Fruit fly AgChemical management: Regulatory trends and challenges

Kevin Bodnaruk

Fruit fly Agchemical management

- Pressures and trends
  - Regulatory
    - Assessment
    - Reconsiderations
  - New chemistry?
- Trade

Regulatory trends

- **Risk assessment**
  - Current methodologies being reviewed, e.g., Dietary exposures
    - Or refined probabilistic vs deterministic
  - New methodologies introduced
  - Aggregate, Anti microbial resistance, Threshold of Toxicological Concern, Global estimate of chronic dietary exposure (GECDE) model
  - New and/or additional data requirements

Regulatory trends

- **Increasing complexity**
  - Residue definitions
    - Metabolites
  - HBGVs

  } Dietary exposure

  - Analytical sensitivity & Measurement uncertainty
  - **Different/refined approaches**
    - EU: Hazard based thresholds, Qualified presumption of safety

Regulatory trends

- **Reconsiderations/re-evaluations**
  - Domestic and international
    - APVMA, Codex, PMRA, US EPA, EFSA etc
  - Cyclic
    - EU: 7-15 years,
    - Canada, Codex, USA: 15 years
  - Special reviews
    - New scientific information or legislative triggers

Regulatory trends

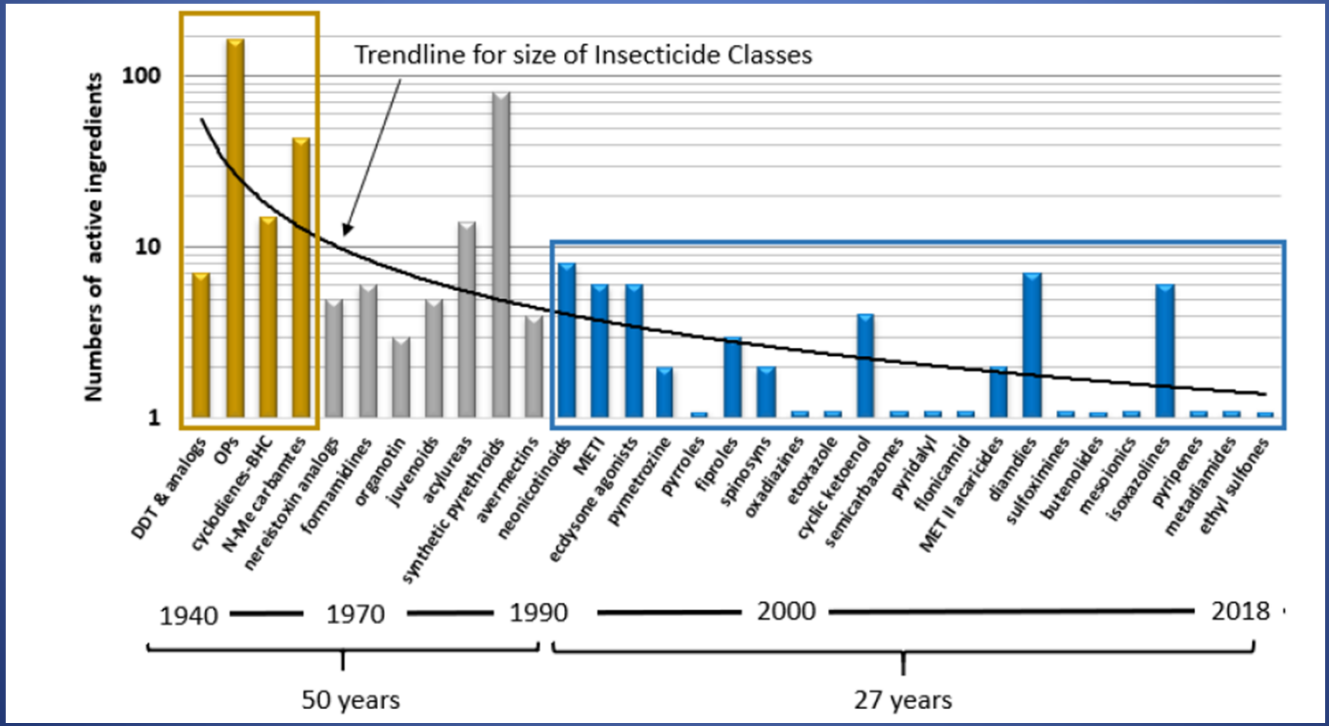
- **Reconsiderations/re-evaluations**
  - Assessed against contemporary standards
    - Gaps in the data will be critical
      - Lack of relevant data - risk assessment and review outcomes uncertain

Regulatory trends

- **Reconsiderations/re-evaluations**
  - **Pressure on older compounds**
    - **Codex** – Reviews scheduled for dimethoate, diazinon & chlorpyrifos;
    - **EU** – Alpha-cypermethrin, clothianidin, dimethoate, indoxacarb, thiacloprid not authorised. Abamectin glasshouse only;
    - **Canada** – Bifenthrin phased-out, Chlorpyrifos cancelled, Methomyl restricted;
    - **USA** – Chlorpyrifos cancelled

New chemistry

- New compound/MOA availability?
  - Potentially problematic
    - MOAs vs number of actives



Sparks *et al*. 2019. Pesticide Biochemistry and Physiology

New chemistry

- Different registrant priorities
  - Market size considerations
  - Focus often on ‘world’ crops
  - Regulatory support of generic compounds uncertain
  - Off-patent products have increased from < 20% in 1995 to near 80% in 2016
- Increased uncertainty

Fruit fly Agchemical management

- Trade considerations
  - MRL alignment – for new & existing insecticides complex
    - Different or nil use patterns
  - Import MRLs
    - Policies/Legislation
      - Reference (Codex) or Default MRLs?
      - MRL application and establishment processes
  - Costs
    - Data generation and fees

Fruit fly Agchemical management

- Import MRL Guideline adopted as an APEC text

  https://www.apec.org/Publications/2016/08/Import-MRL-Guideline-for-Pesticides

- Compendium developed

Fruit fly Agchemical management

- **In summary**
  - Regulatory pressures increasing
  - Access to new insecticides uncertain
- **Challenges**
  - Satisfying regulatory requirements
    - For new and old
    - Availability of data
  - Trade
    - MRL compliance

Fruit fly Agchemical management

- **Going forward**
  - Strategic analyses
    - Short, mid and long-term w.r.t. threats to insecticide availability
  - Prioritise R&D

