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12 **Title: Interactions of tomato and *Botrytis* genetic diversity: Parsing the
13 contributions of host differentiation, domestication and pathogen variation**

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15 Short title: Interactions of tomato and Botrytis genetics

16 Material Distribution Footnote: The author(s) responsible for distribution of materials
17 integral to the findings presented in this article in accordance with the policy described
18 in the Instructions for Authors (www.plantcell.org) is (are): Daniel J. Kliebenstein
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20

21 **Abstract**

22 While the impacts of crop domestication on specialist pathogens are well-studied,
23 less is known about the interaction of crop variation and generalist pathogens. To study
24 how genetic variation within a crop impacts plant resistance to generalist pathogens, we
25 infected a collection of wild and domesticated tomato accessions with a genetically
26 diverse population of the generalist pathogen *Botrytis cinerea*. We quantified variation in
27 lesion size of 97 *B. cinerea* genotypes (isolates) on 6 domesticated *Solanum*
28 *lycopersicum* and 6 wild *S. pimpinellifolium* genotypes. Lesion size was significantly
29 affected by large effects of the host and pathogen's genotype, with a much smaller
30 contribution of domestication. This pathogen collection also enables genome-wide
31 association (GWA) mapping in *B. cinerea*. GWA in the pathogen showed that virulence
32 is highly polygenic and involves a diversity of mechanisms. Breeding against this
33 pathogen would likely need to utilize diverse isolates to capture all possible
34 mechanisms. Critically, we identified a subset of *B. cinerea* genes where allelic variation
35 was linked to altered virulence against the wild versus domesticated tomato, as well as
36 loci that could handle both groups. This generalist pathogen already has a large
37 collection of allelic variation that must be considered when designing a breeding
38 program.

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42 **Introduction**

43 Plant disease is mediated by complex interactions among diverse host and
44 pathogen molecular pathways, and the disease outcome is the sum of host plant
45 susceptibility/resistance and pathogen virulence/sensitivity mechanisms. The specific
46 outcome of any interaction is highly dependent on the genetic variation within these
47 pathways in both the host and pathogen. Over time, mutation and selection have led to
48 distinct genetic architectures in the host and pathogen that are at least partly influenced
49 by the host range of the pathogen. Specialist pathogens are a major focus in plant
50 pathology; virulent on a narrow range of hosts, and often limited to a single species or
51 genus. Most known plant genes for resistance to specialist pathogens confer qualitative

52 resistance through innate immunity via large-effect loci that enable the recognition of the
53 pathogen (Dangl and Jones 2001, Jones and Dangl 2006, Dodds and Rathjen 2010,
54 Pieterse, Van der Does et al. 2012). These recognition signals can be conserved
55 pathogen patterns such as cell-wall polymers or flagellin, or alternatively, specific
56 virulence factors that block perception of the pathogen, and in turn are detected by plant
57 proteins that guard the signaling networks (Jones and Dangl 2006, Bittel and Robatzek
58 2007, Ferrari, Galletti et al. 2007, Boller and He 2009, Dodds and Rathjen 2010). The
59 evolution of large-effect qualitative loci has partly been driven by the narrow host range
60 for the pathogen that enhances co-evolution between host resistance genes and
61 pathogen virulence mechanisms.

62 In contrast to specialist pathogens, generalist pathogens are virulent across a
63 wide range of plant host species. Generalist pathogens potentially have less stringent
64 co-evolution to specific hosts and their accompanying resistance mechanisms, because
65 these pathogens can easily shift to new hosts in the environment. This allows generalist
66 pathogens to evade the rapid evolution of new resistance mechanisms within specific
67 hosts until they evolve to counter this new resistance. This niche-shifting ability may
68 partially explain the observation that most natural resistance to generalist pathogens is
69 highly polygenic, and the underlying plant genes for resistance are quantitative
70 (Glazebrook 2005, Nomura, Melotto et al. 2005, Goss and Bergelson 2006, Rowe and
71 Kliebenstein 2008, Barrett, Kniskern et al. 2009, Corwin, Copeland et al. 2016). Plant
72 quantitative resistance genes to generalist pathogens include a broad array of direct
73 defense genes, like those involved in secondary metabolite production, cell wall
74 formation, and defense proteins (Zhang, Khan et al. 2002, Denby, Kumar et al. 2004,
75 Zipfel, Robatzek et al. 2004, Ferrari, Galletti et al. 2007, Rowe and Kliebenstein 2008,
76 Poland, Balint-Kurti et al. 2009, Corwin, Copeland et al. 2016). Importantly, these
77 quantitative plant resistance loci do not alter resistance to all genotypes (isolates) of a
78 pathogen but interact with the infecting pathogen's genotype. For example, the ability of
79 the *Arabidopsis* defense metabolite, camalexin, to provide resistance to *Botrytis cinerea*
80 depends upon whether the specific isolate is sensitive or resistant to camalexin
81 (Kliebenstein, Rowe et al. 2005, Pedras and Ahiaonu 2005, Stefanato, Abou-Mansour
82 et al. 2009, Pedras, Hossain et al. 2011) and similarly *B. cinerea* virulence on tomato

