



Review

Regulating Death and Disease: Exploring the Roles of Metacaspases in Plants and Fungi

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Abstract: Identified over twenty years ago and distantly related to animal caspases are a group of cysteine proteases known as metacaspases. Throughout the years, much like caspase roles in metazoans, metacaspases have been shown to be involved in regulating cellular death in non-metazoan organisms. Yet, continued research on metacaspases describes these proteins as intricate and multifunctional, displaying striking diversity on distinct biological functions. In this review, we intend to describe the recent advances in our understanding of the divergence of metacaspase functionality in plants and fungi. We will dissect the duality of metacaspase activity in the context of plant-pathogen interactions, providing a unique lens from which to characterize metacaspases in the development, immunity, and stress responses of plants, and the development and virulence of fungi. Furthermore, we explore the evolutionary trajectory of fungal metacaspases to delineate their structure and function. Bridging the gap between metacaspase roles in immunity and pathogenicity of plant-pathogen interactions can enable more effective and targeted phytopathogen control efforts to increase production of globally important food crops. Therefore, the exploitation and manipulation of metacaspases in plants or fungi represent new potential avenues for developing mitigation strategies against plant pathogens.

Keywords: metacaspases; programmed cell death; plant immunity; plant pathogens; pathogenicity; fungal pathogens



Citation: Garcia, N.; Kalicharan, R.E.; Kinch, L.; Fernandez, J. Regulating Death and Disease: Exploring the Roles of Metacaspases in Plants and Fungi. *Int. J. Mol. Sci.* **2023**, *24*, 312. <https://doi.org/10.3390/ijms24010312>

Academic Editor: Lars Matthias Voß

Received: 6 December 2022

Revised: 20 December 2022

Accepted: 22 December 2022

Published: 24 December 2022



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1. Introduction

Plant pathogens are responsible for devastating agricultural losses across a wide array of crops, exacerbating the burden of global food insecurity [1]. Successful plant pathogens must bypass plant defenses while plants must employ a vast range of controlled defense mechanisms to subvert potential pathogenicity [2,3]. This complex interaction entails utilizing a variety of mechanisms, such as pathogen effector proteins and host resistance genes [4]. Intriguingly, a common denominator observed in these plant-pathogen interactions is the implementation and regulation of cellular death. Plant immune responses rely on precise and regulated cell death to impede pathogen invasion while ensuring the protection of the surrounding host cells [5]. Conversely, cell death is an important aspect in the maintenance of pathogen fitness, as it enables the pathogen to effectively cause disease and circumvent defense strategies executed by the plant host [6].

Initially, the regulation of cell death was only known in metazoan organisms. It was found that programmed cell death (PCD), the precise removal of unwanted cells following specific signals, in animals was coordinated by caspases [7,8]. Caspases are proteins found within the family of cysteine proteases. Their name is derived from their composition and amino acid specificity: cysteine aspartic-specific proteases [9]. Given the highly regulated network involved in PCD, caspases are initially synthesized as zymogens, or inactive enzymes. Caspases consist of a prodomain located at the N-terminus, followed by the p20

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Table of Contents Regulating Death

1. Understanding the eBook Regulating Death
 - The Rise of Digital Reading Regulating Death
 - Advantages of eBooks Over Traditional Books
2. Identifying Regulating Death
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Regulating Death
 - User-Friendly Interface
4. Exploring eBook Recommendations from Regulating Death
 - Personalized Recommendations
 - Regulating Death User Reviews and Ratings
 - Regulating Death and Bestseller Lists
5. Accessing Regulating Death Free and Paid eBooks

- Regulating Death Public Domain eBooks
- Regulating Death eBook Subscription Services
- Regulating Death Budget-Friendly Options
- 6. Navigating Regulating Death eBook Formats
 - ePub, PDF, MOBI, and More
 - Regulating Death Compatibility with Devices
 - Regulating Death Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Regulating Death
 - Highlighting and Note-Taking Regulating Death
 - Interactive Elements Regulating Death
- 8. Staying Engaged with Regulating Death
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Regulating Death
- 9. Balancing eBooks and Physical Books Regulating Death
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Regulating Death
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Regulating Death
 - Setting Reading Goals Regulating Death
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Regulating Death
 - Fact-Checking eBook Content of Regulating Death
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development

- Exploring Educational eBooks

14. Embracing eBook Trends

- Integration of Multimedia Elements
- Interactive and Gamified eBooks

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