Australian Citrus

Agrichemical risk management

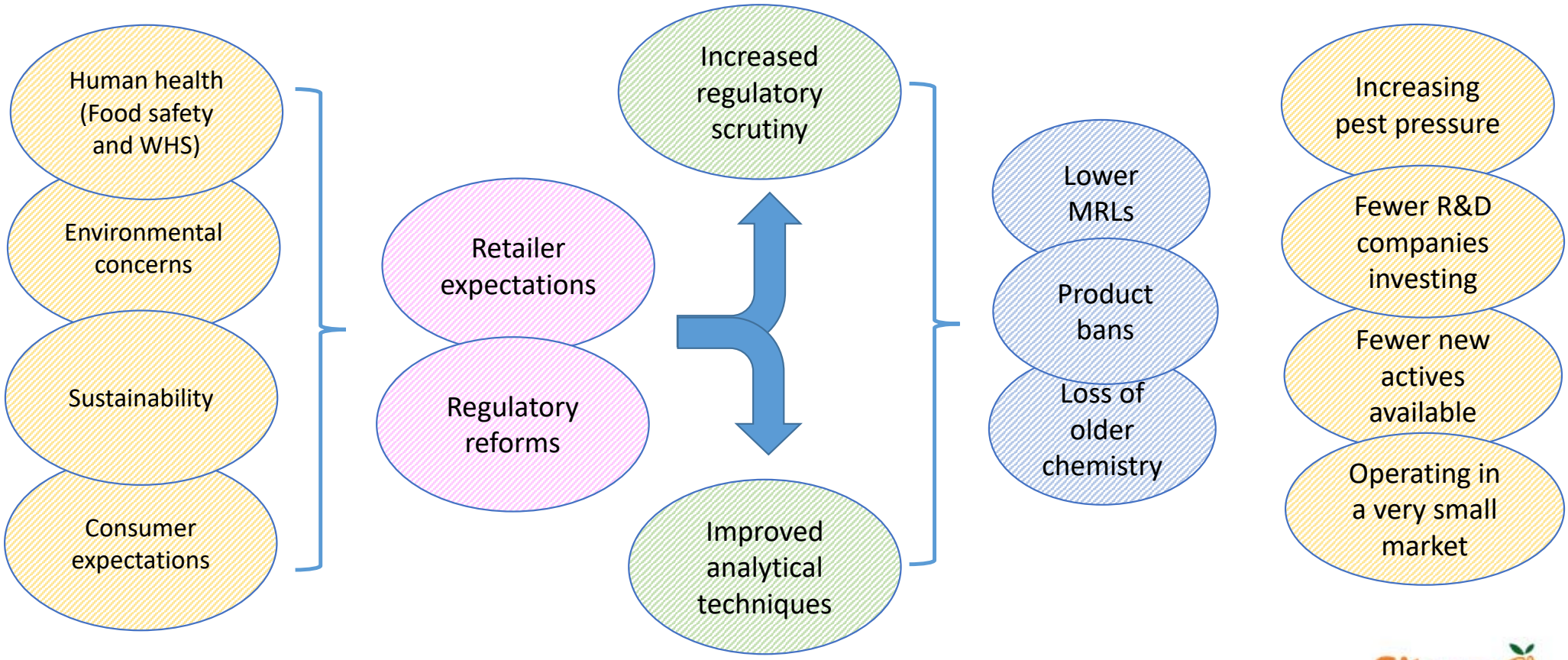
David Daniels

General Manager Market Development, Citrus Australia

david.daniels@citrusaustralia.com.au

Citrus Australia

Current status



Citrus Australia

Current status

- Since 2014 – global downturn
- Increasing regulation
- AgVet companies looking towards alternative technologies (e.g. biostimulatnts, BCAs, GM)
- Industry consolidation
- Less competitive environment

Citrus Australia

Consolidation

- Nufarm Limited
- Bayer CropScience
- BASF
- FMC
- Corteva Agriscience
- Syngenta Australia

Citrus agrichen=mical related investments

1. CT09055 Coordinating a market development program for the Australian citrus value chain
2. CT13022 – Driving citrus industry success through a coordinated market development program – Stage 2
3. CT12005 – Driving citrus exports through improved market access
4. CT11011 – Agrichemical residue monitoring program for Australian citrus exports
5. CT15016 – Agrichemical residue monitoring program for Australian citrus exports – Stage
6. CT15012 – Australian Citrus Industry Innovation and Market Development Program
7. CT18001 – Citrus Agrichemical and Export MRL Program
8. CT18002 – Citrus Market Development, Market Access and Quality
9. MT10029 – Strategic Agrichemical Review Process
10. MT21005 – Strategic Agrichemical Review Process (updates)
11. MT20007 – Regulatory support and coordination (pesticides)
12. MT17019 – Regulatory support and coordination (pesticides)
13. CT14003 – MRL risk analyses and risk management options for major citrus export markets
14. CT14001 – Zero residue concept – scoping study for citrus
15. ST15027 – Generation of residue data for pesticide minor use permit applications

Citrus Australia

Ultra-low residues – in search of the holy grail

Why ??

- Series of MRL breaches in overseas markets
- Immense pressure from import markets (regulators, retailers, consumers, environmentalists)
- Protect reputation
- Loss of options

Citrus Australia

Agrichemical risk management

Monitor MRLs	Communication	Residue testing	Review
WTO notifications	MRL tables	Laboratory proficiency testing	Assist case for new products
Overseas websites	AgChem updates	Maintain and update multi-residue screen	Understand use patterns
Databases	Forums	Negotiate price for testing and freight	Understand risk and protect trade
Government contacts	Citrus Australia committees	Calibrate systems and manage risk	Set priorities

