The Open Agriculture Journal

Content list available at: https://openagriculturejournal.com

REVIEW ARTICLE

Improvement of Wheat Genetic Resistance to Powdery Mildew Retrospects and Prospects

Tamara K. Ternovska[1,*], Tetiana S. Iefimenko[1] and Maksym Z. Antonyuk[1]

[1]*Department of Biology, National University of Kyiv-Mohyla Academy, Kyiv 04655, Ukraine*

Abstract:

Powdery mildew is one of the most noticeable and harmful wheat diseases in countries with temperate climates and sufficient rainfall. The most efficient, economical, and environmentally friendly means to control powdery mildew is the growing of genetically resistant wheat cultivars. The genetic resistance of wheat is quickly overcome due to the evolution of the avirulence genes of the pathogen. The problem of enriching the genetic pool of wheat with new effective resistance genes is relevant. The objective of the work is to show that the basis of the organization of the genetic protection of wheat from powdery mildew cannot be related to the simple expansion of the wheat genetic pool due to new resistance genes. The gene transfer should be preceded by the study of the molecular nature of the resistance gene products. The work presented information about resistance types in wheat against powdery mildew and the molecular nature of *Pm* genes' products. They are NLR-immune receptors, tandem kinase proteins, receptor-like kinases, transporters, plant-specific proteins, and mitogen activated kinases. NLR, in interaction with the pathogen effectors, confers highly specific resistance; all the rest provide resistance of a wide spectrum. Characteristics of pathogen gene products are provided, and a model of interaction between *Pm* and *AvrPm* gene products is described. A certain number of *Pm* genes are present in the current genetic pool of common wheat. The effectiveness of some of the most common genes has already been overcome by the pathogen. This necessitates the renewal of resistance genes in wheat. Prospects for the improvement of wheat genetic resistance to powdery mildew are provided. The prospective direction of research for providing effective long-term wheat genetic resistance to the biotrophic pathogen Blumeria is molecular genetic studies of wheat plants and pathogen races. A clear understanding of the molecular nature of the plant protein conferring resistance and its role in the development of the molecular pattern of plant protection against the pathogen is necessary to assess the prospects of any resistance gene for transfer to the genetic pool of wheat in relation to its ability to confer effective and long-lasting powdery mildew resistance.

Keywords: Powdery mildew wheat, Diseases, Wheat cultivars, Wheat chromosomes, Horizontal resistance, Vertical resistance.

Article History	Received: March 23, 2022	Revised: August 19, 2022	Accepted: September 2, 2022

1. INTRODUCTION

Powdery mildew is one of the most noticeable and harmful wheat diseases in countries with temperate climates and sufficient rainfall [1]. The disease begins to develop early in the vegetation season, affecting all plant's parts, and is amplified in favorable agronomic conditions [2]. Yield loss caused by powdery mildew could be evaluated as 5–40%, and in cases of early disease development [3 - 5], grain quality is decreased [6]. The disease in wheat is caused by the biotrophic fungal pathogen *Blumeria graminis* (DC) E.O. Speer f. sp. *tritici* Em. Marchal (*Bgt*) (syn. *Erysiphe graminis* DC f. sp. *tritici* Marchal) (*Bgt*), which is an obligate parasite [7].

The most efficient, economical, and environmentally friendly means to control powdery mildew is the growing of genetically resistant wheat cultivars [8]. Until recently, in common wheat (*Trtiticum aestivum* L.), durum wheat (*T. durum* Desf.) and their relatives from the subtribe Triticinae at least 90 genes (alleles) in about 50 loci have been identified as genes that prevent the development of powdery mildew spores on wheat leaves, thus conferring resistance of the plant to this pathogen [9, 10].

The resistance of wheat plants to powdery mildew can be horizontal, which is formed as a result of the deployment of a molecular pattern of the interaction of pathogen and host molecules as a result of the expression of several genes involved in ontogenetic processes [11 - 17]. The reaction is not specific to isolate the pathogen and sometimes the disease. Resistance can be vertical when developed in response to the interaction of the products of a particular *Pm* wheat resistance gene and the corresponding *AvrPm* pathogen gene. Such resistance is highly specific, and the vast majority of wheat genes identified today in its gene pool provide it. Products of genes *Pm* and *AvrPm* are components of the gene-for-gene system [18].

* Address correspondence to this author at the Address correspondence to this author at the Department of Biology, National University of Kyiv-Mohyla Academy, Kyiv, 04655, Ukraine;
E-mail: ternovska@ukma.edu.ua

In genotypes of modern commercial wheat cultivars, powdery mildew resistance is conferred by a limited variety of resistance genes, and almost all these genes confer vertical race-specific resistance. These include genes *Pm2*, *Pm3a,b,f, Pm4a*, *Pm30*, inherent to the common wheat genetic pool, and several introgressed genes: *Pm6*, *Pm8*, *Pm13*, *Pm21* [19, 20]. It has been reported that most of the indicated genes were overcome by the pathogen because new races of pathogen appeared with virulence genes, whose products were not recognized by the products of resistance genes [20 - 23]. This has been stated for widely grown cultivars in many regions of the world. That is the reason for the need for constant renewal of genes for resistance to powdery mildew in the cultivated wheat gene pool.

It is believed that the most prospective sources of new resistance genes are wheat wild relatives. They could provide genes for nonhost resistance, and these genes could be effective for a long time, while the pathogen evolves new avirulence genes on the background of positive selection of virulent mutants, which occurs when cultivars contain specific resistance gene (genes) [19, 24 - 29]. However, gene introgression is combined with the performance of a large amount of work and lasts a long time. In order to be sure that the long and hard work will not be in vain due to the rapid overcoming of the new wheat resistance gene by a virulent mutation of a pathogen gene from the gene-for-gene system, the optimal start to such work is the sequencing of the resistance gene to understand what resistance it provides. If vertical, the effectiveness of such a gene is not likely to be long-lasting [24]. If a gene provides broad-spectrum resistance, the effectiveness of such a gene in wheat genotypes can persist for decades [19, 24].

Here, we provide an overview of the current understanding of the possibilities of genetic improvement of wheat relative to resistance to powdery mildew. The objective of the work is to show that the basis of the organization of the genetic protection of wheat from powdery mildew cannot be related to the simple expansion of the wheat genetic pool due to new resistance genes. The gene transfer should be preceded by the study of the molecular nature of the resistance gene products.

1.1. Resistance Types in Wheat

Powdery mildew resistance, similarly to resistance to other pathogens, is firstly classified as passive and active. Passive resistance is conferred by the physical surface barriers of the plant. This type of resistance prevents the penetration of pathogens into plant cells and do not consider here. Active resistance depends on concrete genes and is realized in two main ways: the development of pathogen-associated molecular patterns (PAMP) triggers resistance in which pattern recognition receptors (PRR) are involved. PRRs localize in the plasma membrane and recognize conserved pathogen molecules. Although this resistance reaction is active, it is not specific and develops in response to any pathogen. Such a class of immunity is called “pattern-triggered immunity” (PTI) and may be suppressed by host-adapted pathogens by delivering effector molecules inside host cells [30, 31]. A second line of defense is an active specific reaction to the pathogen. It develops through the action of intracellular multidomain receptors carrying a stereotypical nucleotide binding site (NBS) and leucine-rich repeat (LRR). Their name is NLR (nucleotide-binding leucine-rich repeat) [32, 33]. They are known as immune receptors and are encoded by *R*-genes. Contact between pathogen’s elicitors and *R* gene products directly or with the participation of certain intermediate molecules gives rise to the development of ETI – effector triggered immunity [34].

1.2. *Pm* Genes Products

Genes that provide active resistance to powdery mildew are called *Pm* genes. Their products confer both specific and not specific resistance. Specific resistance is conferred by NLR-receptors, not specific resistance is conferred by tandem kinase proteins, receptor-like kinases, transporters and some other proteins. The functions of proteins encoded by resistance genes have been clarified after sequencing these genes. Currently, nucleotide sequences of more than 300 plant resistance genes are established [35, 36]. For wheat *Pm* genes, sequencing began in 2003, and the number of sequenced genes increases every year. Currently, 13 *Pm* genes are sequenced (Table **1**).

Table 1. List of *Pm* genes in the wheat gene pool.

Gene/Reference	Chromosome	Source of Gene	Product of Gene/Reference
Pm1 a [37, 38]	7AL	[1)]	NLR [39]
Pm1 b [40]		*T.monococcum*	No information
Pm1c [40] =*Pm18*	7AL	[1)]	No information
Pm1d [40]	7AL	*T.spelta*	No information
Pm1e=Pm22 [41, 42]	7AL	[1)]	No information
Pm2a,c [43]	5DS	[1)]	NLR [44]
Pm2b [45]	C-5DS	*Agropyron cristatum*	No information
Pm3 [46]	1AS	[1)]	NLR [47]
Pm4a [48, 49]	2AL	*T.monococcum*	Functional kinase [36]
Pm4b [48, 49]	2AL	*T.carthlicum*	Functional kinase [36]
Pm4c=Pm23 [50]	2AL	[1)]	No information
Pm4d [51]	2AL	*T.monococcum*	No information
Pm5 a[2)]*,b,d,e*[2)] [37]	7BL	*T.dicoccum*	NLR [52]

(Table 1) contd.....

Gene/Reference	Chromosome	Source of Gene	Product of Gene/Reference
Pm5c [37]	7BL	*T.sphaerococcum*	No information
Pm6 [53]	2BL.2GL	*T.timopheevii*	Several LRRs, a trans-membrane domain, and a Ser/Thr protein kinase domain [54]
Pm7 [55]	4BL	*S.cereale*	No information
Pm8 [56, 57]	1BL.1RS	*S.cereale*	Coiled-coil (CC), nucleotide-binding site ARC1 and ARC2 (NB-ARC) and leucine-rich-repeat (LRR) domain protein [58]
Pm9[2)] [59]	7AL	[1)]	No information
Pm10 [60]	1D	[1)]	No information
Pm11 [61]	6BS	[1)]	No information
Pm12 [62]	6BS6SS.6SL	*Ae. speltoides*	No information
Pm13 [55]	T3BL.3BS-3S1 #1S	*Ae. longissima*	No information
Pm14 [63]	6B	[1)]	No information
Pm15 [63]	7DS	[1)]	No information
Pm16 [64]	4A	*T.dicoccoides*	No information
Pm17=Pm8 [65]	T1AL.1R#2S	*S.cereale*	See *Pm8*
Pm18 [66]	7A	[1)]	See *Pm1c*
Pm19 [67]	7D	*Ae.tauschii*	No information
Pm20 [68]	T6BS.6R#2L	*S.cereale*	No information
Pm21 [69]=*Pm31* [70]	T6AL.6VS	*H.villosa*	serine and threonine protein kinase V, Stpk-V) [71]
Pm22= Pm1e			See *Pm1e*
Pm23= Pm4c			See *Pm4c*
Pm24a [72]	1DS	[1)]	(Tandem Kinase Protein, TKP) [13]
Pm24b [73]	1DS	[1)]	No information
Pm25 [74]	1A	*Triticum monococcum* subsp. *aegilopoides*	No information
Pm26[2)] [75]	2BS	*T.dicoccoides*	No information
Pm27 [76]	6B-6G	*T.timopheevii*	No information
Pm28 [77]	1B	[1)]	No information
Pm29 [78]	7DL	*Ae.ovata*	No information
Pm30 [79]	5BS	[1)]	No information
Pm31 [80]=*Pm21* [70]	6VS/6AL	*H.villosa*	No information
Pm32 [81]	1BL.1SS	*Ae.speltoides*	No information
Pm33 [82]	2BL	*T.carthlicum*	No information
Pm34 [82]	5DL	*Ae.tauschii*	No information
Pm35 [83]	5DL	*Ae.tauschii*	No information
Pm36 [84]	5BL	*T.dicoccoides*	No information
Pm37 [85]	7AL	*T.timopheevii*	No information
Pm38 [86]	7DS	[1)]	ABC transporter [16]
Pm39 [87]	1BL	*Ae.umbellulata*	No information
Pm40 [88]	7BS	*Th. intermedium*	CC-NBS-NBS-LRR [89]
Pm41 [90]	3BL	*T. dicoccoides*	Protein with domens CC-NBS-LRR (CNL) [91]
Pm42[2)] [92]	2BS	*T. dicoccoides*	No information
Pm43 [93]	2DL	*Th. intermedium*	No information
Pm44 [94]	3A	[1)]	No information
Pm45 [95]	6DS	[1)]	
Pm46 [96]	5DS	[1)]	Hexose transporter [17]
Pm47 [97]	7BS	[1)]	No information
Pm48 [98]	5DS		No information
Pm49 [99]	2BS	*T.dicoccum*	No information
Pm50 [100]	2AL	*T.dicoccum*	No information
Pm51 [101]	2BL	*Th. ponticum*	No information
Pm52 [102]	2BL	[1)]	No information
Pm53 [94]	5BL	*Ae. speltoides*	No information
Pm54 [103]	6BL	[1)]	No information

(Table 1) contd.....

