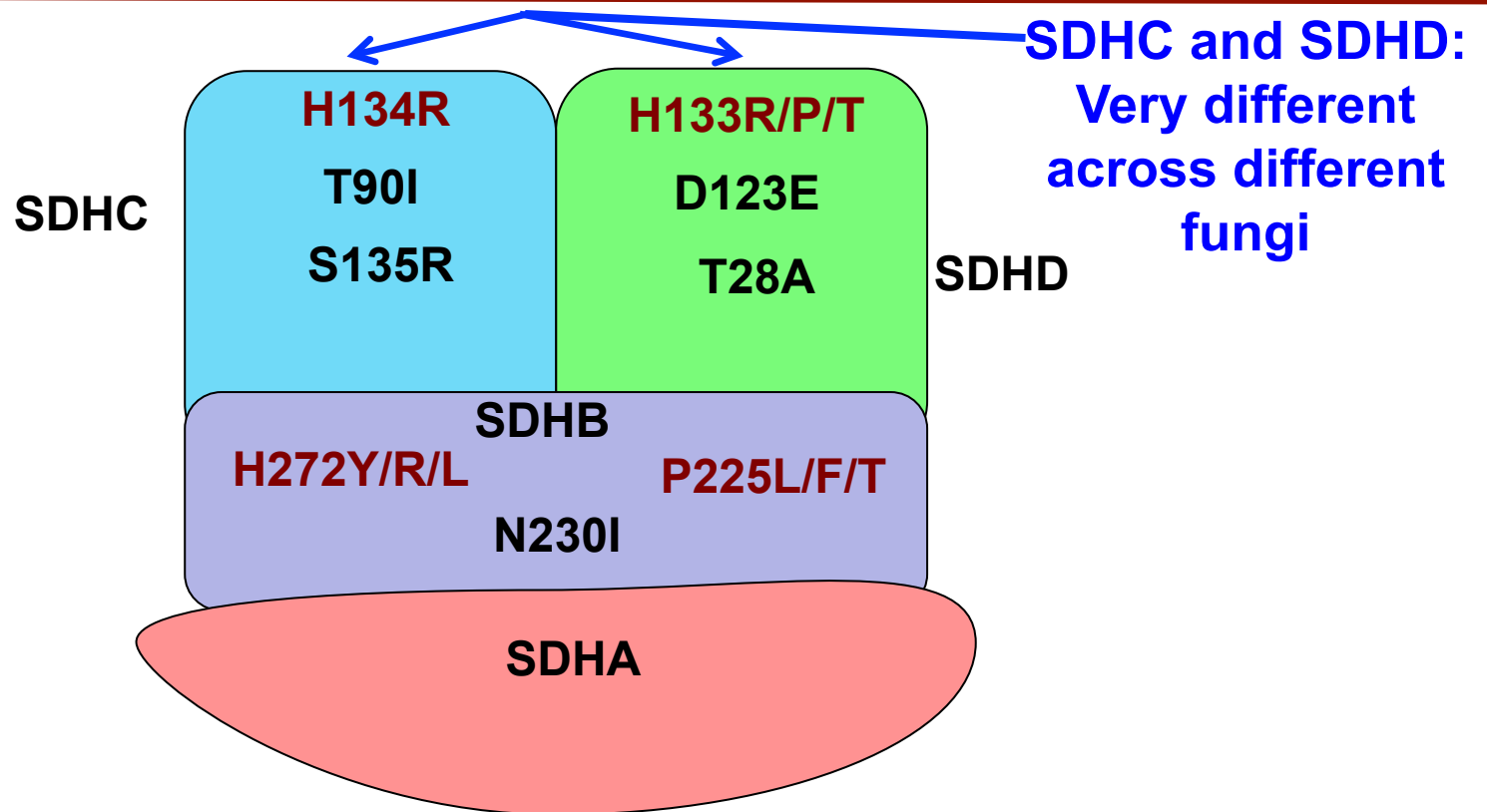


SDHI Fungicide Overview



- Multiple opportunities for mutation
 - Many SDHI fungicide interactions within binding pocket

SDHI Fungicide Overview



- Complete or partial resistance?
 - SDHI fungicide or chemical group
 - Mutation location & substituting residue: Fitness cost
 - # of mutations
 - Pathogen species