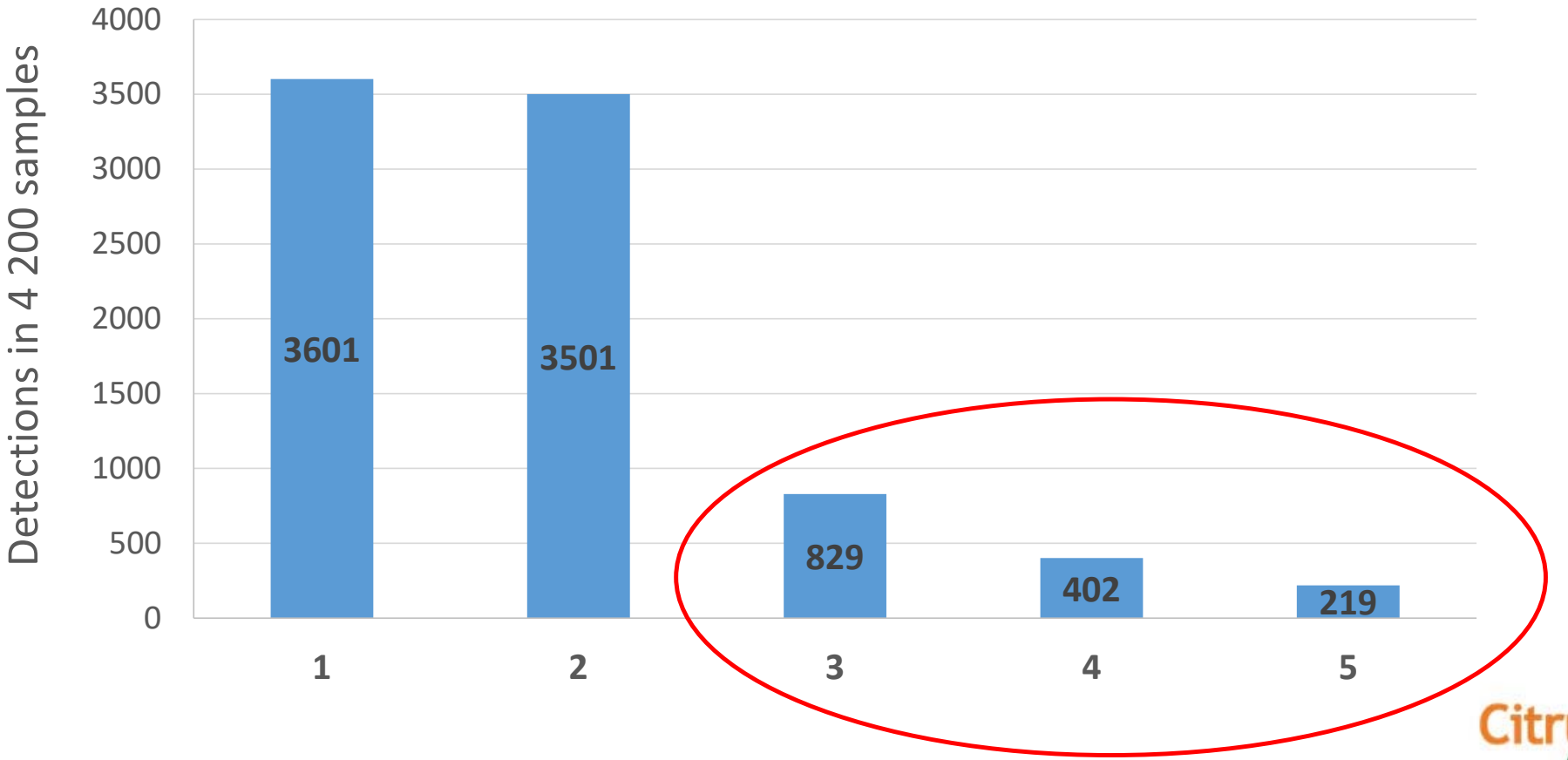
Citrus Australia

Residue testing program

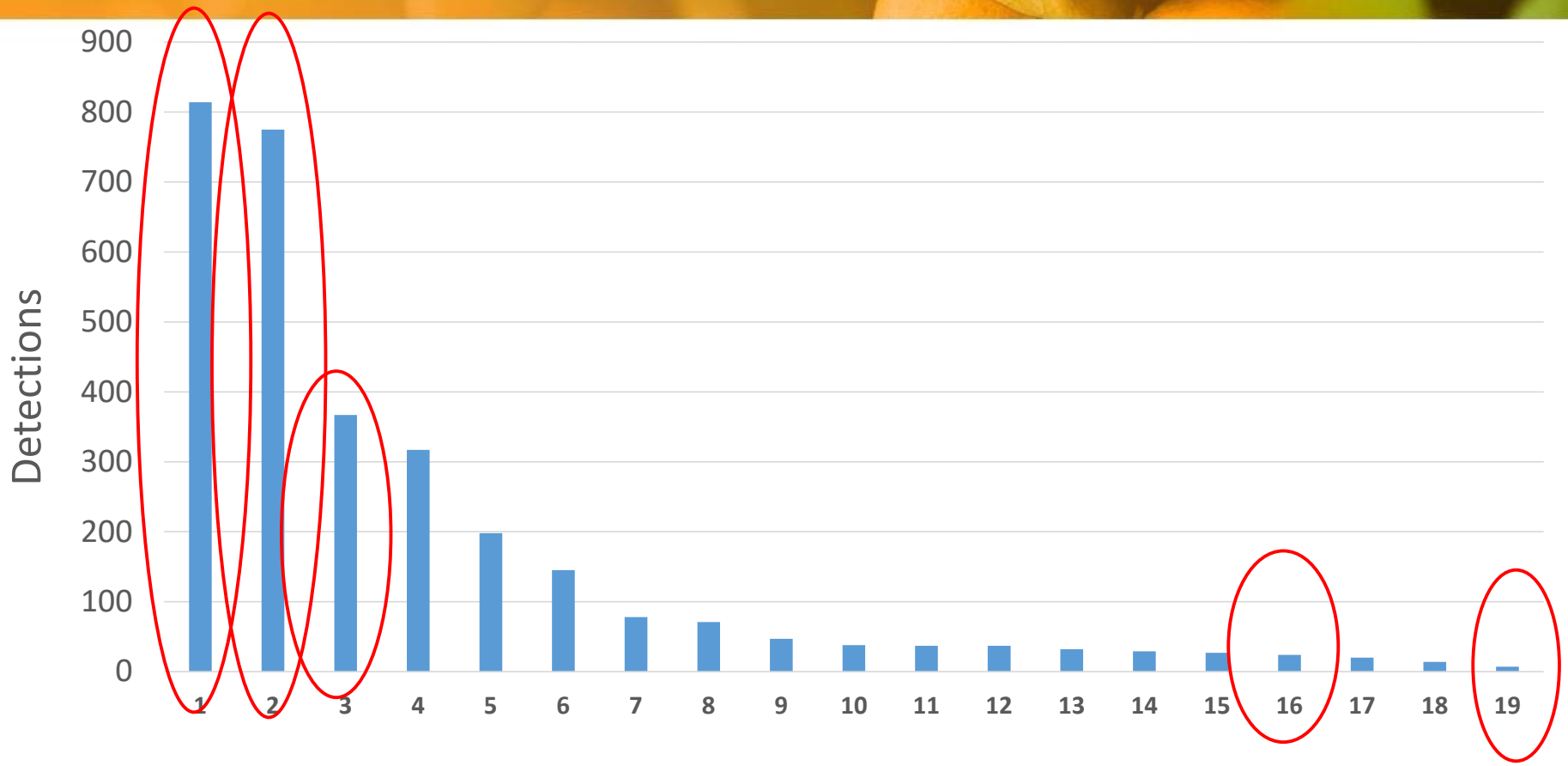
- Over 20 participating businesses
- Operating 11 years
- 4 100 individual samples tested for residues
- multi-residue-screen testing for 310 compounds
- value for money

Citrus Australia

Results post-harvest fungicides



Results – in-field applications.



Citrus Australia

Thank You

Citrus Australia

Acknowledgement of **Country**

The University of Queensland (UQ) acknowledges the Traditional Owners and their custodianship of the lands on which we meet.

We pay our respects to their Ancestors and their descendants, who continue cultural and spiritual connections to Country.

We recognise their valuable contributions to Australian and global society.

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA
CREATE CHANGE

RNA based biopesticides - BioClay™ technology

Prof Neena Mitter

Director, Centre for Horticultural Science,
Director ARC Research Hub for Sustainable Crop protection

QAAFI, The University of Queensland, Australia

n.mitter@uq.edu.au

PESTICIDES:

- RESISTANCE
- RESIDUE
- RUNOFF
- LACK OF SPECIFICITY
- NEW CHEMICALS

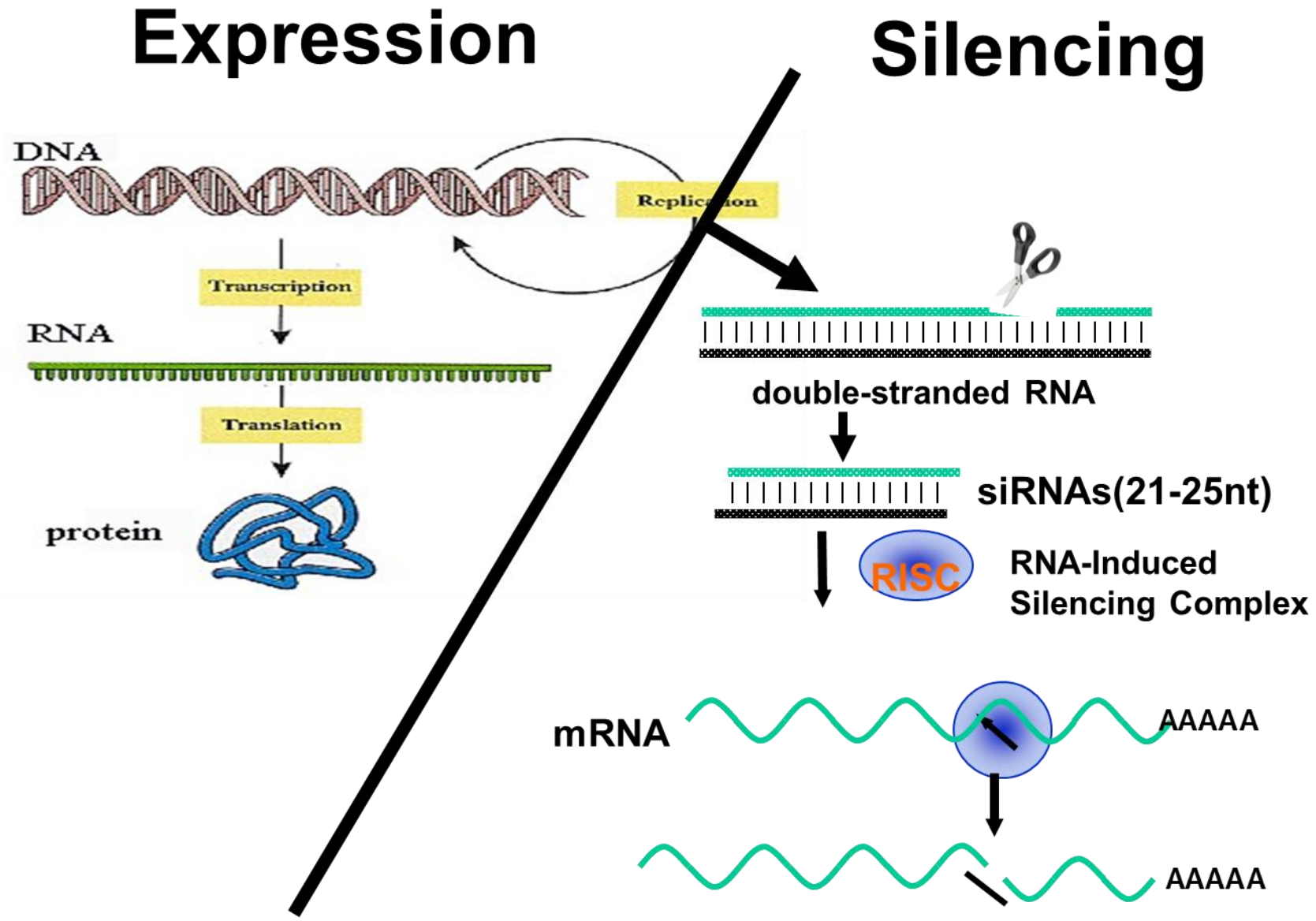
URGENT NEED FOR SAFE METHOD TO PROTECT CROPS

[Pesticide - contaminated meal kills 25 Indian children]

https://www.reuters.com/article/us-india-chidren-poison/contaminated-school-meal-kills-25-indian-children-idUSBRE96G0AY20130717

RNA Interference

"RNA interference or RNA silencing is the most important thing to happen in molecular biology during the last 10 to 20 years"


Expression
Silencing
DNA
Replication
Transcription
RNA
Translation
protein
double-stranded RNA
siRNAs(21-25nt)
RISC
RNA-Induced
Silencing Complex
mRNA
AAAAA
AAAAA

RNA interference for Crop protection

Can we deliver RNA as a topical application instead of genetically modifying the plant?

Limitations of naked dsRNA

- Unstable
- Degradation on plant surface
- Easily washed off leaves
- Short protection window

https://www.britannica.com/science/double-stranded-RNA

Stabilise?

Environmentally friendly?

Degradable?

Stick to the leaf?

How can we convert naked dsRNA experiments into a commercially viable system for farmers?

Protect from rain?

Non-toxic?

Easy to adopt?

