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Progress in the study of genetic and molecular mechanisms of hybridization lethality in plants

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Abstract: *Plant hybrid lethality refers to the phenomenon where the parents are normal, but their hybrid offspring exhibit abnormal development or even death, and it is classified as a post-zygotic form of reproductive isolation. Reproductive isolation plays a crucial role in species formation and maintaining species integrity, but it can also hinder the development of high-quality germplasm resources. Cloning hybrid lethality genes and analyzing their functions helps enrich our understanding of the mechanisms of species evolution and formation. This paper provides a comprehensive overview of the research progress on plant hybrid lethality at the cellular, genetic, and molecular levels, explores the molecular mechanisms of hybrid lethality, deepens our understanding of this phenomenon, and offers some references for future related studies.*

Keywords: *Hybrid lethality, Gene cloning, Functional validation, Molecular mechanism*

1. Introduction

In many species, the biomass of mature hybrid plants often surpasses that of the parent plants due to hybrid vigor or other genetic effects, a phenomenon known as heterosis. However, hybrid disadvantage can occasionally occur, which may be associated with reproductive isolation[1]. Reproductive isolation occurs when closely related populations cannot hybridize and produce offspring under natural conditions, or even if hybridization occurs, the resulting offspring are infertile, or exhibit abnormal growth and development. Reproductive isolation prevents gene flow between closely related species, playing a crucial role in significantly reducing hybrid abundance and maintaining species integrity[2]. However, for plant breeding, reproductive isolation can sometimes pose a barrier. Reproductive isolation is classified into two major categories: pre-zygotic isolation and post-zygotic isolation. Pre-zygotic isolation is caused by factors such as geographical barriers, differences in flowering times, behavioral or morphological isolation. Post-zygotic isolation includes hybrid infertility, hybrid lethality, and hybrid weakness[3]. The phenomenon of hybrid lethality in plants refers to the inability of offspring produced by the cross between two different genotypes to survive, or their death at the seedling stage. This phenomenon is primarily due to the genetic incompatibility between the parent species, which causes abnormalities at the cellular or molecular level in the hybrid offspring, preventing normal growth and development[4]. This review summarizes the progress in the cytological and genetic research on plant hybrid lethality, and discusses its molecular mechanisms in relation to multiple signaling pathways. The review also summarizes the coupling of hybrid lethality with disease resistance loci in previous studies, aiming to provide more insights for research on plant immune systems.

2. Phenotypic, Cytological, and Physiological-Biochemical Studies on Plant Hybrid Lethality

The phenomenon of plant hybrid lethality has been observed in multiple species[5-7]. Based on reported cases of plant hybrid lethality, the main phenotypic characteristics of hybrid lethality include leaf yellowing, chlorosis, reddening, or the appearance of necrotic spots, root growth stagnation, and overall plant development delay. To investigate the cellular changes underlying the hybrid lethality phenotype, researchers stained *Arabidopsis* hybrid lethality plants with trypan blue to observe changes in the number of dead cells[8]. In a case of hybrid lethality in peppers, specific DNA fragmentation patterns were observed using agarose gel electrophoresis, indicating that nuclear DNA was undergoing fragmentation. Moreover, the extent of DNA fragmentation increased as the severity of the hybrid lethality phenotype worsened[9]. Similar phenomena have also been observed in other plants such as

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wheat and tobacco[10,11]. In a study on hybrid lethality in cotton, transmission electron microscopy revealed that as the lethality phenotype intensified, the chloroplast membranes in the dying leaves gradually became blurred, and the vacuoles showed abnormalities[12].

Programmed cell death (PCD) is a key process in plant development and responses to both biotic and abiotic stresses[13]. In plants, PCD is essential for various processes, including development, self-incompatibility, and stress responses[14]. Several studies have shown that pathogen recognition triggers the activation of the mitogen-activated protein kinase (MAPK) cascade, the production of reactive oxygen species (ROS), and salicylic acid (SA), leading to hypersensitive responses that ultimately trigger PCD[15]. Most of the cellular characteristics of PCD in plants and animals are conserved, including cell shrinkage, chromatin condensation, and DNA laddering. These findings directly link the phenomenon of plant hybrid lethality to the biochemical characteristics of PCD, thereby deepening our understanding of the connection between hybrid lethality and PCD in plants.

