Do we always have the tools to manage resistance?

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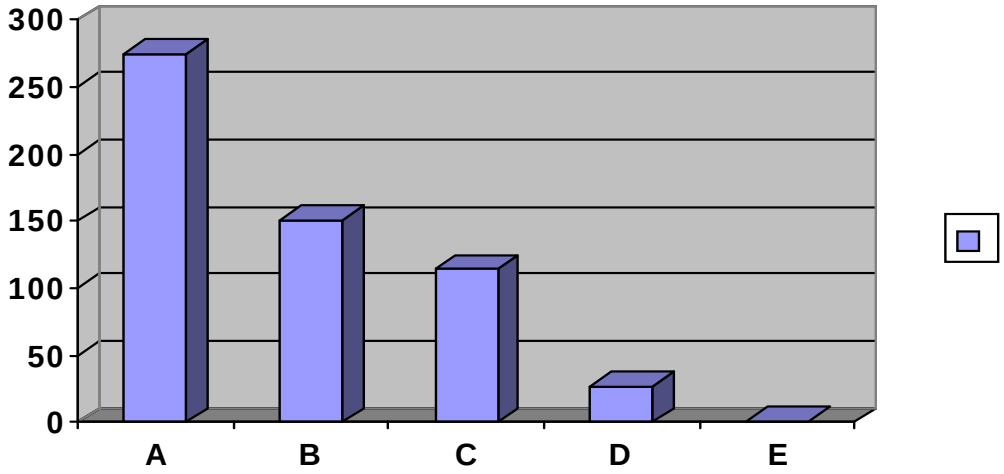
Aim of talk

- Resistance – What cost to growers?
- New biochemistry offers opportunities for novel modes of action
- Use of rapid diagnostics

What is the resistance problem ?

A. Total pathogens **B. Resistance Reports**
C. Found in the field **D. Performance eroded**
E. Control failures



What does resistance cost UK growers ?

Cereal eyespot disease and MBC resistance

	1985 £m	2010 £m	
Lost wheat production (3%)	25.2	67.2	224
Additional cost –prochloraz	2.0	6.0	--
Total	27.2	73.2	224

What is needed?