Gene/Reference	Chromosome	Source of Gene	Product of Gene/Reference
Pm55 [104]	5VS.5DL	*D.villosum*	No information
Pm56 [105]	T6RS.6AL	*S.cereale*	No information
Pm57 [106]	T2BS. 2BL-2SS #1L	*Ae.searsii*	No information
Pm58 [107]	2DS	*Ae.tauschii*	No information
Pm59 [108]	7AL	[1)]	No information
Pm60 [109]	7A	*T.urartu*	Proteins with domens NBS and LRR [110]
Pm61[2)] [111]	4AL	[1)]	No information
Pm62 [112]	2BS.2VL#5	*D.villosum*	No information
Pm63 [108]	2BL	[1)]	No information
Pm64 [113]	2BL	*T.dicoiccoides*	No information
Pm65 [114]	2AL	[1)]	No information
Pm66 [25]	T4S[l]S-4BL	*Ae.longissima*	No information
Pm67 [19]	T1DL·1VS#5	*D.villosum*	No information
Pm68 [115]	2BS	*T.turtgidum*	No information

Note: [1)] Gene is attributable to *T. aestivum*[2)] Recessive gene [3)]Table **1** contains only genes with permanent names mapped to specific chromosomes using traditional methods of linkage mapping and physical mapping using bins. Genes mapped using the modern method of genome-wide association studies (GWAS), in our opinion, should be tested if they are alleles of known mapped genes, and only after this testing, these genes could get the permanent name of a new gene or a new allele, or the allele of the previously mapped *Pm* gene.

1.3. NLR-receptors

Most of the sequenced resistance genes code NLR, which provide vertical resistance to the pathogen [35, 116]. They are classified into two main types depending on the structure of their N-terminal domain (NBS): TIR (Toll and IL-1 receptors) and non-TIR. The majority of non-TIR NLRs have CC (coiled-coil) domain on their N-terminus. It was demonstrated that dicot plants have both TIR and non-TIR NLR, while monocot plants, including wheat, have only non-TIR NLR [116, 117]. When NLR specifically recognizes pathogen's effectors through the LRR domain, structural changes occur in the NB-ARC domain which is a functional ATPase. The binding of nucleotides to the NBS regulates the activity of the R protein. Activated R protein conducts a signal for the subsequent resistance development. Usually, NLR-induced resistance is associated with hypersensitive response – local cell death in the site of pathogen penetration in order to prevent the spread of biotrophic pathogens such as *Blumeria graminis* f.sp. *tritici* [109, 116]. In wheat, NLR-receptors are encoded by the genes *Pm1, Pm2, Pm3, Pm5, Pm8, Pm40,* and *Pm60.*

1.4. TKP (Tandem Kinase Orotein)

In wheat, the *Pm24* gene encodes a tandem kinase protein (TKP) with a predicted kinase pseudokinase domain, which is named WHEAT TANDEM KINASE 3 (WTK3) [13]. *Pm24/WTK* gene confers wheat resistance to 92 Chinese *Bgt*, therefore gene ensures broad-spectrum resistance [51]. A rare 6-nucleotide deletion of Lysine-Glycine codons in kinase domain 1 (Kin I) was identified to be important for the resistant phenotype. This mutation was identified only in wheat from Shaanxi province in China. It is predicted that the absence of these two amino acids could provide the formation of a more compact loop in the kinase structure, which could be important for subsequent protein-protein interactions and signal transduction for resistance development [13].

1.5. RLK (Receptor-like Kinases)

These kinases initiate broad-spectrum resistance (PTI) [14, 15]. Genes of receptor-like kinases *TaRLK1* and *TaRLK2* were identified in the genome of *T. aestivum/T. timopheevi* introgressive line [54]. The genes encode a protein with a signal peptide, several LRRs, a transmembrane domain, and a serine-threonine kinase domain. The lines with *TaRLK1* and *TaRLK2* overexpression demonstrated an increase in the levels of endogenous hydrogen peroxide (H_2O_2) under pathogen invasion sites [54]. This could indicate the possibility of a hypersensitivity reaction, very effective in resistance development, not only due to the immune receptors NLR, but also with the participation of genes with a wide spectrum of action. This makes RLK genes prospective for the development of plants with genetic resistance to powdery mildew. Genes of both kinases are localized in the long arm of wheat chromosome 2B [54], where previously the *Pm6* gene was mapped, but in another region [53, 118, 119]. Perhaps it will be difficult to clearly distinguish the *Pm6* gene from the genes *TaRLK1* and *TaRLK2* through their introgression origination (*T. timopheevi*). Three genes may be members of one gene cluster [119].

1.6. Transporters

Long-term nonspecific resistance to a broad spectrum of pathogens is conferred by transporter proteins. Resistance genes encoding transporters include: *Lr34/Yr18/Pm38/Ltn1* (7DS), which encodes ABC (ATP-binding cassette)-transporter [16], and *Lr67/Sr55/Yr46/Pm46/Ltn* (5DS), which encodes hexose transporter [17]. These genes are valuable as they confer effective, potentially long-term resistance to several important wheat pathogens: leaf rust (*Puccinia triticina*), stripe rust (*P. striiformis*), powdery mildew (*Blumeria graminis* f. sp. *tritici*), as controls a trait of leaf tip necrosis (Ltn1) [16]. The gene has been effective for more than 50 years. ABC transporter could provide resistance development through the export of metabolites affecting fungal pathogens' growth [16]. Developed durum wheat (*T. turgidum*) transgenic lines for the common wheat *Lr34/Yr18/Pm38/Ltn1* gene were resistant to leaf rust, stripe rust and powdery mildew at the seedling stage, and the resistance correlated with transgene expression [120].

Lr67/Sr55/Yr46/Pm46/Ltn3 gene encodes a hexose transporter [17] and confers resistance to the three mentioned before pathogens, and to stem rust. Hexose transporter transports hexoses through the plasma membrane [17, 121]. The gene is mapped in 5DS in wheat.

Fundamentally different groups of genes for active resistance are *Mildew Resistance Locus (MLO)* and *Enhanced Disease Resistance 1 (EDR1)*. Firstly, the recessive alleles of these genes are effective for conferring resistance; secondly, these genes provide broad-spectrum resistance (to different pathogens and races of pathogens), and this resistance has long-term efficiency within the temporal persistence of this genotype. This type of resistance is mediated by loss-of-function mutations in negative regulators of resistance, particularly to powdery mildew.

1.7. Plant-specific Proteins

Resistance of this type was described in 30-40 years of the XX century, and in 1972 loss-of-function mutation was characterized in barley [122]. *MLO* genes encode plant-specific proteins with several transmembrane domains and a specific C-terminal calmodulin-binding domain [11, 123]. Loss-of-function mutation in *MLO* was characterized as universal, conferring permanent resistance to all known barley powdery mildew races. Recently, such mutations were identified in almost all plant species of agricultural importance [124, 125]. They attract attention as potential objects for gene engineering using modern techniques of *in situ* genome editing [126 - 128]. Wheat also has *MLO* genes in the chromosomes of the first homoeological group [129], therefore, recessive mutations of these genes could be identified (or constructed) in wheat, and they could confer resistance to a broad spectrum of powdery mildew races [127, 128, 130].

1.8. Mitogen Activated Kinases

Gene *EDR1* encodes MAPKKK – mitogen activated kinases with nuclear localization. EDR1 functions as negative regulators of MAPK cascade in plants of wild type and plays a role in the transduction of signals from the elicitor to plant cell molecules. The function of these genes was characterized in resistance to the pathogen in Arabidopsis mutants [131]. This pathway is considered very conservative in plants, and the gene could be used for the development of new ways of conferring resistance to pathogens, particularly to powdery mildew in plants. In the wheat genome, this gene, *TaEDR1,* was identified in 2005 through cloning using PCR with primers developed from the sequence of the Arabidopsis gene [12]. It was used as a target gene for CRISPR/CAS in situ editing with a positive result: Taedr1 recessive gene wheat plants showed resistance to powdery mildew without significant pleiotropic effects on plant development. The gene is considered very promising for developing stable lines through targeted mutagenesis [126].

Consequently, all genes whose products are involved in ensuring the resistance of wheat to powdery mildew form two groups: genes of the immune receptors NLR, highly specific to individual races of the pathogen, and genes whose products are involved in the organization of basic processes of interaction of cells and molecules. They form the resistance of a wide spectrum and are now considered the most promising for ensuring the genetic protection of wheat from powdery mildew.

1.9. Blumeria Effectors

Blumeria fungi, from the order Erysiphales, division Ascomycota, are a monophyletic group originating from Leotiomycetes over 120 million years ago. They are obligate biotrophic plant pathogens [132]. Similarly to other biotrophic pathogens, they are able to develop only in the living tissues of the host plants. For the realization of its life cycle, the powdery mildew pathogen must overcome host resistance and switch cellular metabolism to meet its own needs [133, 134]. This is achieved through the action of effector proteins produced by the pathogen and acting as virulence factors [135]. These effectors are considered the main determinants of the interaction between plant and powdery mildew fungus and are classified as candidate secreted effector proteins (CSEPs) [136]. Effectors are secreted via the fungal endoplasmic reticulum. Some of them stay in the plant's apoplast, while other enter the plant cells and are directed to organelles, particularly the nucleus [137]. Blumeria effector candidate (BEC) proteins were identified in high concentrations in isolated haustoria [138]. According to literature [139], the composition of CSEPs and BECs is almost the same. CSEPs are currently classified into two groups: the so-called RNase-like effectors [140], and proteins with structural homologies to the MD2-related lipid-recognition (ML) domain, ML-like CSEPs [141]. RNase-like effectors bind to NLR immune receptors [142 - 144], and currently, more than one hundred genes encoding them are identified in *Bgt* genome [140, 144 - 146]. ML-like CSEPs bind to specific lipids [147].

Genome sequencing of wheat and barley powdery mildew pathogens identified a reduction of gene content compared to other ascomycetes and an expansion of gene complements encoding putative effectors [136, 148]. Currently, at least 35 CSEP genes are cloned. They encode proteins of 63 to 314 amino acid residues, all of which have a secretion signal [142, 144, 149 - 151]. Except for this signal, effector proteins have few similarities, and only one common motif YxC has been identified [152]. This confirms the assumption that effector proteins have different partners for interaction among plant proteins and have different functions [148, 153]. Considerable polymorphism of gene sequences is observed even on the population level, which indicates independent evolution of different alleles of effector genes through various molecular mechanisms [142, 146, 150, 151, 154].

Effector proteins' action is considered to overcome PTI; the first level of plant's nonspecific defense from pathogens. The following defense level is realized when specific *R* genes are present, which encode immune receptors and confer race-specific resistance. Fungal genes encoding effectors activating a specific response in plants are named *Avr* genes.

In *Bgt* genome, currently several *Avr* genes are cloned: *AvrPm3a2/f2*, *AvrPm3b2/c2*, and *AvrPm3d3,* which are recognized by *Pm3a/Pm3f*, *Pm3b/Pm3c* and *Pm3d* gene products, respectively [142, 150]; *AvrPm2* recognized by *Pm2* product [144]; *AvrPm1a* recognized by *Pm1a* product [151];

AvrPm17 recognized by *Pm17* gene product [146]. *Blumeria* AVR effectors are small proteins of 102-130 amino acid residues with N-terminal signal peptide, a very conservative motif after signal sequence, and conservative cysteine residues towards the C-terminus. Similarly to other CSEPs, they are highly variable [140, 145, 150, 154].

