Powdery Mildew Resistance Loci in Vines

Subjects: Plant Sciences

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Grapevine (*Vitis vinifera*) is one of the main fruit crops worldwide, with near of 7.3 million hectares planted in 2020, but along with its economic relevance, it has been associated with diverse pathogens that affect grapevine yield, fruit, and wine quality, of which powdery mildew is the most important disease prior to harvest. Its causal agent is the biotrophic fungus *Erysiphe necator*, which generates a decrease in cluster weight, delays fruit ripening, and reduces photosynthetic and transpiration rates. In addition, powdery mildew induces metabolic reprogramming in its host, affecting primary metabolism. Most commercial grapevine cultivars are highly susceptible to powdery mildew; consequently, large quantities of fungicide are applied during the productive season. These pesticide applications have been associated with high exposure to it, and pesticides are associated with health problems, negative environmental impacts, and high costs for farmers. In parallel, consumers are demanding more sustainable practices during food production. Therefore, new grapevine cultivars with genetic resistance to powdery mildew are needed for sustainable viticulture, while maintaining yield, fruit, and wine quality. Two main gene families confer resistance to powdery mildew in the Vitaceae, *Run* (Resistance to *Uncinula necator*) and *Ren* (Resistance to *Erysiphe necator*), and the resistance they confer is associated with the presence of each locus since there are still no genes that alone can produce a powerful genetic resistance. Because the resistance mediated by the plant immune response is highly complex and considers the evolution and adaptation of the pathogen in parallel to that of the plant.

Keywords: Erysiphe necator ; grapevine ; resistance genes ; Run ; Ren ; powdery mildew ; Vitis ; Resistance to pathogens

1. Introduction

Grapevine (*Vitis vinifera*) is one of the main fruit crops worldwide. In 2020, the total surface area dedicated to this crop was estimated to be 7.3 million hectares [1][2], with a production of approximately 77.8 million tons of grape clusters. Of the total harvest, 57% is destined for wine production; 36% corresponds to table grapes, and 7% is used to produce raisins [1]. Yield and fruit quality are affected by the attack of different fungal pathogens [3]. Of these, powdery mildew is the most important and challenging pre-harvest disease due to its high destructive force, the high susceptibility of most commercial cultivars [3][4], and the broad humidity and temperature ranges in which the pathogen thrives and develops [5]. Its causal agent is the biotrophic fungus *Erysiphe necator* (synonyms: *Uncinula necator* Burr) [6][7]. The main symptoms typically associated with infection are decreased cluster weight, delayed fruit ripening, and reduced photosynthetic and transpiration rates, although Pimentel et al. (2021) [8] observed no differences in berry weight, sugars, organic acids, or main ripening parameters between infected and healthy berries. The determination of yield loss caused by powdery mildew attack is difficult to standardize because multiple factors, such as cultivar susceptibility, production system, and moment of infection, are involved [9][10].

Powdery mildew not only affects crop productivity but also has an impact on fruit quality, altering sugar content, acidity level [11], and anthocyanin levels [12]. Moreover, additional negative sensorial effects on wine quality have been described, such as the reduction in vanilla-like aromas in red wines [13] and tropical fruit-like aromas in Sauvignon blanc [12]. Color is yet another parameter influenced by *E. necator* as reductions in the anthocyanin content in fruits diminish the intensity of color in red wines [14].

In addition, powdery mildew induces metabolic reprogramming in its host [8]. At the primary metabolic level, it reduces the abundance of glycolytic, photorespiratory, and photosynthetic proteins [15] and generates a redistribution of carbon reserves due to an increase in invertase and alpha-amylase activity [16], which degrades starch reserves to glucose and maltose [17]. This metabolic alteration is accompanied by an upregulation of the transcription of the hydroxymethyl-flutary-CoA (*HMG-CoA*) and *HMG-CoA* reductase genes [16]. HMG-CoA synthase enzyme converts Acetoacelyl-CoA into 3-hydroxy-3-methylglutaryl-CoA, which is transformed into mevalonate by HMG-CoA reductase. Both molecules are part of the biosynthesis pathway of terpenes, carotenoids, and sterol compounds [18].

