frontiers | Frontiers in Agronomy

EDITORIAL
published: 27 May 2022
doi: 10.3389/fagro.2022.903841

Editorial: New Applications of Insecticidal RNAi

Thais B. Rodrigues[1], *Lynne K. Rieske*[2], *Kenneth E. Narva*[1], *Andrew Roberts*[3] *and Ana M. Vélez*[4*]

[1] Plant Health Department, Research Triangle Park, GreenLight Biosciences, Medford, NC, United States, [2] Department of Entomology, University of Kentucky, Lexington, KY, United States, [3] Agriculture & Food Systems Institute, Washington, DC, United States, [4] Department of Entomology, University of Nebraska-Lincoln, Lincoln, NE, United States

Keywords: RNA interference, pest management, double-stranded RNA, dsRNA, sprayable RNAi

Editorial on the Research Topic

New Applications of Insecticidal RNAi

OPEN ACCESS

Edited by:
Murray B. Isman,
University of British Columbia, Canada

Reviewed by:
Kun Yan Zhu,
Kansas State University, United States

Correspondence:
Ana M. Vélez
avelezarango2@unl.edu

Specialty section:
This article was submitted to Pest Management, a section of the journal Frontiers in Agronomy

Received: *24 March 2022*
Accepted: *04 May 2022*
Published: *27 May 2022*

Citation:
Rodrigues TB, Rieske LK, Narva KE, Roberts A and Vélez AM (2022) Editorial: New Applications of Insecticidal RNAi Editorial Article. Front. Agron. 4:903841. doi: 10.3389/fagro.2022.903841

INTRODUCTION

Gene silencing, the phenomena where genes are turned off, as a result of RNA was first reported by Napoli and Jorgensen in 1990, who discovered the phenomenon accidentally while trying to overexpress a gene in petunia (Napoli et al., 1990). Referred to as co-suppression, and "quelling" in the early literature, the mechanism of these silencing events remained a mystery until the publication of the 1998 paper from Fire and collaborators describing a mechanism for achieving specific, RNA sequence dependent gene silencing in the model nematode *Caenorhabditis elegans* which they termed "RNA interference" or RNAi (Fire et al., 1998). To say that this observation changed scientific research overnight would not be an overstatement. The classical genetic research paradigm was already yielding to a variety of "reverse genetic" techniques, and the discovery of this ancient, widely conserved gene silencing mechanism provided a powerful new tool for exploring the function of genes with a known sequence. Combined with the exponential growth of genomic sequence information, the process of gene discovery and characterization accelerated its transition from a slow, random process of mutagenesis and laborious genetic mapping through endless crosses and selection into one where known gene sequences could be selected based on similarity to previously known genes and their function assessed through a relatively simple assay. It is not an exaggeration to say genetic research was forever changed, and as a result Andrew Fire and Craig Mello in 2006 were awarded a Nobel Prize in Physiology or Medicine.

Almost immediately, scientists began to imagine its potential for use outside of research, including in agriculture. Modern agriculture is challenged with the need for innovative crop protection technology that will support long term sustainability goals for the environment and ensure food security for the world's rapidly increasing human population. Insects are responsible for significant crop loss, accounting for approximately 20 percent of loss on a global basis (Oerke and Dehne, 2004). Reduced reliance on synthetic chemical pesticides that may negatively impact pollinators and other beneficial insects is an aim of both private industry and governmental agencies alike. The need for environmentally sound methods of insect control has inspired research into a wide range of bio-based technologies. RNA interference has emerged as a highly effective tool with inherent potential to control a wide range of insects. However, translating this potential to real agricultural applications remains a challenging process. This special issue is dedicated to providing up to date information on the latest applications and developments in the use of RNAi for insect control through eight publications.

CURRENT KNOWLEDGE OF SPRAYABLE RNAI

Nitnavare et al. review the successes, challenges, and future prospects for developing RNAi-based pest control. The efficacy of RNAi in insect orders including a majority of pests of agricultural importance, i.e., Hemiptera, Lepidoptera and Coleoptera, and barriers to effective RNA-based are summarized. Delivery technologies aimed at overcoming biological barriers are highlighted with forward-looking safety considerations for RNA insecticides complexed as nanoparticles.

TARGET DISCOVERY

Identification of RNAi-sensitive target genes is an essential first step in developing pesticidal dsRNA. Non-model agricultural insect pests often lack genomic resources and laboratory assay systems to enable large scale RNAi screens. Knorr et al. leveraged the model coleopteran, *Tribolium castaneum*, to identify RNAi target sites and use that knowledge to interrogate candidate genes in a mRNA transcription interaction network and extend those findings to orthologous genes in other Coleopteran pests.

CHALLENGES

Many insects exhibit robust RNAi responses, and most target pests for which the technology has been explored have involved monophagous herbivores. However, ants (Hymenoptera: Formicidae) are important agricultural pests that do not feed directly on crops. Gene silencing using RNAi has been demonstrated in several ant species to evaluate gene function, but Allen explores the potential for utilizing RNAi for pest ant suppression. Application of RNAi technology for ant suppression is complicated by their eusocial nature, which creates unique challenges associated with delivery, targeting, efficacy, and risks.

