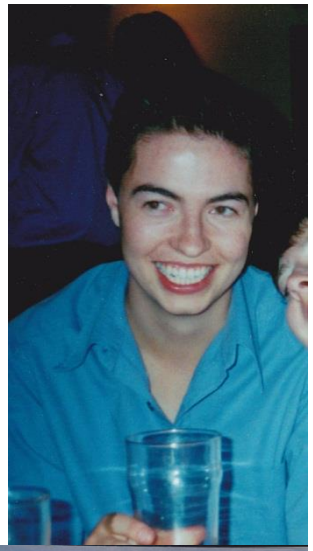
A little bit about me first…..

James Fountaine

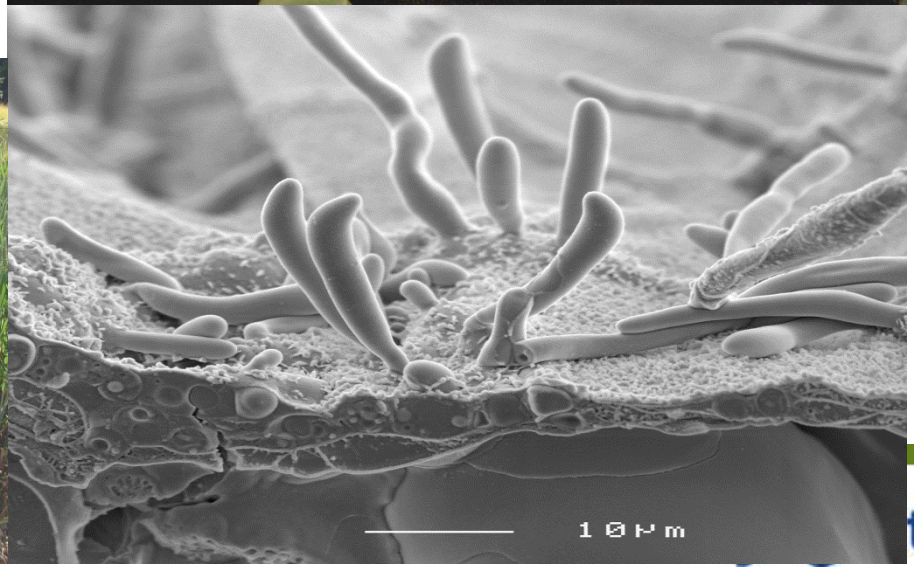
University of the West of England, Bristol (UWE)

- Degree in Applied Biological Sciences
  - Developed an interest in plant pathology
  - Placement year at Cyanamid Agriculture
    - working as a field trials assistant
    - With this Character



PhD at Rothamsted

- On *Rhynchosporium secalis*
  - With Dr Bart Fraaije



Two year Postdoc in Japan

- With Dr Hideo Ishii
  - At the National Institute for Agro-Environmental Sciences (NIAES)
  - Fungicide resistance in a range of different crops

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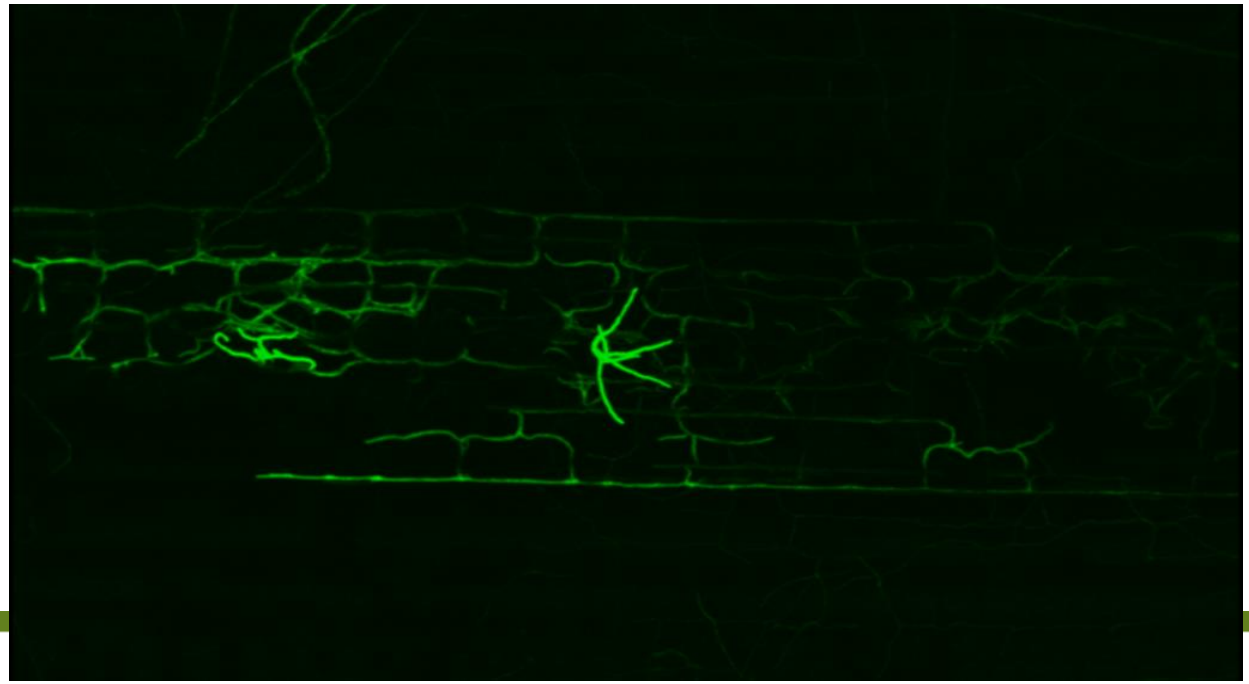
2007-2014 at SAC in Edinburgh