RNA-based Biopesticides - *BioClay™*

Inventors:
Prof. Neena Mitter
Prof. Gordon Xu
Prof. Max Lu

- RNA as the biological active ingredient
- Clay particles as carriers of the active

BILL & MELINDA GATES foundation

QAAFI and AIBN

- **NO RESIDUE**
- **SPECIFIC**
- **STABLE**
- **SUSTAINABLE**
- **SAFE**

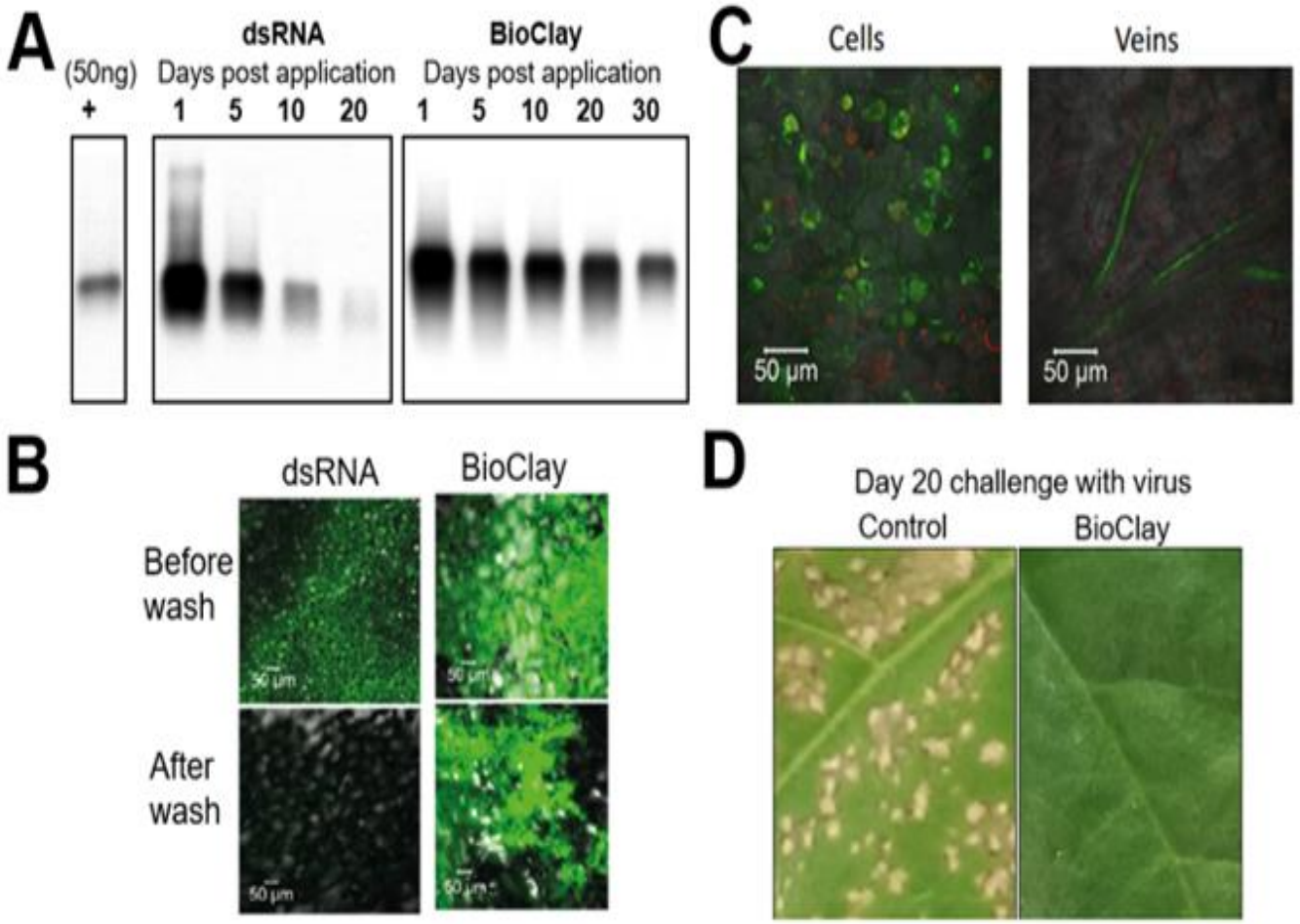
What is BioClay?

Inert biodegradable clay to deliver RNA

- Applied as a spray application without the need to alter the plant genome
- Clay layers degrade naturally leaving no residue
- Extended stability and slow release of dsRNA on plant surface

Double stranded RNA of the pest or pathogen is used to kill the pathogen itself – Nature vs Nature