3. Progress in the Genetic Patterns and Gene Cloning of Plant Hybrid Lethality

3.1. Genetic Patterns of Plant Hybrid Lethality

The genetic patterns of many hybrid lethality cases studied follow the Bateson–Dobzhansky–Muller (BDM) model, which explains how various random mutations accumulate during species evolution and gradually become homozygous within a population. While these mutations do not directly cause apparent phenotypic changes in the parents, hybridization with another homozygous population can result in F1 progeny exhibiting genetic incompatibility due to harmful genetic interactions[16], thus contributing to the barrier of gene flow between populations. This model provides a theoretical framework for understanding plant hybrid lethality, and most cases of plant hybrid lethality align with the genetic pattern described by the BDM model (see Figure 1). In some cases, hybrid lethality is controlled by a single gene (in a physical sense, not a functional single gene)[17]. For example, Jia et al. (2021) revealed a semi-dominant lethality phenomenon in wheat seedlings, regulated by a single gene, *DES* (death of the entire seedling)[18]. In this study, homozygous mutants exhibited seedling lethality, while heterozygotes showed growth retardation. In contrast, wild-type wheat plants grew and developed normally[19]. Some studies have also reported new perspectives on double loci/three-gene interactions, particularly within tandem gene clusters, where genes involved in regulating hybrid lethality may extend beyond two loci[17]. There are also instances involving two genes at a single locus[12]. These lethality genes generally exhibit epistasis, meaning their additive genetic effects come from non-allelic interactions.

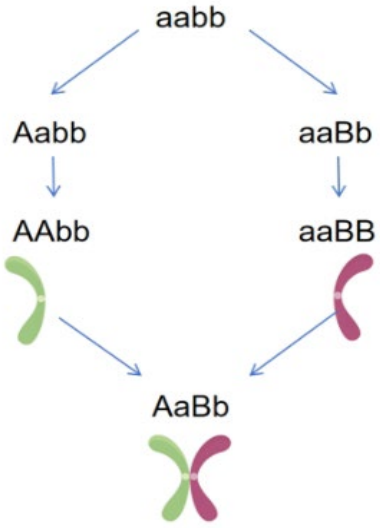

Figure 1: Bateson-Dobzhansky-Muller genetic model

3.2. Progress in Cloning Hybrid Lethality Genes in Plants

As core components of the plant immune defense system, R genes play a key role in resisting pathogen attacks. To date, the functions of more than 140 R genes have been cloned and validated in

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plants[20], with 80% of these being NLR genes[6]. In plant hybrid lethality, NLR alleles and other polymorphic immune genes located in tandem arrays are key factors contributing to intraspecific F1 progeny programmed death. Most NLRs are characterized by nucleotide-binding site and leucine-rich repeat (NBS-LRR, NBS) genes. NBS genes are classified into two types based on the presence of a TIR receptor at the protein amino acid N-terminus: TIR-NBS-LRR (TNL) and nTIR-NBS-LRR (nTNL). Since the protein N-terminus of most nTNL genes contains a coiled-coil (CC) domain, nTNL genes are also referred to as CC-NBS-LRR (CNL) genes[19]. A small number of nTNL genes contain an RPW8 domain at the N-terminus. The plant immune system consists of two main layers: PAMP-triggered immunity (PTI), mediated by pattern recognition receptors, and effector-triggered immunity (ETI), induced by effectors. NLR proteins are primarily involved in the ETI stage[21]. Numerous studies in various species have reported examples where interactions between disease resistance genes activate PCD, leading to the occurrence of plant hybrid lethality.

In existing studies, genes associated with hybrid lethality[12,22,23] and hybrid weakness[24,25] [26] have been cloned in various species, and the functions of some of these genes have been validated. Deng et al. (2019) discovered that the *Gh_D11G2949* gene, which encodes a CC-NBS-LRR protein, regulates hybrid lethality in cotton. Silencing this gene using VIGS restored normal development in cotton plants exhibiting hybrid lethality, confirming it as a regulatory gene for cotton hybrid lethality[12]. In wheat, a gene encoding a CC-NBS-LRR protein was identified as a candidate gene for the wheat hybrid lethality gene *Ne1*. Gene editing of *TraesCS2B01G182800* produced T0 positive transgenic lines, and all homozygous mutants in the T2 generation grew normally[18]. In rice, the hybrid lethality genes *Hwi1* and *Hwi2* have been identified. *Hwi1* consists of two LRR-RLK genes, while *Hwi2* encodes a protein kinase-type R gene. Genetic transformation of the *Hwi1* candidate gene into a background carrying *Hwi2* validated its function in the hybrid lethality phenotype, and *Hwi2* was also confirmed as a key gene [27] (see Table 1). In addition to R genes, some hybrid lethality genes are of other types, and they activate immune responses leading to plant death through interactions with R genes. For example, the hybrid lethality gene *Rin4* in lettuce encodes an RPM1-interacting protein[20]; the hybrid lethality gene *hl14* in monkeyflower is related to chloroplast synthesis[28]; the hybrid lethality gene *DM3* in *Arabidopsis* encodes an α/β hydrolase protein[25]; the hybrid lethality gene *Hwi2* in rice encodes a secreted, presumed Bacillus-like protease[27]. Further research indicates that NLR alleles and other polymorphic immune genes located in tandem repeat sequences are the primary cause of programmed cell death in intraspecific F_1 progeny.