- Worked mainly on *Ramularia collo-cygni* (NG sequencing, fungicide resistance and population genetics and understanding it's biology)



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Introduction to Discovery Biology

James Fountaine
Discovery Fungicide Technical Lead

Crop Protection Research - what do we do ?

Crop Protection	selective and non-selective herbicides, fungicides, insecticides, nematicides
Seed Care	Seed treatment with insecticides; fungicides; nematicides
Lawn & Garden	insecticides; fungicides; herbicides; nematicides; biologicals

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Global CP R&D capabilities

Major R&D sites located on three continents

JEALOTT'S HILL
Chemical Discovery
Weed Control
Formulation
Bioscience
Environmental Science

GREENSBORO
Formulation
Environmental Science

GOA
Chemistry

BEIJING
Biotechnology
R&D

RTP
Biotechnology
R&D

STEIN
Fungicides, Insecticides &
Lawn & Garden Controls

Other sites

- breeding centers
- global field station network

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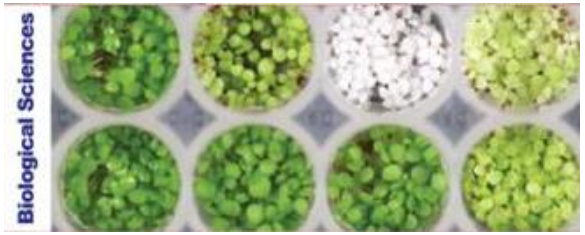
Biological Sciences – Twin Site Locations

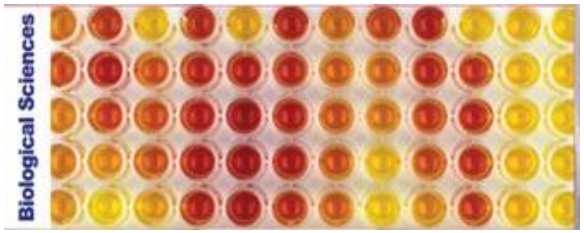
Functional Split by Site – Jealott's Hill