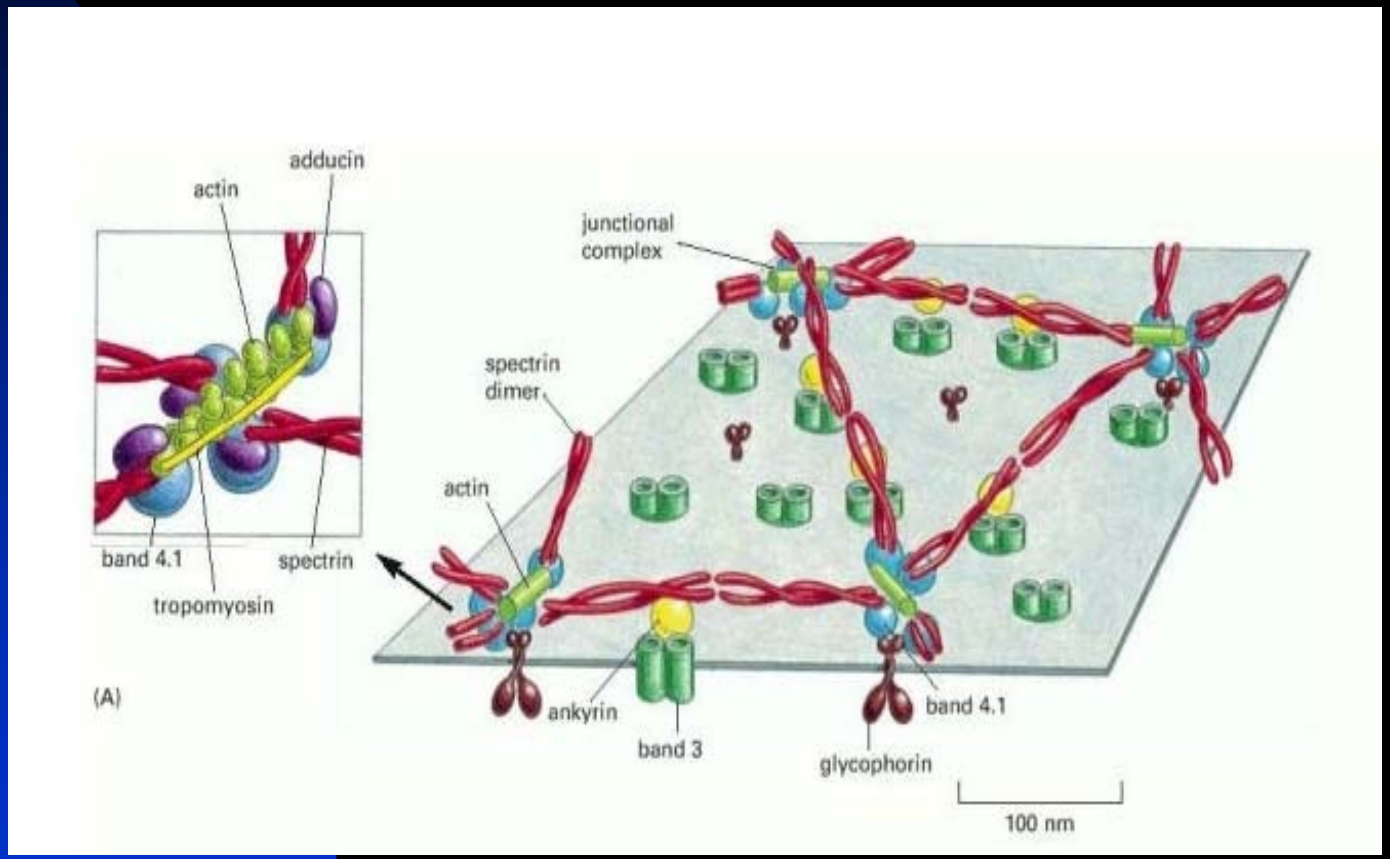
New modes of action

More Biochemistry

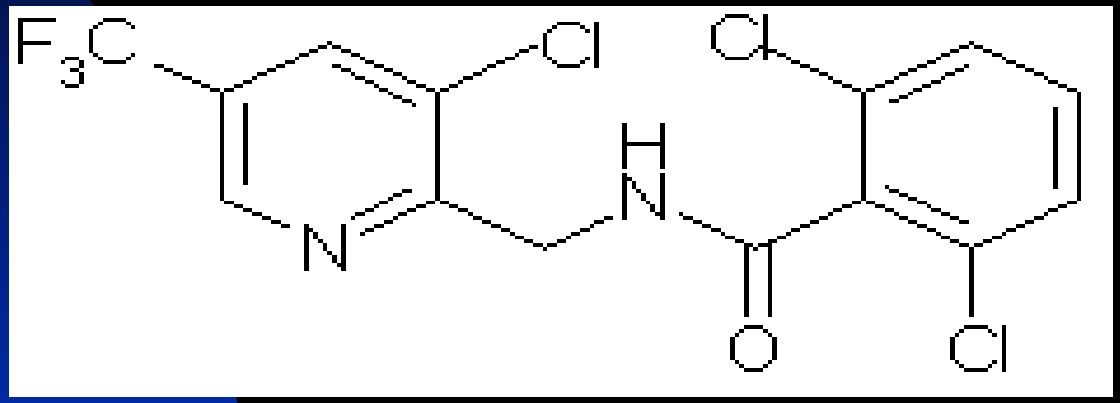
New modes of action for resistance management