Consequently, pathogen effectors play a determinant role in initiating processes that culminate in wheat injury by powdery mildew or the development of a resistance reaction. The initiation of the process lies in the interaction of effectors with the products of plant resistance genes.

1.10. Interaction of *Pm* Gene Products with Pathogen Effectors (*Avr* Gene Products)

For their development in living plant tissues, biotrophic pathogens need to suppress the protective reactions of the plant. For this purpose, pathogens use their effectors, which overcome PTI. Subsequently, pathogen effectors are recognized by NLR plant proteins, and ETI resistance reaction is activated. Plant resistance acquired as a result of NLR protein and pathogen effector interaction is usually associated with local cell death (hypersensitive response) [155].

Pathogen effectors (*Avr* gene products), which are recognized by plant R-proteins, are often polymorphic for different fungal isolates. For the recognition of different pathogen effectors, plants have various resistance genes or different alleles at one locus. The set of *Blumeria graminis* isolates includes many sub-lineages, which are named *formae speciales (f.sp.)*. Belonging to a certain sub-lineage depends on the specificity of certain cereal species which could be affected, and this type of resistance is named host resistance. In the case when wheat is affected, this is *B.g. tritici formae speciales* (*Bgt f.sp.*), for rye – *B.g. secalis formae speciales* (*Bgs f.sp.*), for barley – *B.g. hordei formae speciales*. If effectors *Bgs f.sp*, for example, may be recognized by wheat immune receptors, this kind of resistance is named nonhost [156]. It is assumed that in the presence of host resistance to *Bgs f.sp* in wheat, effectors of *Bgs f.sp* are not subject to selection on the background of wheat immune receptors and these *formae speciales* remain nonadapted [150].

Several studies have been conducted for the *Pm3* gene to understand the mechanisms of interaction between plant's *Pm* gene and pathogen's *AvrPm* gene products. The study has been conducted by mapping populations from crosses of different Blumeria genotypes (different *Bgt f.sp.*), modern methods of analyzing DNA sequences, including rapid genotyping methods and development of genetic constructions with the studied elements controlling virulence/avirulence trait using transient expression systems in *Nicotiana benthamiana* after agrobacterial transformation [142]. Wheat *Pm3* gene is recognized as contributing to both host and nonhost resistance, because the products of its alleles are recognized by not only *Bgt f.sp,* but also *Bgs f.sp*. According to a study [149], these effectors are ancient conservative virulence factors, and they have been present in genotypes of *Bgt f.sp.* even before the introgression of the *Pm17* gene into the wheat genome. *Pm8* (in 1BS.1RL translocation) and *Pm17* (in 1AL.1RS translocation) resistance genes were introgressed from rye into the wheat genome; these genes are homologous to wheat *Pm3* gene, and are likely of orthologous origin [146]. For this reason, race-specific resistance conferred by these genes has been rapidly overcome by the virulent effector AvrPm17, encoded by two paralogous genes mapped in dynamic effector clusters specific to *Bgs* and *Bgt* genomes [146].

For the *Pm3* locus, currently, the greatest number of alleles (17) were identified (*Pm3a-g; Pm3k-Pm3t*) [157, 158]. Protein products of these different alleles have high sequence similarity (>97%), however, they recognize effectors of different *Bgt* isolates [158]. Studies of the interaction of wheat *Pm* genes' products (particularly different *Pm3* alleles) with *Bgt* pathogen effectors are an important model for understanding the mechanisms underlying resistance specificity [145, 150]. *Pm3a, Pm3b, Pm3c, Pm3d, Pm3e*, and *Pm3f* alleles of the polymorphic Pm3 gene were studied in wheat genotypes for their response to corresponding *AvrPm* alleles in fungal genotypes [143, 150]. For the determination of genetic control of avirulence/virulence trait, the results of F_1 segregation were studied. F_1 generations were obtained from crosses of pathogen genotypes with alternative trait manifestation: one genotype was avirulent for plants with any of the specified *Pm3* alleles, while the other genotype was virulent. It was determined that depending on plant resistance allele pathogen avirulence could be conferred by one (alleles $AvrPm3^{a}$, $AvrPm3^{c}$, $AvrPm3^{e}$), two (haplotype $AvrPm3^{f1}$-$AvrPm3^{f2}$), or three (haplotypes $AvrPm3^{b1}$-$AvrPm3^{b2}$-$AvrPm3^{b3}$, $AvrPm3^{d1}$-$AvrPm3^{d2}$-$AvrPm3^{d3}$) loci. Each of these proteins is specifically recognized by the corresponding Pm3 alleles. On the part of the pathogen, another gene is involved in controlling the virulence reaction, $SvrPm3^{a1/f1}$ [143]. The product of this gene acts as a suppressor of recognition of avirulence effectors $AvrPm3a^{2/f2}$, $AvrPm3^{b2/c2}$ and $AvrPm3^{d3}$ by-products of plant *Pm3a-f* allele [142].

Pathogen avoidance from recognition by immune receptors occurs in case of its change that it is not recognized by the plant receptor. Mechanisms of changes of the effector gene include missense mutations with a change of at least one amino acid [150, 154], truncation or deletion of the *Avr* gene [145, 146], and, as it was demonstrated for the interaction *AvrPm3-Pm3*, involvement of one more gene in the control of recognition reaction. That is gene *SvrPm3*, the product of which suppresses recognition of the respective effector [149]. The other type of polymorphism, which underlies the gain of virulence, is effector gene duplication, which enables independent diversification of the two virulence genes [158].

So, to date, it has been experimentally proven that the development of ETI is the result of the interaction of products of highly specific plant *Pm* genes and *AvrPm/SvrPm* genes of the pathogen. There may be more than one gene on both sides. A long, multi-stage experiment involving alleles of the plant gene *Pm3* and the corresponding effectors of the pathogen showed that to understand the genetic basis of a highly specific reaction between immune receptors and pathogen effectors for each individual case, the task is very difficult and, as it seems to us, will not acquire practical significance.

1.11. *Pm* Genes Present in the Current Genetic Pool of Common Wheat

The first *Pm* gene in wheat was identified in the Thaw cultivar by Australian researcher Waterhouse in 1910 [159], and currently, the identification of new resistance genes and alleles continues. Resistance genes, first of all, could be classified into two groups: genes from the native genetic pool of common wheat and genes introgressed from cultivated and wild relatives (Table **1**).

As can be seen from Table **1**, some parts of *Pm* genes identified in modern cultivars and local varieties of common wheat have an introgression origin. This is the result of long-lasting work using initially only cytogenetic methods of work with plant material obtained by wide hybridization of wheat with numerous wild relatives. Later studies in this area became optimized by the use of molecular genetic markers and methods of work with DNA sequences. Significant interest in resistance gene introgression to the common wheat genome could be explained by two reasons. Firstly, among researchers of the last century, the idea of the impoverishment of the common wheat genetic pool by resistance genes has arisen, and this impoverishment involved resistance genes to biotic stresses [160]. This was explained, on the one hand, by the hypothesis of monophyletic wheat origin; however, this hypothesis is not supported by all researchers [161 - 164]. Possible monophyletic wheat origin by itself could be the reason to believe that the wheat genetic pool did not include many resistance genes, and its resistance could have quite a limited variety of molecular genetic mechanisms. On the other hand, as it is always indicated, the genetic pool of modern cultivars is limited by the variability inherent to commercial varieties and local landraces or lines, which could be used for intraspecific hybridization [165, 166]. Quite a long time ago, the assumption was made [167, 168] that for the wheat genetic pool widening, its numerous wild relatives could be used, including those having genomes different from wheat. This idea turned out to be constructive, and for several decades the common wheat genome, and, to a lesser extent, the durum wheat genome, were artificially supplemented by genes (alleles), which had not been naturally inherent to these species. Wheat genetic pool became enriched in resistance genes to many devastating diseases, including powdery mildew (Table **1**). The second reason making introgression popular was very widespread at the beginning of such work confidence that genetic resistance introgressed from wild relatives could be more long-lasting compared to resistance controlled by wheat genes [24]. Practical experience over several decades demonstrated that this was not always the case.

Resistance genes introgressed from wild relatives have limitations in their use in wheat cultivars' resistance improvement, because they are often part of alien chromatin of some amount, which could also contain genes deteriorating cultivars' agricultural traits (linkage drag) [169]. For the separation of resistance genes from other genes with negative effects, many backcrosses are usually needed; moreover, recombination between alien chromosomes of wild relatives and wheat homoeologous chromosomes is limited by *Ph* (pairing homoeologous) gene [106, 114]. To obtain recombination between alien chromosome fragments containing resistance genes and wheat chromosomes, *ph* gene mutants could be used [106]. In the case when sexual hybridization and recombination of genetic material in hybrid genomes are, for some reason, impossible, genetic engineering and transformation of plant cells could be used. Clearly, for the development of genetic constructs with particular resistance genes, these genes must be cloned and available for use as nucleotide sequences [170, 171].

Thus, the main characteristic of modern wheat varieties relative to powdery mildew resistance genes is the limited number of effective genes in the genetic pool of these varieties. This creates favorable conditions for overcoming plant resistance through the positive selection of pathogen isolates with such mutations in the *AvrPm* genes that their products are no longer recognized by the plant's immune receptors. The most common conclusion in the relevant literature is the belief of researchers in need to constantly replenish the genetic pool of wheat with new genes of resistance to powdery mildew.

1.12. Prospects for Improvement of Wheat Genetic Resistance to Powdery Mildew

The review of the present literature on wheat genetic resistance to powdery mildew demonstrates that the transfer of resistance genes from wild relatives to wheat remains an urgent problem. Genetic engineering methods began to be used to develop constructs containing target resistance genes. However, resistance genes must be previously cloned and available for constructs' development [170, 171]. Furthermore, currently, introgressive hybridization has been associated with the induction of plant genome variability [172, 173], and due to this, rearrangements of common wheat genetic material could arise in its genome with the following formation of a new allele of the resident resistance gene [89], and changes in transcription regulation could occur [106]. Many NBS-LRR encoding resistance genes are known to be localized in plant genomes in clusters [174, 175]. These gene clusters and repeated sequences (encoding LRR-repeats) provide more opportunities for recombination and gene conversion, which could provide the formation of new resistance alleles and new races of the pathogen [176], and alien chromatin could be a trigger of these processes. Furthermore, it has been demonstrated that nonfunctional resistance genes (pseudogenes) are widespread in plant populations, and they could promote the formation of new functional genes [177]. Alternative splicing of mRNAs of many NBS-LRR genes also adds complexity and variety to plant defense reactions [175, 176]. All information mentioned above does not add confidence that the resistance of descendants from distant crosses is conferred exactly by the alien resistance gene. Nevertheless, according to modern research, it could be predicted that wild relatives would be further used for wheat gene pool enrichment in resistance genes to powdery mildew.

Compared to previous decades, when attention was focused on resistance genes' introgression, currently, the search of new resistance genes in wheat genotypes has been activated. Wheat landraces and local varieties which have limited distribution, possibly would not create a genetic

background for high selective pressure for the new virulent fungus mutant's evolution [97, 108, 111, 114, 178, 179]. In addition, their use is more convenient at least because the transfer of resistance genes is not associated with linkage drag, an integral part of distant hybridization [114, 180, 181].

For the search of new resistance genes and their characterization, modern methods of direct genome analysis are increasingly involved. To map the resistance genes within the wheat genome, a variety of molecular genetic markers designed for different types of cereals [106, 111, 130, 182], and fine mapping of *Pm* genes [183 - 186]. The most modern map-based cloning method could be used, which is essentially the method of position cloning: a resistance gene is identified only through its localization in a particular chromosome or its part through the association of the desired phenotype (resistance) and a number of molecular markers, previously mapped on the chromosomes of the genome. That is, the candidate region is identified by the traditional linkage analysis with the following sequencing of the region of interest and identification of the DNA fragment with different sequences for two alternative phenotypes [13, 25, 45, 52, 73, 96, 182, 185, 187, 188]. Next fine mapping enables the identification of all polymorphisms in the region of interest and the determination of haplotypes (combination of particular genetic elements) associated with resistance [182, 184, 186, 189]. Both the data on the sequencing of the resistance gene and the determination of the haplotype associated with resistance provide information about the molecular nature of the product of the resistance gene and its participation in the initiation of the plant's protective reaction against the pathogen. The use of the RNA-Seq method could be especially effective, because this method enables the comparison of transcriptomes obtained in the conditions of pathogen attack or without pathogen. This enables the identification of the gene of interest and the determination of its function without the mapping of this gene in the genome [89, 109, 190]. Modification of this method BSR-Seq (bulked segregant RNASequencing) allows to work with segregating populations and to determine the localization of resistance genes in the genome using molecular markers with known localization and polymorphic for different resistance phenotypes [52].