Biology Support

Discovery Biology



Fungicide Bioscience



Herbicide Bioscience

Insecticide Bioscience

Biometrics

Weed Control Biology

Functional Split by Site – Stein

Disease Control Biology

Insect Control Biology

Environmental & Crop Modelling

Abiotic Stress Management

Seed Care

Biology Support

Lawn & Garden

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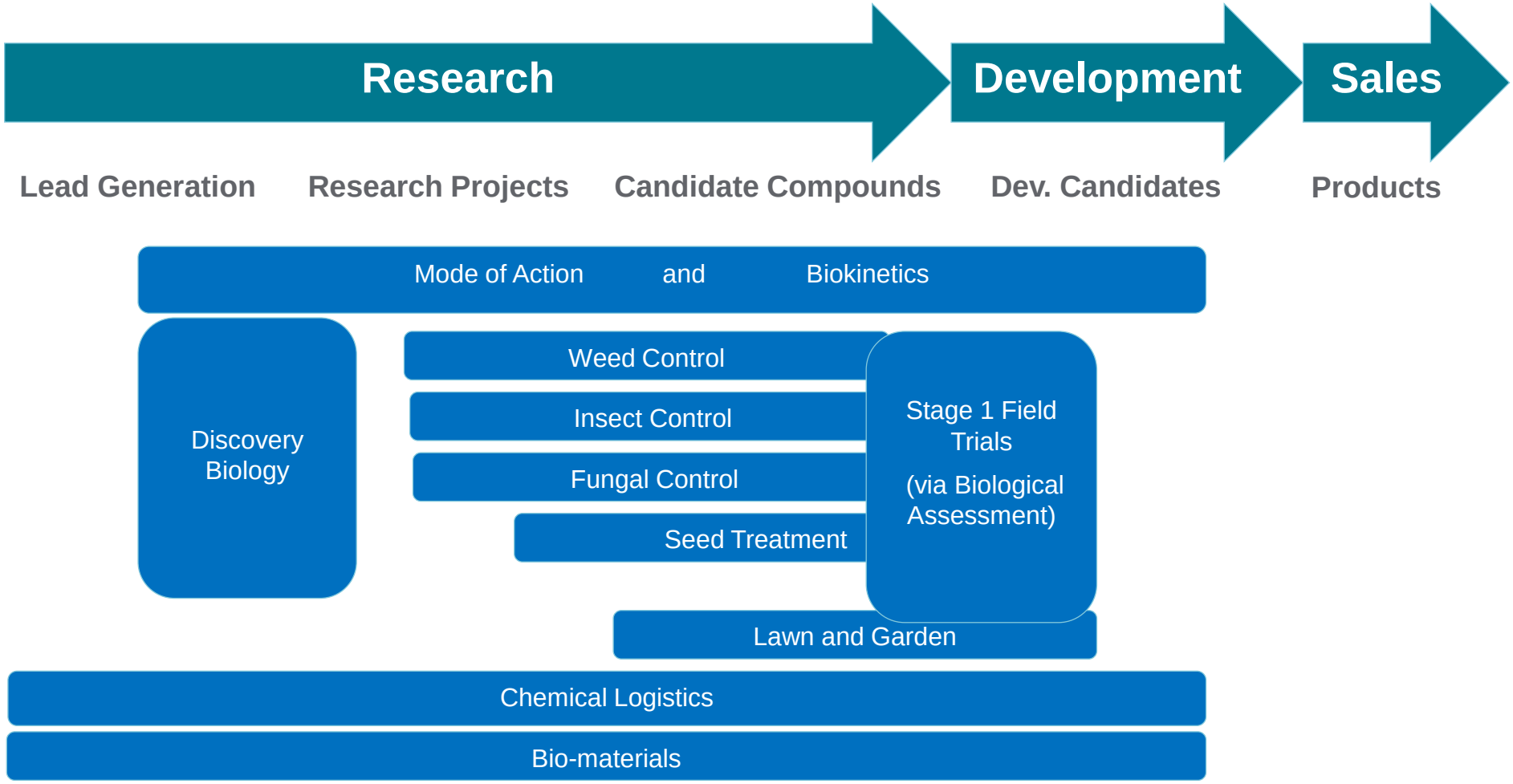
Core Activities: Supporting Chemical AI Invention



The invention process is driven by whole organism biology and crucially supported by our understanding of the mechanism of action

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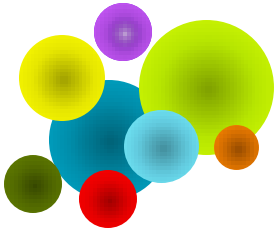
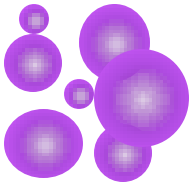
Finding new starting points

Novelty



Initial compounds



Leads

Products

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Obtaining new chemicals

Natural Products

Serendipity

Chemical Libraries

Patent and Literature

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Discovery Biology: High Throughput Screening

- First level testing of chemical samples on whole organisms for indications of biological activity: simultaneous screening on weeds, insects and fungi
- Tests designed to be:
  - Simple, sensitive, reliable, predictive of desired activity
  - Scalable, fast, efficient (sample and labour)
  - Tend to be miniaturised and automated
- Typically yes/no (“hit”) result based on pest mortality

Discovery Early Screens

Herbicide

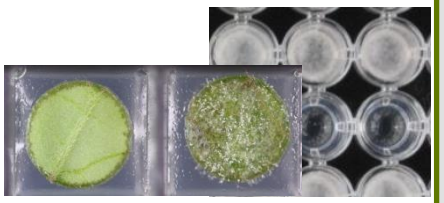
Assays give clear active/inactive data

Insecticide

Activity evaluated against chewing and sucking pests

Fungicide

Activity evaluated in agar and leaf disc assays



These screens dictate what is found and we must guard against missing signals!