Transient expression is one of the methods used to verify the function of lethality genes. Jeuken (2009) performed transient expression of the lettuce hybrid lethality candidate gene *Rin4* in bacterial suspension into 36 lettuce materials, and severe leaf necrosis was observed only in the *L. sativa* variety exhibiting hybrid lethality[20]. Additionally, *Rin4* was silenced to verify its role in resistance to *Lactobacillaceae* Bl:16. Similarly, Deng et al. (2019) used VIGS to silence the hybrid lethality candidate gene *Le4*, restoring the normal leaf phenotype in F1 hybrids of *Gossypium barbadense* and *Gossypium hirsutu*[12].Peng Xu et al. (2023) selected nine hybrid lethality candidate genes through map-based cloning and constructed the pTRV2 vector. By using the VIGS system to silence these genes in cotton hybrid F1, they found that only the pTRV2::GoanoORF3 line showed a normal phenotype[7].Chen et al. introduced the natural promoter of the *Hwi2* candidate gene *LOC_Os01g58290* through genetic transformation into materials containing the hybrid lethality gene *Hwi1*. The resulting F1 generation exhibited a hybrid weakness phenotype[27].

Cloning hybrid lethality genes is a key step in exploring and understanding the molecular mechanisms of hybrid incompatibility in plants. This process not only reveals the molecular basis of hybrid incompatibility but also provides a fundamental approach to further elucidate the phenomenon of hybrid incompatibility between species. Through this approach, we can gain a deeper understanding of the important role hybrid lethality genes play in reproductive isolation and speciation in plants. This also highlights the evolutionary significance of these genes in promoting species diversity and stability, providing an important scientific foundation for future applications in plant breeding and genetic diversity conservation research.

Table 1: The localization and cloning of planthybrid lethality genes.

Types	Gene1	Gene2	Progress in Gene Cloning Research	References
Arabidopsis thaliana	*DM2d*(NLR)	*DM1* (NLR)	Genomic, amiRNA Verification of *DM2d* and *DM1* interaction leading to hybrid lethality	Chae et al., 2014

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Table 1

Types	Gene1	Gene2	Progress in Gene Cloning Research	References
Arabidopsis thaliana	*DM2h* (RPP1)	*DM3* (prolylamino peptidase)	amiRNA/genomic, MIGS Verification of DM2d and DM1 Interaction Leading to Hybrid Lethality	Chae et al., 2014
	DM2 (RPP1)	*DM4* (RPP8)	Mapping/mapping	Chae et al., 2014
	DM2 (RPP1)	*DM5*	Mapping/mapping	Chae et al., 2014
	DM6 (RPP7)	*DM7* (RPW8)	amiRNA and Gene Editing	Chae et al., 2014
	DM6 (RPP7)	*DM8*(RPP4/5 NLR clusters)	amiRNA	Chae et al., 2014
	DM10 (NLR)	*DM11*	Transgenic *DM10* was introduced into Arabidopsis and crossed with lethality materials, resulting in a lethality phenotype in the F1 generation.	Barragan et al., 2021b
cotton	*Le3*(unkown)	*Le4* (CC-NBS-LRR)	VIGS and Transcriptome Analysis	Deng et al., 2019
	GoanoHBD1 (NLR)	-	Silencing the gene using VIGS restored the normal phenotype in the hybrid lethality plants.	Xu et al., 2023
wheat	*Ne1* (unkown)	*Ne2* (NLR)	Mutagenesis, VIGS, and Transcriptome Analysis	Hewitt et al., 2021b; LI et al., 2021
	mDES1 (NLR)	-	Edited Lines Restore Normal Phenotype	Jia et al., 2021
rice	*Hwi1* (NLR)	*Hwi2* (a secreted putative subtilisin-like Protease)	Positive complementation lines for hybrid lethality showed the lethality phenotype.	Chen et al., 2014
	Hwc1	*Hwc2* (NLR)	Hwc1 was mapped to a 60 Kb region on chromosome 1; Hwc2 was mapped to a 19 Kb region on chromosome 4.	Ichitani et al., 2007
	Hwj1	*Hwj2* (maybe a NLR gene)	-	Than et al., 2022
Nicotiana tabacum	*NtHL1* (NLR)	Maybe a homolog of *NtHL1*	Through gene editing, plants with the edited genotype restored the normal phenotype.	Ma et al., 2020