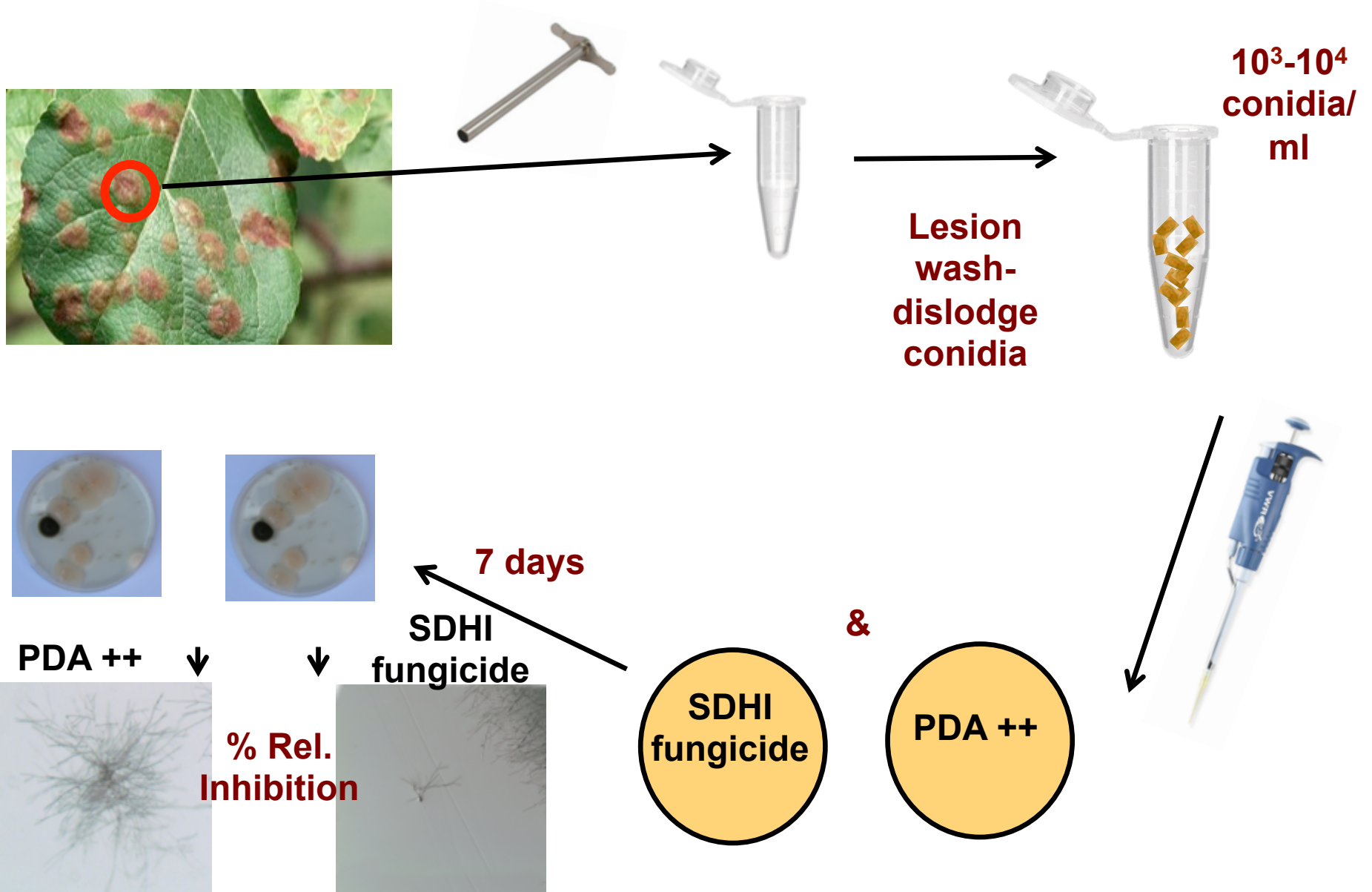
Questions Surrounding the SDHIs

- Are all similarly effective against specific tree fruit pathogens?
- What growth stage should we be targeting?
 - Protectant/germination? Curative/mycelial growth inhibition?
- Is there cross-sensitivity between SDHI fungicides?

In vitro studies (completed in lab with *Venturia inaequalis*)

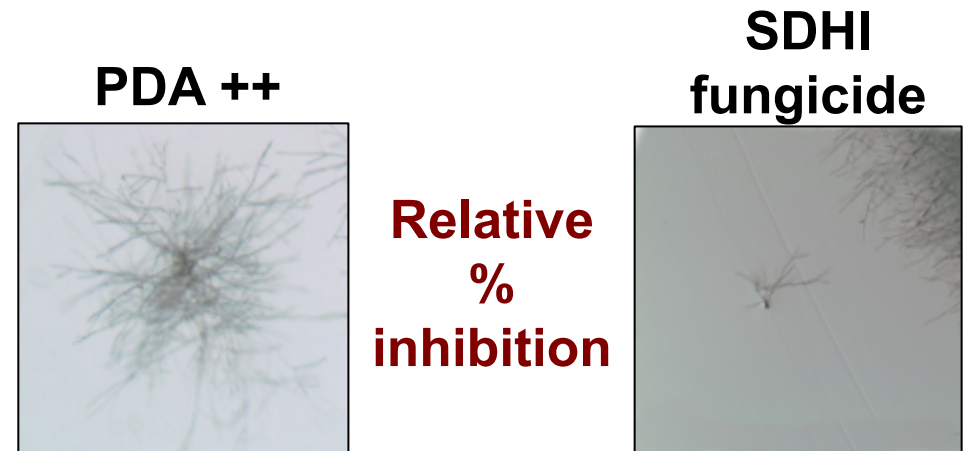
- How do SDHI fungicides perform with fungal populations resistant to other single-site fungicide classes (i.e. QoI, DMI)
- What is the risk of resistance development among the SDHI fungicides?