DELIVERY TECHNOLOGIES

The deployment of dsRNA (double-stranded RNA) as a biopesticide faces several environmental and biological barriers. Pugsley et al. present a comprehensive overview of chemicals and biological nanoparticles as potential solutions to these challenges. The review covers 1) synthetic and natural charged polymers that can complex with dsRNA and protect the molecule from degradation and 2) alternative nanocarriers such as nanoclays and liposomes developed and tested in insects and showing promising results. In addition to polymers and nanoparticles, they explored studies for RNA-based therapeutic application as future research directions in agriculture.

Hunter et al. report the development, evaluation, and efficacy of a new RNA-targeting technology, antisense oligonucleotide FANA (2'-deoxy-2'fluoro-arabinonucleotide). FANA was tested in citrus trees and potato plants for the management of both bacterial pathogens and arthropod pests. FANA technology is a new and novel RNAi technology that solves issues of stability, cell entry, and binding affinity experienced by other exogenous RNAi strategies and can move systemically in plants and animals. Importantly, this is the first RNAi technology to successfully target bacterial plant pathogens, not possible with other RNAi technologies.

EFFECTS ON NON-TARGETS

Sequence complementarity of the RNAi pathway permits targeted silencing of essential genes and reduces the likelihood of impacts on non-target organisms. However, demonstrating specificity to target organisms remains an essential step for RNAi risk analysis and eventual deployment. Pampolini and Rieske evaluated the spectrum of activity of orally ingested emerald ash borer (EAB) specific dsRNAs. Model insects were exposed and evaluated for lethal effects, and when possible, evaluated for gene expression and *in silico* analysis.

GENE CHARACTERIZATION AND APPLICATION

The first sprayable RNAi-based biopesticide product (active ingredient ledprona) targets an essential gene in *Leptinotasa decemlineata*, Colorado potato beetle (CPB). Rodrigues et al. showed ledprona has a new mode of action, where long dsRNA is processed into 21 nucleotides small interfering RNAs (siRNAs) that complement, bind, and cleave CPB proteasome 20S subunit beta-5 (PSBM5) mRNA and compromise its protein production. Ledprona represents a new biopesticide class for integrated pest management (IPM) and insecticide resistance management programs against CPB (Rodrigues et al.).

Willow et al. provides another example of the evaluation of RNAi for the potential management of an insect pest, the pollen beetle *Brassicogethes aeneus*, a major pest of oilseed rape in Europe. This study demonstrated the successful silencing of the *B. aeneus coatomer subunit* α (*aCOP*) and subsequent mortality of larvae. Research in semi-field-realistic conditions spraying dsRNA formulations and bioengineering crops and exploring additional dsRNA targets are the proposed next steps to evaluate the potential use of RNAi for the management of *B. aeneus*.

CONCLUSIONS

The characterization of the RNAi pathway as a conserved mechanism of gene silencing across taxonomic phyla has already revolutionized basic biological research. As researchers and product developers move forward, they are increasingly overcoming the practical challenges to using this knowledge to accomplish human goals for pest control in agriculture. The sequence specific nature of RNAi presents an opportunity to design target sequences that minimize the impacts to non-target organisms and to the environment while providing pest control programs with a new tool for integrated pest management. This collection of publications provides an overview of the current progress and remaining challenges for maximizing the potential benefits of these technologies.

AUTHORS CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

REFERENCES

Fire, A., Xu, S., Montgomery, M. K., Kostas, S. A., Driver, S. E., and Mello, C. C. (1998). Potent and Specific Genetic Interference by Double-Stranded RNA in *Caenorhabditis Elegans*. *Nature* 391, 806–811. doi: 10.1038/35888

Napoli, C., Lemieux, C., and Jorgensen, R. (1990). Introduction of a Chimeric Chalcone Synthase Gene Into Petunia Results in Reversible Co-Suppression of Homologous Genes in Trans. *Plant Cell* 2, 279–289. doi: 10.2307/3869076

Oerke, E. C., and Dehne, H. W. (2021). Safeguarding Production—losses in Major Crops and the Role of Crop Protection. *Crop Protection* 23 (4), 275–285. doi: 10.1016/j.cropro.2003.10.001

Conflict of Interest: AV has received funding for research on RNAi from Dow AgroSciences, DuPont Pioneer, Monsanto Company, Corteva Agriscience, Bayer Crop Science, and Greenlight Biosciences. TR and KN work at GreenLight Biosciences. LR has received research funding from Greenlight Biosciences. KN, TR, LR, and AV hold multiple RNAi patents. The information and views represented in this editorial are those of the authors as individuals and experts in the field and do not represent those of their organizations. The mention of a product does not constitute an endorsement or a recommendation for its use.

The remaining author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.