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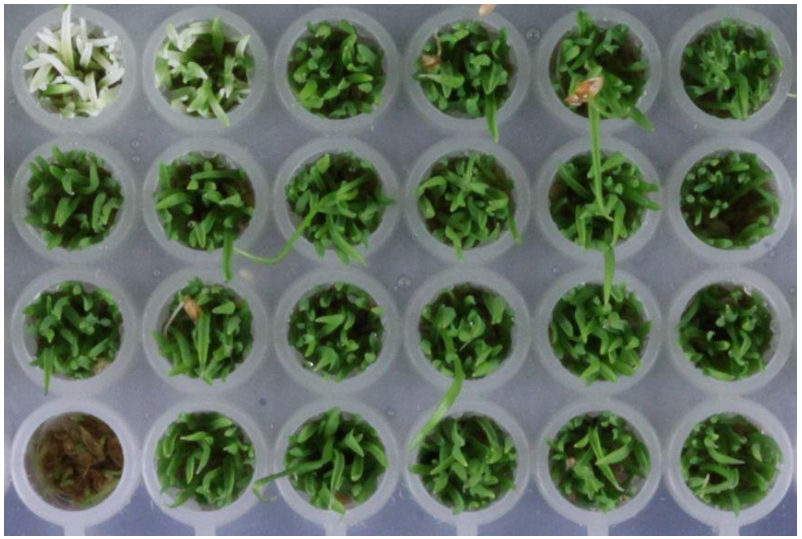
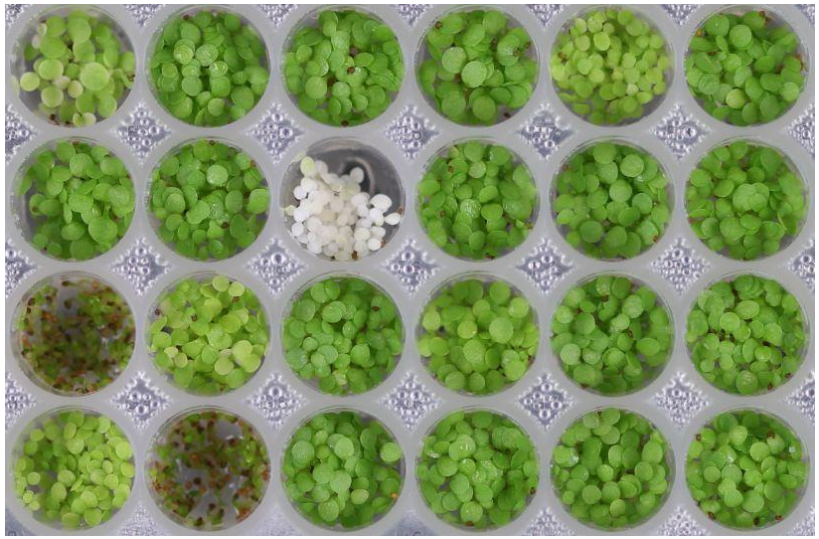
Discovery Early Screen - Herbicide



Poa annua



Arabidopsis thaliana

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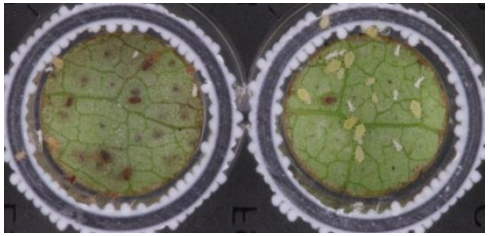
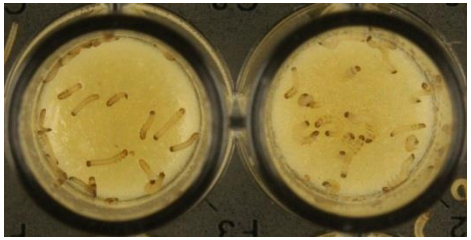
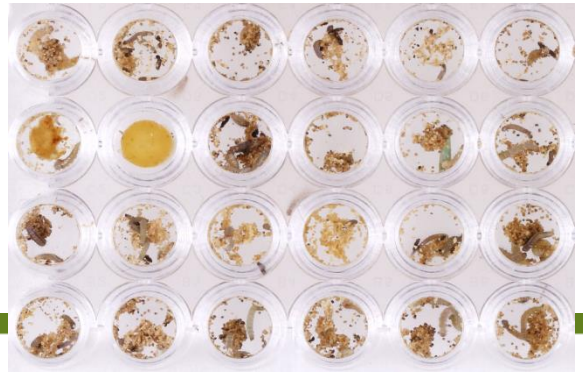
Discovery Early Screen– Insecticide