Question 1: Efficacy of SDHI Fungicides



Baseline Fungicide Sensitivity: Apple Scab

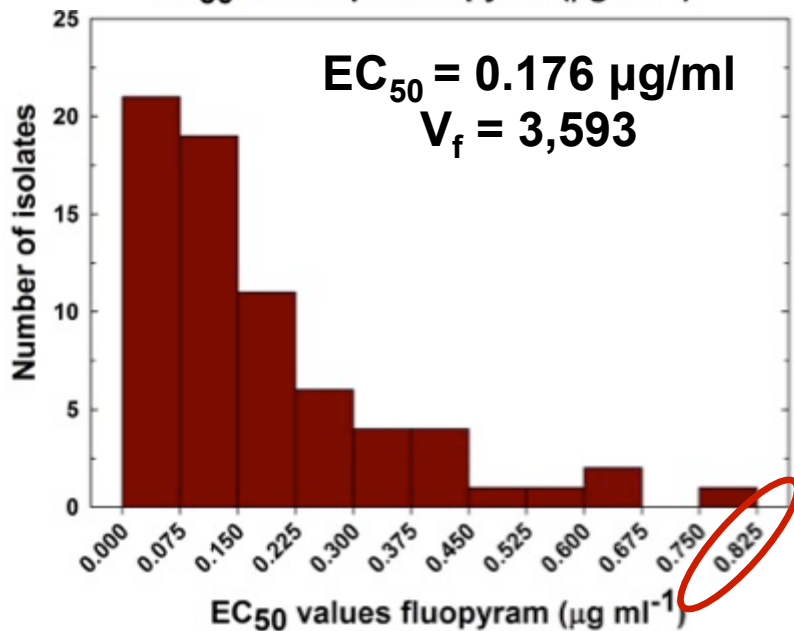
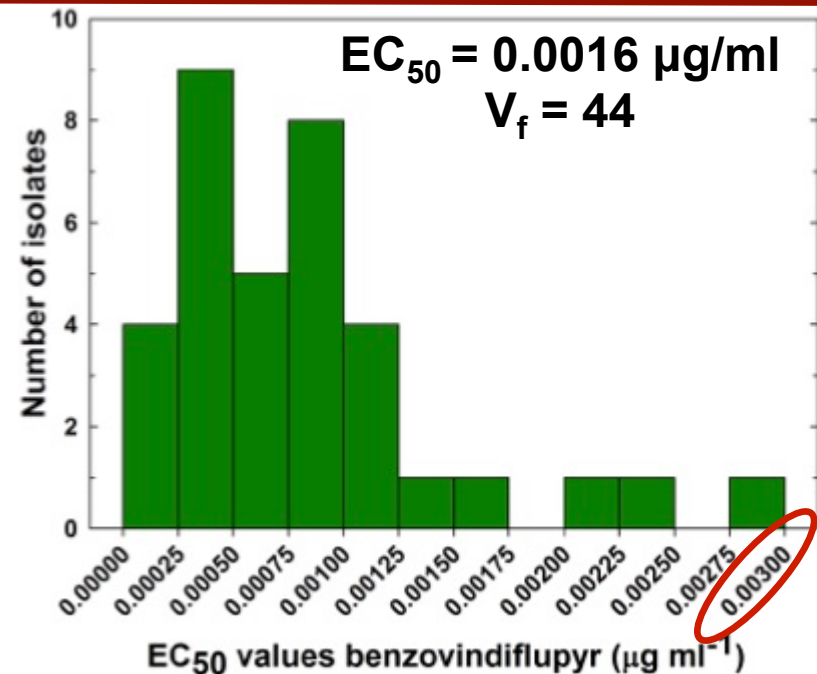
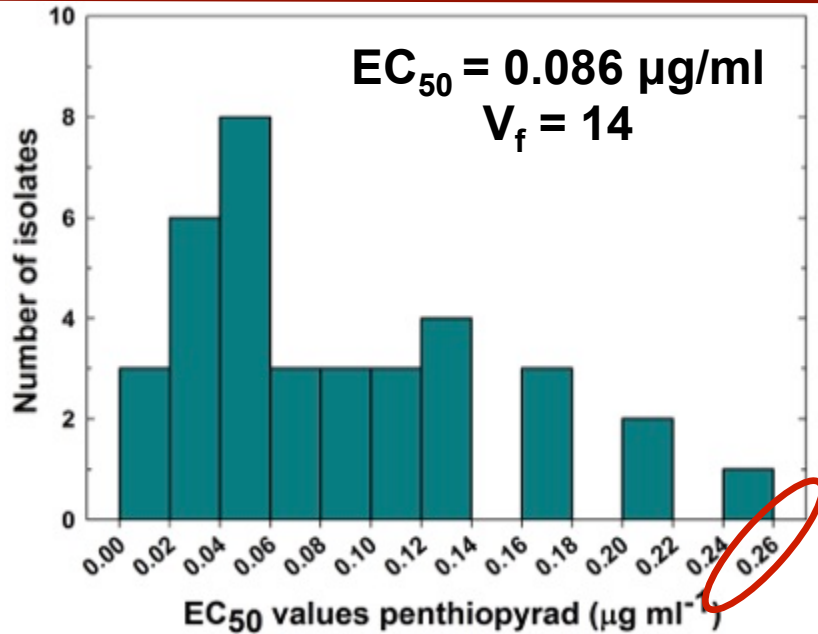
- Conidial germ tube growth inhibition assay
 - Protective mode-targets conidial germination/germ tube elongation
- 2012-2014: 105 (**70**) baseline *V. inaequalis* isolates collected



Round 1 (n = 35)	Round 2 (n = 35)
Penthiopyrad (Fontelis)	Benzovindiflupyr (Aprovia)
Fluopyram (Luna)	Fluopyram (Luna)