Most commercial grapevine cultivars are highly susceptible to *E. necator* [19]. For that reason, in order to achieve stable yields and good-quality fruits, powdery mildew is controlled by the intensive application of fungicides during the productive season [20]. However, chemical control is expensive for farmers and is associated with health hazards for field workers, animals, and consumers of table grapes and wine [20][21][22][23][24]. In addition, fungicide application has negative consequences on the environment, such as soil and groundwater contamination [25]. In response to these detrimental effects, governments and consumers are demanding more sustainable production methods, including decreased pesticide applications [26]. One example of this is the Green Deal Farm Fork strategy, which aims to reduce the use of pesticides in Europe by 50% [27]. These demands and legislations are a great challenge for viticulture farmers, who, at the same time, are facing the effects of climate change that threaten the yield and quality of their production [26]. In this context, the approach of replacing conventional grapevine cultivars with fungus-resistant cultivars is a sustainable alternative for disease control [28].

2. Host Response

The plant's immune system is summarized by the zig-zag model, which distributes the plant's response to the presence of pathogens into three main stages. The initial stage is related to the recognition of Pathogen-Associated Molecular Patterns (PAMPs) or Microbe-Associated Molecular Patterns (MAMPs) by Pattern Recognition Receptors (PRRs), resulting in PAMP-triggered immunity (PTI). This triggers nonspecific physiological and molecular responses, such as the accumulation of reactive oxygen species (ROSs) and phytoalexins, and/or stomata closure through the phosphorylation of a MAP kinase pathway (MAPKKK–MAPKK–MAPK), which activates transcription factors, such as WRKY22, thus inducing related genetic responses. In the second stage, and in response to plant defense, pathogens initiate effector-triggered susceptibility (ETS) [29] whereby through effectors (Secreted Effector Proteins), such as coat proteins [30] or other specific proteins, the defensive response pathway of plants is stopped. For instance, some effectors, such as AvrPto and AvrPtoB, have been shown to block the phosphorylation of MAPKs in the case of *Pseudomonas syringae* [31], while *EqCSEP01276* produced by powdery mildew inhibits the biosynthesis of abscisic acid (ABA) [32]. In this ETS phase, pathogens may overcome the immune response of plants and infect the host's cells. Cells of certain plant species possess resistance proteins (R) that directly or indirectly recognize the presence of pathogenic effectors and trigger an immune response, called effector-triggered immunity (ETI). This final phase generates an immune response of greater intensity than PTI. This switch between ETS–ETI is maintained until the hypersensitive cell death response is triggered or the pathogen overwhelms the cell [33].

Most *R* genes encode nucleotide-binding site (NBS) leucine-rich repeat (LRR) domain proteins (NBS–LRR proteins) [29]. This is the case of the *R* genes transcribed in the Vitaceae plant family in response to *E. necator* infection. In Vitaceae, the *R* genes are clustered in tandem repeats of genomic regions. These have been genetically mapped, uncovering nine loci that encode *R* gene sequences conferring resistance to *E. necator*, such as *Run1*, *Run2*, *Ren1*, *Ren2*, *Ren3*, *Ren4*, *Ren5*, *Ren6,* and *Ren7* [34], which have been used to obtain plants resistant to this infection by pseudo-backcrossing [35]. On the other hand, more recent "New Breeding Technologies" (NBTs) have been employed for genetic improvements in *Vitis* plants through the elimination of the endogenous genetic material using the thermal shock FRP/FLP system [36][37] or the generation of DNA-free modifications using ribonucleoproteins [38]. This, together with new rapidly developing *Vitis* models, such as Microvine or Picovine, have helped to accelerate the discovery of new target genes to decipher the resistance of *Vitis* to powdery mildew, such as the PATHOGENESIS-RELATED 4b (*VvPR4b*) gene, whose loss of function decreases *Vitis* resistance to downy mildew [39]. As expected, the overexpression of *VvPR4b* is related to enhanced resistance to *E. necator* [40], while the DIMERIZATION PARTNER-E2F-LIKE 1 (*VviDEL1)* double-cut transgenic *Vitis* has 90% fewer symptoms of powdery mildew infection than the control plants [40].