The results of sequencing of resistance genes and their products have demonstrated that there was a fundamental difference in the structures of protein products conferring race-specific and broad-spectrum resistance. It was demonstrated that race-specific resistance controlled by *R* genes is based on the molecular level of mutual recognition of plant immune receptors and pathogen's effectors. Effector is avirulent as long as this recognition occurs. When the effector gene mutates (this process is random and permanent) and the effector becomes no longer recognizable by the plant immune receptor, a resistance reaction does not develop. The main and determining factor for developing a strategy for the genetic protection of plants is that the plant gene acts as a passive element. Certainly, a plant gene can also mutate, however, its mutation is also random, the probability that the new mutation will provide complementation (recognition) of the mutated effector is insignificant, and expecting this mutation is not a promising method to deal with the problem. Other types of proteins participating in conferring resistance are kinase proteins. Usually they confer broad-spectrum resistance, like receptor-like kinases *TaRLK1* and *TaRLK* [54], whose products initiate a non-race-specific hypersensitive response in plants. This means that the effectiveness of the effector mutation is lost. *Pm21* gene product is a serine/threonine kinase with nonspecific action [71]. This gene was transferred to the wheat genome from Haynaldia and was effective against powdery mildew for about 20 years despite its wide distribution in wheat cultivars. The *Pm24/WTK* gene also encodes kinase; this gene was identified in wheat local landraces of provinces of China and conferred resistance to many *Bgt* races. The effectiveness of this gene depends on the presence of a rare 6-bp deletion in the kinase domain [13]. Such molecular structure of the resistant allele makes it prospective to artificially modified susceptible alleles of this gene through the introduction of deletion, possibly using the *CRISPR/Cas* method of genome editing [126, 130]. The example given confirms the effectiveness of studding rare wheat genotypes as prospective sources of useful genes. These genes, unlike resistance genes of wild relatives, are also prospective because they could be transferred to commercial wheat cultivars easily, with any recombination level, and without linkage drag. They emphasize the significance of the determination of the molecular nature of a resistance gene product for making predictions about its prospects for introgression to the wheat genetic pool because this work requires much time and effort. In our opinion, simply increasing the number of introgressed to wheat genetic pool resistance genes without determination of the molecular nature of their products could appear to be a direction with reduced prospects.

CONCLUSION

The prospective direction of research for providing effective long-term and controlled wheat genetic resistance to the biotrophic pathogen Blumeria is molecular genetic studies of wheat plants and pathogen races. For this, it can be applied both traditional methods of crossing and mapping populations' development for plants and fungi, and modern methods of genome analysis for direct (not through phenotype) genotyping of members of segregating populations of plant or fungus. Clear understanding of the molecular nature (structure and function) of the plant protein conferring resistance, and its role in the development of the molecular picture of plant protection against the pathogen, will enable to evaluate any new gene (introgressed to the wheat genetic pool or identified in wheat local varieties, or edited *in situ* using corresponding technologies) on how prospective could this gene be for introduction into commercial wheat cultivars for conferring reliable and long-lasting powdery mildew resistance.

LIST OF ABBREVIATIONS

PAMP	=	Pathogen-Associated Molecular Patterns
PRR	=	Pattern Recognition Receptors
PTI	=	Pattern-Triggered Immunity
NBS	=	Nucleotide Binding Site
LRR	=	Leucine-Rich Repeat

TKP	=	Tandem Kinase Protein
GWAS	=	Genome-Wide Association Studies
WTK3	=	Wheat Tandem Kinase 3
Ltn1	=	Leaf Tip Necrosis
MLO	=	Mildew Resistance Locus
EDR1	=	Enhanced Disease Resistance 1
CSEPs	=	Candidate Secreted Effector Proteins
BEC	=	Blumeria Effector Candidate
ETI	=	Effector Triggered Immunity

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Conner RL, Kuzyk AD, Su H. Impact of powdery mildew on the yield of soft white spring wheat cultivars. Can J Plant Sci 2003; 83(4): 725-8.
[http://dx.doi.org/10.4141/P03-043]

[2] Cowger C, Miranda L, Griffey C, Hall M, Murphy JP, *et al.* Wheat powdery mildew.Disease Resistance in Wheat. Oxfordshire, UK: CABI 2012; pp. 84-119.
[http://dx.doi.org/10.1079/9781845938185.0084]

[3] Mehta YR. Wheat Diseases and Their Management. Switzerland: Springer 2014.
[http://dx.doi.org/10.1007/978-3-319-06465-9]

[4] Singh RP, Singh PK, Rutkoski J, *et al.* Disease impact on wheat yield potential and prospects of genetic control. Annu Rev Phytopathol 2016; 54(1): 303-22.
[http://dx.doi.org/10.1146/annurev-phyto-080615-095835] [PMID: 27296137]

[5] Gao H, Niu J, Li S. Impacts of wheat powdery mildew on grain yield & quality and its prevention and control methods. J Agric For 2018; 6(5): 141-7.
[http://dx.doi.org/10.11648/j.ajaf.20180605.14]

[6] Samobor V, Vukobratovic M, Jost M. Effect of powdery mildew attack on quality parameters and experimental bread baking of wheat. Acta Agric Slov 2006; 87(2): 381-91.

[7] Bennett FGA. Resistance to powdery mildew in wheat: A review of its use in agriculture and breeding programmes. Plant Pathol 1984; 33(3): 279-300.
[http://dx.doi.org/10.1111/j.1365-3059.1984.tb01324.x]

[8] Pietrusińska A, Tratwal A. Characteristics of powdery mildew and its importance for wheat grown in Poland. Plant Prot Sci 2020; 56(3): 141-53.
[http://dx.doi.org/10.17221/99/2019-PPS]

[9] McIntosh RA, Yamazaki Y, Dubcovsky J, Rogers J, Morris C. Catalogue of gene symbols for wheat In: KOMUGI-integrated wheat science database. 2013. Available from: www.shigen.nig.ac.jp/wheat/komugi/genes/download.jsp

[10] McIntosh RA, Dubcovsky J, Rogers WJ, Xia XC, Raupp WJ. Catalogue of gene symbols for wheat, 2020 supplement. Annu Wheat Newsl 2020; 66: 19-28.

[11] Büschges R, Hollricher K, Panstruga R, *et al.* The barley *Mlo* gene: A novel control element of plant pathogen resistance. Cell 1997; 88(5): 695-705.
[http://dx.doi.org/10.1016/S0092-8674(00)81912-1] [PMID: 9054509]

[12] Niu JS, Zhang LN, Hong DF, Wang YH. Cloning, characterization and expression of wheat EDR1 (enhanced disease resistance) gene. J Plant Physiol Mol Biol 2005; 31(5): 477-84.
[PMID: 16222089]

[13] Lu P, Guo L, Wang Z, *et al.* A rare gain of function mutation in a wheat tandem kinase confers resistance to powdery mildew. Nat Commun 2020; 11(1): 680.
[http://dx.doi.org/10.1038/s41467-020-14294-0] [PMID: 32015344]

[14] Hervé C, Serres J, Dabos P, *et al.* Characterization of the arabidopsis lecRK-a genes: Members of a superfamily encoding putative receptors with an extracellular domain homologous to legume lectins. Plant Mol Biol 1999; 39(4): 671-82.
[http://dx.doi.org/10.1023/A:1006136701595] [PMID: 10350082]

[15] Kaku H, Nishizawa Y, Ishii MN, *et al.* Plant cells recognize chitin fragments for defense signaling through a plasma membrane receptor. Proc Natl Acad Sci USA 2006; 103(29): 11086-91.
[http://dx.doi.org/10.1073/pnas.0508882103] [PMID: 16829581]

[16] Krattinger SG, Lagudah ES, Spielmeyer W, *et al.* A putative ABC transporter confers durable resistance to multiple fungal pathogens in wheat. Science 2009; 323(5919): 1360-3.
[http://dx.doi.org/10.1126/science.1166453] [PMID: 19229000]

[17] Moore JW, Herrera FS, Lan C, *et al.* A recently evolved hexose transporter variant confers resistance to multiple pathogens in wheat. Nat Genet 2015; 47(12): 1494-8.
[http://dx.doi.org/10.1038/ng.3439] [PMID: 26551671]

[18] Van Der Plank JE. Horizontal and vertical resistance.Disease resistance in plants. Orlando, FL: Academic 1984.
[http://dx.doi.org/10.1016/B978-0-12-711442-2.X5001-6]

[19] Zhang R, Xiong C, Mu H, *et al.* Pm67, a new powdery mildew resistance gene transferred from Dasypyrum villosum chromosome 1V to common wheat (*Triticum aestivum* L.). Crop J 2021; 9(4): 882-8.
[http://dx.doi.org/10.1016/j.cj.2020.09.012]

[20] Cowger C, Mehra L, Arellano C, Meyers E, Murphy JP. Virulence differences in *Blumeria graminis* f. sp. *tritici* from the Central and Eastern United States. Phytopathology 2018; 108(3): 402-11.
[http://dx.doi.org/10.1094/PHYTO-06-17-0211-R] [PMID: 29082810]

[21] Zhou YL, Duan XY, Chen G, Sheng BQ, Zhang Y. Analyses of resistance genes of 40 wheat cultivars or lines to wheat powdery mildew. Acta Phytopathol Sin 2002; 32: 301-5.

[22] Lijun Y, Xiang L, Zeng F, Wang H, Shi W, *et al.* Virulence gene structure analysis of *Blumeria graminis* f. sp. *tritici* in Hubei. Plant Protection 2009; 3(5): 76-9.

[23] Shi Y, Wang B, Li Q, Wu X, Wang F, *et al.* Analysis of the virulent genes of *Erysiphe graminis* f. sp. *tritici* and the resistance genes of wheat commercial cultivars in Shaanxi Province. Mailei Zuowu Xuebao 2009; 29(4): 706-11.

[24] Tang S, Hu Y, Zhong S, Luo P. The potential role of powdery mildew-resistance gene *Pm40* in Chinese wheat-breeding programs in the post-*Pm21* era. Engineering 2018; 4(4): 500-6.
[http://dx.doi.org/10.1016/j.eng.2018.06.004]

[25] Li H, Dong Z, Ma C, *et al.* A spontaneous wheat-Aegilops longissima translocation carrying Pm66 confers resistance to powdery mildew. Theor Appl Genet 2020; 133(4): 1149-59.
[http://dx.doi.org/10.1007/s00122-020-03538-8] [PMID: 31932954]

[26] Wang Y, Quan W, Peng N, *et al.* Molecular cytogenetic identification of a wheat–*Aegilops geniculata* roth 7mg disomic addition line with powdery mildew resistance. Mol Breed 2016; 36(4): 40.
[http://dx.doi.org/10.1007/s11032-016-0463-1]

[27] Liu W, Koo DH, Xia Q, *et al.* Homoeologous recombination-based transfer and molecular cytogenetic mapping of powdery mildew-resistant gene *Pm57* from *Aegilops searsii* into wheat. Theor Appl Genet 2017; 130(4): 841-8.
[http://dx.doi.org/10.1007/s00122-017-2855-y] [PMID: 28116459]

[28] Zhu C, Wang Y, Chen C, *et al.* Molecular cytogenetic identification of a wheat – *Thinopyrum ponticum* substitution line with stripe rust resistance. Genome 2017; 60(10): 860-7.
[http://dx.doi.org/10.1139/gen-2017-0099] [PMID: 28759728]

[29] Wang Y, Long D, Wang Y, *et al.* Characterization and evaluation of resistance to powdery mildew of wheat–*Aegilops Geniculata* roth $7M^g$ (7A) alien disomic substitution line w16998. Int J Mol Sci 2020; 21(5): 1861.
[http://dx.doi.org/10.3390/ijms21051861] [PMID: 32182810]