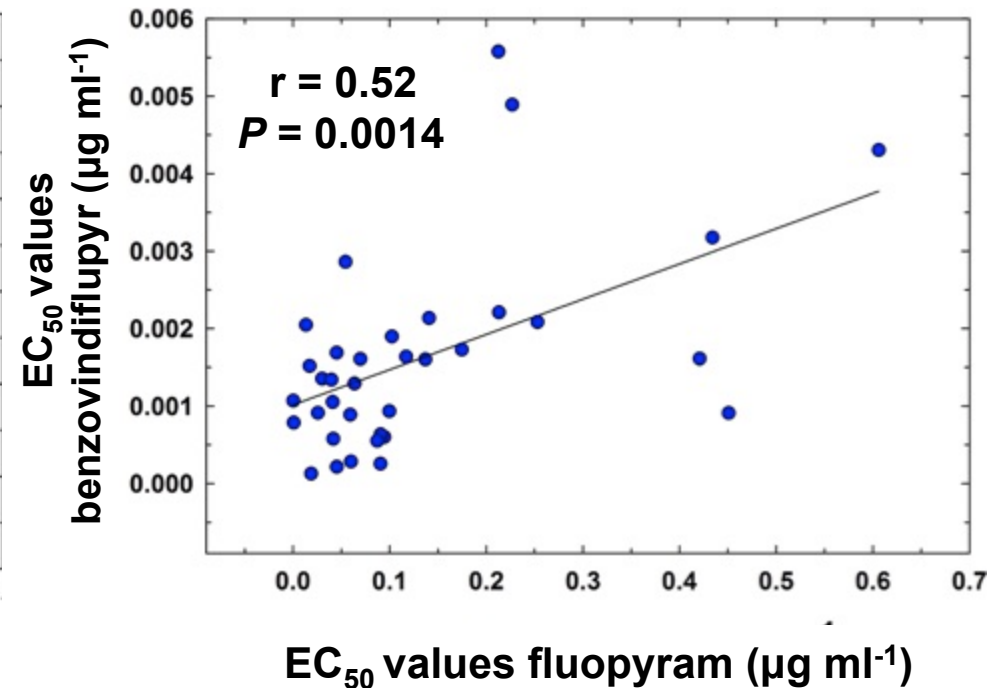
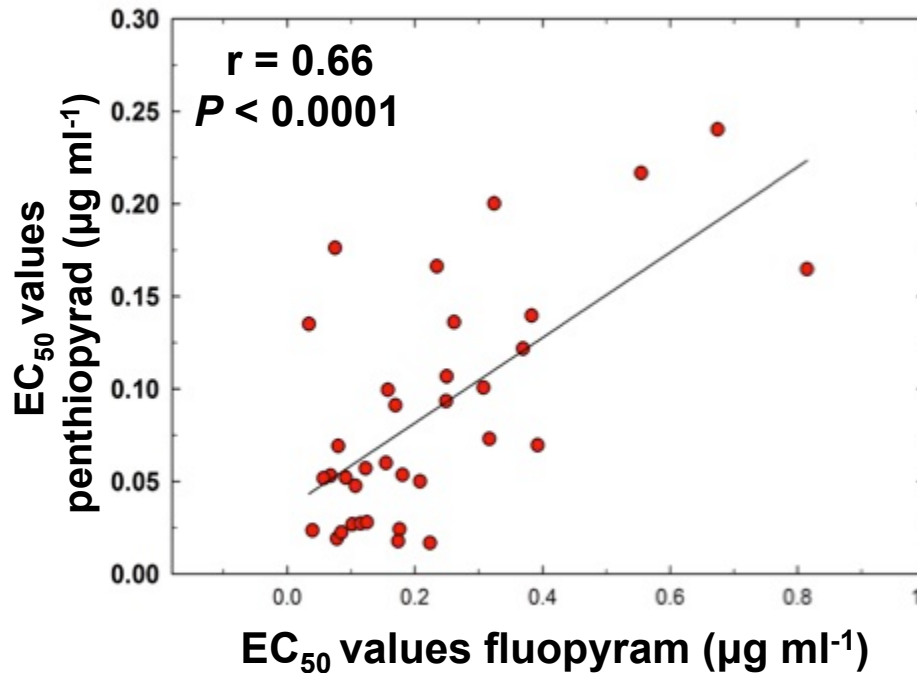
- EC_{50} values using 11 SDHI fungicide concentrations (0.0001 to 10 $\mu\text{g ml}^{-1}$)

SDHI Baseline Sensitivity: Conidial Inhibition



- Benzovindiflupyr (Aprovia) demonstrated highest level of activity during initial growth stages
 - Enhanced interaction with A.A. residues inside binding pocket?