Hormones play a key role in plant defense responses, particularly jasmonic acid (JA) and ethylene (Et) for necrotrophic pathogens and salicylic acid (SA) for hemibiotrophic and biotrophic pathogens, such as powdery mildew [3][8]. In *Arabidopsis thaliana*, SA is synthesized in response to a pathogen attack, mainly from chorismic acid by the activity of the enzymes isochorismate synthase (ICS) and isochorismate pyruvate lyase (IPL) [41]. A mobile derivative of SA is methyl salicylate (MeSa), which can be transported through the phloem to distal parts of plants, generating a Systemic Acquired Response (SAR). This activates various physiological immune responses, such as programmed cell death (PCD) and accumulation of ROS, such as hydrogen peroxide and nitric oxide [42]. Thus, to achieve an effective resistance response in grapevines upon infection by *E. necator*, it is necessary to enhance SAR [3]. Although the most well-described hormonal response pathway against the attack of powdery mildew is that of SA, it has also been shown that Et and JA contribute to the response against *E. necator* in grapevines [43][44]. Furthermore, recent data show that when *V. vinifera* cv. 'Cabernet Sauvignon' plants are treated with exogenous Et, a defense response against *E. necator* is triggered [44]. Such a response mechanism is associated with the induction of a series of defense proteins, such as acidic class IV chitinase (CHIT4c),

protease inhibitor (PIN), polygalacturonase-inhibiting protein (PGIP), and ß-1,3-glucanase (GLU). Although there is no direct evidence linking the induction of these defense proteins with the phenylpropanoid pathway, a correlation has been seen in the increased biosynthesis of phytoalexins and the upregulation of phenylalanine ammonia-lyase (*PAL*) and stilbene synthase (*STS*) genes. These increases are positively correlated with the increased accumulation of stilbenes with known antimicrobial activity, which emphasizes the participation of these enzymes in the host response against biotrophic fungi [45]. In support of the above, the transcriptomic analysis of the response to *E. necator* infection of two *Vitis* species, one susceptible (*V. pseudoreticulata*) and the other resistant (*V. quinquangularis*), showed the induction of genes and metabolites associated with the defense response [46]. Specifically, the repression of the flavonoid pathway genes was reported in the susceptible cultivar *V. pseudoreticulata*, alongside differential responses of genes and processes related to hormones, such as SA and JA [47]. A high accumulation of arachidic acid has been reported in berries infected by *E. necator*, meaning that it is now considered a quantitative biomarker for infection by this fungus [8][48]. Interestingly, Jiao et al. [46] described the suppression of genes related to the biosynthesis and elongation of fatty acids in the resistant cultivar, suggesting the participation of these types of lipids in the interaction of *E. necator* with the host in a developing infection. Additionally, genes involved in the biosynthesis and signaling of phytohormones, such as JA and cytokinins (CK), were identified, as were ones that code for protein kinases and proteins with NBS–LRR repeats [46] (**Figure 1**).