83 varies with the isolate's ability to detoxify tomatine (Quidde, Osbourn et al. 1998,
84 Quidde, Büttner et al. 1999). In contrast to the polygenic nature of plant resistance to
85 generalist pathogens, little is known about the genetic architecture of virulence within
86 generalist pathogens, and how this is affected by genetic variation in the plant (Bartoli
87 and Roux 2017). There are no reported naturally variable large-effect virulence loci in
88 generalist pathogens, suggesting that virulence in generalist pathogens is largely
89 quantitative and polygenic. This potential for interaction between polygenic virulence in
90 generalist pathogens and equally polygenic resistance in host plants suggests that we
91 need to work with genetic variation in both the host and pathogen to truly understand
92 quantitative host-pathogen interactions.

93 Domestication of crop plants is a key evolutionary process in plants that has
94 affected resistance to specialist pathogens. Domesticated plant varieties are typically
95 more sensitive to specialist pathogens than their wild relatives (Smale 1996, Rosenthal
96 and Dirzo 1997, Couch, Fudal et al. 2005, Dwivedi, Upadhyaya et al. 2008), and
97 pathogens may evolve higher virulence on domesticated hosts (Stukenbrock and
98 McDonald 2008). Further, domestication typically imposes a genetic bottleneck that
99 reduces genetic diversity in the crop germplasm, including decreased availability of
100 resistance alleles against specialist pathogens (Tanksley and McCouch 1997, Doebley,
101 Gaut et al. 2006, Chaudhary 2013). These general evolutionary patterns, of reduced
102 resistance and allelic diversity found when studying the interaction of specialist
103 pathogens with crop plants, are assumed to hold for generalist pathogens and their
104 domesticated hosts. However, there is less information about how crop host
105 domestication affects disease caused by generalist pathogens, when the resistance to
106 these pathogens is quantitative and polygenic rather than qualitative and monogenic. As
107 such, there is a need to quantify the effect of domestication on a broad generalist
108 pathogen in comparison to the rest of the crop's standing variation to test how and if
109 domestication influences the pathogen.

110 *Botrytis cinerea* provides a model generalist pathogen for studying quantitative
111 interactions with plant hosts and underlying evolutionary processes. *B. cinerea* is a
112 broad generalist pathogen that can infect most tested plants, from bryophytes to
113 eudicots, and causes wide ranging pre- and post-harvest crop losses (Nicot and Baille