- Cytoskeleton
- Signal transduction
- Protein structure
- Gene silencing - RNAi

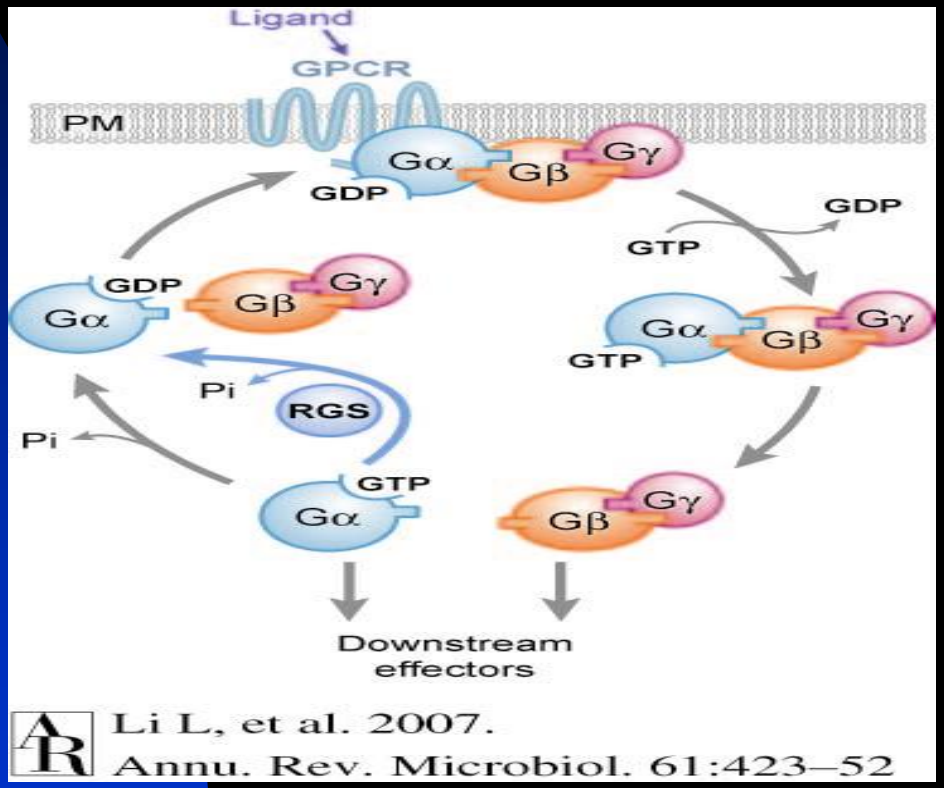
Membrane cytoskeleton



Fluopicolide – Oomycete fungicide



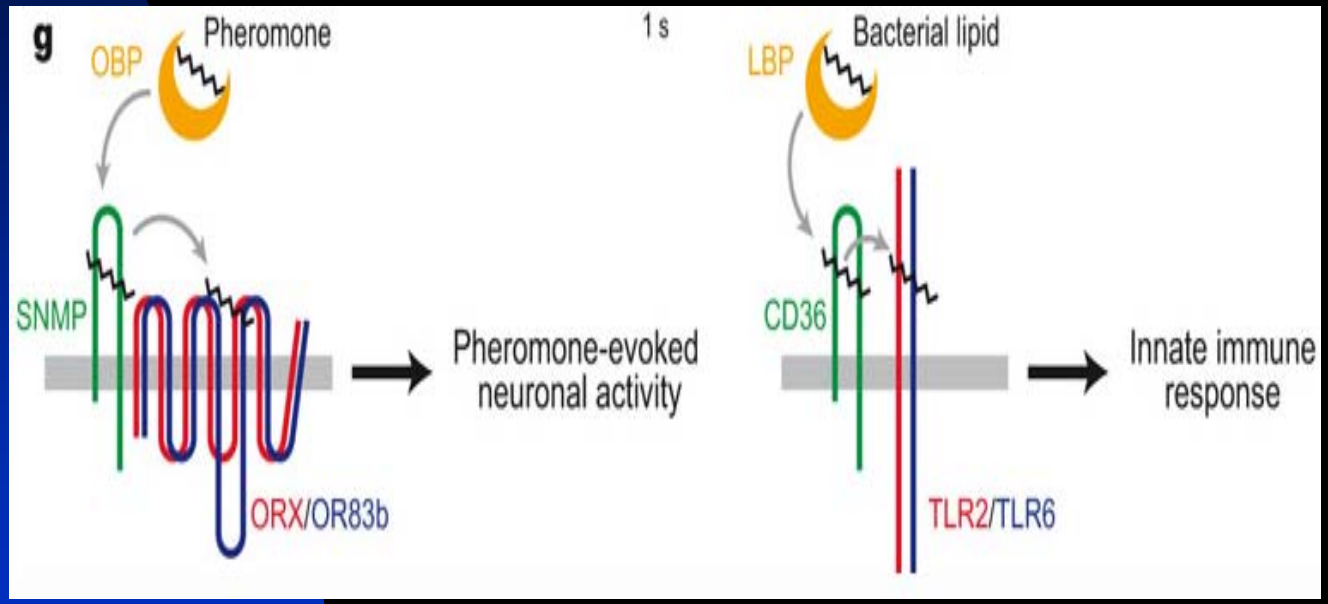
Signal transduction - GPCR



Li L, et al. 2007.
Annu. Rev. Microbiol. 61:423–52

Pheromone traps in crop protection

Pheromone transport to Odorant Binding Protein



Benton *et al.* (2007) *Nature* 450 289-93

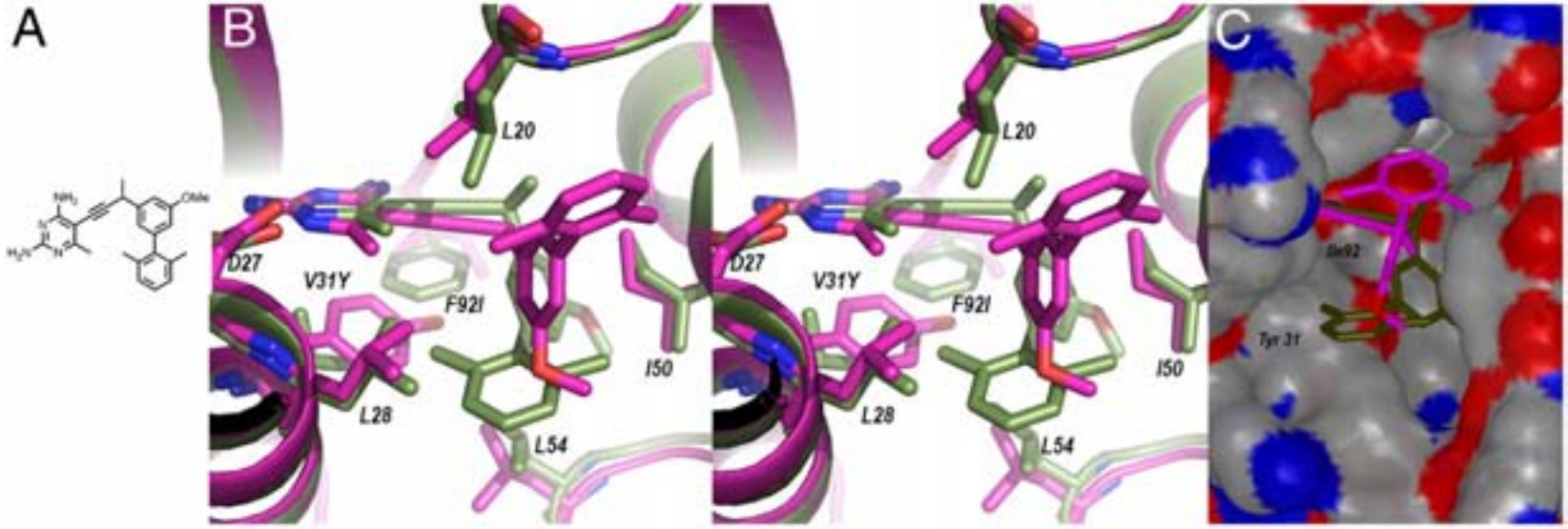
B

Frey, K.M., Georgiev, I., Donald, B.R. & Anderson, A.C.

Predicting resistance mutations using protein design algorithms.

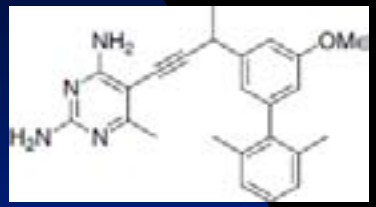
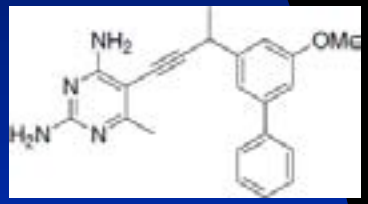
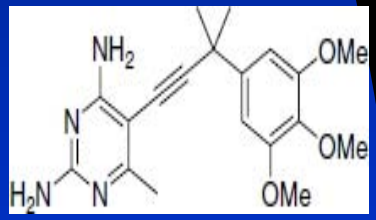
***Proc. Nat. Acad. Sci. USA*, (2010) 107, 13707-13712.**

Stereo view of the superposition of the ternary crystal structures of Sa (WT) DHFR (green) and Sa(V31Y/F92I) DHFR (magenta) bound to NADPH and compound 1 (A) as B) stick models and C) surface rendering.