[30] Maekawa T, Kufer TA, Schulze LP. NLR functions in plant and animal immune systems: so far and yet so close. Nat Immunol 2011; 12(9): 817-26.
[http://dx.doi.org/10.1038/ni.2083] [PMID: 21852785]

[31] Hückelhoven R, Seidl A. PAMP-triggered immune responses in barley

and susceptibility to powdery mildew. Plant Signal Behav 2016; 11(7): e1197465.
[http://dx.doi.org/10.1080/15592324.2016.1197465] [PMID: 27348336]

[32] McDowell JM, Woffenden BJ. Plant disease resistance genes: Recent insights and potential applications. Trends Biotechnol 2003; 21(4): 178-83.
[http://dx.doi.org/10.1016/S0167-7799(03)00053-2] [PMID: 12679066]

[33] Martin GB, Bogdanove AJ, Sessa G. Understanding the functions of plant disease resistance proteins. Annu Rev Plant Biol 2003; 54(1): 23-61.
[http://dx.doi.org/10.1146/annurev.arplant.54.031902.135035] [PMID: 14502984]

[34] Wu L, Chen H, Curtis C, Fu ZQ. Go in for the kill: How plants deploy effector-triggered immunity to combat pathogens. Virulence 2014; 5(7): 710-21.
[http://dx.doi.org/10.4161/viru.29755] [PMID: 25513772]

[35] Xing L, Hu P, Cui C, Wang H, Di Z, *et al. NLR1-V*, a CC-NBS-LRR encoding gene, is a potential candidate gene of the wheat powdery mildew resistance gene *Pm21*. bioRxiv 2017.
[http://dx.doi.org/10.1101/114058]

[36] Sánchez MJ, Widrig V, Herren G, *et al.* Wheat *Pm4* resistance to powdery mildew is controlled by alternative splice variants encoding chimeric proteins. Nat Plants 2021; 7(3): 327-41.
[http://dx.doi.org/10.1038/s41477-021-00869-2] [PMID: 33707738]

[37] Hsam SLK, Huang XQ, Zeller FJ. Chromosomal location of genes for resistance to powdery mildew in common wheat (Triticum aestivum L. em Thell.) 6. Alleles at the Pm5 locus. Theor Appl Genet 2001; 102(1): 127-33.
[http://dx.doi.org/10.1007/s001220051627]

[38] Sears ER, Briggle LW. Mapping the gene *Pm1* for resistance to *Erysiphe graminis* f. sp. *tritici* on chromosome 7A of wheat. Crop Sci 1969; 9(1): 96-7.
[http://dx.doi.org/10.2135/cropsci1969.0011183X000900010033x]

[39] Liu N, Bai G, Lin M, Xu X, Zheng W. Genome-wide association analysis of powdery mildew resistance in U.S. winter wheat. Sci Rep 2017; 7(1): 11743.
[http://dx.doi.org/10.1038/s41598-017-11230-z] [PMID: 28924158]

[40] Hsam SLK, Huang XQ, Ernst F, Hartl L, Zeller FJ. Chromosomal location of genes for resistance to powdery mildew in common wheat (Triticum aestivum L. em Thell.). 5. Alleles at the Pm1 locus. Theor Appl Genet 1998; 96(8): 1129-34.
[http://dx.doi.org/10.1007/s001220050848]

[41] Singrün C, Hsam SLK, Hartl L, Zeller FJ, Mohler V. Powdery mildew resistance gene Pm22 in cultivar Virest is a member of the complex Pm1 locus in common wheat (Triticum aestivum L. em Thell.). Theor Appl Genet 2003; 106(8): 1420-4.
[http://dx.doi.org/10.1007/s00122-002-1187-7] [PMID: 12750784]

[42] Peusha H, Hsam SLK, Zeller FJ. Chromosomal location of powdery mildew resistance genes in common wheat (*Triticum aestivum* L. em. Thell.) 3. Gene *Pm22* in cultivar Virest. Euphytica 1996; 91(2): 149-52.
[http://dx.doi.org/10.1007/BF00021064]

[43] McIntosh RA, Baker EP. Cytogenetical studies in wheat iv. Chromosome location and linkage studies involving thePM2 locus for powdery mildew resistance. Euphytica 1970; 19(1): 71-7.
[http://dx.doi.org/10.1007/BF01904668]

[44] Manser B, Koller T, Praz CR, *et al.* Identification of specificity‐defining amino acids of the wheat immune receptor *Pm2* and powdery mildew effector AvrPm2. Plant J 2021; 106(4): 993-1007.
[http://dx.doi.org/10.1111/tpj.15214] [PMID: 33629439]

[45] Ma P, Xu H, Xu Y, *et al.* Molecular mapping of a new powdery mildew resistance gene *Pm2b* in Chinese breeding line KM2939. Theor Appl Genet 2015; 128(4): 613-22.
[http://dx.doi.org/10.1007/s00122-015-2457-5] [PMID: 25673140]

[46] Yahiaoui N, Srichumpa P, Dudler R, Keller B. Genome analysis at different ploidy levels allows cloning of the powdery mildew resistance gene *Pm3b* from hexaploid wheat. Plant J 2004; 37(4): 528-38.
[http://dx.doi.org/10.1046/j.1365-313X.2003.01977.x] [PMID: 14756761]

[47] Srichumpa P, Brunner S, Keller B, Yahiaoui N. Allelic series of four powdery mildew resistance genes at the *Pm3* locus in hexaploid bread wheat. Plant Physiol 2005; 139(2): 885-95.
[http://dx.doi.org/10.1104/pp.105.062406] [PMID: 16183849]

[48] The TT, McIntosh RA, GA Bennett F. Cytogenetical studies in wheat. IX. Monosomic analyses, telocentric mapping and linkage relationships of genes Sr21, Pm4 and Mle. Aust J Biol Sci 1979; 32(1): 115-26.
[http://dx.doi.org/10.1071/BI9790115]

[49] Ma ZQ, Sorrells ME, Tanksley SD. RFLP markers linked to powdery mildew resistance genes *Pm1*, *Pm2*, *Pm3*, and *Pm4* in wheat. Genome 1994; 37(5): 871-5.
[http://dx.doi.org/10.1139/g94-123] [PMID: 18470129]

[50] Hao Y, Liu A, Wang Y, *et al. Pm23*: A new allele of *Pm4* located on chromosome 2AL in wheat. Theor Appl Genet 2008; 117(8): 1205-12.
[http://dx.doi.org/10.1007/s00122-008-0827-y] [PMID: 18818899]

[51] Schmolke M, Mohler V, Hartl L, Zeller FJ, Hsam SLK. A novel powdery mildew resistance allele at the *Pm4* locus from einkorn wheat (*Triticum monococcum*). Mol Breed 2010; 29(2): 449-56.
[http://dx.doi.org/10.1007/s11032-011-9561-2]

[52] Xie J, Guo G, Wang Y, *et al.* A rare single nucleotide variant in *Pm5e* confers powdery mildew resistance in common wheat. New Phytol 2020; 228(3): 1011-26.
[http://dx.doi.org/10.1111/nph.16762] [PMID: 32569398]

[53] Jørgensen JH, Jensen CJ. Gene *Pm6* for resistance to powdery mildew in wheat. Euphytica 1973; 22: 423.
[http://dx.doi.org/10.1007/BF00022656]

[54] Chen T, Xiao J, Xu J, *et al.* Two members of TaRLK family confer powdery mildew resistance in common wheat. BMC Plant Biol 2016; 16(1): 27.
[http://dx.doi.org/10.1186/s12870-016-0713-8] [PMID: 26810982]

[55] Friebe B, Jiang J, Raupp WJ, McIntosh RA, Gill BS. Characterization of wheat-alien translocations conferring resistance to diseases and pests: Current status. Euphytica 1996; 91(1): 59-87.
[http://dx.doi.org/10.1007/BF00035277]

[56] Lukaszewski AJ. Manipulation of the 1RS.1BL translocation in wheat by induced homoeologous recombination. Crop Sci 2000; 40(1): 216-25.
[http://dx.doi.org/10.2135/cropsci2000.401216x]

[57] Zeller FJ, Fuchs E. Cytologie und Kronkheitsresistanz einer 1A/1R- und meherer 1B/1R-Weizen-Roggen-Translocationssorten/Zeitschrift fur Pflanzenzuchtung.AGRIS 1983; 90: pp. 284-96. Available from: https://agris.fao.org/agris-search/search.do?recordID=US201302165791

[58] Hurni S, Brunner S, Buchmann G, *et al.* Rye *Pm8* and wheat *Pm3* are orthologous genes and show evolutionary conservation of resistance function against powdery mildew. Plant J 2013; 76(6): 957-69.
[http://dx.doi.org/10.1111/tpj.12345] [PMID: 24124925]

[59] McIntosh RA, Dubcovsky J, Rogers WJ, Morris C, Xia XC. Catalogue of Gene Symbols for Wheat 2017. Available from: https://shigen.nig.ac.jp/wheat/komugi/genes/macgene/supplement2017.pdf

[60] Tosa Y, Tsujimoto H, Ogura H. A gene involved in the resistance of wheat to wheatgrass powdery mildew fungus. Genome 1987; 29(6): 850-2.
[http://dx.doi.org/10.1139/g87-145]

[61] Tosa Y, Tokunaga H, Ogura H. Identification of a gene for resistance to wheatgrass powdery mildew fungus in the common wheat cultivar Chinese Spring. Genome 1988; 30(4): 612-4.
[http://dx.doi.org/10.1139/g88-103]

[62] Jia J, Devos KM, Chao S, Miller TE, Reader SM, Gale MD. RFLP-based maps of the homoeologous group-6 chromosomes of wheat and their application in the tagging of Pm12, a powdery mildew resistance gene transferred from Aegilops speltoides to wheat. Theor Appl Genet 1996; 92(5): 559-65.
[http://dx.doi.org/10.1007/BF00224558]

[63] Tosa Y, Sakai K. The genetics of resistance of hexaploid wheat to the wheatgrass powdery mildew fungus. Genome 1990; 33(2): 225-30.
[http://dx.doi.org/10.1139/g90-035]

[64] Reader SA, Miller T. The introduction into bread wheat of a major gene for resistance to powdery mildew from wild emmer wheat. Euphytica. 1991; 53: pp. 57-60.

[65] Hsam SLK, Zeller FJ. Evidence of allelism between genes Pm8 and Pm17 and chromosomal location of powdery mildew and leaf rust resistance genes in the common wheat cultivar'Amigo'. Plant Breed 1997; 116(2): 119-22.
[http://dx.doi.org/10.1111/j.1439-0523.1997.tb02164.x]

[66] Hartl L, Weiss H, Stephan U, Zeller FJ, Jahoor A. Molecular identification of powdery mildew resistance genes in common wheat (*Triticum aestivum* L.). Theor Appl Genet 1995; 90(5): 601-6.
[http://dx.doi.org/10.1007/BF00222121] [PMID: 24174015]

[67] Lutz J, Hsam SLK, Limpert E, Zeller FJ. Chromosomal location of

powdery mildew resistance genes in Triticum aestivum L. (common wheat). 2. Genes *Pm2* and *Pm19* from *Aegilops squarrosa* L. Heredity 1995; 74(2): 152-6.
[http://dx.doi.org/10.1038/hdy.1995.22]

[68] Friebe B, Heun M, Tuleen N, Zeller FJ, Gill BS. Cytogenetically monitored transfer of powdery mildew resistance from rye into wheat. Crop Sci 1994; 34(3): 621-5.
[http://dx.doi.org/10.2135/cropsci1994.0011183X003400030003x]

[69] Qi LL, Chen PD, Liu DJ, Zhou B, Zhang SZ, *et al.* The gene *Pm21* - A new source of resistance to wheat powdery mildew. Acta Agriculture Sinica 1995; 21: 257-61.