114 1996, Elad, Williamson et al. 2007, Fillinger and Elad 2015). Individual isolates of *B.*
115 *cinerea* show the same broad host range (Deighton, Muckenschnabel et al. 2001,
116 Finkers, van Heusden et al. 2007, Ten Have, van Berloo et al. 2007, Corwin, Subedy et
117 al. 2016). This is in contrast to pathogens like *Fusarium oxysporum* where the species
118 can infect diverse hosts, but each isolate is highly host specific (Katan 1999, Ormond,
119 Thomas et al. 2010, Loxdale, Lushai et al. 2011, Barrett and Heil 2012). *B. cinerea*
120 isolates display significant variation in virulence phenotypes, partly due to genetic
121 variation in specific virulence mechanisms, like the production of the phytotoxins,
122 botrydial and botcnic acid (Siewers, Viaud et al. 2005, Dalmais, Schumacher et al.
123 2011). This genetic variation also influences cell wall degrading enzymes and key
124 regulators of virulence like *VELVET* that quantitatively control virulence on multiple host
125 plants (Rowe and Kliebenstein 2007, Schumacher, Pradier et al. 2012). This standing
126 diversity in virulence mechanisms can contribute to the formation of quantitative
127 differences in virulence between the isolates (ten Have, Mulder et al. 1998). The
128 phenotypic variation is driven by a high level of sequence diversity spread across the
129 genome (Rowe and Kliebenstein 2007, Fekete, Fekete et al. 2012). The polymorphism
130 rate in *B. cinerea*, 37 SNP/kb, is much more variable than most previously studied plant
131 pathogens (1-2 SNP/kb in *Blumeria graminis*, 1.5 SNP/kb in *Melampsora larici-populina*,
132 5.5 SNP/kb in the compact genome of the obligate biotroph *Plasmodiophora brassicae*,
133 12.3 SNP/kb in the wheat stem rust pathogen *Puccinia graminis* f. sp. *tritici*) and human
134 pathogens (3-6 SNP/kb in *Mycobacterium tuberculosis*). In addition to SNP diversity, the
135 genomic sequencing showed that *B. cinerea* has a high level of recombination and
136 genomic admixture, as if it were a randomly intermating population (Supplemental
137 Figure 1) (Atwell, Corwin et al. 2018). As such, a collection of *B. cinerea* isolates contain
138 genetic variation in a wide range of virulence mechanisms, offering the potential to
139 challenge the host with a blend of diverse virulence mechanisms to identify the
140 pathogen variation controlling quantitative virulence .

141 A model pathosystem for studying quantitative host-pathogen interactions is the
142 tomato-*B. cinerea* system, where the pathogen causes crop loss due to both pre- and
143 post-harvest infection (Dean, Van Kan et al. 2012, Hahn 2014, Romanazzi and Droby
144 2016). Resistance to *B. cinerea* is a quantitative trait in tomato as with most other

species, with identified tomato QTLs each explaining up to 15% of phenotypic variation for lesion size on stems (Diaz, ten Have et al. 2002, Finkers, van Heusden et al. 2007, Ten Have, van Berloo et al. 2007, Rowe and Kliebenstein 2008, Corwin, Copeland et al. 2016). Tomato is also a key model system to study how domestication influences plant physiology and resistance, including alterations in the circadian clock (Tanksley 2004, Bai and Lindhout 2007, Panthee and Chen 2010, Bergougnoux 2014, Müller, Wijnen et al. 2016), which can modulate resistance to *B. cinerea* (Sauerbrunn and Schlaich 2004, Weyman, Pan et al. 2006, Bhardwaj, Meier et al. 2011, Hevia, Canessa et al. 2015). This suggests that host plant diversity within tomato can alter traits known from other systems to influence *B. cinerea* resistance. Tomato domestication is typically considered a single event, followed by extensive crop improvement (Lin, Zhu et al. 2014, Blanca, Montero-Pau et al. 2015). Thus, we are using the tomato-*B. cinerea* pathosystem to directly measure the interaction of domesticated crop variation with genetic variation in a generalist pathogen to better understand the evolution of this pathosystem.

In this study, we infected 97 genetically diverse *B. cinerea* isolates on a collection of domesticated tomato, *S. lycopersicum*, and wild tomato, *S. pimpinellifolium*, and quantified the interaction through lesion size in a detached leaf assay. Previous studies have examined *B. cinerea* resistance between domesticated and wild tomato species using single isolates of pathogens (Egashira, Kuwashima et al. 2000, Nicot, Moretti et al. 2002, Guimaraes, Chetelat et al. 2004, Ten Have, van Berloo et al. 2007, Finkers, Bai et al. 2008). These previous studies typically used individual wild and domesticated tomato accessions that were the founders of mapping populations and found a wide range of *B. cinerea* resistance. However, it is still unknown how domesticated and wild tomatoes compare for *B. cinerea* resistance using multiple plant genotypes and a population of the pathogen. We selected accessions to sample major geographic origins of the progenitor species, and focused the domesticated germplasm on diverse mid- to late- 20th century improved germplasm (Lin, Zhu et al. 2014, Blanca, Montero-Pau et al. 2015). In this study, we asked whether *B. cinerea* virulence was controlled by host variation, pathogen variation, or the interaction between them. Lesion size of *B. cinerea* is a quantitative trait that was controlled by plant domestication status, plant genotype