BioClay- It works



A – BioClay dsRNA survives on leaves even after 30 days of spray

B – The sprayed dsRNA can enter into the plant system

C – BioClay does not get washed off by water/rain

D – The sprayed leaves are protected from virus even after 20 days of spray

Mitter et al, Nature Plants 2017

Novel Topical Vegetable, Cotton Virus and Whitefly Protection –VG16037

BioClay it works….Zucchini yellow mosaic virus

Water

Unpublished

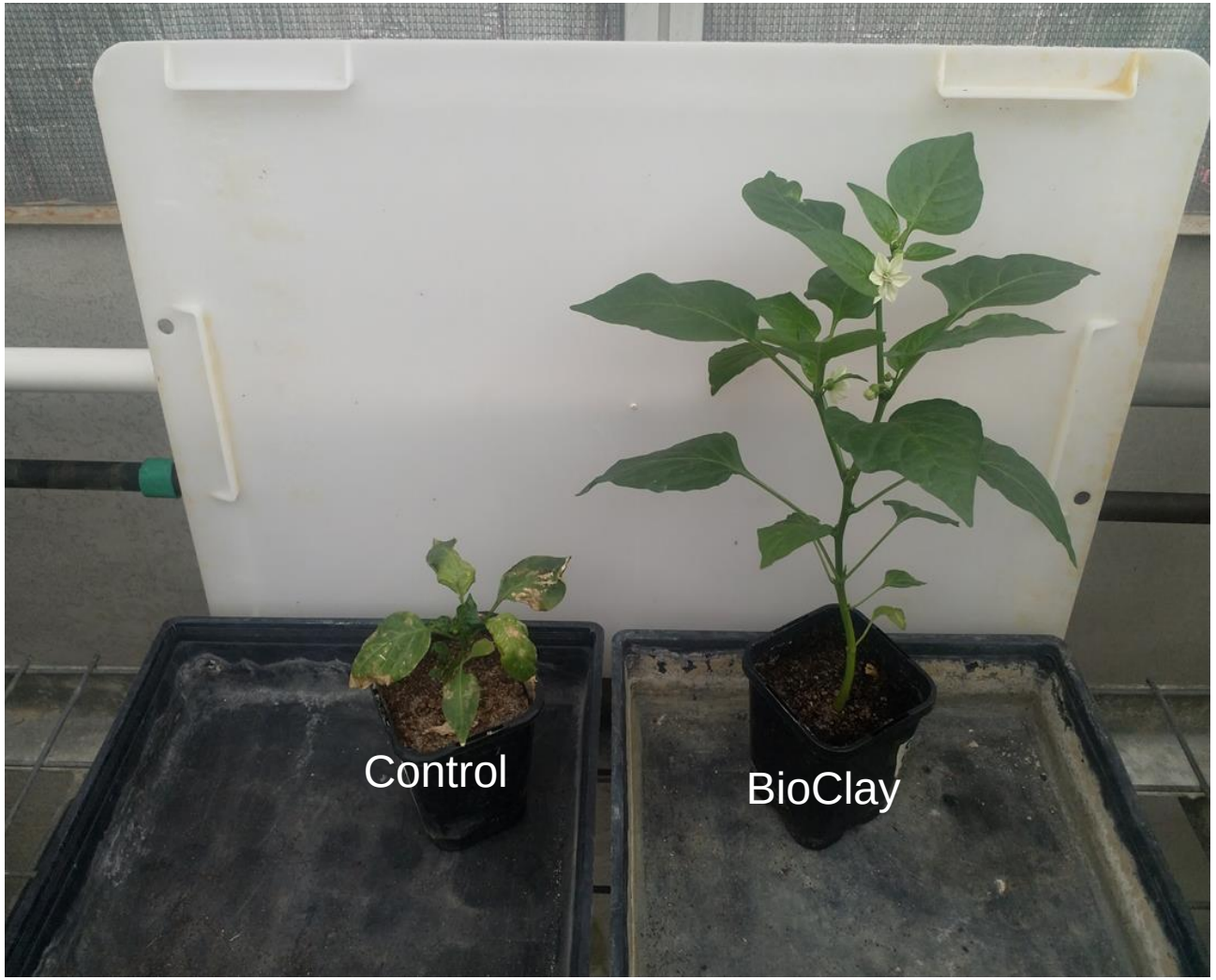
Naked
dsRNA

BioClay

Figure 12. Zucchini Field trial site Redlands

Unpublished

BioClay it works - Control of Tomato Spotted Wilt Virus



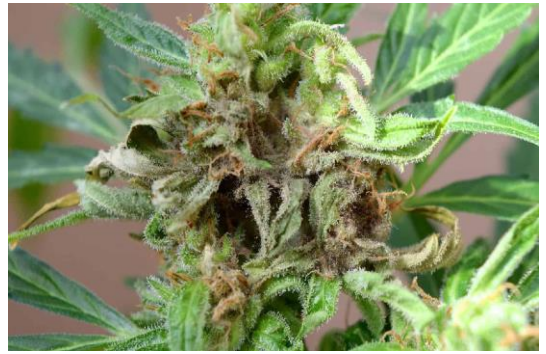
Viruses	Insect pests	Fungi
Tospoviruses	Whiteflies	Botrytis
Potyviruses	Aphids	Sclrerotinia
Cucumovirus	Thrips	Fusarium
		Verticillium



extension@sdtstate.edu


www.appsnet.org


growveg.com.au


Growdiaries.com

The University Of Queensland AUSTRALIA
QAAFI Queensland Alliance for Agriculture and Food Innovation
Queensland Government

nature plants

Article | Published: 16 May 2022

Foliar application of clay-delivered RNA interference for whitefly control

Ritesh G. Jain, Stephen J. Fletcher, Narelle Manzie, Karl E. Robinson, Peng Li, Elvin Lu, Christopher A. Brosnan, Zhi Ping Xu & Neena Mitter ✉

Nature Plants **8**, 535–548 (2022) | Cite this article

1595 Accesses | **502** Altmetric | Metrics

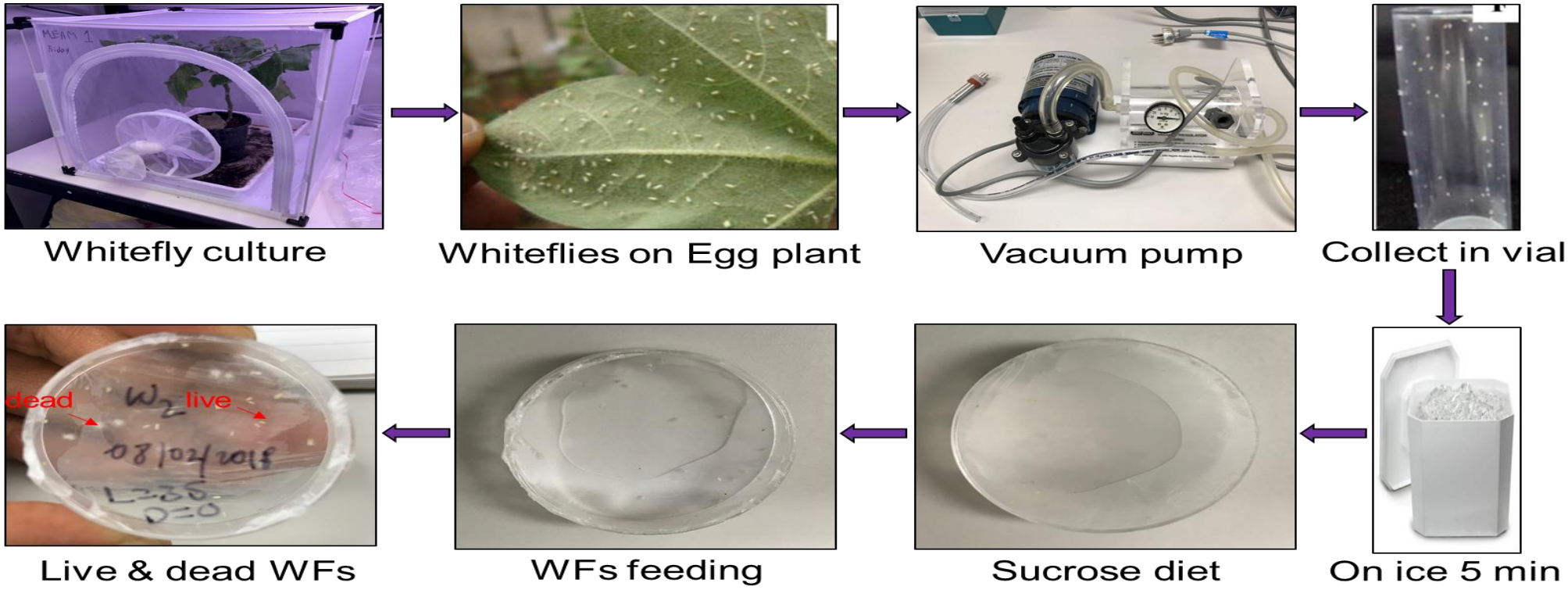
Summary of whitefly work – Cotton/Tomato as the host

1. Screening of >100 targets – AD & Plant assays
2. Effective 13 targets
3. Combination and stacking of dsRNAs
4. Uptake of dsRNA in cotton and whitefly
5. Insectary trials – mortality between 30 - 80% targeting various stages of life cycle
6.

Whitefly and virus work – ready for translation to horticultural crops- cotton- protected cropping

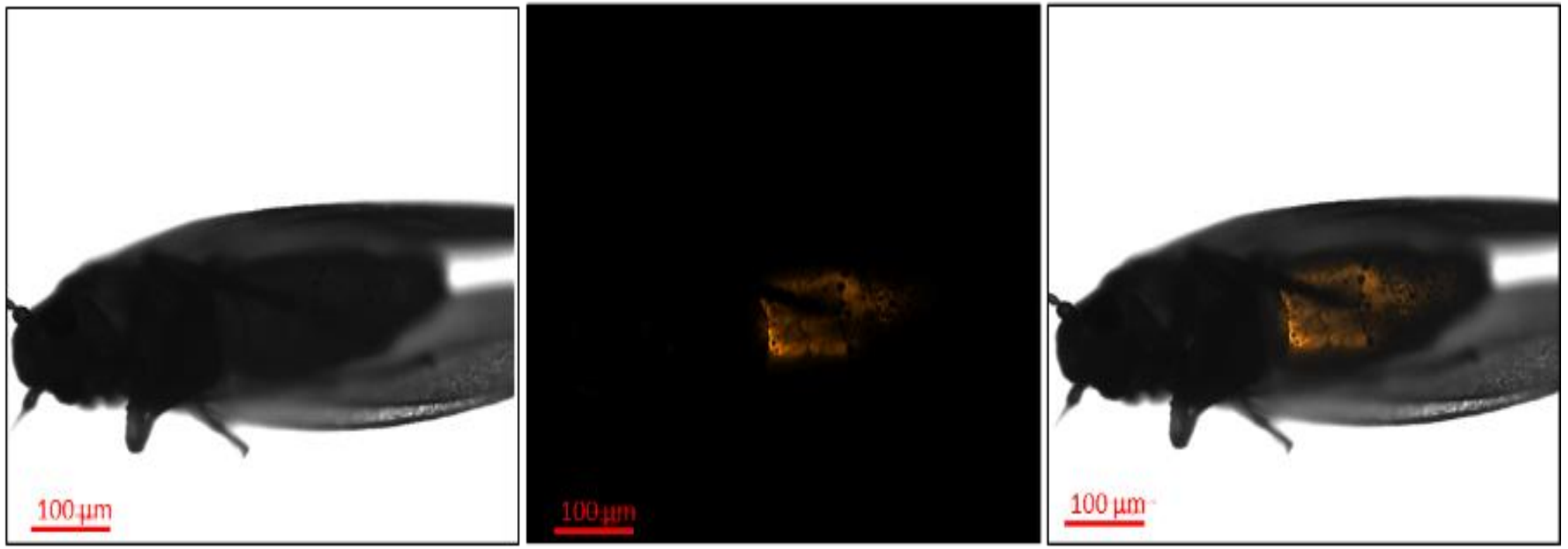
Unpublished

Workflow of RNAi screening bioassays



Artificial diet assay (AD)