[70] Xie W, Ben DR, Zeng B, *et al.* Suppressed recombination rate in 6VS/6AL translocation region carrying the *Pm21* locus introgressed from *Haynaldia villosa* into hexaploid wheat. Mol Breed 2012; 29(2): 399-412.
[http://dx.doi.org/10.1007/s11032-011-9557-y]

[71] Cao A, Xing L, Wang X, Yang X, Wang W, *et al.* Serine/threonine kinase gene Stpk-V, a key member of powdery mildew resistance gene Pm21, confers powdery mildew resistance in wheat. PNAS 2011; 108(19): 7727-32.
[http://dx.doi.org/10.1073/pnas.1016981108]

[72] Huang XQ, Hsam SLK, Zeller FJ. Chromosomal location of genes for resistance to powdery mildew in common wheat (*Triticum aestivum* L. em. Thell.) 4. Gene *Pm 24* in Chinese landrace Chiyacao. Theor Appl Genet 1997; 95(5-6): 950-3.
[http://dx.doi.org/10.1007/s001220050646]

[73] Xue F, Wang C, Li C, *et al.* Molecular mapping of a powdery mildew resistance gene in common wheat landrace Baihulu and its allelism with *Pm24.* Theor Appl Genet 2012; 125(7): 1425-32.
[http://dx.doi.org/10.1007/s00122-012-1923-6] [PMID: 22772588]

[74] Shi AN, Leath S, Murphy JP. A major gene for powdery mildew resistance transferred to common wheat from wild einkorn wheat. Phytopathology 1998; 88(2): 144-7.
[http://dx.doi.org/10.1094/PHYTO.1998.88.2.144] [PMID: 18944983]

[75] Rong JK, Millet E, Manisterski J, Feldman M. A new powdery mildew resistance gene: Introgression from wild emmer into common wheat and RFLP-based mapping. Euphytica 2000; 115(2): 121-6.
[http://dx.doi.org/10.1023/A:1003950431049]

[76] Järve K, Peusha HO, Tsymbalova J, Tamm S, Devos KM, Enno TM. Chromosomal location of a *Triticum timopheevii* - derived powdery mildew resistance gene transferred to common wheat. Genome 2000; 43(2): 377-81.
[http://dx.doi.org/10.1139/g99-141] [PMID: 10791827]

[77] Peusha H, Enno T, Priilinn O. Chromosomal location of powdery mildew resistance genes and cytogenetic analysis of meiosis in common wheat cultivar Meri. Hereditas 2000; 132(1): 29-34.
[http://dx.doi.org/10.1111/j.1601-5223.2000.00029.x] [PMID: 10857256]

[78] Zeller FJ, Kong L, Hartl L, Mohler V, Hsam SLK. Chromosomal location of genes for resistance to powdery mildew in common wheat (*Triticum aestivum* L. em Thell.) 7. Gene *Pm29* in line Pova. Euphytica 2002; 123(2): 187-94.
[http://dx.doi.org/10.1023/A:1014944619304]

[79] Liu Z, Sun Q, Ni Z, Nevo E, Yang T. Molecular characterization of a novel powdery mildew resistance gene *Pm30* in wheat originating from wild emmer. Euphytica 2002; 123(1): 21-9.
[http://dx.doi.org/10.1023/A:1014471113511]

[80] Xie C, Sun Q, Ni Z, Yang T, Nevo E, Fahima T. Chromosomal location of a Triticum dicoccoides-derived powdery mildew resistance gene in common wheat by using microsatellite markers. Theor Appl Genet 2003; 106(2): 341-5.
[http://dx.doi.org/10.1007/s00122-002-1022-1] [PMID: 12582861]

[81] Hsam SLK, Lapochkina IF, Zeller FJ. Chromosomal location of genes for powdery mildew resistance in common wheat (*Triticum aestivum* L. em Thell.). 8. Gene *Pm32* in a wheat-*Aegilops speltoides* translocation line. Euphytica 2003; 133(3): 367-70.
[http://dx.doi.org/10.1023/A:1025738513638]

[82] Miranda LM, Murphy JP, Marshall D, Leath S. Pm34: A new powdery mildew resistance gene transferred from Aegilops tauschii Coss. to common wheat (*Triticum aestivum* L.). Theor Appl Genet 2006; 113(8): 1497-504.
[http://dx.doi.org/10.1007/s00122-006-0397-9] [PMID: 16953419]

[83] Miranda LM, Murphy JP, Marshall D, Cowger C, Leath S. Chromosomal location of Pm35, a novel Aegilops tauschii derived powdery mildew resistance gene introgressed into common wheat (*Triticum aestivum* L.). Theor Appl Genet 2007; 114(8): 1451-6.
[http://dx.doi.org/10.1007/s00122-007-0530-4] [PMID: 17356863]

[84] Blanco A, Gadaleta A, Cenci A, Carluccio AV, Abdelbacki AMM, Simeone R. Molecular mapping of the novel powdery mildew resistance gene *Pm36* introgressed from *Triticum turgidum* var. *dicoccoides* in durum wheat. Theor Appl Genet 2008; 117(1): 135-42.
[http://dx.doi.org/10.1007/s00122-008-0760-0] [PMID: 18392800]

[85] Perugini LD, Murphy JP, Marshall D, Brown GG. Pm37, a new broadly effective powdery mildew resistance gene from Triticum timopheevii. Theor Appl Genet 2008; 116(3): 417-25.
[http://dx.doi.org/10.1007/s00122-007-0679-x] [PMID: 18092148]

[86] Spielmeyer W, McIntosh RA, Kolmer J, Lagudah ES. Powdery mildew reaction and *Lr34/Yr18* genes for adult plant resistance to leaf rust and stripe rust cosegregate at a locus on the short arm of chromosome 7D of wheat. Theor Appl Genet 2005; 111(4): 731-5.
[http://dx.doi.org/10.1007/s00122-005-2058-9] [PMID: 15965649]

[87] Zhu Z, Zhou R, Kong X, Dong Y, Jia J. Microsatellite marker identification of a *Triticum aestivum* - *Aegilops umbellulata* substitution line with powdery mildew resistance. Euphytica 2006; 150(1-2): 149-53.
[http://dx.doi.org/10.1007/s10681-006-9103-x]

[88] Luo PG, Luo HY, Chang ZJ, Zhang HY, Zhang M, Ren ZL. Characterization and chromosomal location of *Pm40* in common wheat: A new gene for resistance to powdery mildew derived from *Elytrigia intermedium.* Theor Appl Genet 2009; 118(6): 1059-64.
[http://dx.doi.org/10.1007/s00122-009-0962-0] [PMID: 19194691]

[89] Yang H, Zhong S, Chen C, *et al.* Identification and cloning of a CC-NBS-NBS-LRR gene as a candidate of *Pm40* by integrated analysis of both the available transcriptional data and published linkage mapping. Int J Mol Sci 2021; 22(19): 10239.
[http://dx.doi.org/10.3390/ijms221910239] [PMID: 34638580]

[90] Li G, Fang T, Zhang H, *et al.* Molecular identification of a new powdery mildew resistance gene Pm41 on chromosome 3BL derived from wild emmer (Triticum turgidum var. dicoccoides). Theor Appl Genet 2009; 119(3): 531-9.
[http://dx.doi.org/10.1007/s00122-009-1061-y] [PMID: 19471905]

[91] Li M, Dong L, Li B, *et al.* A CNL protein in wild emmer wheat confers powdery mildew resistance. New Phytol 2020; 228(3): 1027-37.
[http://dx.doi.org/10.1111/nph.16761] [PMID: 32583535]

[92] Hua W, Liu Z, Zhu J, *et al.* Identification and genetic mapping of pm42, a new recessive wheat powdery mildew resistance gene derived from wild emmer (Triticum turgidum var. dicoccoides). Theor Appl Genet 2009; 119(2): 223-30.
[http://dx.doi.org/10.1007/s00122-009-1031-4] [PMID: 19407985]

[93] He R, Chang Z, Yang Z, *et al.* Inheritance and mapping of powdery mildew resistance gene *Pm43* introgressed from *Thinopyrum intermedium* into wheat. Theor Appl Genet 2009; 118(6): 1173-80.
[http://dx.doi.org/10.1007/s00122-009-0971-z] [PMID: 19214392]

[94] Petersen S, Lyerly JH, Worthington ML, *et al.* Mapping of powdery mildew resistance gene *Pm53* introgressed from *Aegilops speltoides* into soft red winter wheat. Theor Appl Genet 2015; 128(2): 303-12.
[http://dx.doi.org/10.1007/s00122-014-2430-8] [PMID: 25425170]

[95] Ma H, Kong Z, Fu B, *et al.* Identification and mapping of a new powdery mildew resistance gene on chromosome 6D of common wheat. Theor Appl Genet 2011; 123(7): 1099-106.
[http://dx.doi.org/10.1007/s00122-011-1651-3] [PMID: 21755339]

[96] Gao H, Zhu F, Jiang Y, *et al.* Genetic analysis and molecular mapping of a new powdery mildew resistant gene *Pm46* in common wheat. Theor Appl Genet 2012; 125(5): 967-73.
[http://dx.doi.org/10.1007/s00122-012-1886-7] [PMID: 22660629]

[97] Xiao M, Song F, Jiao J, Wang X, Xu H, Li H. Identification of the gene Pm47 on chromosome 7BS conferring resistance to powdery mildew in the Chinese wheat landrace Hongyanglazi. Theor Appl Genet 2013; 126(5): 1397-403.
[http://dx.doi.org/10.1007/s00122-013-2060-6] [PMID: 23429903]

[98] Fu BS, Liu Y, Zhang QF, *et al.* Development of markers closely linked with wheat powdery mildew resistance gene *Pm48.* Zuo Wu Xue Bao 2017; 43(2): 307-12.
[http://dx.doi.org/10.3724/SP.J.1006.2017.00307]

[99] Piarulli L, Gadaleta A, Mangini G, *et al.* Molecular identification of a new powdery mildew resistance gene on chromosome 2BS from Triticum turgidum ssp. dicoccum. Plant Sci 2012; 196: 101-6.
[http://dx.doi.org/10.1016/j.plantsci.2012.07.015] [PMID: 23017904]

[100] Mohler V, Bauer C, Schweizer G, Kempf H, Hartl L. Pm50: A new powdery mildew resistance gene in common wheat derived from cultivated emmer. J Appl Genet 2013; 54(3): 259-63.
[http://dx.doi.org/10.1007/s13353-013-0158-9] [PMID: 23794194]

[101] Zhan H, Li G, Zhang X, *et al.* Chromosomal location and comparative

genomics analysis of powdery mildew resistance gene *Pm51* in a putative wheat-*Thinopyrum ponticum* introgression line. PLoS One 2014; 9(11): e113455.
[http://dx.doi.org/10.1371/journal.pone.0113455] [PMID: 25415194]

[102] Zhao Z, Sun H, Song W, *et al.* Genetic analysis and detection of the gene MlLX99 on chromosome 2BL conferring resistance to powdery mildew in the wheat cultivar Liangxing 99. Theor Appl Genet 2013; 126(12): 3081-9.
[http://dx.doi.org/10.1007/s00122-013-2194-6] [PMID: 24061485]

[103] Hao Y, Parks R, Cowger C, *et al.* Molecular characterization of a new powdery mildew resistance gene *Pm54* in soft red winter wheat. Theor Appl Genet 2015; 128(3): 465-76.
[http://dx.doi.org/10.1007/s00122-014-2445-1] [PMID: 25533209]

[104] Zhang R, Sun B, Chen J, *et al. Pm55*, a developmental-stage and tissue-specific powdery mildew resistance gene introgressed from *Dasypyrum villosum* into common wheat. Theor Appl Genet 2016; 129(10): 1975-84.
[http://dx.doi.org/10.1007/s00122-016-2753-8] [PMID: 27422445]

[105] Hao M, Liu M, Luo J, *et al.* Introgression of powdery mildew resistance gene *Pm56* on rye chromosome arm 6RS into wheat. Front Plant Sci 2018; 9: 1040.
[http://dx.doi.org/10.3389/fpls.2018.01040] [PMID: 30065746]

[106] Dong Z, Tian X, Ma C, Xia Q, Wang B. Physical mapping of Pm57, a powdery mildew resistance gene derived from Aegilops searsii. Intern J of Mol Sci 2020; 21322.
[http://dx.doi.org/10.3390/ijms21010322]

[107] Wiersma AT, Whetten RB, Zhang G, *et al.* Registration of two wheat germplasm lines fixed for *Pm58.* J Plant Regist 2018; 12(2): 270-3.
[http://dx.doi.org/10.3198/jpr2017.06.0036crg]

