Killer yeasts: Mechanisms, Applications in Medicine and Biocontrol, and Future Prospects

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Abstract—**The discovery of the yeast killer system, particularly in Saccharomyces cerevisiae, has significantly advanced various areas of biology. Researchers have gained insights into fundamental processes like protein processing and secretion, shedding light on how proteins are synthesized and transported within cells. Studies of killer toxins, similar to secreted proteins, have revealed mechanisms involved in post-translational modifications and secretion, providing a deeper understanding of eukaryotic cell biology. Additionally, the mode of action of killer toxins, which target specific receptors, has facilitated the study of yeast and fungal cell wall structures, helping to develop strategies for combating infections caused by pathogens like Candida albicans and Sporothrix schenckii. Over the past three decades, research on killer yeasts has also advanced our knowledge of virus-host interactions and yeast virology. Researchers like Schmitt & Breinig have explored killer strains' effects on related species, providing insights into ecological and industrial applications. Furthermore, Pieczynska et al. found that around 10% of strains carry killer viruses, while 25% resist viral toxins. While killer yeasts are valued for their antimicrobial properties, they pose challenges in large-scale fermentation processes, where they can inhibit starter cultures and disrupt production. Nonetheless, their potential in biomedicine and gene technology remains an active research area.**

Index Terms—**Killer toxins, *Saccharomyces cerevisiae*, protein secretion, yeast virology, antimicrobial properties.**

I. INTRODUCTION

The discovery of the yeast killer system has led to extensive research that has greatly advanced our knowledge in several areas of biology. This research has provided us with a deeper understanding of how cells work, including processes involved in protein processing and secretion. It has also helped us gain insights into how viruses interact with their host cells and how yeast and fungal cell walls are structured, which is useful for fighting infections caused by harmful yeasts in humans. Moreover, the study of killer yeasts, toxins, and viruses has sparked interest in their potential applications in biomedicine and gene technology. They could be explored for their therapeutic properties, such as using killer toxins to develop new antimicrobial treatments. Additionally, killer yeasts and viruses might have uses in gene technology, like delivering genes or editing them. Overall, the research on the yeast killer system has expanded our understanding of basic cell biology, virus-host interactions, and opened up possibilities for biomedical and gene technology applications.(1)Over the past three decades, extensive research on the killer system, particularly in the yeast species Saccharomyces cerevisiae, has led to significant advancements in various fields of biology. These investigations have provided valuable insights into fundamental aspects of eukaryotic cell biology, interactions between viruses and host cells, and the study of yeast viruses. The detailed analysis of killer toxins, which bear similarities to naturally secreted proteins or glycoproteins, has significantly enhanced our understanding of the mechanisms involved in post-translational prepro-protein processing in the eukaryotic secretion pathway. By studying the structure and synthesis of killer toxins, researchers have gained important knowledge about how proteins are processed and transported within cells. Furthermore, the analysis of killer toxins and their mode of action, which involves interacting with specific receptors, has proven to be an effective approach for investigating the molecular structure and in vivo assembly of yeast and fungal cell walls. This research has provided valuable information that can be applied to combatting yeast infections caused by certain pathogenic strains of Candida albicans and/or Sporothrix schenckii, which can affect humans. The intensive investigations of the killer system in S. cerevisiae over the past three decades have resulted in significant progress in various fields of biology. This review has deepened our understanding of eukaryotic cell biology, virus-host interactions, and yeast virology. Moreover, the study of killer toxins has provided insights into protein processing and secretion mechanisms, while also offering valuable information for combating specific yeast infections in humans. Building upon the initial discovery by Bevan and Makower in Saccharomyces cerevisiae[2],researchers such as Schmitt & Breinig have further explored killer strains that target related species, further investigations have focused on studying the effects of killer strains on phenotype, fitness, and the association with host-virus interactions. By understanding how killer strains affect the characteristics and behaviour of related species, researchers gain insights into the potential applications and implications of these strains in different ecological and industrial contexts toxin .[1]Furthermore, Pieczynska et al. have contributed to our understanding of killer yeasts by examining the prevalence of killer viruses among different strains. Their findings reveal that approximately 10% of strains carry killer viruses, while 25% show resistance to viral toxins.[3]