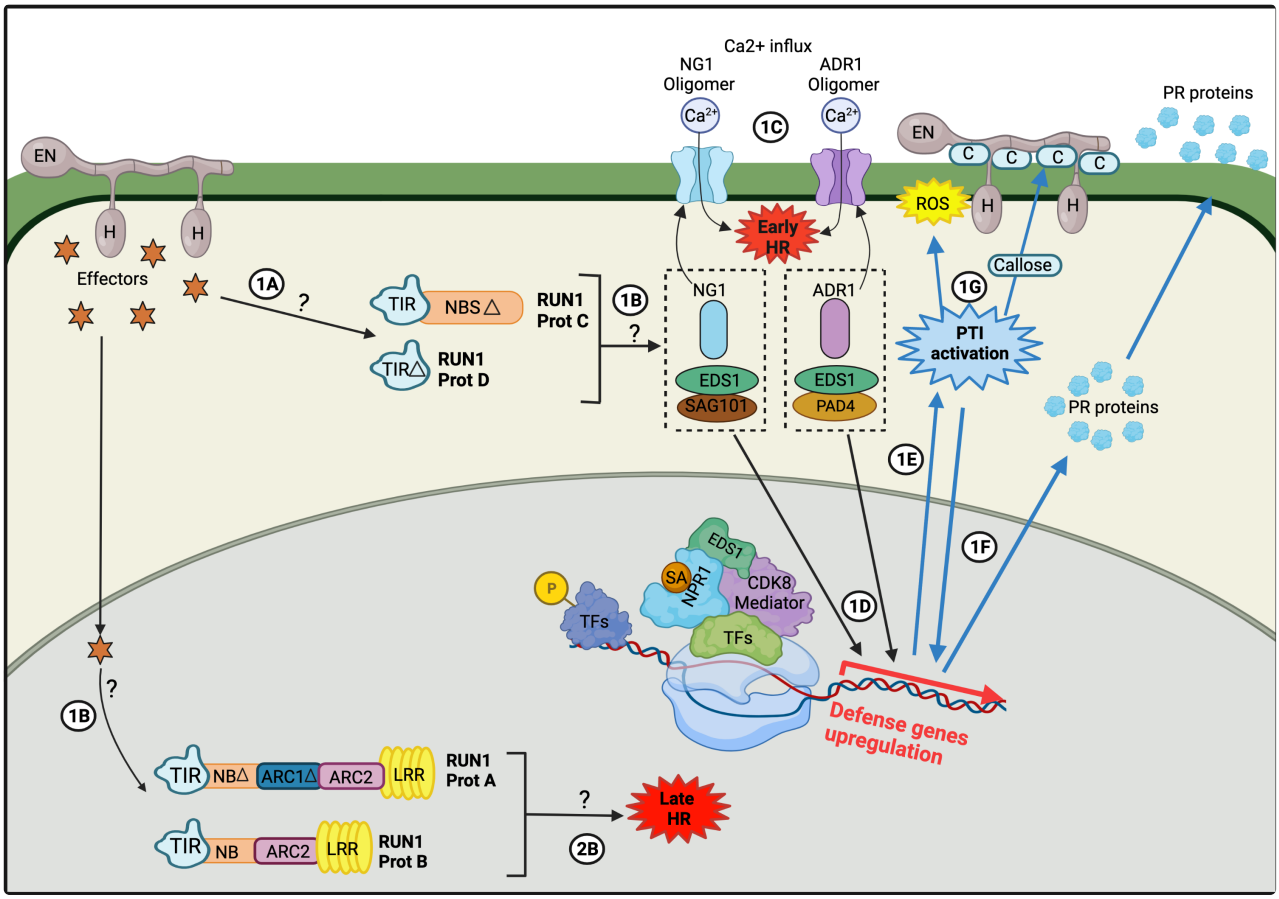

Figure 1. Illustrative figure adapted to summarize the host (*V. vinifera*) response to fungal *(E. necator),* showing a theoretical pathway for *Run1*: *MrRUN1* proteins recognize pathogen effectors, which activate PTI. It is proposed that *Run1* proteins modulate two response pathways, one generated by truncated proteins (Prot C and Prot D, pathway1) located in the cytoplasm, and another produced by full-length *MrRUN1* proteins in the cell nucleus (Prot A and Prot B, pathway 2). Pathway 1: **1A**) Truncated *Run1* proteins detect fungal effectors in the cytoplasm. **1B**) Activation of signaling nodes of PTI: EDS1-PAD4-ADR1 and EDS-SAG10-NGR1. **1C**) Activation of Ca2+ influx, which culminates with an early PCD. **1D**) EDS1 acts as a transcriptional factor that recruits CDK8 and RNA polymerase II to start the expression of defence genes. **1E**) The activation of ETI triggers PTI (blue arrows). **1F**) PTI generates the transcription of Plant-pathogenesis Related Proteins (PR proteins). **1G**) PTI increases the ROS production and produces callose deposits (C) in the cell areas where the fungus penetrated. Pathway 2: **1B**) *E. necator* effectors move to the cell nucleus, recognized by the full-length And B RUN1 proteins. **2B**) Prot A and prot B triggers a late HR. This illustrative figure was made specifically for this publication by Viviana Sosa-Suñiga, it is adapted to summarize the response pathways to fungi in plants. This representation is general and can only be used as a guide.

3. Mapping Resistance Genes for Powdery Mildew Resistance Using Interspecific Crosses

The use of F_1 families derived from the cross of two parents with contrasting phenotypes is the most used strategy for genetic mapping in grapevines [49]. Based on the pseudo-testcross strategy [50], it is suitable for highly heterozygous plants with long juvenile periods, such as grapevines.

Although *V. vinifera* is the most widely cultivated *Vitis* species, the levels of powdery mildew resistance in this species are lower than that of other *Vitis* or *Muscadinia* species from North America or Asia. These contrasting phenotypes have been exploited for genetic mapping. To date, 15 loci responsible for grapevine powdery mildew resistance have been reported, leveraging information from 24 F_1 interspecific families or descendants [51].