Table 1

Types	Gene1	Gene2	Progress in Gene Cloning Research	References
Brassica oleracea	*BoHL1*(NLR)	*BoHL2*(unkown)	Transient Expression and Transgenic Verification; The genes *BoHL1* and *BoHL2* were localized to chromosome 4.	Xiao et al., 2017
Mimulus	*pTAC14*(properchloroplastdevelopment)	-	Mutation Analysis, Transcriptome Sequencing	Zuellig et al., 2018

Note:'-'indicates that there are currently no relevant reports

4. Preliminary Exploration of the Molecular Mechanisms of Plant Hybrid Lethality

Transcriptome sequencing analysis is currently one of the most popular methods for studying the molecular mechanisms of plant hybrid lethality. Through transcriptome analysis, researchers can analyze the expression patterns of differentially expressed genes in hybrid lethality plants, revealing key regulatory networks and signaling pathways involved in hybrid lethality. This approach helps identify biological processes and metabolic pathways that are upregulated or downregulated in hybrid lethality and unveils the underlying pathological mechanisms of the lethal phenotype, further validating the

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connection between hybrid lethality and self-immune responses. In recent years, transcriptome sequencing has been applied not only to model plants[29,30] but also to non-model plants. Several studies on plant hybrid lethality have reported the use of transcriptome sequencing to analyze the differential gene expression patterns in hybrid lethality plants, thereby revealing the molecular mechanisms behind the lethality phenomenon at the genetic level. For example, transcriptome analysis of parental materials and F1 hybrids in wheat hybrid weakness revealed a significant upregulation of self-immune-related genes and protein degradation-related genes. In contrast, genes associated with carbohydrate metabolism, nitrogen metabolism, and lipid metabolism were significantly downregulated in the F1 generation, indicating that these metabolic disruptions contribute to the observed growth weakness in the F1 plants. In rice hybrid weakness, the expression levels of pathogenesis-related (PR) genes, which are closely linked to plant defense and immune mechanisms, were significantly elevated. Additionally, several biological processes related to programmed cell death (PCD) and immune responses were enhanced, including those associated with cell death and programmed cell death. Salicylic acid (SA), a key plant hormone, plays a role in regulating plant immune responses. Transcriptome analysis showed a significant upregulation of SA expression in rice hybrid weakness materials[10]. These findings collectively highlight the close link between rice hybrid weakness and immune defense responses. Similarly, in transcriptome sequencing studies of cotton hybrid lethality, biological processes related to immune responses were significantly enriched, with the expression of PR genes being markedly upregulated. Additionally, immune defense signaling pathways, including the mitogen-activated protein kinase (MAPK) signaling pathway, were highly enriched. The MAPK signaling pathway is one of the key signaling pathways throughout the plant life cycle, playing a crucial role in responding to biotic and abiotic stresses, regulating hormones, immune and defense responses, and supporting plant growth and development. The significant enrichment of these immune-related genes and pathways provides evidence for the activation of immune responses during cotton hybrid lethality[12].

In plant-related research, protein-protein interactions are an essential foundation and method for studying molecular mechanisms. Currently, common methods for studying protein-protein interactions include yeast two-hybrid (Y2H), bimolecular fluorescence complementation (BiFC), co-immunoprecipitation (CoIP), and more recently, firefly luciferase complementation (Luc), which has been gradually applied in recent years.

The molecular mechanisms underlying plant hybrid lethality are still not well understood. However, preliminary studies in *Arabidopsis* [25], cotton[12], and rice[27] suggest that the occurrence of hybrid lethality requires an intermediate product to activate NBS-LRR genes, triggering programmed cell death (PCD). In cotton, genes associated with ATP binding and DNA-dependent ATPase activity are upregulated during early developmental stages, promoting the conversion of *Le4* (an NBS-LRR gene) from an OFF to an ON state, generating immune signals that lead to the lethality phenotype[12]. The activation of plant NBS-LRRs is determined by the nucleotide binding to the NB-ARC domain, with the OFF and ON states corresponding to ADP and ATP binding, respectively[31]. Bernoux et al. (2016) reported a balanced switch model, where NBS-LRRs cycle between inactive/ADP binding (OFF) and active/ATP binding (ON) states. This model strongly favors the OFF state, and effector recognition shifts this balance towards the ON state to activate defense signaling[32].