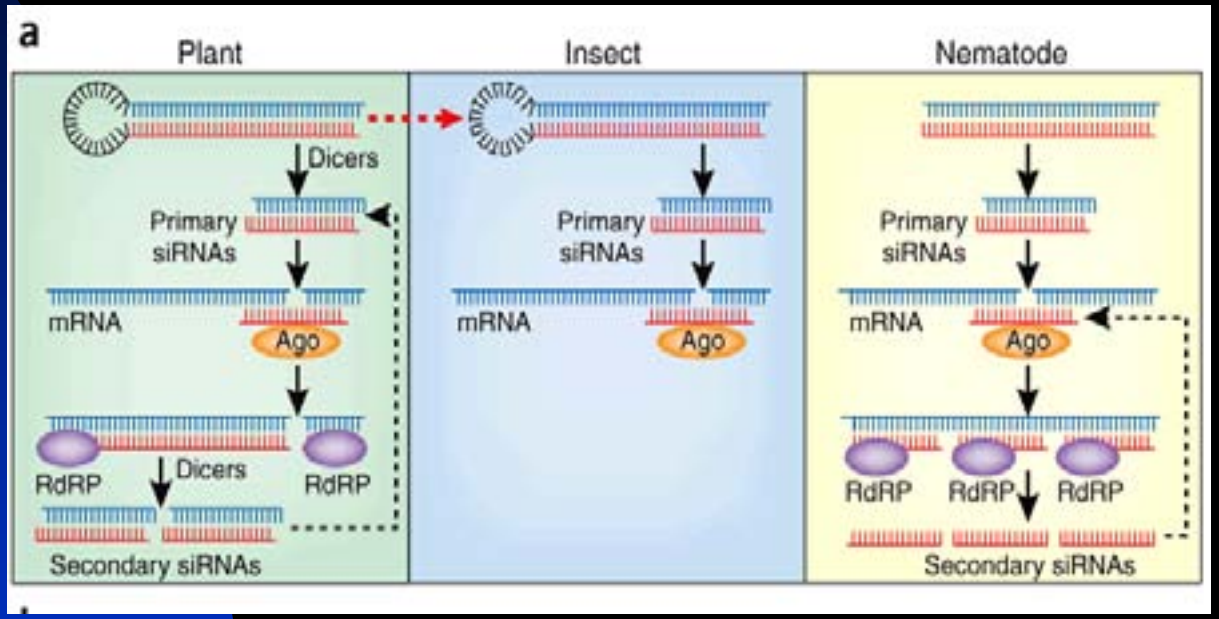
Frey K M et al. PNAS 2010;107:13707-13712

Inhibition assays (K_i nM) for Dihydrofolate Reductase and propargyl-linked anti-folates

	V31Y,F92 I	Wild-type	Resistance Factor
	180	10	18
	60	8.5	7.1
	65	9.0	7.2

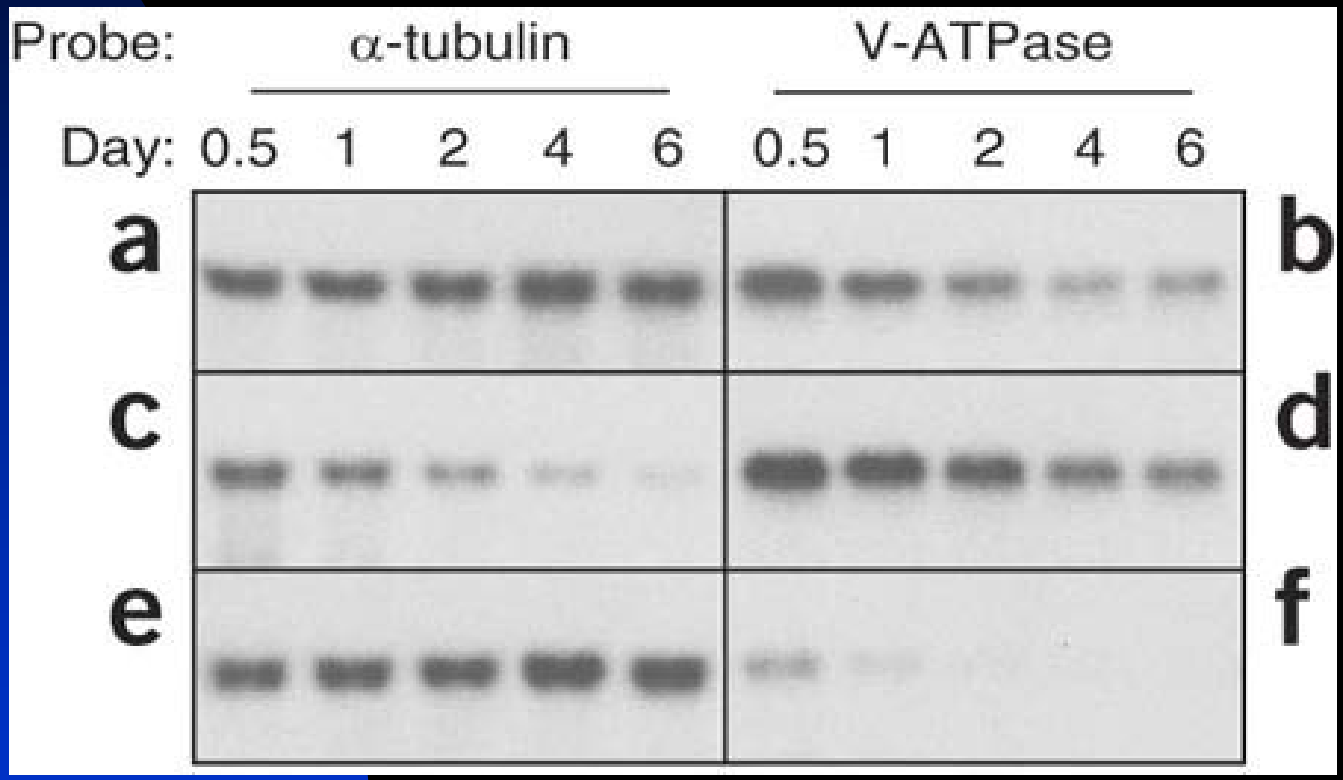
From Frey *et al.* PNAS (2010) 107, 13707-12