BioClay for insect pests: RNA uptake in Whitefly

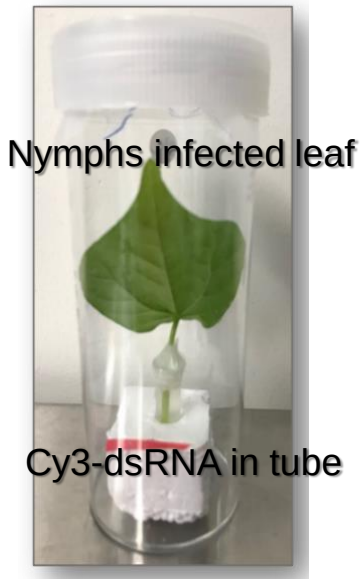


Adult whitefly showing presence of dsRNA in the abdomen 48 after after feeding on a sprayed leaf

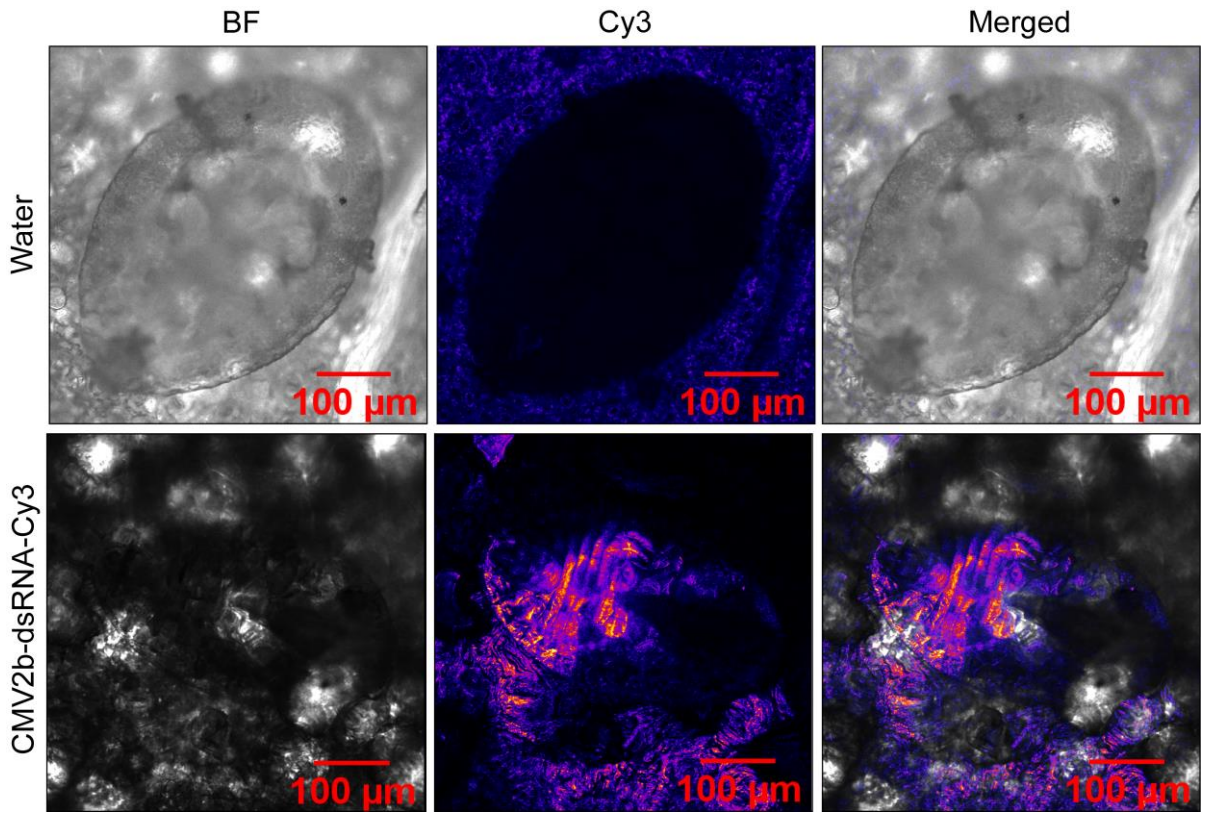
Unpublished

Jain, Ritesh G., Robinson, Karl E., Asgari, Sassan and Mitter, Neena (2020).Current scenario of RNAi -based hemipteran control. Pest Management Science, 77 (5) ps.6153, 2188-2196

Leaf-mediated uptake of dsRNA in whitefly nymphs



Set up



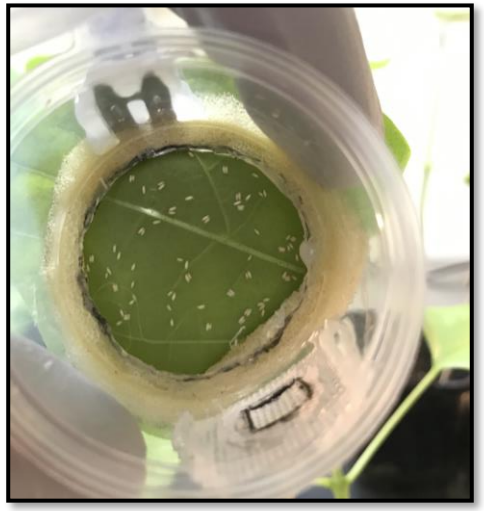
Whitefly nymphs can uptake dsRNA from petiole dip assay