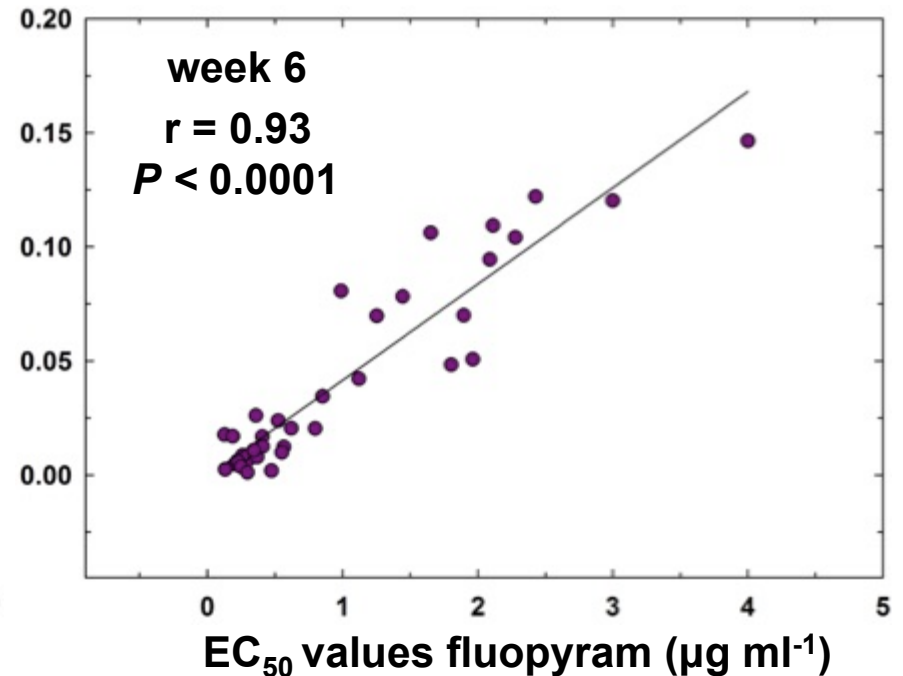
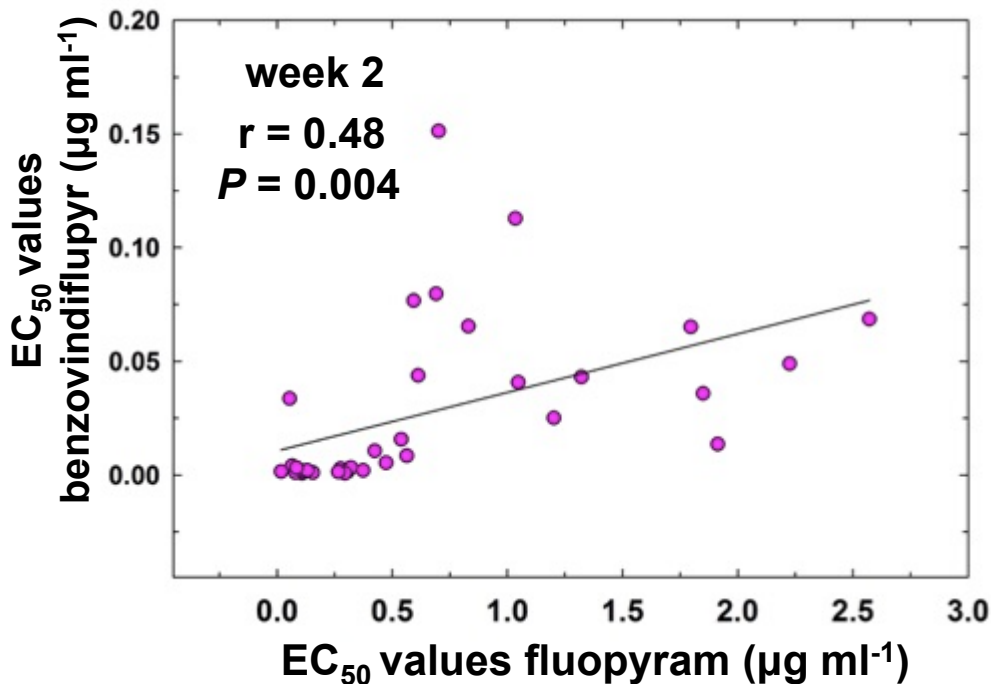
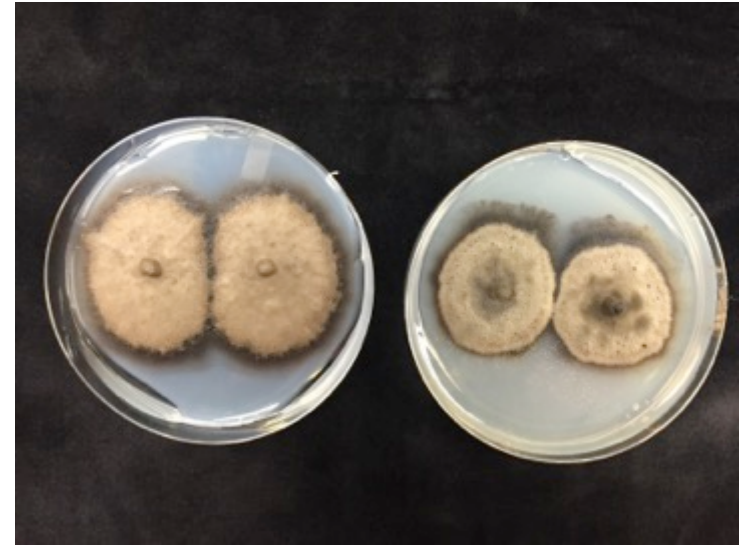
SDHI Baseline Sensitivity: Conidial Inhibition



- Similar and significant levels of cross-sensitivity observed between penthiopyrad or benzovindiflupyr and fluopyram
= Cross resistance between fungicides?
- Role of mutations within different subunits in SDHI sensitivity?
 - *A. alternata*, *D. bryoniae*, *C. cassicola*, and *P. xanthii*

SDHI Baseline Sensitivity: Mycelial Inhibition

- Mycelial growth inhibition assay
 - Curative/kick-back mode
 - Benzovindiflupyr & fluopyram only
- 2012-2014: 105 (35) baseline *V. inaequalis* isolates collected
 - measured biweekly for 6 weeks



SDHI Baseline Sensitivity Summary

- SDHI fungicides can inhibit both conidial germ tube growth and mycelial growth however greater efficacy during early growth stages
 - Benzovindiflupyr EC₅₀: 0.002 vs. 0.043 µg/ml
 - Fluopyram EC₅₀: 0.176 vs. 2.02 µg/ml
 - Higher energy requirements during different growth stages?
- Greatest control when applied in protective mode?
- Cross-sensitivity observed across SDHI chemical groups, but more apparent during later stage mycelial growth

Questions Surrounding the SDHIs

- Are all similarly effective against specific tree fruit pathogens?
 - What stage of growth should we be targeting?
 - Protectant/germination? Curative/mycelial growth inhibition?
 - Is there cross-sensitivity between SDHI fungicides?
-
- How do SDHI fungicides perform with fungal populations resistant to other single-site fungicide classes (i.e. QoI, DMI)
 - What is the risk of development for resistance among the SDHI fungicides?