[108] Tan C, Li G, Cowger C, Carver BF, Xu X. Characterization of *Pm59*, a novel powdery mildew resistance gene in Afghanistan wheat landrace PI 181356. Theor Appl Genet 2018; 131(5): 1145-52.
[http://dx.doi.org/10.1007/s00122-018-3067-9] [PMID: 29453526]

[109] Zou S, Wang H, Li Y, Kong Z, Tang D. The NB-LRR gene *Pm60* confers powdery mildew resistance in wheat. New Phytol 2018; 218(1): 298-309.
[http://dx.doi.org/10.1111/nph.14964] [PMID: 29281751]

[110] Zhang Q, Li Y, Li Y, Fahima T, Shen Q, Xie C. Introgression of the powdery mildew resistance genes *Pm60* and *Pm60b* from *Triticum urartu* to common wheat using durum as a "bridge.". Pathogens 2021; 11(1): 25.
[http://dx.doi.org/10.3390/pathogens11010025] [PMID: 35055973]

[111] Sun H, Hu J, Song W, *et al. Pm61*: A recessive gene for resistance to powdery mildew in wheat landrace xuxusanyuehuang identified by comparative genomics analysis. Theor Appl Genet 2018; 131(10): 2085-97.
[http://dx.doi.org/10.1007/s00122-018-3135-1] [PMID: 29967989]

[112] Zhang R, Fan Y, Kong L, *et al. Pm62*, an adult-plant powdery mildew resistance gene introgressed from *Dasypyrum villosum* chromosome arm 2VL into wheat. Theor Appl Genet 2018; 131(12): 2613-20.
[http://dx.doi.org/10.1007/s00122-018-3176-5] [PMID: 30167758]

[113] Zhang DY, Zhu KY, Dong LL, Liang Y, Li G, *et al.* Wheat powdery mildew resistance gene Pm64 derived from wild emmer (Triticum turgidum var. dicoccoides) is tightly linked in repulsion with stripe rust resistance gene Yr5. Crop J 2019; 7(6): 7761-0.

[114] Li H, Dong Z, Ma C, *et al.* Discovery of powdery mildew resistance gene candidates from *Aegilops biuncialis* chromosome 2Mb based on transcriptome sequencing. PLoS One 2019; 14(11): e0220089.
[http://dx.doi.org/10.1371/journal.pone.0220089] [PMID: 31710598]

[115] He H, Liu R, Ma P, *et al.* Characterization of *Pm68*, a new powdery mildew resistance gene on chromosome 2BS of Greek durum wheat TRI 1796. Theor Appl Genet 2021; 134(1): 53-62.
[http://dx.doi.org/10.1007/s00122-020-03681-2] [PMID: 32915283]

[116] Araujo AC, De Assid FC, Cotta MG, Alves GS, Millar RN. Plant NLR receptor proteins and their potential in the development of durable genetic resistance to biotic stresses. Biotechnol Res Innov 2019; 3: pp. 80-94.
[http://dx.doi.org/10.1016/j.biori.2020.01.002]

[117] Sánchez MJ, Keller B. NLR immune receptors and diverse types of non-NLR proteins control race-specific resistance in Triticeae. Curr Opin Plant Biol 2021; 62: 102053.
[http://dx.doi.org/10.1016/j.pbi.2021.102053] [PMID: 34052730]

[118] Tao W, Liu D, Liu J, Feng Y, Chen P. Genetic mapping of the powdery mildew resistance gene *Pm6* in wheat by RFLP analysis. Theor Appl Genet 2000; 100(3-4): 564-8.
[http://dx.doi.org/10.1007/s001220050074]

[119] Ji JH, Cao AZ, Wang HY, *et al.* Discrimination of the *Triticum aestivum-T. timopheevii* introgression lines using PCR-based molecular markers. Yi Chuan 2007; 29(10): 1256-62.
[http://dx.doi.org/10.1360/yc-007-1256] [PMID: 17905717]

[120] Rinaldo A, Gilbert B, Boni R, *et al.* The *Lr34* adult plant rust resistance gene provides seedling resistance in durum wheat without senescence. Plant Biotechnol J 2017; 15(7): 894-905.
[http://dx.doi.org/10.1111/pbi.12684] [PMID: 28005310]

[121] Breia R, Conde A, Badim H, Fortes AM, Gerós H, Granell A. Plant sweets: From sugar transport to plant–pathogen interaction and more unexpected physiological roles. Plant Physiol 2021; 186(2): 836-52.
[http://dx.doi.org/10.1093/plphys/kiab127] [PMID: 33724398]

[122] Jørgensen IH. Discovery, characterization and exploitation of Mlo powdery mildew resistance in barley. Euphytica 1992; 63(1-2): 141-52.
[http://dx.doi.org/10.1007/BF00023919]

[123] Devoto A, Piffanelli P, Nilsson I, *et al.* Topology, subcellular localization, and sequence diversity of the *Mlo* family in plants. J Biol Chem 1999; 274(49): 34993-5004.
[http://dx.doi.org/10.1074/jbc.274.49.34993] [PMID: 10574976]

[124] Chen Y, Wang Y, Zhang H. Genome-wide analysis of the Mildew Resistance Locus O (*MLO*) gene family in tomato (*Solanum lycopersicum* L.). Plant Omics 2014; 7(2): 87-93.

[125] Kusch S, Panstruga R. mlo-based resistance: an apparently universal "Weapon" to defeat powdery mildew disease. Mol Plant Microbe Interact 2017; 30(3): 179-89.
[http://dx.doi.org/10.1094/MPMI-12-16-0255-CR] [PMID: 28095124]

[126] Zhang Y, Bai Y, Wu G, *et al.* Simultaneous modification of three homoeologs of *TaEDR1* by genome editing enhances powdery mildew resistance in wheat. Plant J 2017; 91(4): 714-24.
[http://dx.doi.org/10.1111/tpj.13599] [PMID: 28502081]

[127] Acevedo GJ, Spencer D, Thieron H, *et al. mlo* -based powdery mildew resistance in hexaploid bread wheat generated by a non-transgenic tilling approach. Plant Biotechnol J 2017; 15(3): 367-78.
[http://dx.doi.org/10.1111/pbi.12631] [PMID: 27565953]

[128] Ingvardsen CR, Massange SJA, Borum F, Uauy C, Gregersen PL. Development of mlo-based resistance in tetraploid wheat against wheat powdery mildew. Theor Appl Genet 2019; 132(11): 3009-22.
[http://dx.doi.org/10.1007/s00122-019-03402-4] [PMID: 31317234]

[129] Várallyay É, Giczey G, Burgyán J. Virus-induced gene silencing of Mlo genes induces powdery mildew resistance in Triticum aestivum. Arch Virol 2012; 157(7): 1345-50.
[http://dx.doi.org/10.1007/s00705-012-1286-y] [PMID: 22446884]

[130] Wang Y, Cheng X, Shan Q, *et al.* Simultaneous editing of three homoeoalleles in hexaploid bread wheat confers heritable resistance to powdery mildew. Nat Biotechnol 2014; 32(9): 947-51.
[http://dx.doi.org/10.1038/nbt.2969] [PMID: 25038773]

[131] Frye CA, Innes RW. An arabidopsis mutant with enhanced resistance to powdery mildew. Plant Cell 1998; 10(6): 947-56.
[http://dx.doi.org/10.1105/tpc.10.6.947] [PMID: 9634583]

[132] Takamatsu S. Origin and evolution of the powdery mildews (Ascomycota, Erysiphales). Mycoscience 2013; 54(1): 75-86.
[http://dx.doi.org/10.1016/j.myc.2012.08.004]

[133] Jones JDG, Dangl JL. The plant immune system. Nature 2006; 444(7117): 323-9.
[http://dx.doi.org/10.1038/nature05286] [PMID: 17108957]

[134] Ellis JG, Lawrence GJ, Luck JE, Dodds PN. Identification of regions in alleles of the flax rust resistance gene L that determine differences in gene-for-gene specificity. Plant Cell 1999; 11(3): 495-506.
[http://dx.doi.org/10.1105/tpc.11.3.495] [PMID: 10072407]

[135] Schmidt SM, Panstruga R. Pathogenomics of fungal plant parasites: What have we learnt about pathogenesis? Curr Opin Plant Biol 2011; 14(4): 392-9.
[http://dx.doi.org/10.1016/j.pbi.2011.03.006] [PMID: 21458359]

[136] Spanu PD, Abbott JC, Amselem J, *et al.* Genome expansion and gene loss in powdery mildew fungi reveal tradeoffs in extreme parasitism. Science 2010; 330(6010): 1543-6.
[http://dx.doi.org/10.1126/science.1194573] [PMID: 21148392]

[137] Koeck M, Hardham AR, Dodds PN. The role of effectors of biotrophic and hemibiotrophic fungi in infection. Cell Microbiol 2011; 13(12): 1849-57.
[http://dx.doi.org/10.1111/j.1462-5822.2011.01665.x] [PMID: 21848815]

[138] Bindschedler LV, McGuffin LJ, Burgis TA, Spanu PD, Cramer R. Proteogenomics and *in silico* structural and functional annotation of the barley powdery mildew *Blumeria graminis* f. sp. *hordei.* Methods 2011; 54(4): 432-41.
[http://dx.doi.org/10.1016/j.ymeth.2011.03.006] [PMID: 21453771]

[139] Bindschedler LV, Panstruga R, Spanu PD. Mildew-omics: how global analyses aid the understanding of life and evolution of powdery mildews. Front Plant Sci 2016; 7: 123. [http://dx.doi.org/10.3389/fpls.2016.00123] [PMID: 26913042]

[140] Spanu PD. Cereal immunity against powdery mildews targets RN Ase□Like Proteins Associated With Haustoria (RALPH) effectors evolved from a common ancestral gene. New Phytol 2017; 213(3): 969-71. [http://dx.doi.org/10.1111/nph.14386] [PMID: 28079937]

[141] Menardo F, Praz CR, Wicker T, Keller B. Rapid turnover of effectors in grass powdery mildew (Blumeria graminis). BMC Evol Biol 2017; 17(1): 223. [http://dx.doi.org/10.1186/s12862-017-1064-2] [PMID: 29089018]

[142] Bourras S, McNally KE, Ben DR, *et al.* Multiple avirulence loci and alele-specific effector recognition control the *Pm3* race-specific resistance of wheat to powdery mildew. Plant Cell 2015; 27(10) [http://dx.doi.org/10.1105/tpc.15.00171] [PMID: 26452600]

[143] Parlange F, Roffler S, Menardo F, *et al.* Genetic and molecular characterization of a locus involved in avirulence of *Blumeria graminis* f. sp. *tritici* on wheat *Pm3* resistance alleles. Fungal Genet Biol 2015; 82: 181-92. [http://dx.doi.org/10.1016/j.fgb.2015.06.009] [PMID: 26165518]

[144] Praz CR, Bourras S, Zeng F, *et al. AvrPm2* encodes an RN ase□like avirulence effector which is conserved in the two different specialized forms of wheat and rye powdery mildew fungus. New Phytol 2017; 213(3): 1301-14. [http://dx.doi.org/10.1111/nph.14372] [PMID: 27935041]

[145] Saur IML, Bauer S, Lu X, Schulze LP. A cell death assay in barley and wheat protoplasts for identification and validation of matching pathogen AVR effector and plant NLR immune receptors. Plant Methods 2019; 15(1): 118. [http://dx.doi.org/10.1186/s13007-019-0502-0] [PMID: 31666804]

[146] Müller M, Kunz L, Schudel S, Kammerecker S, Isaksson J, *et al.* Standing genetic variation of the *AvrPm17* avirulence gene in powdery mildew limits the effectiveness of an introgressed rye resistance gene in wheat. bioRxiv 2021. [http://dx.doi.org/10.1101/2021.03.09.433749]

[147] Inohara N, Nuñez G. ML — A conserved domain involved in innate immunity and lipid metabolism. Trends Biochem Sci 2002; 27(5): 219-21. [http://dx.doi.org/10.1016/S0968-0004(02)02084-4] [PMID: 12076526]

[148] Wicker T, Oberhaensli S, Parlange F, *et al.* The wheat powdery mildew genome shows the unique evolution of an obligate biotroph. Nat Genet 2013; 45(9): 1092-6. [http://dx.doi.org/10.1038/ng.2704] [PMID: 23852167]