Strong disease-resistant loci have been mapped to chromosomes 12, 18, and 9, named *Run1* [52][53], *Ren4* [54][55][56], and *Ren6* [57], respectively. These loci originate from *M. rotundifolia*, *V. romanetii*, and *V. piasezkii* and provide strong quantitative disease resistance [58].

Other moderate to minor disease-resistant sources have been found on chromosomes 2, 9, 13, 14, 15, and 18 [51]. In some of these loci, the study of the infection process demonstrated a postpenetration resistance mechanism, with delayed hyphal growth, as in the case of *Ren1* [59], *Ren5* [60], *Ren7* [57], and *Ren11* [61][62]. Some of these moderate to minor resistance loci come from *V. vinifera*, *V. rotundifolia* [60], *V. piasezkii* [57], and complex hybrids involving *V. cinerea*, *V. rupestris*, or ‘Seibel’ selections [63][64][65][66][67].

4. *Run* and *Ren* Resistance Loci

Several loci associated with powdery mildew resistance have been identified in different species of the Vitaceae family. These loci have been named *Ren1* [59], *Ren1.2* [68], *Ren2* [63][69], *Ren3* [65][70], *Ren4* [54], *Ren5* [60], *Ren6* [57], *Ren7* [57], *Ren8* [66], *Ren9* [65], R*en10* [67], *Ren11* [61], *Run1* [52][53], *Run1.2a* and *b* [71], *Run2.1* [55][71], and *Run2.2* [55][71] (**Figure 2**). In the case of most *Run* and *Ren* loci, it is not clear which genes are responsible for powdery mildew resistance and their mechanism of action [34]. The only exception to this is the resistance gene *MrRUN1* (*MrRGA10*), whose sequence was described by Feechan et al. (2013) [53]. The *MrRUN1* gene encodes an NBS–LRR resistance protein containing a Toll/interleukin-1 receptor-like (TIR) domain, which recognizes pathogen effectors, thus triggering the hypersensitive response (HR), which is characterized by an increase in ROS production leading eventually to programmed cell death (PCD) in infected cells [69]. The same defense response has been seen in grapevine plants that carry the *Run1*, *Run1.2a*, *Run1.2b*, *Run2*, *Ren1*, *Ren2*, *Ren3*, *Ren4*, *Ren5*, *Ren6*, *Run7*, or *Ren9* loci (**Table 1**). These facts suggest that the immune response generated by these loci is mediated by resistance proteins that recognize *E. necator* effectors and activate ETI [34]. This hypothesis is supported by the presence in other species of resistance genes to powdery mildew that encode for NBS–-LRR proteins [72][73][74][75][76][77][78][79].