Killer yeasts are microorganisms, which can produce and secrete proteinaceous toxins, a characteristic gained via infection by a virus. These toxins are able to kill sensitive cells of the same or a related species. From a biotechnological perspective, killer yeasts have been considered as beneficial due to their antifungal/antimicrobial activity, but also regarded as problematic for large-scale fermentation processes, whereby those yeasts would kill species off starter cultures and lead to stuck fermentations.[5]

II. PATHOGENESIS OR THE MECHANISM

In recent years, significant progress has been made in our understanding of the basic biology of virus-carrying killer yeasts, specifically focusing on the toxin-encoding killer viruses and the intracellular processes associated with the maturation and toxicity of viral protein toxins. This research has shed light on the strategy employed by these eukaryotic viral toxins to effectively enter and ultimately eliminate target cells of eukaryotic organisms. Additionally, investigations have addressed the cellular mechanisms involved in self-defence and protective immunity against these killer yeasts and their toxins. Scientists have delved into the intricate details of how killer yeasts, harbouring killer viruses, utilize their viral protein toxins to penetrate target cells. This research has uncovered the mechanisms by which these toxins are processed and matured within the host cell, enabling them to exert their toxic effects. Understanding these processes contributes to our knowledge of how these viruses interact with host cells and manipulate cellular machinery. Furthermore, researchers have explored the cellular mechanisms that eukaryotic organisms employ in response to the presence of killer yeasts and their toxins. This includes the activation of self defence mechanisms aimed at neutralizing or eliminating the threat posed by these pathogens. Additionally, investigations have focused on protective immunity, which involves the development of immune responses to recognize and combat killer yeasts and their toxins.

By studying the basic biology of virus-carrying killer yeasts, their toxin-encoding killer viruses, and the intracellular processing, maturation, and toxicity of viral protein toxins, researchers have made significant strides in unravelling the intricate dynamics of these systems. These advancements deepen our understanding of the mechanisms employed by these pathogens and provide insights that could potentially contribute to the development of strategies for combating them and protecting against their harmful effects.[4][8]

III. USAGE OF KILLER TOXIN

Killer toxins (KTs) have shown significant promise as potential treatments for both animal and human infections, demonstrating effectiveness against various disease-causing bacteria and fungi. However, before KTs can be widely applied, further research is needed to evaluate their safety, effectiveness, and methods for more efficient production. This research will be crucial in unlocking the full potential of KTs as natural antimicrobials and therapeutic agents.

KTs can be used directly in laboratory settings or animal models to study their effects on disease-causing microorganisms. By understanding how KTs interact with specific pathogens, scientists can develop new therapeutic strategies, either using KTs alone or in combination with existing treatments to improve efficacy[6].Furthermore, through the idiotypic network—the interactions between antibodies and antigens—scientists can produce immunological derivatives of KTs. These derivatives may stimulate the immune system to recognize and target pathogens, potentially enhancing immune responses against infections. KTs also have potential applications in vaccine development. By harnessing the properties and structures of KTs, vaccines could be created to stimulate the production of antibodies that neutralize harmful microorganisms, offering protection against various infectious diseases. While these applications show great promise, ongoing research is essential to fully explore their potential and ensure their safety and effectiveness in medical use.

IV. PRESENT

Yeasts possess various characteristics that make them well-suited for protection and survival. They have a rapid nutrient utilization and high proliferation rate, allowing them to compete effectively with other organisms. Yeasts are capable of colonizing fruit surfaces for extended periods, even enduring dry conditions. They also produce extracellular polysaccharides that enhance their own survival while limiting the growth of pathogens. Moreover, yeasts have a sufficient tolerance to commonly used pesticides such as imazalil, tiabendazole, pyrimethanil, or fludioxonil. [(9)]Despite the existence of numerous reports on the use of yeasts as biological control agents, the availability of commercial products is limited and does not fully meet the potential market demand. This is primarily due to the multiple and time-consuming steps involved in product development and implementation. To successfully address these challenges, it is crucial to involve a commercial company with expertise in upscaling production, formulation development, registration procedures, and an established marketing network. Collaborating with such a company is necessary to overcome the obstacles and effectively bring yeast-based biological control products to the market. [(10)]

V. FUTURE

In spite of the numerous studies which have clearly demonstrated the advantages and benefits of using killer yeasts as biocontrol agents, commercial formulations are still not available. However, due to the obvious abundance and diversity of epiphytically thriving killer yeasts on fruit surfaces, and the continuous increase in the number of publications with respect to the search for novel killer strains as biocontrol agents, commercial formulations may soon be on hand. [(11)]

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