Jain..Mitter et al Nature Plants, 2022

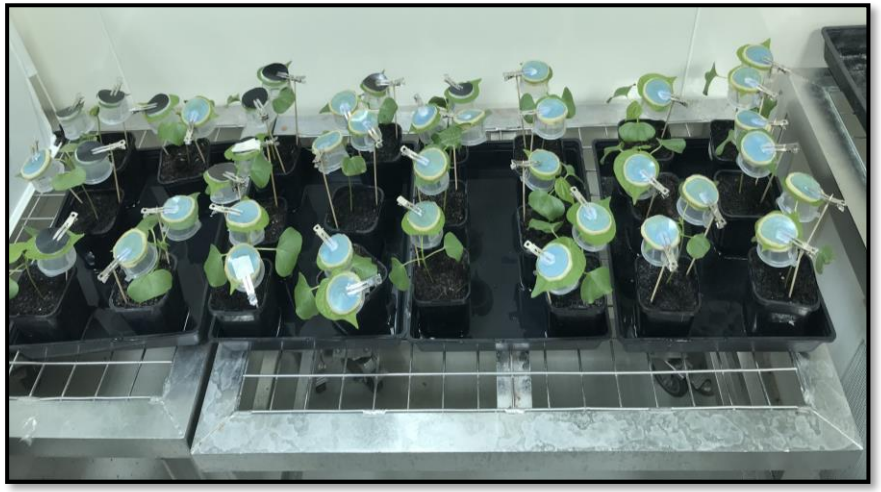
White Fly - Insectary Trials

insectary room

Cotton plants



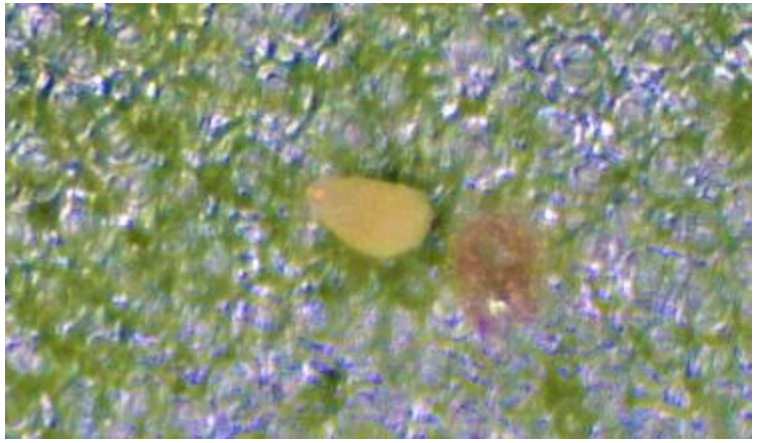
Adult Wfs into clip cage



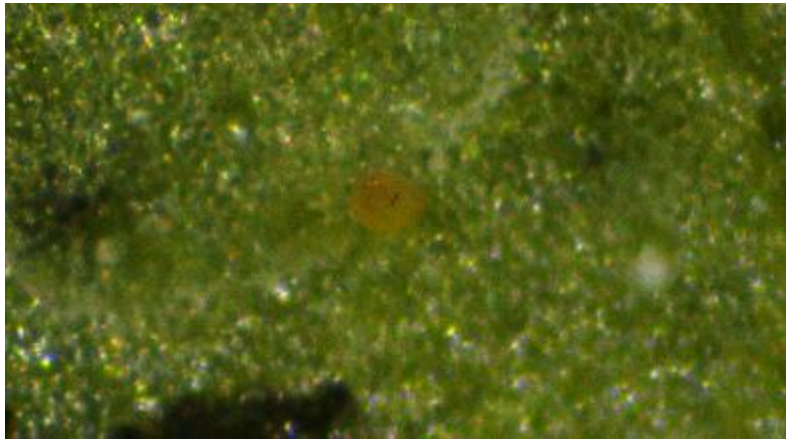
3D printed clip cage

Phenotypic effects of dsRNA/BioClay

Jain..Mitter et al Nature Plants, 2022



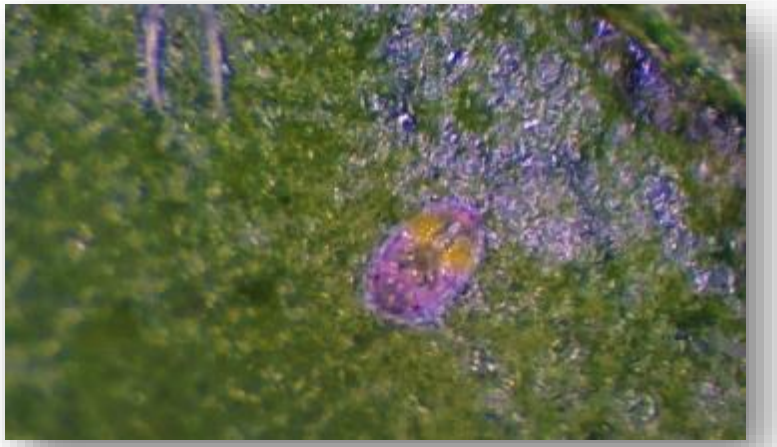
Water treated egg



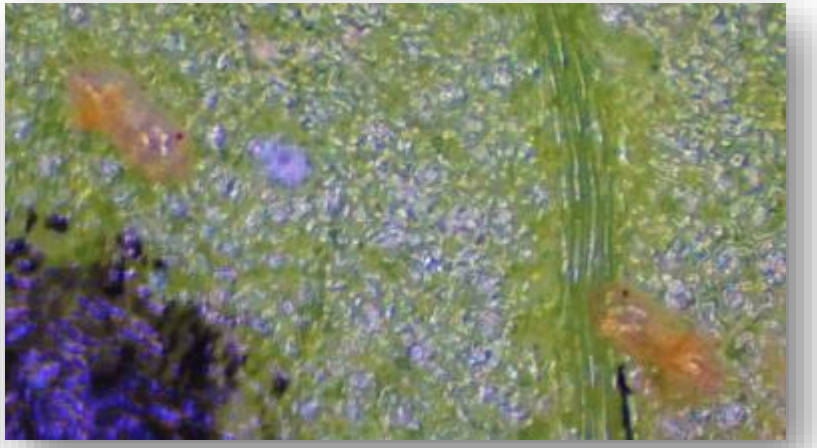
BioClay treated egg

Live Whitefly

BioClay Dead Whitefly



Water treated nymph

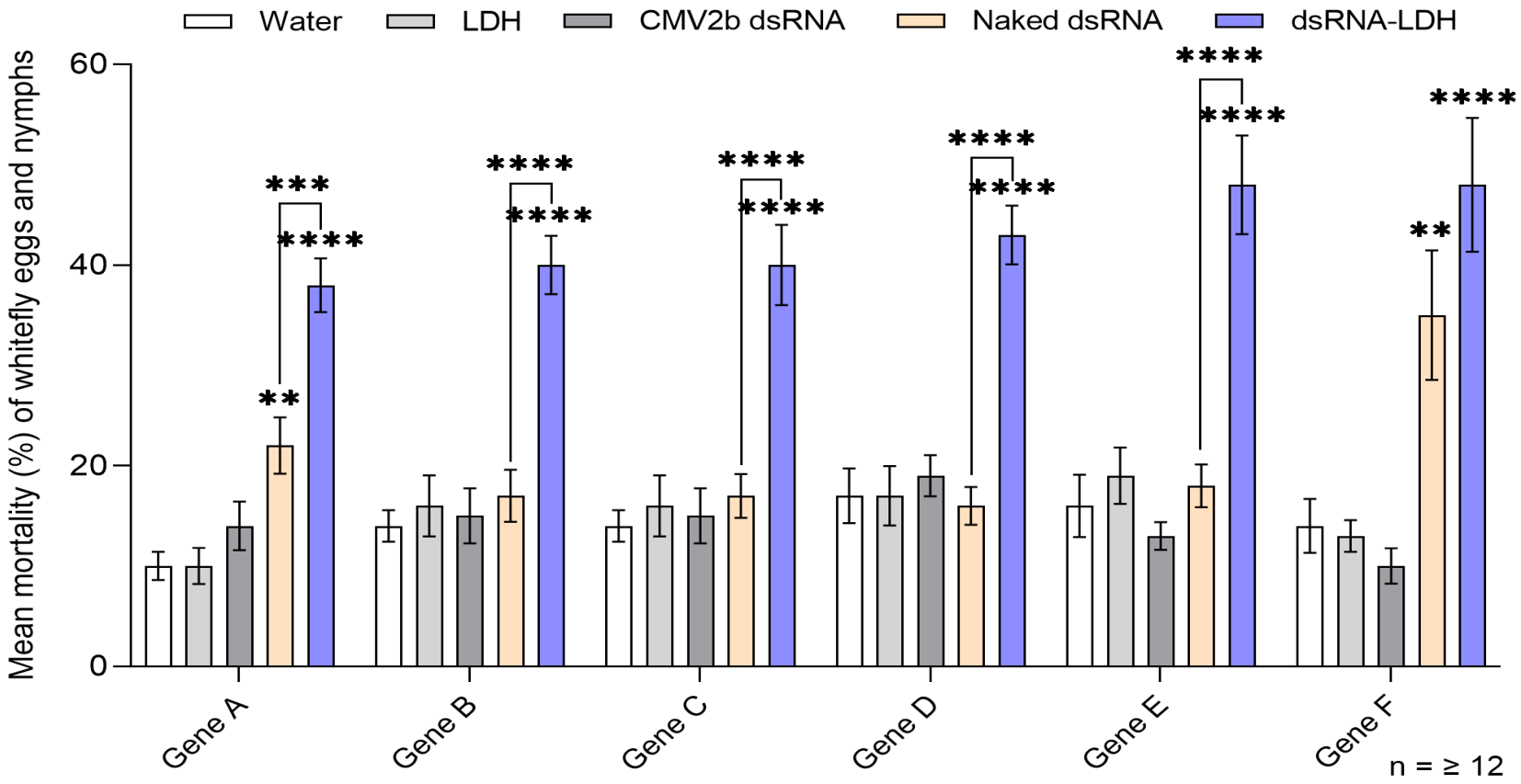


BioClay treated nymphs

Tested :
No effect on Stingless Bees
No effect on aphids

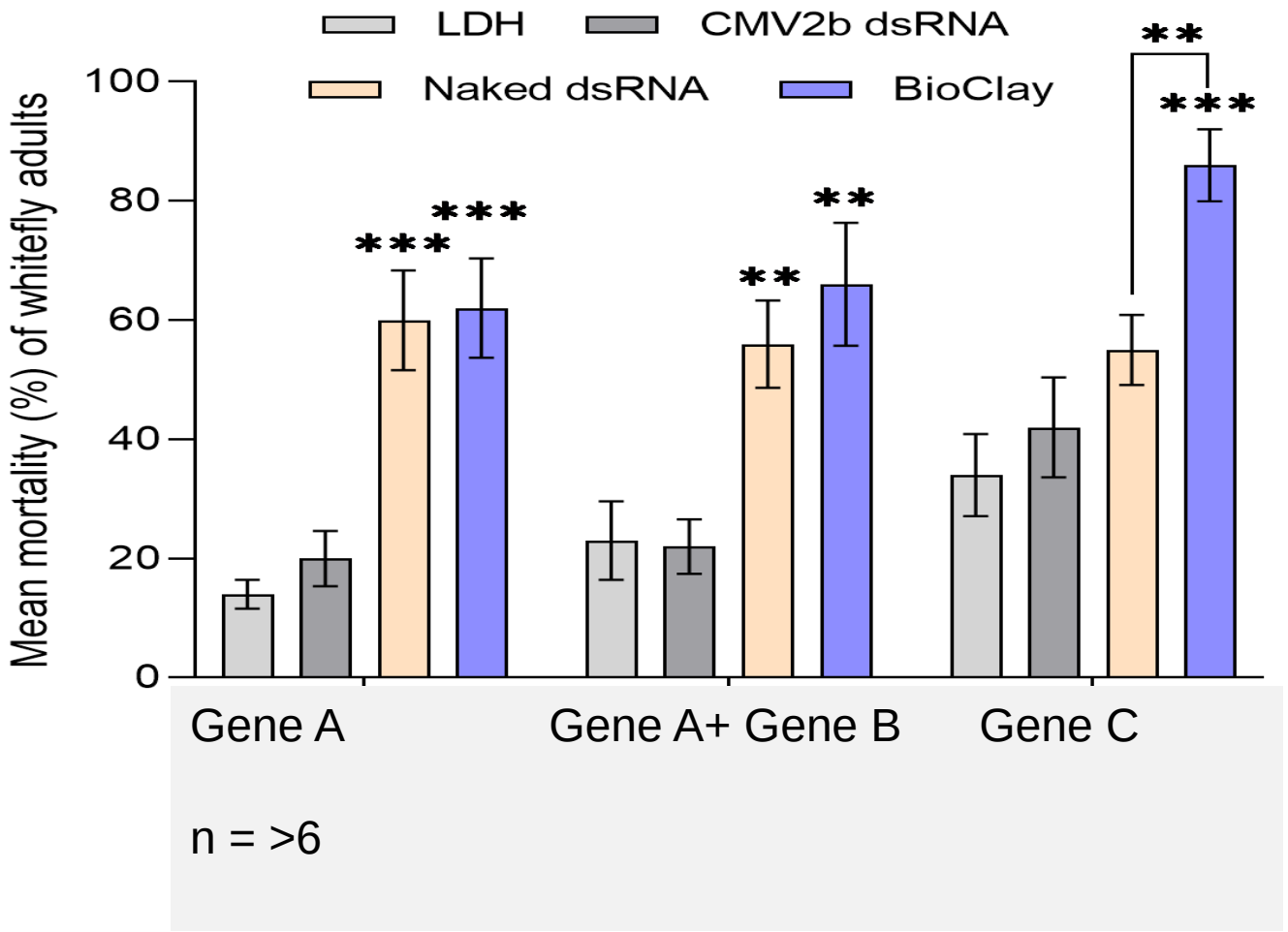
Jain..Mitter et al Nature Plants, 2022

Percentage eggs and nymphs mortality caused by foliar spray of BioClay on Cotton



Jain..Mitter et al Nature Plants, 2022

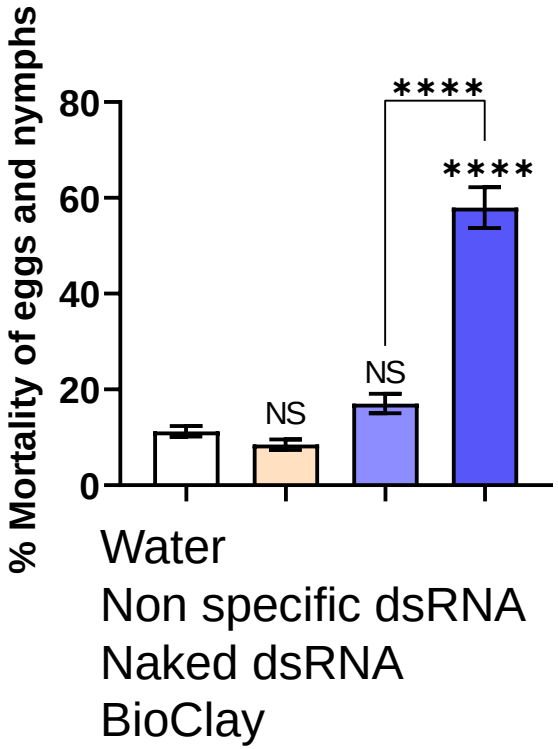
Percentage adult mortality caused by foliar spray of BioClay on Cotton



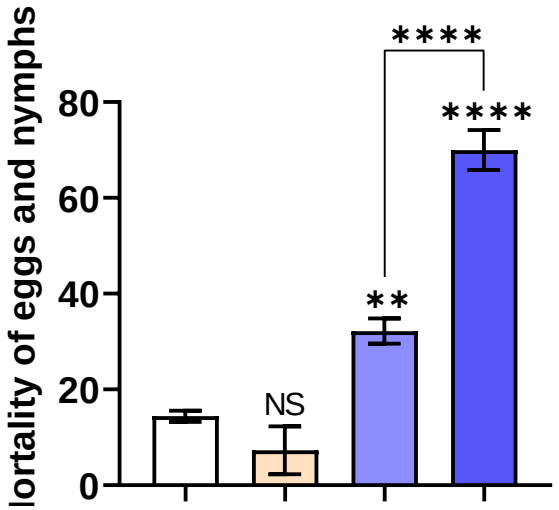
Unpublished

BioClay showed better protection against eggs/nymphs on Tomato plants

Trial_1



Trial_2



Jain..Mitter et al Nature Plants, 2022

BioClay for control of Fungal diseases

Australian Research Council Research Hub for Sustainable Crop Protection -
Targeting Fungal Diseases and Officially Opened in Aug 2020

~$18 million cash and in-kind

Universities, multiple RDCs, State Governments and Industry partners

https://crophub.com.au/

RNA-based biopesticides – a paradigm shift

- Pre- and post-harvest application possible
- Increased pest/pathogen specificity
- Easy deployment of new sequences to address resistance
- Finite amount of dsRNA
- Non GM

Photo by Sushobhan Badhai on Unsplash

On 8th October 2019 the Australian Parliament formally agreed with the Office of the Gene Technology Regulator's proposal that topically-applied dsRNA be exempt from GMO regulations

Gene Technology Amendment (2019 Measures No. 1) Regulations 2019

24 Schedule 1A (at the end of the table)

Add:

11	Introduction of RNA into an organism, if: (a) the RNA cannot be translated into a polypeptide; and (b) the introduction of the RNA cannot result in an alteration of the organism's genome sequence; and (c) the introduction of the RNA cannot give rise to an infectious agent.