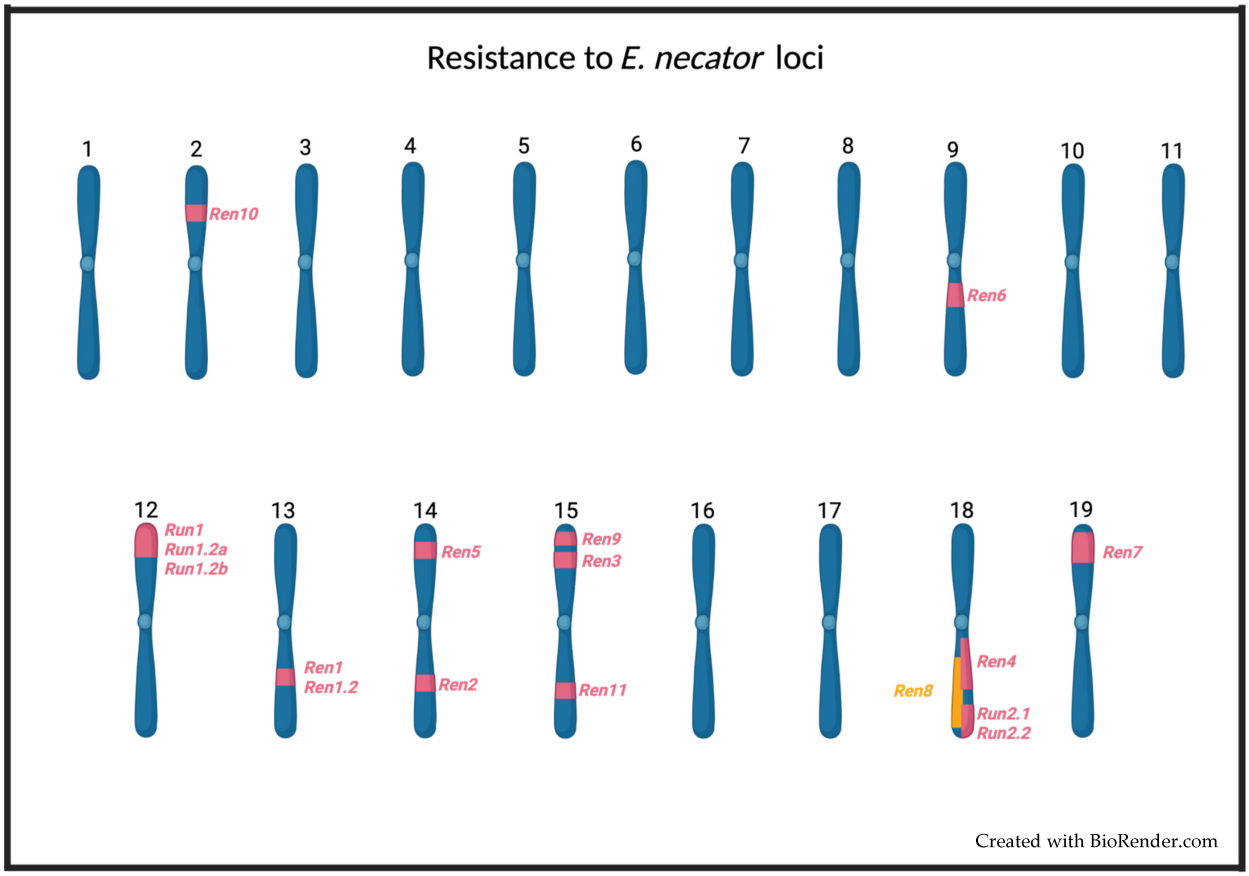

Figure 2. Illustration of the chromosomal location of loci of resistance to *E. necator* in *Vitis vinifera* *Run1–Run1.2a/b* (Chr12) [52][53][71][80][81]; *Run2.1–Run2.2* (Chr18) [55]; *Ren1–Ren1.2* (Chr13) [59][68][82][83][84]; *Ren2* (Chr14) [63][85]; *Ren3* (Chr15) [64][70]; *Ren4* (Chr18) [54]; *Ren5* (Chr14) [60]; *Ren6* (Chr9) [57]; *Ren7* (Chr17) [57]; *Ren9* (Chr15) [64]; *Ren10* (Chr2) [67]; and *Ren11* (Chr15) [61] are marked in red on the figure. *Ren8* [66] is marked in orange to highlight that it may overlap with *Ren4* and *Ren2.1–Ren2.2* [66].

Table 1. Summary of powdery mildew resistance loci discovered in Vitaceae family. The origin, host response, and resistance level to powdery mildew of each locus are shown. Donor species and area of origin are also specified. In the host, the responses are programmed cell death (PCD), the production of callose, and the increase in ROSs. The level of resistance is considered as 'total' in the absence of visible symptoms and 'partial' for cases where the symptomatology decreases without disappearing completely. The variable classification was used for cases in which a race-specific response was observed, being 'total' for some strains and 'partial' for others.

Locus	Donor	Host Response			Resistance Level	Reference
		PCD	Callose	ROS		
Run1	*M. rotundifolia* G52 [1]	Yes	Yes	Yes	Variable *	[35][52][53]
Run1.2a	*M. rotundifolia*[1]	Yes	n.i.	n.i.	Variable *	[71]
Run1.2b	*M. rotundifolia*[1]	Yes	n.i.	n.i.	Variable *	[71]
Run2.1	*M. rotundifolia* 'Magnolia' [1]	Yes	n.i.	n.i.	Partial	[55]
Run2.2	*M. rotundifolia* 'Trayshed' [1]	Yes	n.i.	n.i.	Partial *	[55]
Ren1	*V. vinifera* cv. 'Kismish vatkana' [2]	Yes	Yes	Yes	Total	[59]