Aphid *sp.*



Diabrotica balteata



Plutella xylostella

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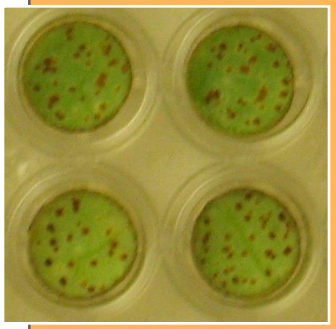
Discovery Early Screen – Fungicide

- Focussed on major business relevant targets



Fungicide assays

***Septoria tritici* /wheat**
***Phytophthora infestans* /tomato**
***Uromyces viciae-fabae* /bean**

Semi-solid:
Fusarium graminearum
Alternaria solani
Pythium dissimile
Botrytis cinerea

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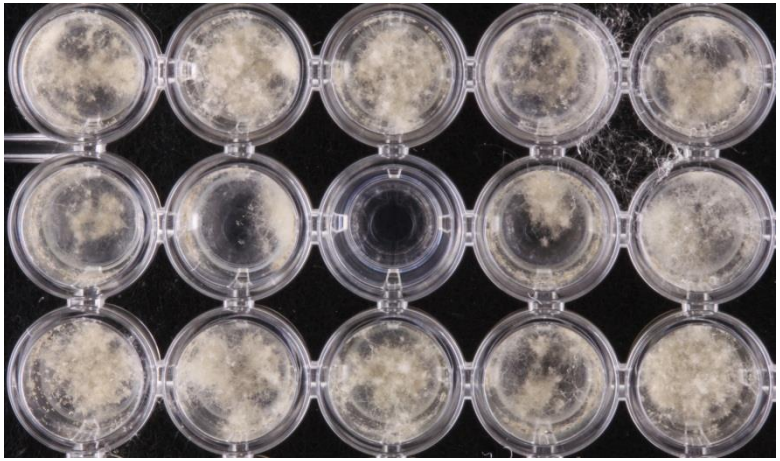
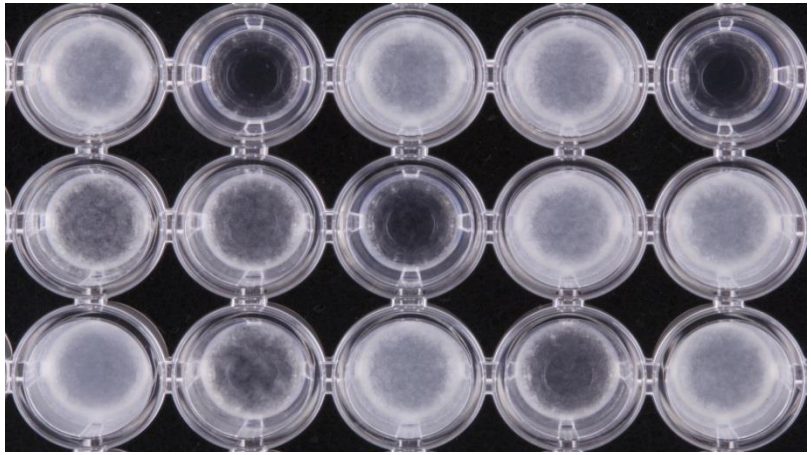
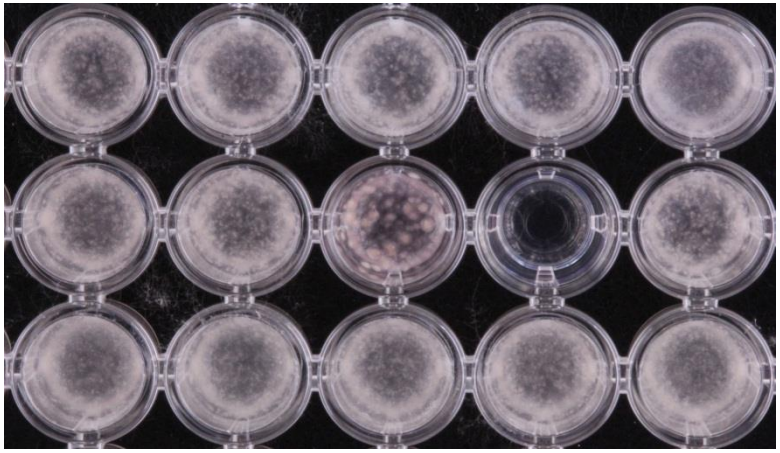
Discovery Early Screen – Fungicide