RNA interference (RNAi)



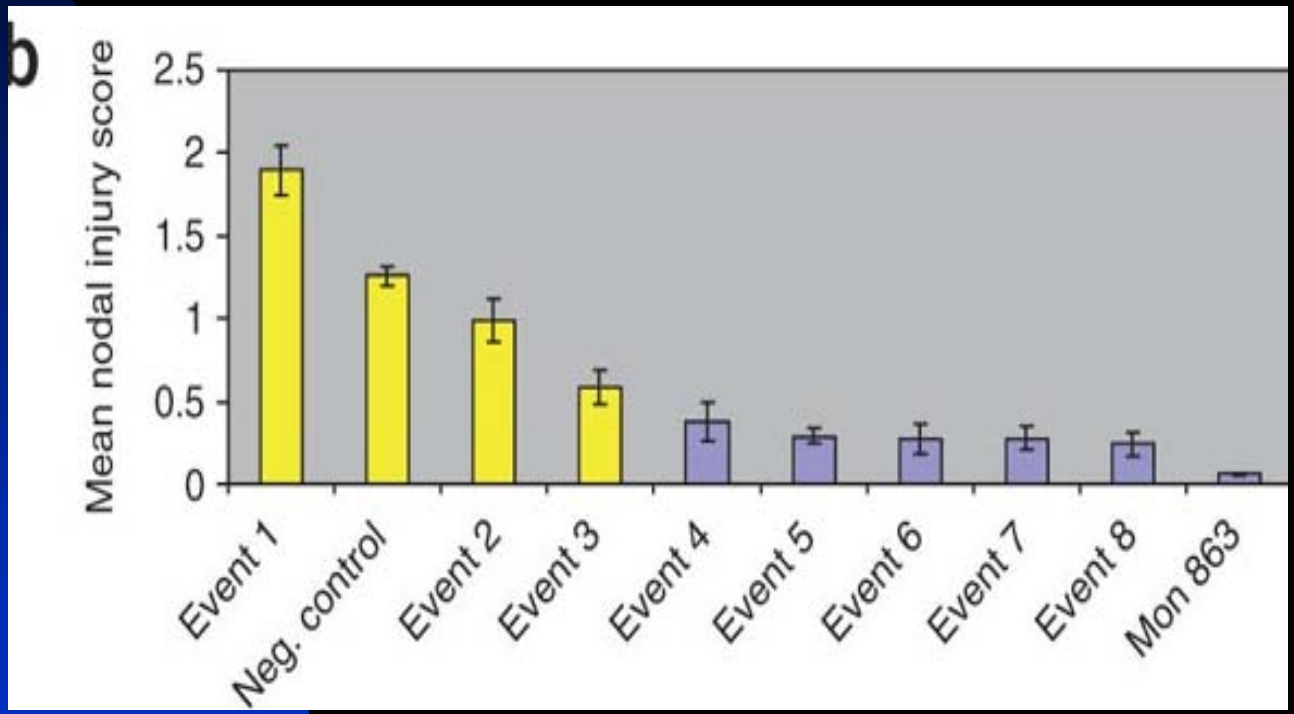
From Gordon &Waterhouse *Nature Biotechnology* (2007) 25, 1231- 1232

RNAi and suppression of target mRNA in Western Corn Rootworm



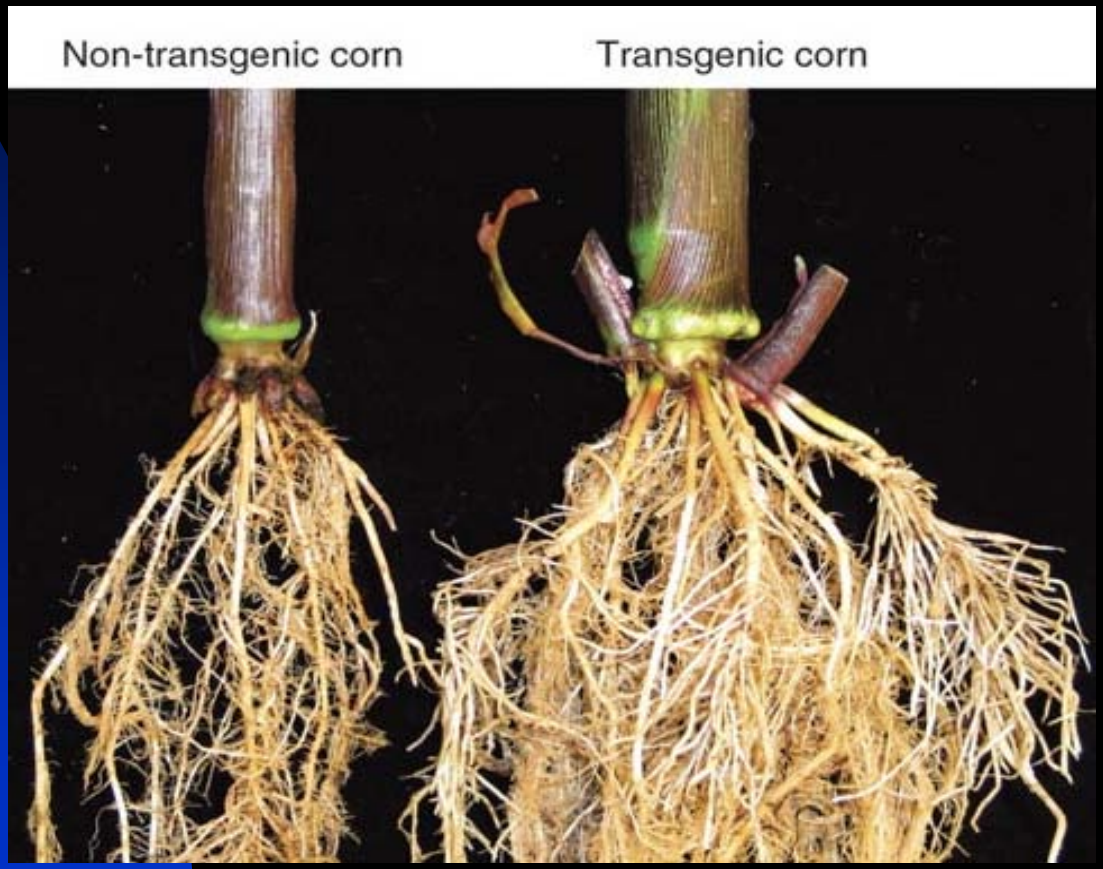
Baum *et al* (2007) *Nature Biotechnology* 25 1322-1326