176 and pathogen isolate. Finally, we aimed to identify the genetic basis of variation in *B.*
177 *cinerea* virulence on *S. lycopersicum* and *S. pimpinellifolium*. We conducted genome-
178 wide association (GWA) in *B. cinerea* to identify pathogen loci where genetic variation
179 leads to altered virulence across the host genotypes, including a specific test for loci
180 that influence responses to crop domestication. Few studies have conducted GWA in
181 plant pathogens for virulence phenotypes, and most of these were limited by few
182 variable loci or few genetically distinct isolates (Dalman, Himmelstrand et al. 2013, Gao,
183 Liu et al. 2016, Talas, Kalih et al. 2016, Wu, Sakthikumar et al. 2017). Our previously-
184 sampled isolate collection includes genetic diversity across 272,672 SNPs
185 (Supplemental Figure 1) (Atwell, Corwin et al. 2015, Zhang, Corwin et al. 2017, Atwell,
186 Corwin et al. 2018). We found that the genetic architecture of virulence of *B. cinerea* is
187 highly quantitative, with hundreds of significant SNPs with small effect sizes associated
188 with lesion area on each tomato genotype. Importantly, there is a subset of loci in the
189 pathogen where allelic variation gives the isolates opposing responses to crop
190 domestication. These pathogen loci could provide tools for understanding how
191 domestication in tomato has influenced generalist pathogen resistance, to inform
192 breeding efforts.

193

194 **Results**

195 **Experimental Design**

196 To measure how tomato genetic variation affects quantitative resistance to a
197 population of a generalist pathogen, we infected a collection of 97 diverse *B. cinerea*
198 isolates (genotypes) on wild and domesticated tomato genotypes. We selected 6
199 domesticated *Solanum lycopersicum* and 6 wild *S. pimpinellifolium* accessions, the
200 closest wild relative of *S. lycopersicum*, to directly study how domestication has
201 influenced resistance to *B. cinerea* (Peralta, Spooner et al. 2008, Müller, Wijnen et al.
202 2016)(Supplemental Figure 2). Our previously collected *B. cinerea* sample includes 97
203 isolates obtained from various eudicot plant hosts, including tomato stem tissue (2
204 isolates; T3, KT) and tomato fruit (3 isolates; KGB1, KGB2, Supersteak) (Atwell, Corwin
205 et al. 2015, Zhang, Corwin et al. 2017, Atwell, Corwin et al. 2018). We infected all 97 *B.*
206 *cinerea* isolates onto each of the 12 plant genotypes in 3-fold replication across 2

207 independent experiments in a randomized complete block design, giving 6
208 measurements per plant-pathogen combination, for a total of 3,276 lesions. Digital
209 measurement of the area of the developing lesion provides a composite phenotype
210 controlled by the interaction of host and pathogen genetics. This measurement of the
211 plant-*B. cinerea* interaction has been used successfully in a number of molecular and
212 quantitative genetic studies (Ferrari, Plotnikova et al. 2003, Denby, Kumar et al. 2004,
213 Kliebenstein, Rowe et al. 2005, Ferrari, Galletti et al. 2007, Ten Have, van Berloo et al.
214 2007, AbuQamar, Chai et al. 2008, Rowe and Kliebenstein 2008, Liu, Hong et al. 2014).
215 It should be noted that we are not focusing on MAMP or PAMP specific host/pathogen
216 interactions with this study; we are instead allowing the identification of any mechanism
217 that may influence the host/pathogen interaction including metabolism, development or
218 any other unknown component. If there is genetic variation affecting the trait, and the
219 trait influences the interaction of host and pathogen, it will be a component of the
220 experiment. This fits with the recently developing view that growth, development and
221 resistance in plants are highly integrated processes that may not be as distinct as once
222 believed (Campos, Yoshida et al. 2016, Ballaré and Pierik 2017, Züst and Agrawal
223 2017, Izquierdo-Bueno, González-Rodríguez et al. 2018).