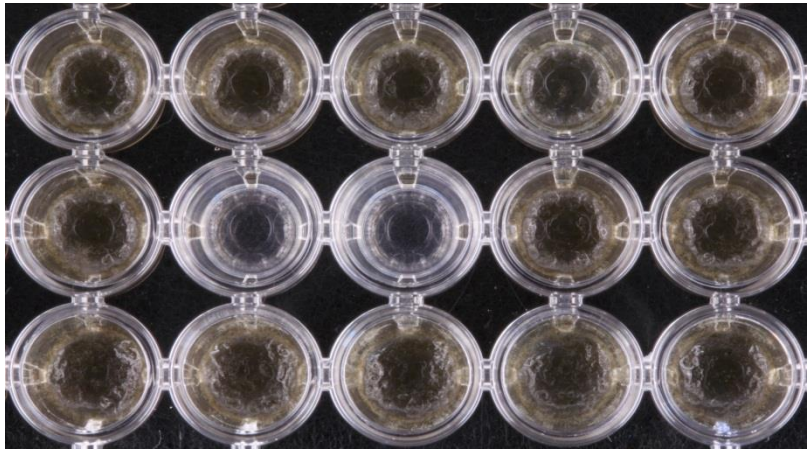
Botryotinia fuckeliana (Botrytis cinerea)



Pythium dissimile

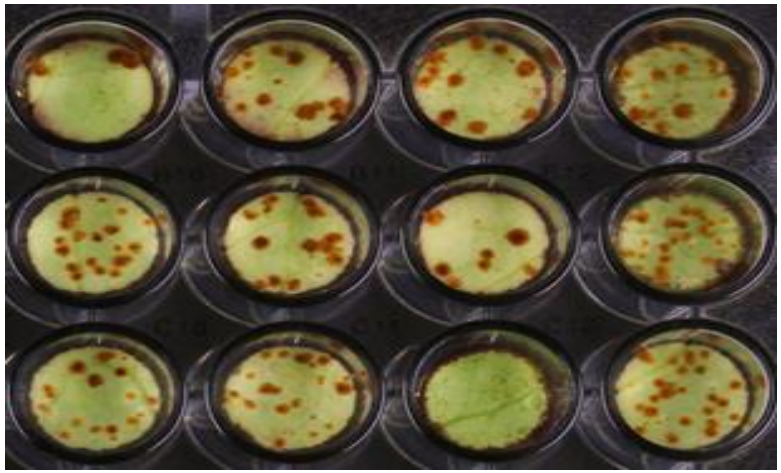


Fusarium graminearum (Gibberella zeae)