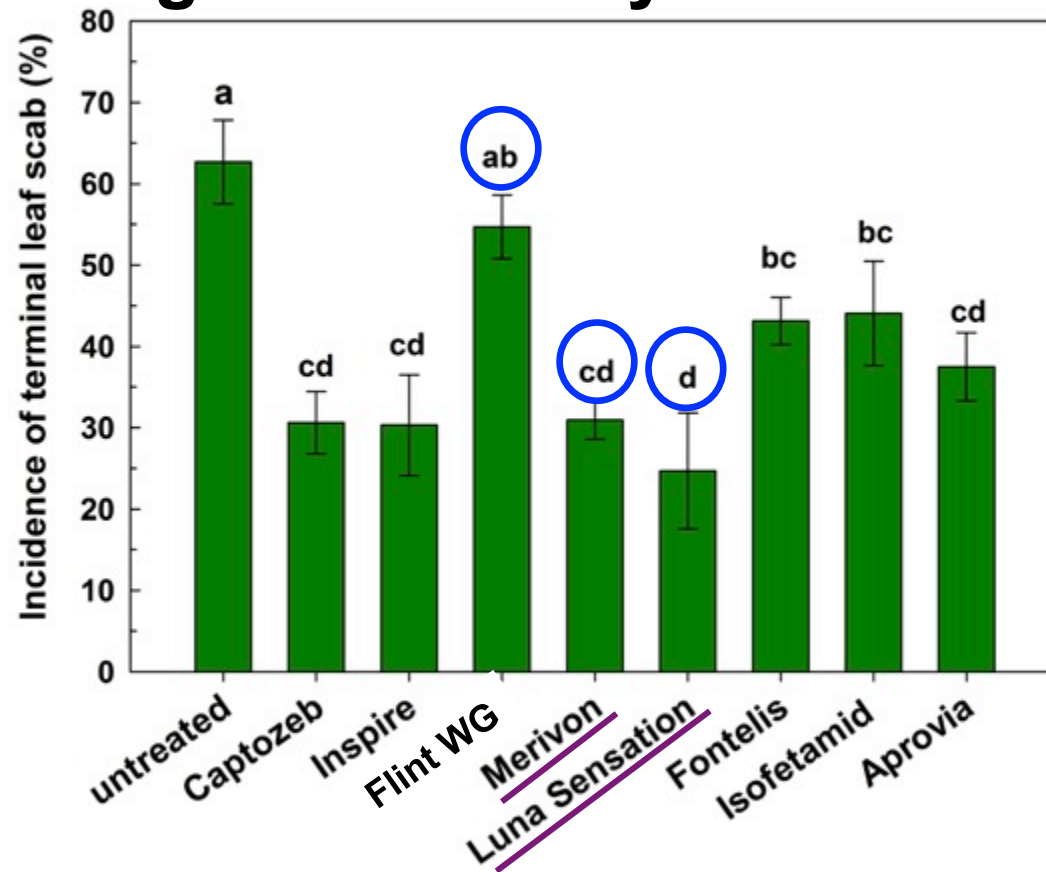
2015 SDHI Efficacy Trial

- Mature orchard site of paired ‘Empire’ and ‘Jonagold’ trees on M.9/M.111 interstem
- *V. inaequalis* population resistant to DMIs (2010) and Qols (2011); no confirmed SDHI resistance
 - Applied dilute to run-off w/handgun sprayer (200psi)
 - Dodine, DMIs, Qols, SDHIs, protectants



SDHI Efficacy Trials: Apple Scab

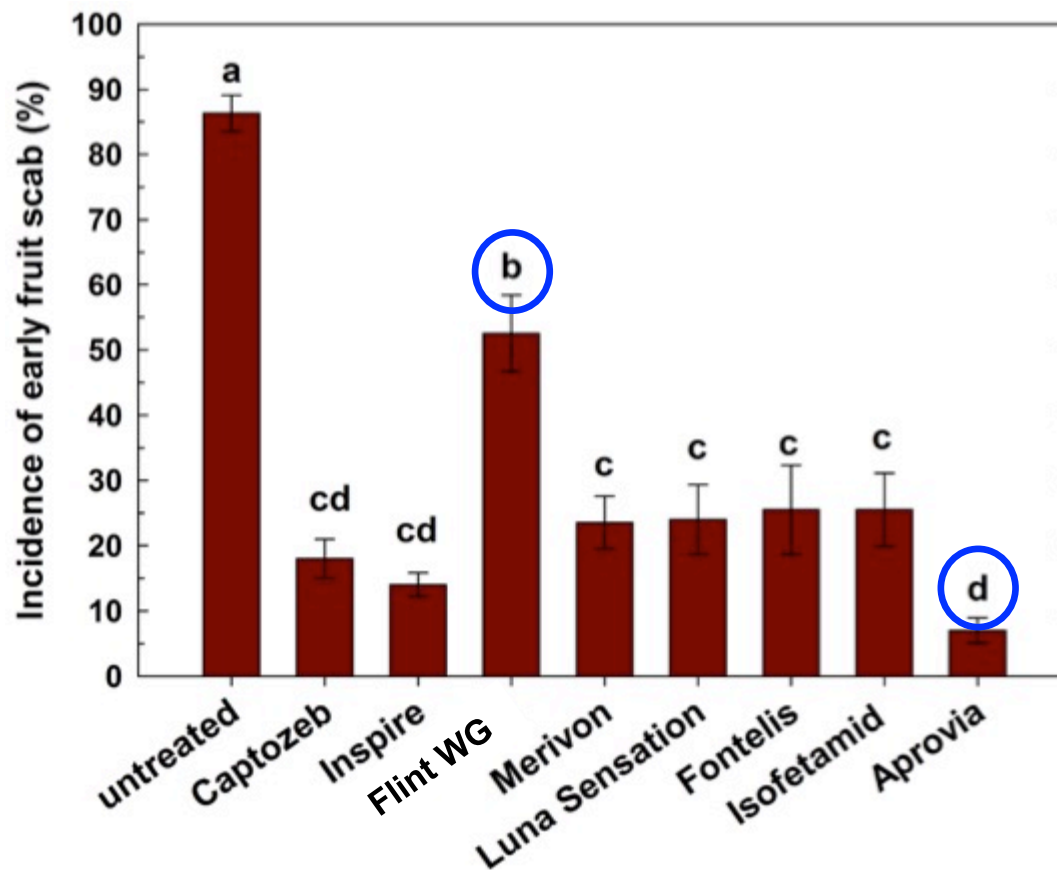
SDHI fungicide efficacy: Terminal leaves



- Primary apple scab infections still occurring mid- late June: high incidence in general
- SDHI/QoI premix products: lower incidence of apple scab on leaf terminals