5. Other Factors Contributing to Plant Hybrid Lethality

5.1. The Effect of Temperature on Plant Hybrid Lethality

Environmental temperature is a key factor influencing the intensity of plant immune responses and pathogen virulence. Currently, most plant hybrid lethality phenomena are suppressed by high temperatures[33-35]. For example, in tobacco hybrid lethality, F1 plants exhibit extensive cell apoptosis at lower temperatures (28°C), while no cell apoptosis is observed at higher temperatures (36°C). In rice, high temperatures can delay the occurrence of hybrid weakness, as high temperatures slow down the growth weakness caused by root development stagnation[36], thus delaying the onset of growth weakness. Generally, low temperatures induce immune responses, while high temperatures suppress them, which is related to the NLR protein family that is typically involved in immunity. In plant immune responses, high temperatures reduce the activity of effector proteins in the ETI response, leading to the suppression of NLR-mediated ETI signal transduction, thereby weakening disease resistance and hypersensitive response (HR)[37]. However, there are also cases where high temperatures promote immune responses. In rice, *Hwi1* and *Hwi2* play roles in temperature-triggered resistance, leading to the induction of hybrid weakness, and as temperature increases, the expression of PR genes in hybrid weak rice also increases[10].

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In cotton hybrid lethality studies, F1 plants do not exhibit hybrid lethality phenotypes below 26°C, with the phenotype only appearing above 26°C[12].

In summary, whether hybrid lethality is triggered by high or low temperatures is closely related to the type of hybrid lethality gene. In cases of hybrid lethality induced by low temperatures, most genes involved are NLR genes, while in cases of hybrid lethality induced by high temperatures, the lethality genes are usually members of the immune receptor family, encoding receptor kinases or receptor proteins. These findings further support the idea that plant hybrid lethality is part of the plant immune response, providing an important foundation for studying the molecular mechanisms of hybrid lethality.

5.2. The Effect of Plant Hormones on Hybrid Lethality

Compared to wild-type tomato seedlings, TRK1 RNAi seedlings showed reduced ethylene production, suggesting that TRK1 may mediate the plant's resistance to fungi through ethylene accumulation[38]. The plant immune system consists of several complex mechanisms. Pathogen-associated molecular patterns (PAMPs), microbe-associated molecular patterns (MAMPs), and damage-associated molecular patterns (DAMPs) are recognized by pattern recognition receptors, activating PAMP-triggered immunity (PTI). PTI induces various cellular signaling events, including the production of reactive oxygen species (ROS) and the biosynthesis of defense hormones such as salicylic acid (SA)[39]. Pathogens that evade this defense line produce effector proteins, which are specifically recognized by R proteins, triggering effector-triggered immunity (ETI). Downstream of PTI and ETI, various plant hormones play critical roles in regulating plant immunity. Among these, salicylic acid (SA) [40]and jasmonic acid (JA) are the most important defense hormones, while ethylene (ET)[41], abscisic acid (ABA), gibberellins (GA), auxins, cytokinins (CK), and brassinosteroids are also regulatory hormones involved in plant immunity[42]. The synergistic and antagonistic interactions between various plant hormone signaling pathways, known as hormone crosstalk, add an additional layer of defense to plant immunity. Among these, the SA-JA crosstalk is considered a central component of the plant immune signaling network[43]. As plant hybrid lethality has been recognized as a form of plant immune regulation, increasing attention has been focused on the impact of plant hormones(especially SA and JA)on hybrid lethality. Several plant hormones have been shown to respond to hybrid lethality phenomena. For example, in tobacco studies, it was found that the levels of auxin (AUX) and ethylene (ET) were significantly higher in hybrid lethality lines compared to normal lines. When auxin and ethylene synthesis inhibitors were applied, the hybrid lethality phenotypes were restored to normal[8]. In rice hybrid weakness studies, plants were treated with different concentrations of zeatin, auxin, ethylene, brassinosteroids, jasmonic acid (JA), and salicylic acid (SA). The results indicated that only the SA treatment restored normal phenotypes, suggesting that the salicylic acid signaling pathway directly regulates the process of hybrid weakness in plants[27].