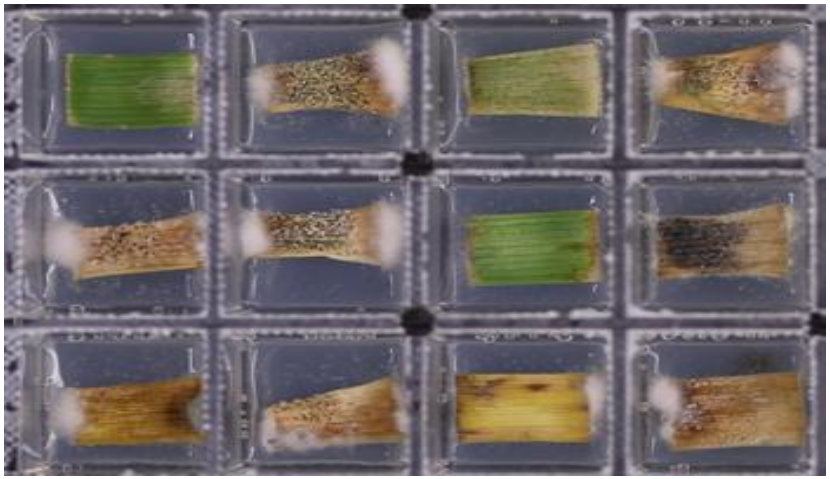


Alternaria solani

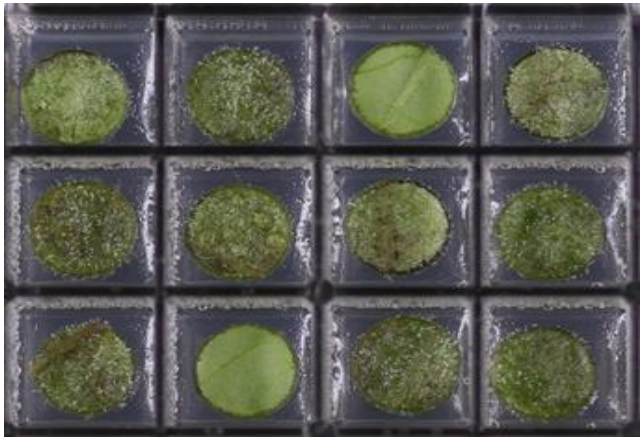
Discovery Early Screen – Fungicide



Uromyces viciae-fabae



Zymoseptoria tritici (formerly *Septoria tritici*)



Phytophthora infestans

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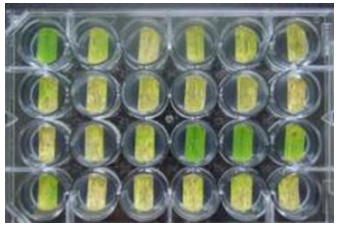
Glasshouse Screening Cascade - Fungicides

Discovery Biology

DCR Biology – Lab/Glasshouse Screening



Discovery Early Screen (DES)

- Potential fungicide activity
- 7 species:

3 leaf discs, 4 semi solid

- 96 well plate assays
- Standard rates
- <1mg

Micro Profiling Screens (MPS)

- Initial potency and spectrum evaluations
- 10 species/application timings on leaf disc
  - 10 species in ss
- 24 and 96 well plate
- Up to 6 rates according the project needs
- < 1mg

Whole Plant Screen (WPS)

- Broad spectrum
- Different application timings

-14 Foliar test methods

- Whole plant assay

Foliar Comparison/ Characterisation (CCS)

- Extended spectrum and timings
- Different application types
- Optimised formulations
- Selection of field candidates
- 20 pathogens
- Assays tailored to project needs
- Whole plant - and special assays

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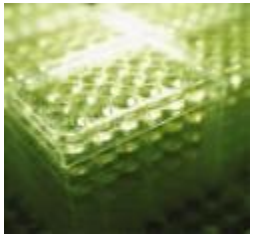
Turning leads into products – the screening process






Discovery

Crop Protection Profiling

Project A

Project B

Project C

Development Candidate

Lawn & Garden Controls Profiling

Development Candidate

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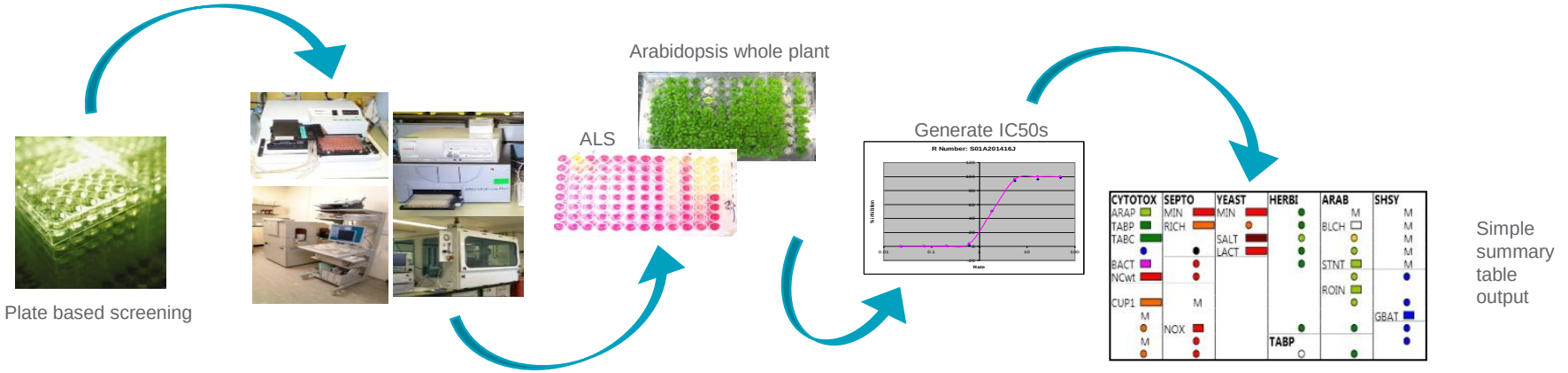
Discovery Biology: Mode of Action Platform