224

225 **Lesion size (phenotypic) variation**

226 We collected images of all lesions at 24, 48, and 72 hours post inoculation. At 24 hours,
227 no visible lesions were present on the tomato leaves. At 48 hours, a thin ring of primary
228 lesion became visible surrounding the location of the spore droplet, but no expansion
229 was visible. At 72 hours significant lesion growth was visible, but no lesions had spread
230 to infect over half of the leaflet. We digitally measured the area of all developing lesions
231 at 72 hours post infection (HPI) as a measure of virulence (Figure 1). We use the linear
232 measurement of lesion area for several reasons. First, in previous work 72 HPI *B.*
233 *cinerea* lesion area growth appears to enter a relatively linear growth phase (Rowe,
234 Walley et al. 2010). Secondly, previous research has shown that the linear
235 measurement behaves as a normally distributed trait (Kliebenstein, Rowe et al. 2005,
236 Corwin, Copeland et al. 2016, Atwell, Corwin et al. 2018, Fordyce, Soltis et al. 2018).
237 And finally, previous work has shown that *Botrytis* isolates display large variation in their

unit biomass per lesion area and as such growth in biomass is not the sole factor driving this measure (Corwin, Subedy et al. 2016). We observed a mean lesion size of 0.67 cm² across the full experiment, with 0.94 CV across the full isolate population on all tomato genotypes. Individual isolates were highly variable in their lesion size across tomato genotypes (Figure 1c-h), with mean lesion size per isolate of 0.14 cm² to 1.29 cm², and individual isolate coefficient of variation (CV) from 0.51 to 1.68 across all observations on all tomato genotypes (Supplemental Data Set 1). A subset of these isolates is highly virulent on tomato (mean lesion size > 1.05 cm², Figure 1e), and a subset can be considered saprophytic (mean lesion size < 0.3 cm², Figure 1f). Lesion size of *B. cinerea* on tomato showed a weak positive correlation with lesion size on *A. thaliana* from previous studies; both on domesticated tomato ($r=0.247$, $p= 0.003$) and on wild tomato ($r=0.301$, $p= 0.016$) (Supplemental Figure 3)(Zhang, Corwin et al. 2017). This lack of correlation suggests the presence of both shared and unique mechanisms of quantitative virulence in the two species.

To measure the relative contribution of genetic diversity in the plant and the pathogen to variation in the virulence/ susceptibility phenotype, we used a general linear model (R lme4 package;(Bates, Maechler et al. 2015)). This model directly tested the contribution of pathogen genotype (isolate), plant genotype, and plant domestication status to variation in lesion size. The final model showed that genetic variation within both the host plant and the pathogen had significant effects on lesion growth, each explaining approximately the same portion of the variance (Table 1 and Figure 1c). Interestingly, while tomato domestication status significantly impacted *B. cinerea* virulence, it was to a much lower level than the other factors (Table 1). There was no evidence for significant interaction effects between pathogen isolate and plant genotype. Thus, the interaction between tomato and *B. cinerea* was significantly controlled by genetic diversity within the host plant and the pathogen, including a slight effect of domestication status.

Table 1. ANOVA results of the interaction between 12 tomato accessions and 95 *B. cinerea* isolates measured as lesion area.

269 Results of general linear modelling of lesion area for 12 tomato accessions by 95 *B.*
 270 *cinerea* isolates is shown (R lme4 package version 1.1-18-1;(Bates, Maechler et al.
 271 2015)). Two of our 97 isolates did not have replication across 2 experiments, so they
 272 were dropped at this stage of analysis. The terms are as follows; Isolate is the 95 *B.*
 273 *cinerea* isolates, Domestication is wild tomato, *S. pimpinellifolium*, versus domesticated
 274 tomato, *S. lycopersicum*, Plant is 12 tomato genotypes nested within their respective
 275 domestication groupings, Experiment tests the random effect of 2 independent replicate
 276 experiments. The nested random effects of whole plant sampled, leaf sampled, and
 277 leaflet pair are included. In addition, interactions of these factors are tested (:). The
 278 degrees of freedom and p-value are shown. For fixed effects, the type II sum of squares
 279 and F-value are shown, and for random effects the likelihood ratio test statistic (LRT) is
 280 shown.
 281