5.3. Changes in reactive oxygen species in plant hybrid lethality

In plants, reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2), superoxide anion (O^{2-}), and hydroxyl radicals (OH^-), are stress-response molecules[44]. The production of ROS is an important signal for programmed cell death (PCD), and changes in H_2O_2 levels have been detected in several studies on plant hybrid lethality. A significant accumulation of reactive oxygen species can also result from both biotic and abiotic stresses, leading to cell death through PCD. In addition, ROS act as important secondary messengers in core plant signaling pathways[44]. PTI induces a variety of cellular signaling events, including ROS production and hormone signal transduction. ROS play a crucial role in plant defense responses, with pathogen invasion activating PTI and triggering a burst of reactive oxygen species. ROS are widely produced in plant cells under both biotic and abiotic stress conditions[41]. Extrafacial ROS production is induced and regulated by abscisic acid (ABA), and it participates in the ABA signaling pathway, which is involved in regulating the plant immune system[44]. The interaction between auxin and ROS signaling pathways under biotic or abiotic stress has been increasingly reported[45]. Auxin regulates the increase and decrease of ROS levels in plant cells[46,47]. When a plant's metabolic responses fail to neutralize the excess production of reactive oxygen species, it activates programmed cell death (PCD), attempting to eliminate damaged cells in order to prevent plant death[13]. In cotton hybrid lethality, the levels of H_2O_2 and MAPK at various stages in hybrid lethality F1 plants were higher than in normal F1 plants. This provides evidence that the interaction between *Le4* and *Le3*, triggering an immune response, is mediated by ROS crosstalk and the MAPK signaling pathway, which integrates defense and growth hormone signals. Constitutive activation of defense responses suppresses plant growth and ultimately induces plant death[7,12]. Excessive accumulation of ROS, such as superoxide radicals (O^{2-}) and hydrogen peroxide (H_2O_2), disrupts the balance of cellular redox status and can even

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cause oxidative damage to cellular genetic material. Higher levels of ROS are closely related to the occurrence of PCD, as demonstrated in *Arabidopsis*[48], wheat[49], and rice[50].

5.4. Effect of hybrid lethality on resistance to Phytophthora disease

It was found that in some hybrid combinations where postzygotic segregation occurred, the expression levels of defense genes of pathogen-related genes were up-regulated, and the hybrid F1s showed enhanced resistance to certain diseases. For example, defense-related genes and WRKY genes accumulated in large quantities in mildly greenish wheat and enhanced HR, which led to increased resistance to rice blast and powdery mildew in wheat[51]; even the loci of hybrid lethality in some species were the same as the disease resistance loci: crossing 29 *Ne2-containing* wheat mutants with *Ne1-containing* material restored the wild-type phenotype of progeny that simultaneously lost stripe rust resistance to stripe rust, while crossing plants carrying the *Lr3* transgene with plants carrying the *Ne1* gene resulted in a necrotic phenotype in the $_{F1}$, confirming that the wheat stripe rust resistance gene *, Lr3*, is at the same locus as the lethal gene, *Ne2*[11]. The above demonstrates a strong linkage between plant hybrid lethality and disease resistance loci, which may be due to the similarity in the types of genes (mostly NLR genes). And the coupling between hybrid lethality and disease resistance loci points to a certain effector that possesses multiple host specificities. Plant-pathogen interactions can often be explained by interactions between two or more loci, a pattern of interactions consistent with the two-locus genetic model of DM.

6. Conclusions

The occurrence of plant hybrid lethality is not only related to the lethality genes but also associated with multiple plant immune defense signaling pathways. Gene cloning studies of hybrid lethality have been reported in many species, and currently, more research is focused on uncovering the molecular mechanisms of hybrid lethality. Specifically, advances are being made through techniques such as transcriptomics and proteomics to further explore the interactions of hybrid lethality genes in the parents and the key regulatory factors that control the development of hybrid offspring.

Despite significant progress in research, the molecular mechanisms of plant hybrid lethality are still not fully understood. Published studies on plant hybrid lethality suggest that lethality genes do not directly interact to cause plant death. Instead, they interact indirectly through intermediate products that activate the plant's immune responses. However, the details of this process are still under investigation, and the molecular mechanisms of hybrid lethality vary across different species, indicating that hybrid lethality may be influenced by species-specific genetic factors. Thus, there is still wild space for further development in the study of plant hybrid lethality. Researching the molecular mechanisms of plant hybrid lethality not only contributes to the production of high-quality germplasm resources but also helps deepen our understanding of reproductive isolation and plant immune responses.

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