RNAi and root damage by Western Corn Rootworm



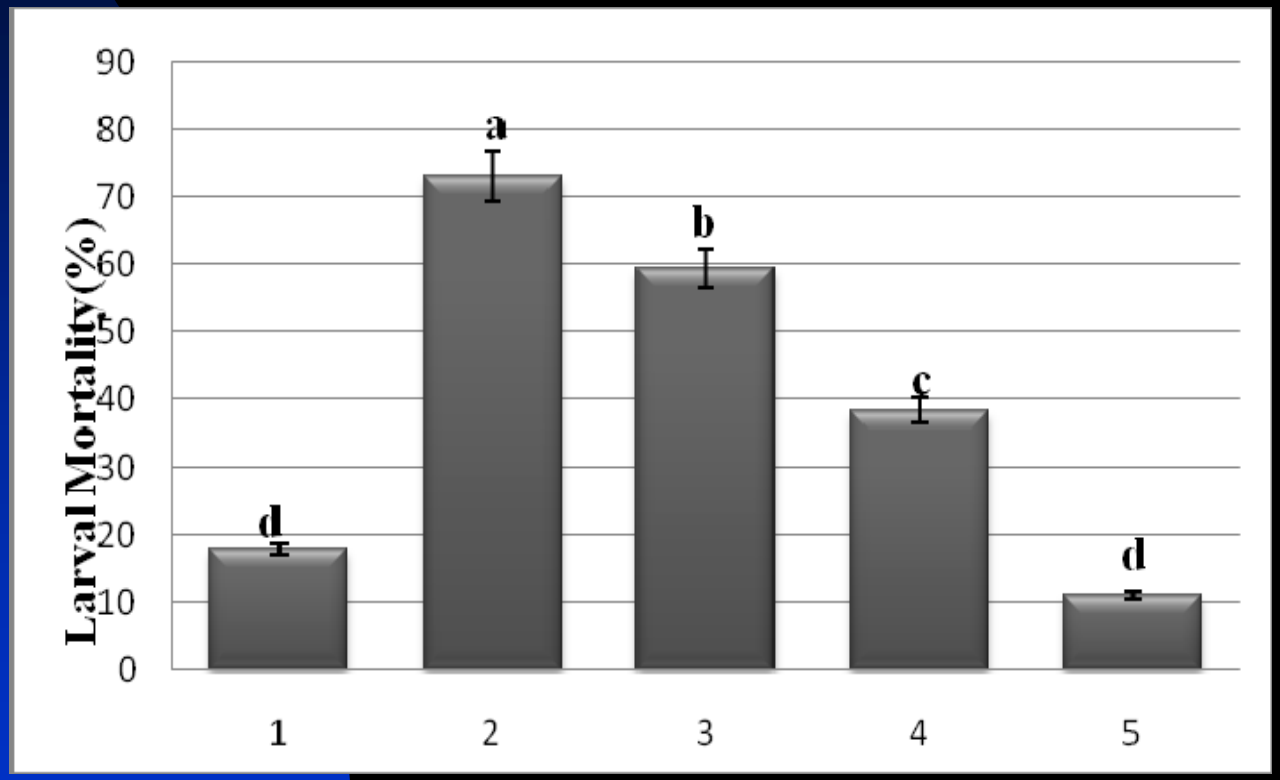
From Baum *et al.* *Nature Biotechnology (2007) 25, 1324-1326*