[149] Bourras S, McNally KE, Müller MC, Wicker T, Keller B. Avirulence genes in cereal powdery mildews: The gene-for-gene hypothesis. Front Plant Sci 2016; 7: 241. [http://dx.doi.org/10.3389/fpls.2016.00241] [PMID: 26973683]

[150] Bourras S, Kunz L, Xue M, *et al.* The *AvrPm3-Pm3* effector-NLR interactions control both race-specific resistance and host-specificity of cereal mildews on wheat. Nat Commun 2019; 10(1): 2292. [http://dx.doi.org/10.1038/s41467-019-10274-1] [PMID: 31123263]

[151] Hewitt T, Müller MC, Molnár I, *et al.* A highly differentiated region of wheat chromosome 7AL encodes a *Pm1a* immune receptor that recognizes its corresponding *AvrPm1a* effector from *Blumeria graminis*. New Phytol 2021; 229(5): 2812-26. [http://dx.doi.org/10.1111/nph.17075] [PMID: 33176001]

[152] Pedersen C, Van Themaat EVL, McGuffin LJ, *et al.* Structure and evolution of barley powdery mildew effector candidates. BMC Genomics 2012; 13(1): 694. [http://dx.doi.org/10.1186/1471-2164-13-694] [PMID: 23231440]

[153] Pliego C, Nowara D, Bonciani G, *et al.* Host-induced gene silencing in barley powdery mildew reveals a class of ribonuclease-like effectors. Mol Plant Microbe Interact 2013; 26(6): 633-42. [http://dx.doi.org/10.1094/MPMI-01-13-0005-R] [PMID: 23441578]

[154] McNally KE, Menardo F, Lüthi L, *et al.* Distinct domains of the AVRPM3 $^{A2/F2}$ avirulence protein from wheat powdery mildew are involved in immune receptor recognition and putative effector function. New Phytol 2018; 218(2): 681-95. [http://dx.doi.org/10.1111/nph.15026] [PMID: 29453934]

[155] Dodds PN, Lawrence GJ, Catanzariti AM, *et al.* Direct protein interaction underlies gene-for-gene specificity and coevolution of the flax resistance genes and flax rust avirulence genes. Proc Natl Acad Sci USA 2006; 103(23): 8888-93. [http://dx.doi.org/10.1073/pnas.0602577103] [PMID: 16731621]

[156] Troch V, Audenaert K, Bekaert B, Höfte M, Haesaert G. Phylogeography and virulence structure of the powdery mildew population on its 'new' host triticale. BMC Evol Biol 2012; 12(1): 76. [http://dx.doi.org/10.1186/1471-2148-12-76] [PMID: 22658131]

[157] Yahiaoui N, Brunner S, Keller B. Rapid generation of new powdery mildew resistance genes after wheat domestication. Plant J 2006; 47(1): 85-98. [http://dx.doi.org/10.1111/j.1365-313X.2006.02772.x] [PMID: 16740148]

[158] Müller MC, Praz CR, Sotiropoulos AG, *et al.* A chromosome□scale genome assembly reveals a highly dynamic effector repertoire of wheat powdery mildew. New Phytol 2019; 221(4): 2176-89. [http://dx.doi.org/10.1111/nph.15529] [PMID: 30388298]

[159] Wu X, Bian Q, Gao Y, *et al.* Evaluation of resistance to powdery mildew and identification of resistance genes in wheat cultivars. PeerJ 2021; 9: e10425. [http://dx.doi.org/10.7717/peerj.10425] [PMID: 33510966]

[160] Gill BS, Friebe B, Raupp WJ, *et al.* Wheat genetic resource center: the first 25 years. Adv Agron 2006; 89: 73-136. [http://dx.doi.org/10.1016/S0065-2113(05)89002-9]

[161] El Baidouri M, Murat F, Veyssiere M, *et al.* Reconciling the evolutionary origin of bread wheat (*Triticum aestivum*). New Phytol 2017; 213(3): 1477-86. [http://dx.doi.org/10.1111/nph.14113] [PMID: 27551821]

[162] Feldman M. The origin of cultivated wheat.The Wheat Book. Paris: Lavoisier Tech and Doc 2001; pp. 1-56.

[163] Li LF, Liu B, Olsen KM, Wendel JF. Multiple rounds of ancient and recent hybridizations have occurred within the *Aegilops – Triticum* complex. New Phytol 2015; 208(1): 11-2. [http://dx.doi.org/10.1111/nph.13563] [PMID: 26147650]

[164] Marcussen T, Sandve SR, Heier L, *et al.* Ancient hybridizations among the ancestral genomes of bread wheat. Science 2014; 345(6194): 1250092. [http://dx.doi.org/10.1126/science.1250092] [PMID: 25035499]

[165] Mujeeb KA, Gul A, Ahmad I, Farooq M, Rauf Y, *et al.* Genetic resources for some wheat abiotic stress tolerances.Salinity and water stress: improving crop efficiency. Germany: Springer 2008; pp. 149-63. [http://dx.doi.org/10.1007/978-1-4020-9065-3_16]

[166] Kellogg EA. What happens to genes in duplicated genomes. Proc Natl Acad Sci USA 2003; 100(8): 4369-71. [http://dx.doi.org/10.1073/pnas.0831050100] [PMID: 12682287]

[167] Mains EB. Host specialization of *Erysiphe graminis tritici.* Proc Natl Acad Sci USA 1933; 19(1): 49-53. [http://dx.doi.org/10.1073/pnas.19.1.49] [PMID: 16587748]

[168] Morris R, Sears ER. The cytogenetics of wheat and its relatives.Wheat and wheat improvement. Madison: American Society of Agronomy 1967; pp. 19-87.

[169] Li G, Xu X, Bai G, Carver BF, Hunger R, Bonman JM. Identification of novel powdery mildew resistance sources in wheat. Crop Sci 2016; 56(4): 1817-30. [http://dx.doi.org/10.2135/cropsci2015.09.0551]

[170] Brunner S, Stirnweis D, Diaz QC, *et al.* Transgenic *Pm3* multilines of wheat show increased powdery mildew resistance in the field. Plant Biotechnol J 2012; 10(4): 398-409. [http://dx.doi.org/10.1111/j.1467-7652.2011.00670.x] [PMID: 22176579]

[171] Koller T, Brunner S, Herren G, Hurni S, Keller B. Pyramiding of transgenic *Pm3* alleles in wheat results in improved powdery mildew resistance in the field. Theor Appl Genet 2018; 131(4): 861-71. [http://dx.doi.org/10.1007/s00122-017-3043-9] [PMID: 29302719]

[172] Antonyuk MZ, Shpylchyn VV, Ternovska TK. Permanent genetic variability in the introgressive lines and amphidiploids of *Triticeae.* Cytol Genet 2013; 47(4): 242-51. [http://dx.doi.org/10.3103/S0095452713040026]

[173] Iefimenko TS, Antonyuk MZ, Martynenko VS, Navalihina AG, Ternovska TK. Introgression of Aegilops mutica genes into common wheat genome. Cytol and Genet 2018; 52(1): 21-30.

[174] Nepal M, Andersen E, Neupane S, Benson B. Comparative genomics of non-TNL disease resistance genes from six plant species. Genes 2017; 8(10): 249. [http://dx.doi.org/10.3390/genes8100249] [PMID: 28973974]

[175] Andersen EJ, Nepal MP, Purintun JM, Nelson D, Mermigka G, Sarris PF. Wheat disease resistance genes and their diversification through integrated domain fusions. Front Genet 2020; 11: 898. [http://dx.doi.org/10.3389/fgene.2020.00898] [PMID: 32849852]

[176] Gong C, Cao S, Fan R, *et al.* Identification and phylogenetic analysis

of a CC-NBS-LRR encoding gene assigned on chromosome 7B of wheat. Int J Mol Sci 2013; 14(8): 15330-47.
[http://dx.doi.org/10.3390/ijms140815330] [PMID: 23887654]

[177] Mizuno H, Katagiri S, Kanamori H, *et al.* Evolutionary dynamics and impacts of chromosome regions carrying *R*-gene clusters in rice. Sci Rep 2020; 10(1): 872.
[http://dx.doi.org/10.1038/s41598-020-57729-w] [PMID: 31964985]

[178] Xu H, Yi Y, Ma P, *et al.* Molecular tagging of a new broad-spectrum powdery mildew resistance allele *Pm2c* in Chinese wheat landrace Niaomai. Theor Appl Genet 2015; 128(10): 2077-84.
[http://dx.doi.org/10.1007/s00122-015-2568-z] [PMID: 26133735]

[179] Li N, Jia H, Kong Z, *et al.* Identification and marker-assisted transfer of a new powdery mildew resistance gene at the *Pm4* locus in common wheat. Mol Breed 2017; 37(6): 79.
[http://dx.doi.org/10.1007/s11032-017-0670-4]

[180] Jia M, Xu H, Liu C, *et al.* Characterization of the powdery mildew resistance gene in the elite wheat cultivar jimai 23 and its application in marker-assisted selection. Front Genet 2020; 11: 241.
[http://dx.doi.org/10.3389/fgene.2020.00241] [PMID: 32300355]

[181] Summers RW, Brown JKM. Constraints on breeding for disease resistance in commercially competitive wheat cultivars. Plant Pathol 2013; 62(1): 115-21.
[http://dx.doi.org/10.1111/ppa.12165]

[182] Wang Z, Li H, Zhang D, *et al.* Genetic and physical mapping of powdery mildew resistance gene *MlHLT* in Chinese wheat landrace hulutou. Theor Appl Genet 2015; 128(2): 365-73.
[http://dx.doi.org/10.1007/s00122-014-2436-2] [PMID: 25471672]

[183] Xie J, Wang L, Wang Y, *et al.* Fine mapping of powdery mildew resistance gene *PmTm4* in wheat using comparative genomics. J Integr Agric 2017; 16(3): 540-50.
[http://dx.doi.org/10.1016/S2095-3119(16)61377-1]

[184] Qin B, Cao A, Wang H, *et al.* Collinearity-based marker mining for the fine mapping of *Pm6*, a powdery mildew resistance gene in wheat. Theor Appl Genet 2011; 123(2): 207-18.
[http://dx.doi.org/10.1007/s00122-011-1577-9] [PMID: 21468676]

[185] Ouyang S, Zhang D, Han J, *et al.* Fine physical and genetic mapping of powdery mildew resistance gene *MlIW172* originating from wild emmer (*Triticum dicoccoides*). PLoS One 2014; 9(6): e100160.
[http://dx.doi.org/10.1371/journal.pone.0100160] [PMID: 24955773]

[186] Wu Q, Zhao F, Chen Y, *et al.* Bulked segregant CGT□Seq□facilitated map□based cloning of a powdery mildew resistance gene originating from wild emmer wheat (*Triticum dicoccoides*). Plant Biotechnol J 2021; 19(7): 1288-90.
[http://dx.doi.org/10.1111/pbi.13609] [PMID: 33949081]

[187] Xu H, Yao G, Xiong L, *et al.* Identification and mapping of *pm2026*: a recessive powdery mildew resistance gene in an einkorn (*Triticum monococcum* L.) accession. Theor Appl Genet 2008; 117(4): 471-7.
[http://dx.doi.org/10.1007/s00122-008-0791-6] [PMID: 18504540]

[188] Li J, Li Y, Ma L. Recent advances in CRISPR/Cas9 and applications for wheat functional genomics and breeding. aBIOTECH 2021; 2: 375-85.
[http://dx.doi.org/10.1007/s42994-021-00042-5]

[189] Qiu L, Liu N, Wang H, *et al.* Fine mapping of a powdery mildew resistance gene MlIW39 derived from wild emmer wheat (Triticum turgidum ssp. dicoccoides). Theor Appl Genet 2021; 134(8): 2469-79.
[http://dx.doi.org/10.1007/s00122-021-03836-9] [PMID: 33987716]

[190] Shi X, Wu P, Hu J, *et al.* Molecular characterization of all-stage and adult-plant resistance loci against powdery mildew in winter wheat cultivar Liangxing 99 using BSR-Seq technology. Plant Dis 2021; 105(11): 3443-50.
[http://dx.doi.org/10.1094/PDIS-03-21-0664-RE] [PMID: 34010023]