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Fusion Proteins as a Resistance Factor against Insect Pests

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Abstract

The development of insect-resistant crops has been a significant challenge in agriculture. Fusion proteins technology, a promising approach, combines the properties of different proteins to confer resistance against insect pests. These fusion proteins are engineered by fusing genes from different sources, such as *Bacillus thuringiensis* (Bt), scorpion toxin-based, spider venom-based and other insecticidal proteins. The resulting fusion proteins exhibit enhanced insecticidal activity, broader insect target range and improved stability compared to individual proteins. Moreover, they can overcome the development of resistance in insect populations, a major concern with conventional insect-resistant crops. Fusion proteins have shown promising results in various crop systems against lepidopteran, coleopteran and hemipteran pests. However, optimizing their expression, stability and bio-safety requires further research for sustainable insect pest management.

Keywords: Fusion proteins, Insect-resistant crops, Insecticidal proteins, Resistance

Introduction

The world's population is projected to reach 10 billion by 2050 (Zsögön *et al*., 2022), necessitating a 56% increase in food production (van Dijk *et al*., 2021). However, factors like population growth, resource depletion, climate change and insect pests pose challenges to agricultural productivity, with insect pests causing 25%-30% losses (Fernández *et al*., 2021). Conventional synthetic pesticides have led to concerns over pest resistance, non-target impacts, water contamination and poisoning, prompting the withdrawal of many broad-spectrum insecticides. Sustainable and modern agricultural practices, including protein-based biopesticides, offer a promising solution, combining efficacy, specificity and environmental biodegradability. Biotechnological methods can produce recombinant insecticidal fusion proteins, consisting of a toxic peptide or protein fused to a carrier that facilitates oral delivery and targeted toxicity against pests (Fitches *et al*., 2004).

What are Fusion Proteins?

A fusion protein is a unique type of protein that combines two or more functional components from different sources into a single molecule. These components, originally encoding separate proteins, are merged together through genetic engineering techniques. There are two main types of fusion proteins: Type-I fusion proteins, in which the individual proteins or protein subunits are joined end-to-end, typically with a linker sequence acting as a bridge between them and Type-II fusion proteins, where the amino acids from the different sources are interspersed throughout the final fusion protein product, creating a more intertwined structure (Figure 1). These fusion proteins exhibit specific structural features, such as breakpoints occurring in disordered regions to preserve function, non-random combinations of domains from the parent proteins and increased disorder or lack of stable structure, promoting domain recombination and flexibility.

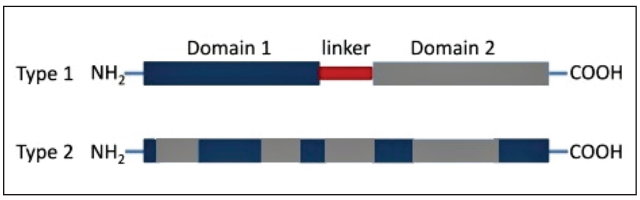

Figure 1: Types of fusion proteins

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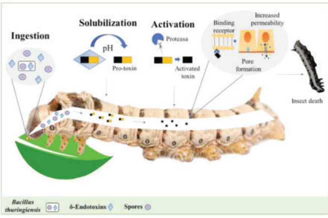
Application of Fusion Proteins in Agricultural Crops against Insect Pests

Application of fusion proteins can evolve as a promising strategy for developing insect-resistant crops in future. When expressed in transgenic crops, these fusion constructs can confer targeted resistance against a broad range of insect pests, reducing crop losses and enhancing food security. There are different types of fusion proteins (Table 1).

Table 1: Types of fusion proteins

Type of Fusion Protein	Mechanism	Example
Cry-based Fusion Proteins  Toxic potential of *B. thuringiensis*	Combines Cry proteins (derived from *B. thuringiensis*) with protease inhibitors, binding proteins, or multiple Cry proteins for enhanced efficacy, broadened activity and delayed resistance development.	Cry1Ac + Cowpea Trypsin Inhibitor (Bt Cotton); Cry1Ab + Cadherin Receptor-Binding Domain (Bt Maize); Cry1Ab + Cry1Ac + Cry2A (Bt Cotton)
Allatostatin-based Fusion Proteins  *Manduca sexta*	Fuses insect-specific allatostatin (a neuropeptide) with a carrier protein to disrupt allatostatin signaling pathways, affecting insect growth, development and reproduction.	*Galanthus nivalis* agglutinin (GNA) + *Manduca sexta* allatostatin
Scorpion Toxin-based Fusion Proteins  *Androctonus australis*	Combines scorpion neurotoxins (modulators of voltage-gated sodium channels) with carrier proteins for delivery across the insect gut, causing paralysis and insect death.	ButaIT/GNA (ButaIT toxin from red scorpion + GNA); AaIT/GNA (AaIT toxin + GNA)
Spider Venom-based Fusion Proteins  *Pireneitega luctuosus*	Fuses spider venom toxins (specific for ion channels or receptors) with carrier proteins to modulate intended molecular targets upon delivery across the insect gut.	PI1a/GNA (δ-amaurobitoxin-PI1a toxin + GNA)
TAT-PTD-Diapause Hormone-based Fusion Proteins  *Clostera anastomosis*	Incorporates the cell-penetrating TAT peptide and insect diapause hormone to disrupt insect metamorphosis and life cycle progression upon ingestion.	TAT-caDH (TAT peptide + *Clostera anastomosis*)

Fusion Proteins in Agriculture: Opportunities and Challenges

Fusion proteins offer advantages such as activity against a broad range of insect pests and pathogens, lower toxicity for vertebrates compared to chemical pesticides and potential to enhance micronutrient contents of crops. However, challenges include applicability to well-characterized genes, difficulties in recalcitrant crops, regulatory hurdles and public acceptance. Ensuring protein stability, efficacy, specificity and developing insect resistance management strategies are crucial. Future directions involve improving protein designs through multi-mode fusions, integrating fusion proteins into Integrated Pest Management strategies and continuous research and development efforts to drive progress in this field.

Conclusion

Fusion proteins, engineered by combining insecticidal toxins with carrier proteins or cell-penetrating peptides, offer a promising approach for sustainable management of pest in agriculture when expressed in transgenic crops. This technology can confer targeted resistance against insect pests, reducing crop losses and enhancing food security. However, successful development and deployment require collaborative efforts, extensive research to optimize design, efficacy, specificity and bio-safety and implementation of resistance management strategies. With continued innovation, regulatory support and responsible stewardship, fusion proteins could become a vital component of integrated pest management for sustainable agriculture and global food production.

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