RNAi and root damage by Western Corn Rootworm



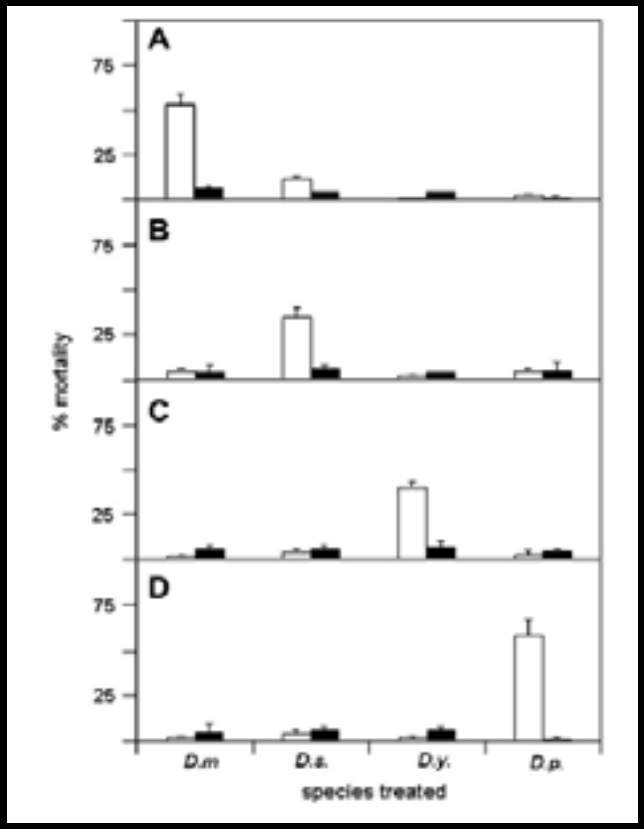
From Baum *et al. Nature Biotechnology* (2007) 25, 1324-1326

RNAi and larval mortality in Diamond Back Moth



Gong *et al. Pest Management Science* in press

Selective mortality between Drosophila species using a short ds3'UTR γTUB23 C



From Whyard *et al. Insect Biochem. Mol. Biol.* (2009) 39, 824-32

RNA silencing in plant pathogens

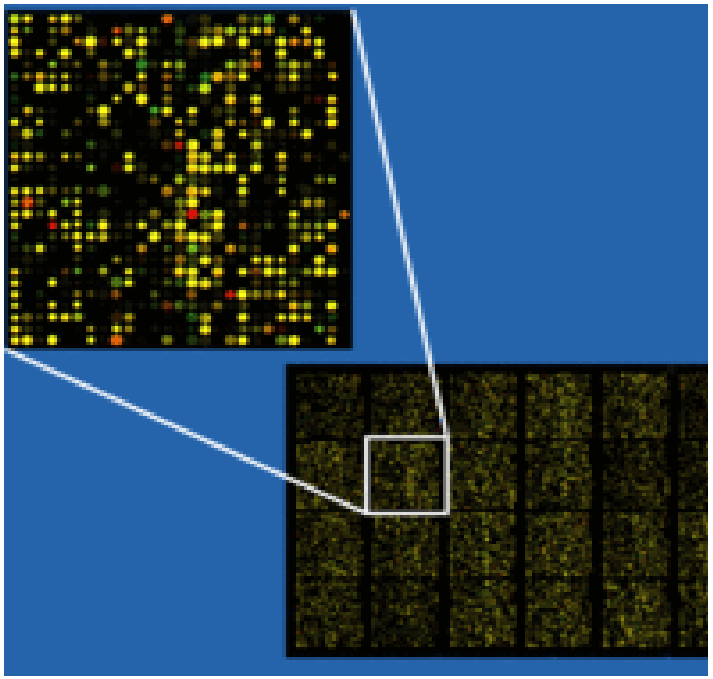
- *Magnaporthe oryzae* Rice blast
- *Venturia inaequalis* Apple scab
- *Botrytis cinerea* Grey mould
- *Phytophthora infestans* Potato late blight

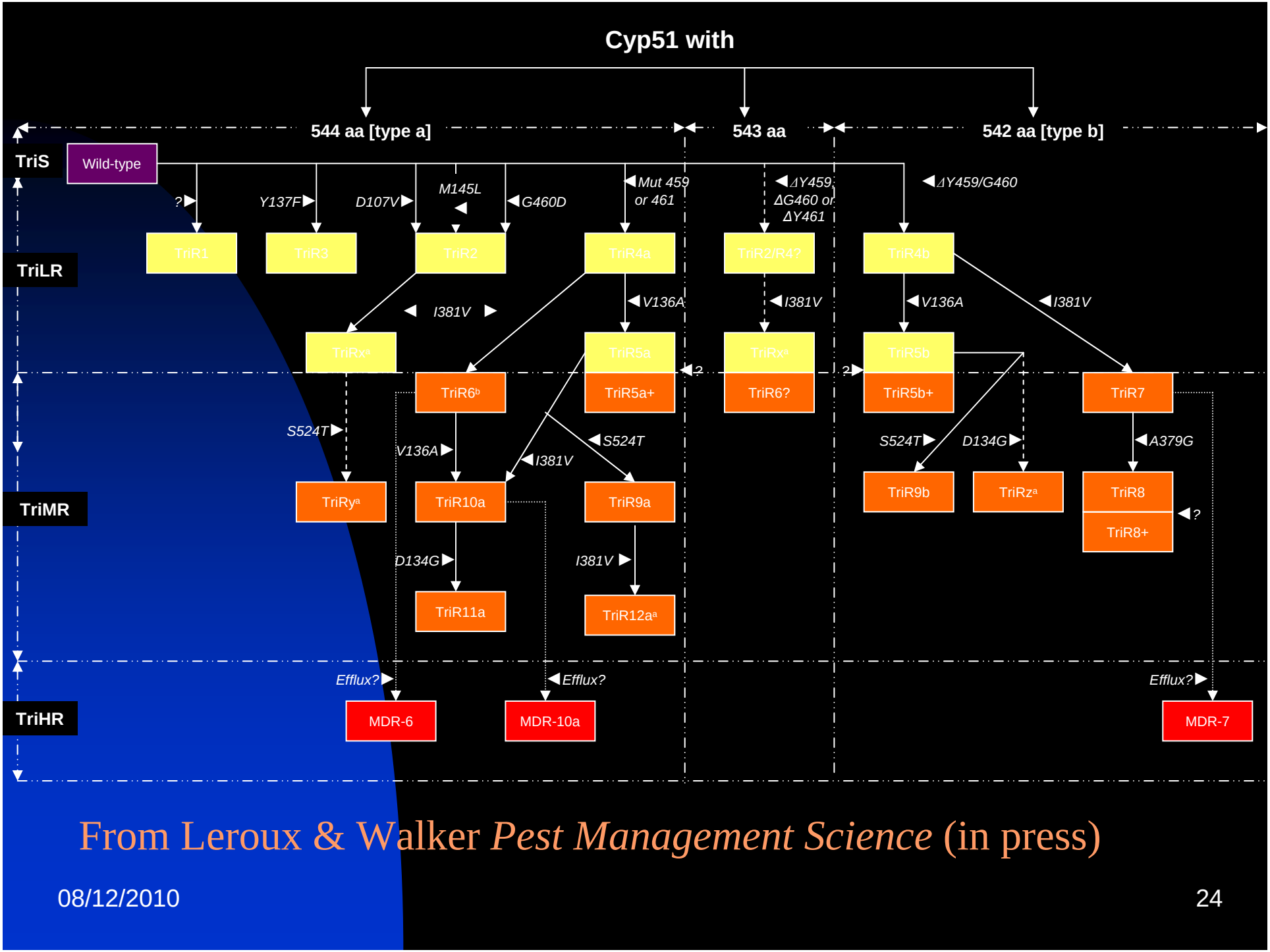
- also the parasitic weed Striga
- Virus infections