Locus	Donor	Host Response			Resistance Level	Reference
		PCD	Callose	ROS		
Ren1.2	*V. vinifera* cv. 'Shavtsitka' [3]	Yes	n.i.	n.i.	Partial	[68]
Ren2	*V. cinerea*[2]	Yes	n.i.	n.i.	Partial	[63][69]
Ren3	'Regent' [4]	Yes	Yes	Yes	Partial	[64][70]
Ren4	*V. romanetii*[2]	Yes	n.i.	n.i.	Partial	[54]
Ren5	*M. rotundifolia* 'Regale' [1]	n.i.	n.i.	n.i.	Total	[60]
Ren6	*V. piasezki*[2]	Yes	n.i.	n.i.	Total	[57]
Ren7	*V. piasezki*[2]	Yes	n.i.	n.i.	Partial	[57]
Ren8	Unknown [4]	n.i.	n.i.	n.i.	Partial	[66]
Ren9	'Regent' [4]	Yes	n.i.	n.i.	Partial	[64][65]
Ren10	'Seyval blanc' [4]	n.i.	n.i	n.i.	Partial	[67]
Ren11	*Vitis aestivalis*[2]	n.i.	n.i.	n.i	Partial	[61]

[1] North American *Vitis*, [2] Asian *Vitis*, [3] Caucasian *V. vinifera* cultivar, [4] Interspecific hybrids of *V. vinifera* with North American *Vitis* species, * Genetic resistance was overcome by Musc4 *E. necator* isolates [69][85], and n.i.: No information available.

For example, in wheat (*Triticum* spp.), several powdery mildew (*Pm*) genes that encode NBS–LRR proteins have been described. These genes confer a broad-spectrum or a race-specific or a quantitative resistance to the host. Further, their expression could change depending on the plant's phenological stage. For example, *Pm21* gene encodes an NBS–LRR protein that confers broad-spectrum resistance to powdery mildew (*Blumeria graminis* f.sp. *tritici*) throughout the life of the plant [75]. On the other hand, *Pm6* and *Pm8* genes confer a race-specific resistance that is only present during the adult stage of plant development [77]. One example of quantitative resistance is the Reaction to Puccinia recondite Rob. ex Desm. 22a (*LRR22a*) gene that gives a quantitative resistance at the adult stage of the plant [79].

Another example is the presence of NBS–LRR resistance to powdery mildew (*Sphaerotheca pannosa*) genes in chestnut rose (*Rosa roxburghii* Tratt.). Xu et al. [78] identified and cloned 23 NonTIR–NBS–LRRR and 11 TIR–NBS–LRR genes associated with powdery mildew resistance.

It is important to consider that NBS–LRR resistance proteins confer a level of response that can vary depending on the allele, environmental conditions, and pathogen genotype, an example of which is the race-specific performance of some *Run* and *Ren* loci (**Table 1**).

5. Locus Stacking: The Search for Durable and Broad-Spectrum Resistance

Currently, one of the main objectives of grapevine breeding programs worldwide is the development of durable and strong resistance to powdery mildew, through independent modes of action. The most important desirable outcome of such programs is that the resistance must be durable. Because grapevine plants are productive for at least twenty years, resistance needs to be maintained through that period of time [55][57]. To achieve this goal, a pyramiding strategy has been

proposed, which combines various resistance loci in the same genotype [86]. To ensure the durability of this resistance, it is necessary to mix loci that have different mechanisms of action, spectrums of target isolates, and contributions (minor and major) to the resistance [83][87]. Referring to this last aspect, it is important to consider that even though initially more promising results are observed when a gene or locus with a major effect is used, this can favor the selection of isolates of the fungus that are capable of overcoming this major resistance loci [87][88], and if resistance is based only on the presence of one gene, the fungus could mutate its effector and evade immune recognition [57]. A clear example of this is what happened between the *Run*1 locus and the Musc4 isolate, which is probably due to a long coexistence with *M. rotundifolia*, the donor specie of *Run1*, which likely mutated its effector to overcome the resistance conferred by this gene [51][85]. This response has not only been observed with *Run1*; *Ren3* and *Ren9* loci resistance were also overcome by a North American *E. necator* strain, despite these loci only conferring partial resistance [67]. These results suggest that in the case of the development of new grapevine cultivars with resistance to powdery mildew, it is important to consider the origin of the genes or loci when pyramiding, prioritizing the combination of resistance sources from species with diverse geographical origins. In the case of the development of resistant cultivars in North America, the high genetic variability of powdery mildew in that area [83] is a challenge for breeders.