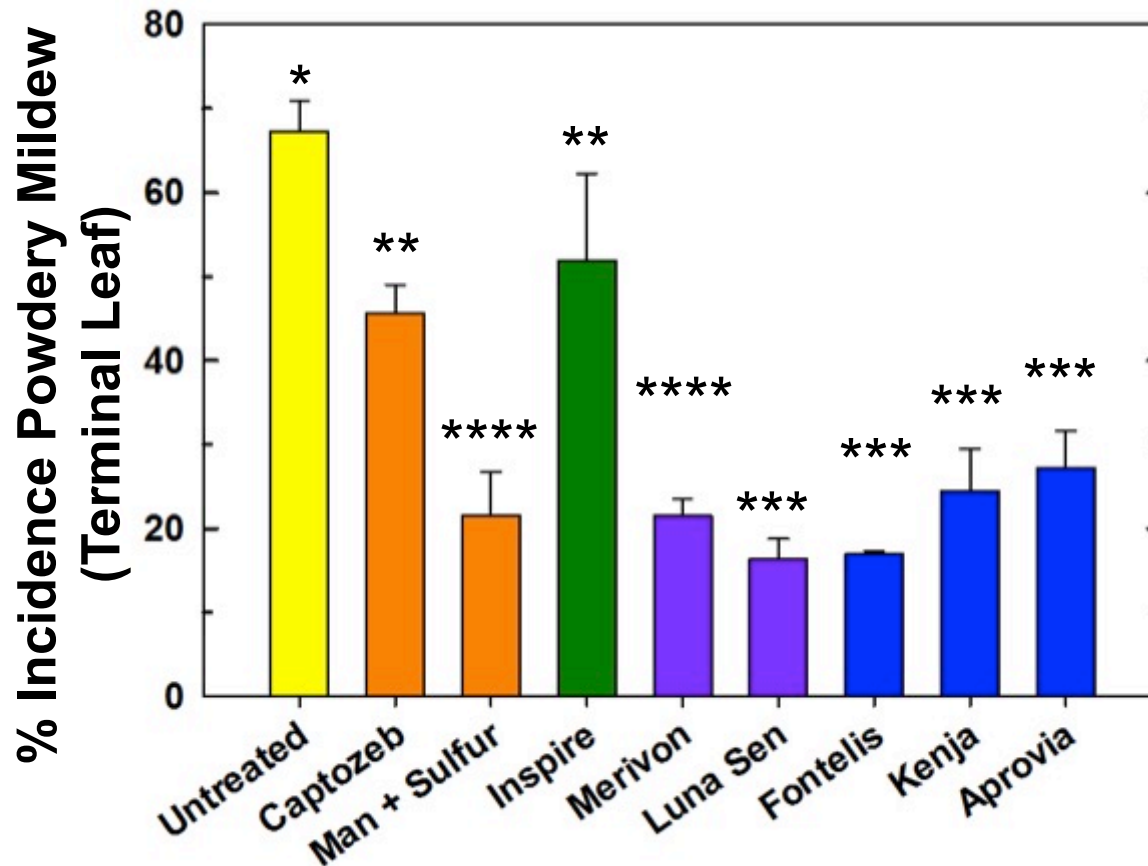
SDHI Efficacy Trials: Apple Scab

SDHI fungicide efficacy: Mature fruit



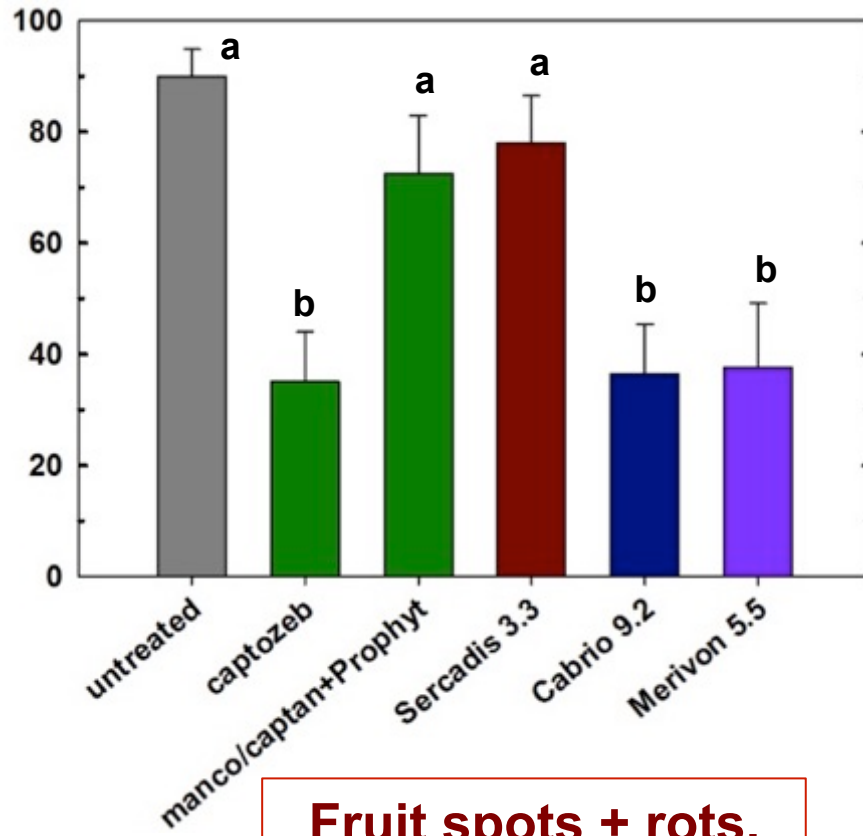
- No difference in apple scab incidence on fruit between stand alone SDHI and SDHI/QoI premix
 - Aprovia (benzovindiflupyr) exception