Trade and Markets

Naked dsRNA:

- Short or nil withholding periods (set to allow chemical residues in edible commodities for domestic markets)

- Short or nil export intervals (to satisfy the standards imposed by overseas trading partners)

RNAi based biopesticides

Topical spray
Tissue Culture
Seedling applications
Baits
Feed

- ✓ Non - GM
- ✓ No residue
- ✓ Specificity
- ✓ Minimal issue of resistance development
- ✓ Value across plant and animal health

Fruit Fly – Can it work???

RNA based approach can be designed and tested in artificial diet, baits, traps, and cover sprays for reducing reproductive fitness, targeting ovipositor, and inducing mortality of Qfly and Medfly.

.

Vinegar fly (Drosophila melanogaster) is a model genetic organism, which has been extensively used in RNAi studies

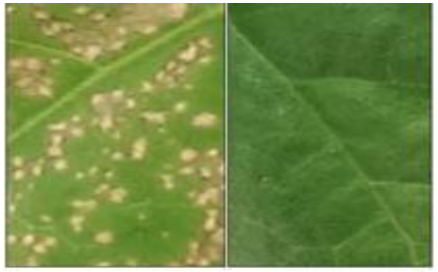
- Dietary dsRNA could knockdown expression of Oriental fly genes related to spermatogenesis resulting in reduced fecundity of treated males (Dong et al, 2016)
- Demonstration of similar effect in Qfly genes (Cruz et al, 2018)
- Other fruit fly species have also been successfully targeted using RNAi, including the South American fruit fly (Dias et al 2019) ,

Innovations aimed at contributing to the supermarket trolley

Endless possibilities…

Design of regulation and public opinion are crucial

VIRUSES



FUNGI

INSECTS

PROTECTED CROPPING !!

PACKHOUSES!!

ANIMAL HEALTH !!

agric.wa.gov.au

BIOSECURITY!!

Nufarm

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QAAFI Queensland Alliance for Agriculture and Food Innovation

Australian Government
Australian Research Council

Griffith UNIVERSITY Queensland, Australia

LA TROBE UNIVERSITY

Curtin University

UNIVERSITY of TASMANIA
TIA Tasmanian Institute of Agriculture

UC RIVERSIDE

Government of South Australia
Department of Primary Industries and Regions

SARDI
SOUTH AUSTRALIAN RESEARCH AND DEVELOPMENT INSTITUTE

The Australian Wine Research Institute

Queensland Government
Department of Agriculture and Fisheries

BIOPLATFORMS AUSTRALIA

Hort Innovation

CRDC
COTTON RESEARCH AND DEVELOPMENT CORPORATION

GRDC
GRAINS RESEARCH & DEVELOPMENT CORPORATION

Wine Australia

AUSVEG