Challenges for RNAi

- Identify suitable gene for silencing
- Will the technology extend to other insects or pathogens ?
- Will sequence polymorphism allow selection for resistance ?
- Will laboratory results translate to effective crop protection in the field ?

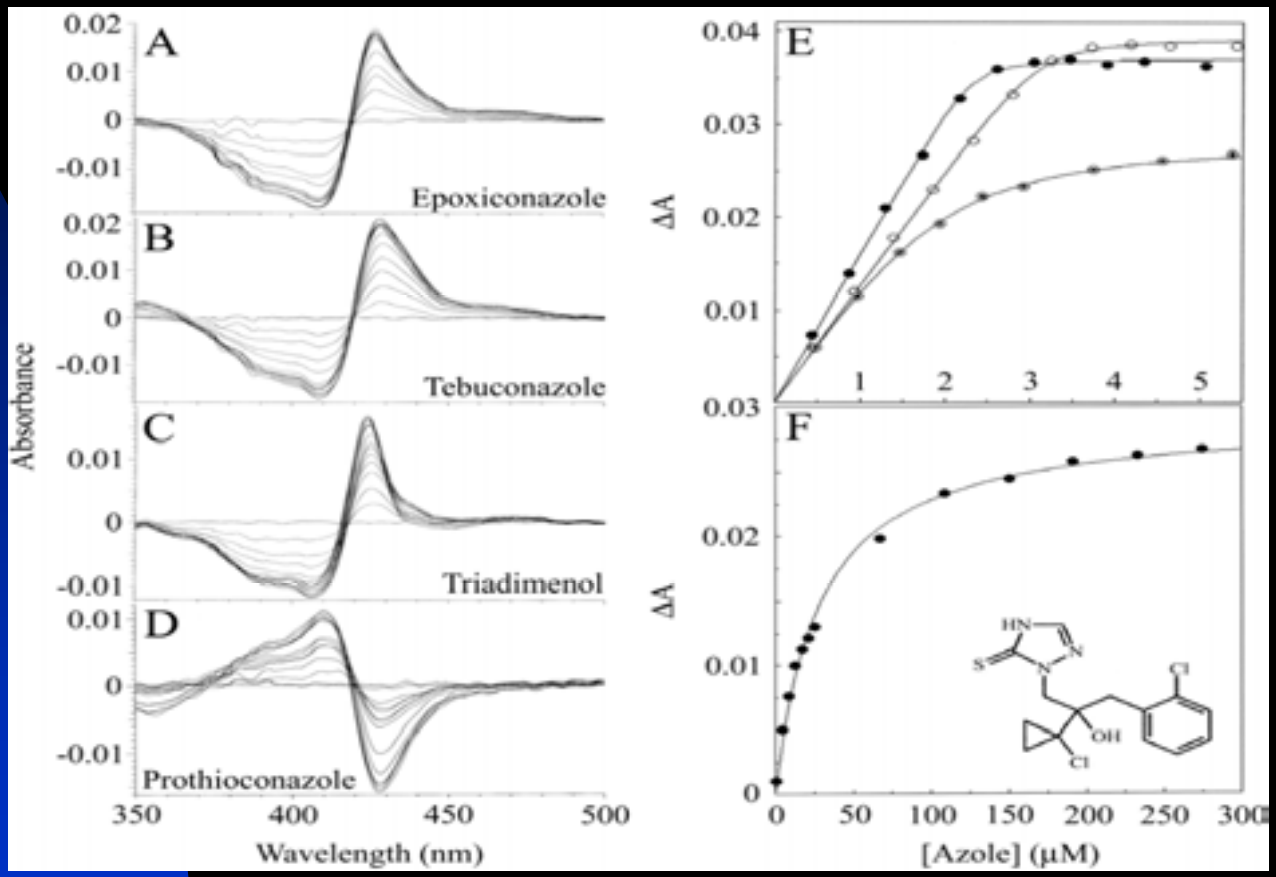
Microarray





From Leroux & Walker *Pest Management Science* (in press)

Azole binding spectra



Parker, J.E., *et al.* (2011) *Appl. Environ. Microbiol.* 77, (in press).

SUMMARY

- **New modes of action continue to underpin resistance management**
- **New findings from biochemistry and cell biology provide opportunities for novel targets – but these need to be explored in pests, diseases and weeds – not just model organisms**

SUMMARY

- New modes of action not necessarily chemical
- Host plant resistance provides new modes of action