SDHI Efficacy Trials: Powdery Mildew

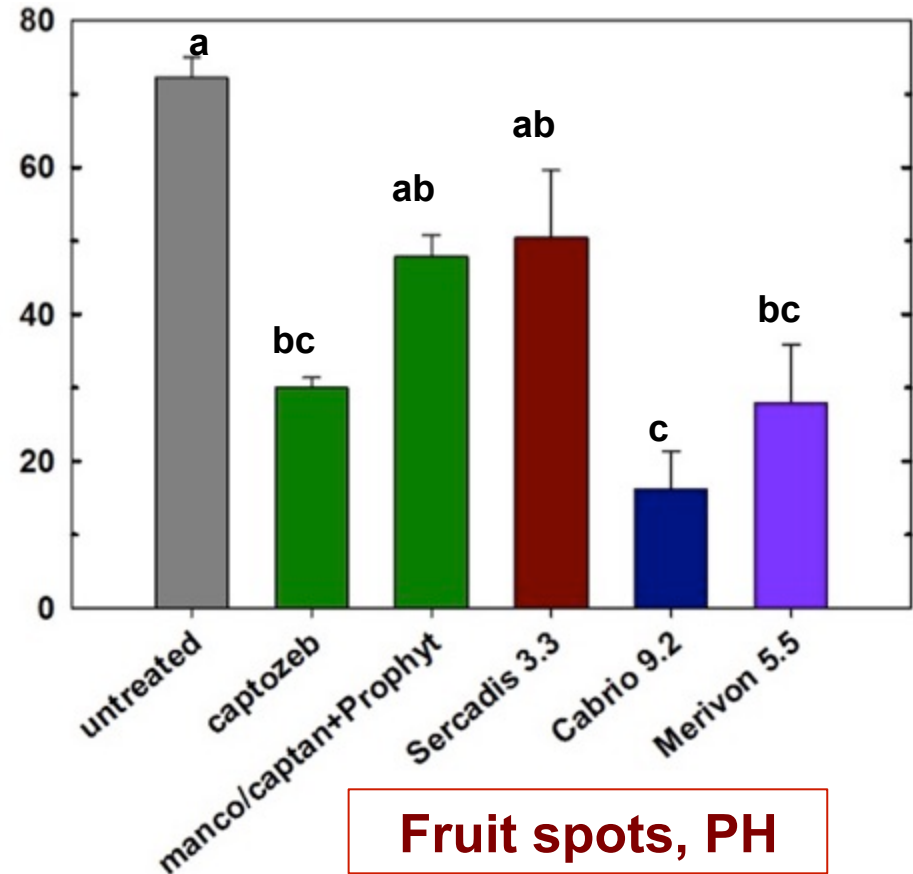


- Aprovia: Best for apple scab, among worst against powdery mildew

SDHI Efficacy Trials: *Colletotrichum* spp.



**Fruit spots + rots,
Harvest**



Fruit spots, PH

- Cabrio (Pyraclostrobin, Group 11) and Merivon provided greater control against fruit rot caused by *Colletotrichum* at harvest and post-harvest compared to Sercadis (fluxapyroxad, Group 7)

Questions Surrounding the SDHIs

- Are all similarly effective against specific tree fruit pathogens?
- What stage of growth should we be targeting?
 - Protectant/germination? Curative/mycelial growth inhibition?
- Is there cross-sensitivity between SDHI fungicides?
- How do SDHI fungicides perform with fungal populations resistant to other single-site fungicide classes (i.e. QoI, DMI)
- What is the risk of development for resistance among the SDHI fungicides?

Mitigating SDHI Resistance: What We Know

- Mutation #, location, and SDHI active ingredient can all affect resistance level (partial resistance vs. complete)
- Cross-resistance has been observed across some SDHIs and not others
 - Depends on where mutation is: Mutation in SDHC subunit may result in cross-resistance between 2 SDHI fungicides, but mutation in SDHB may only confer resistance to one of those fungicides:
- Pre-selection and multiple applications

Mitigating SDHI Resistance

- Apply fungicides when fungal population numbers are low-apply before infection when possible



OR



- Use highest legal rates of fungicide
- Get complete coverage of host, make sure sprayer is calibrated, avoid ARM

Mitigating SDHI Resistance

- Apply fungicides in tank mixture with effective, unrelated fungicides
 - i.e. Mancozeb + Fontelis: Mancozeb should “clean up” any resistant “survivors”

mancozeb

Fontelis



Mitigating SDHI Resistance

- Use correct SDHI fungicide for target pathogen
 - Be aware that SDHI fungicide may not be efficacious against other major pathogens (Aprovia: apple scab and powdery mildew)
- Rotate and be careful of promoting pre-mix partner resistance (QoI)



Restrictions: Do not apply more than 11 oz of Flint Fungicide per acre per season. Do not apply Flint Fungicide within 14 days of harvest. To reduce the potential for resistance, limit Group 11 fungicides to two sequential applications and alternate with at least two applications of fungicides from a different Group before making a third application with a Group 11 fungicide. Do not apply more than 4 applications of Flint Fungicide or any other Group 11 fungicide per season. Do not apply Flint Fungicide where spray drift may reach Concord grapes or crop injury may occur. Spray equipment must be rinsed after applying Flint Fungicide before application of other products to Concord grapes or crop injury may occur.



Restrictions:

- Do not apply more than 21.0 fl oz of LUNA SENSATION per acre per year.
- Apply using ground, aerial, or chemigation equipment.
- Regardless of formulation or method of application, do not apply more than 0.446 lbs fluopyram or 0.343 lbs trifloxystrobin per acre per year, including soil and foliar uses.
- Do not make more than 4 applications per year.

Acknowledgements and Questions?

- State, federal, and institutional funds appropriated to the Cornell NYSAES and to NCSU, NYSAES
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