More studies are needed to evaluate the best combination of genes and loci for each viticultural area. Currently, the immune responses of some genotypes that have more than one source of resistance have already been characterized (**Table 2**). The presence of more than one resistant gene or loci does not generate a more intense resistance response in all the cases studied, demonstrating that combinations do not always generate additive effects (**Table 2**). This is the case of the *Run1.2a/b* genotypes that did not show any difference in PCD induction and secondary hyphae formation, compared to genotypes carrying just one of these loci [68]. Another example is the combination of *Ren3* and *Ren9*, which did not generate an immune response that has an advantage in terms of the intensity or speed of the response compared to *Ren3* alone [64]. This response has also been observed in *Ren*6*Ren*7 genotypes, which had an equal response to the *Ren6* locus alone [57]. On the other hand, the combinations of *Run1Run1.2a/b, Run1Ren1*, and *Run1Ren2* did show an additive effect, as the combination of both genes/loci generated a stronger immune response than the one triggered by each one individually. For example, *the Run1Run1.2a/b* genotypes showed less formation of secondary hyphae than each gene/locus separately [68], while in the case of *Run1Ren1* genotypes, a more intense defense response was observed in terms of ROS production, callose accumulation, PCD, and activation of STILBENE SYNTHASE 36 (*Vv*STS36) and PENETRATION 1 (*VvPEN*1) than each of them separately [35]. The STS gene family encodes stilbene synthases, which catalyse the production of the stilbenes, compounds that have antimicrobial activities in plant defense [39]. *PEN1* has a role in the traffic of secretory vesicles that could be associated with penetration resistance against powdery mildews [88]. For *Run1Ren2* genotypes, a significant decrease in colony formation was seen compared to genotypes containing only *Run1* or *Ren2* [68].

Table 2. Effect on resistance reported by pyramiding different loci in the same genotype. Additive effect refers to the fact that the combination of loci generated a stronger immune response compared to the effect of each locus separately.

Effect Type	Loci	Reference
Additive	*Run1Run1.2a/b*	[69]
	Run1Ren1	[35]
	Run1Ren2 *	[69]
	Run1.2a/bRun2.2	[69]
Nonadditive	*Ren3Ren9*	[64]
	Ren6Ren7	[57]

* Race-specific, as this effect was not seen with the Musc4 isolate.

6. Development of Genetic Resistance by Gene Editing

As an alternative approach to identify genes conferring resistance to *E. necator*, searching for susceptibility genes (*S* genes) can be an interesting strategy since inactivation of those S genes should lead to resistance to powdery mildew. An example of these S genes is the mildew locus O (*MLO*), which is conserved throughout the plant kingdom. Loss of function of certain members of the *MLO* gene family increases resistance to powdery mildew in *A. thaliana*, pea, tomato, wheat, and pepper. In *Vitis*, the combined silencing of *VvMLO6*, *VvMLO7,* and *VvMLO11* produced a 77% decrease in *E. necator* infection [89]. However, although gene editing by Crispr–Cas9 of *VvMLO3* did lead to an increase in resistance to powdery mildew, this was only observed in heterozygous plants, as the homozygous mutation produced plant death by necrosis, which suggests a pleiotropic function of this gene in *Vitis* [90].

7. Final Remarks

We are experiencing a devastated climate change phenomenon, which among its most important effects for food production are drought, the increase of insects and the elevated spread of pathogenic fungi. This scenario is especially worrying in woody plants such as vitis, because the study of its genome becomes very complex, due to the long waiting times for transformations, the genetic differences between each cultivar, and the high susceptibility of this plant to biotic and abiotic stress. Therefore, it becomes very important for current scientists to work to ensure the presence of this genus for future generations, in areas from biotechnology for genetic modifications, to engineering to create specific irrigation systems. But above all, take advantage of the knowledge that we have generated as a scientific community, disperse it in the population, and be able to achieve regulatory changes that allow us to dream, without irrational fears, in genetic improvements that benefit everyone.

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