- Evaluation of interesting chemicals on for initial mode of action (MoA) determination
- Highly efficient use of sample (96 or 384 well plates)
- Study ca. 500 compounds per annum
- Platform covers ca. 50 known agrochemical MoAs
- Helps us decide what is interesting and what is not…

- Whole plant phytotoxicity & symptomology
- Genetically modified resistant plants
- Fungal phenotypic assays
- Insect, plant and bacterial cell lines
- Gene knock-out cell line
- Cellular organelles (mitochondria, chloroplasts)
- Enzyme assays
- Receptor assays
- Chemical reactivity assay
- Reporter gene assays

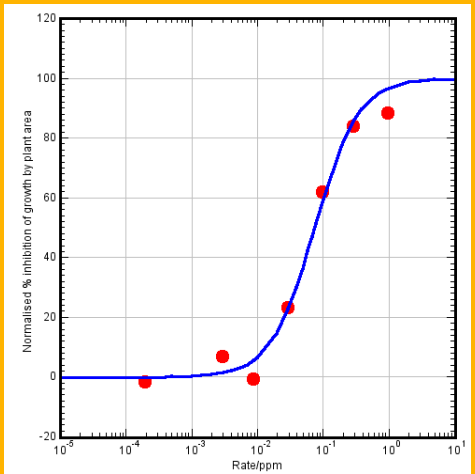


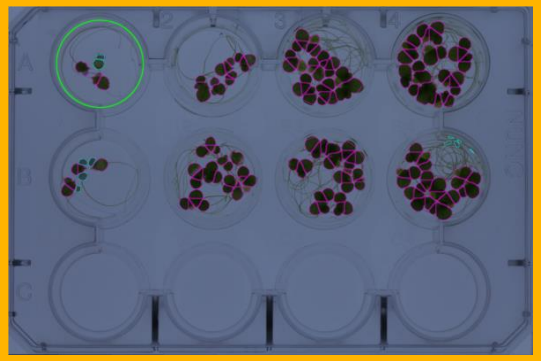
MOA testing helps prevent “reinvention of the wheel” and points out novel “unknowns”

Discovery Biology – Aquatic Plant Safety

Lemna gibba – Duck Weed

- Assessment at 7DAT
- EbC50 calculated on green frond area using image analysis
- Symptomology recorded

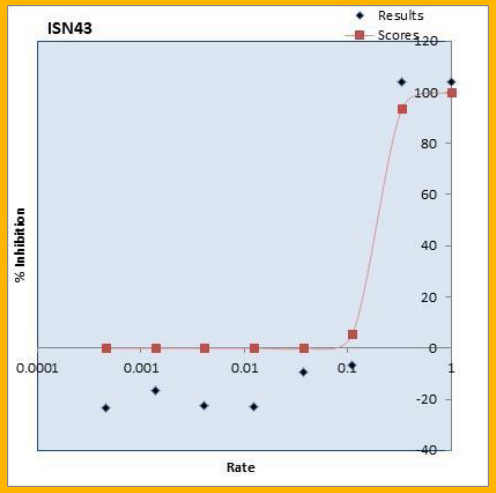


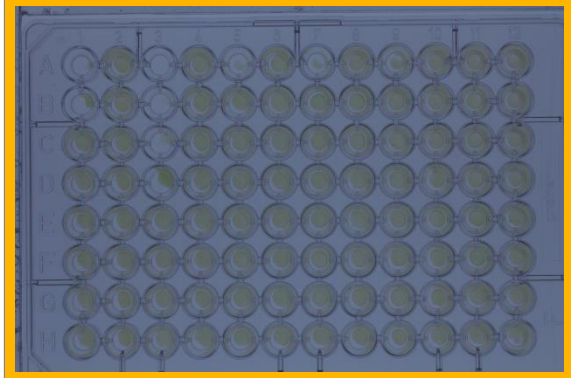


Bleach Morphological Stunt

Pseudokirchneriella subcapitata – Green Algae species

- Plate read Assessment at 0DAT and 3DAT
- EbC50 – calculated using absorbance measurements of cell growth





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Bringing plant potential to life