Fixed Effect	SS	F value	DF	p
Isolate	37.8	1.7	94	0.007
Domestication	3.4	14.1	1	0.0006
Domest/Plant	39.3	16.2	10	5e-11
Iso:Domest	15.8	0.7	94	0.99
Iso:Domest/Plant	179.1	0.8	940	1
Random Effect	LRT	DF	p	
1 Experiment	136	1	<2e-16	
1 Whole Plant	0.21	1	0.65	
1 WP/Leaf	22.4	1	2e-06	
1 WP/Leaf/Leaflet Pair	0	1	1	
1 Exp:Iso	321	1	<2e-16	

282

283 Pathogen Specialization to Source Host

284 One evolutionary model of plant-generalist pathogen interactions suggests that
 285 pathogen isolates within a generalist species may specialize for interaction with specific
 286 hosts. Alternatively, generalist isolates may show no host specialization or preference.
 287 Our collection of *B. cinerea* includes five isolates that may be adapted to tomato, as
 288 they were collected from *S. lycopersicum*. To test if there is evidence for specialization
 289 to the source host, we compared the virulence of the *B. cinerea* isolates obtained from
 290 tomato to the broader pathogen population. For *B. cinerea* genotypes isolated from
 291 tomato tissue vs. other hosts, there was no significant difference in lesion size across all
 292 tomato genotypes (t-test; n = 97, p=0.14) (Figure 1g). In fact, one isolate collected from
 293 tomato tissue (KGB1) was within the 10 least-virulent isolates and another (Triple3) was
 294 within the 10 most-virulent isolates (Figure 1g). This demonstrated significant genetic

295 variation in virulence across the *B. cinerea* isolates, and that this collection of *B. cinerea*
296 isolates from tomato do not display a strong host-specificity for tomato (Martinez,
297 Blancard et al. 2003, Ma and Michailides 2005, Rowe and Kliebenstein 2007, Samuel,
298 Veloukas et al. 2012).

299

300 **Pathogen Specialization to Host Genotype**

301 Though we did not find evidence for *B. cinerea* preference for tomato based on isolate
302 host source, the *B. cinerea* isolates may contain genetic variation at individual loci that
303 allow them to better attack subsets of the tomato genotypes (Rowe and Kliebenstein
304 2007, Kretschmer and Hahn 2008, Corwin, Subedy et al. 2016). A visual analysis of the
305 data suggested an interaction between the genomes of *B. cinerea* and tomato (Figure 1
306 c-h). However, when using the full model, we found no significant interaction between
307 isolate and individual host genotype, even though there was a large fraction of variance
308 within these terms (Table 1). This may indicate a lack of interaction between genetic
309 variation in the host and pathogen. Interaction effects in large datasets can be difficult to
310 identify using mixed models, so we used a second standard statistical approach, a
311 Wilcoxon signed-rank test. We used model-adjusted lesion sizes as input to test if the
312 rank of *B. cinerea* isolate-induced lesion size significantly changes between pairs of
313 tomato genotypes. This showed that when using the full isolate population, the rank
314 performance of the isolates does significantly vary between host genotypes. When
315 comparing mean lesion size between paired plant genotypes, 59% (39 out of 66) of
316 tomato accession pairs had significantly different ranking of the isolates (Wilcoxon
317 signed-rank test with Benjamini-Hochberg FDR-correction, Table 2, Supplemental
318 Figure 4). A significant p-value indicates that the two host genotypes show evidence for
319 different virulence interactions with the population of *B. cinerea* isolates, providing
320 evidence for host x pathogen genotypic interactions. This pattern was consistent across
321 domesticated host pairs, wild host pairs, or between-species host pairs (Wilcoxon
322 signed-rank test with B-H FDR-correction, Table 2). This provides evidence that the
323 population of *B. cinerea* does display differential responses to the tomato genetic
324 variation.

325 To focus on whether specific *B. cinerea* isolates may be sensitive to tomato
326 domestication, we applied a Wilcoxon and ANOVA approach. Overall, most isolates
327 (78/97, 80%) are more virulent on domesticated than wild tomato (Figure 3;
328 Supplemental Data Set 1). Using a Wilcoxon signed-rank test to compare the rank of
329 model-corrected mean lesion size of all the *B. cinerea* isolates on wild versus
330 domesticated tomato we found a significant difference (Wilcoxon signed-rank test, $W =$
331 5801, p -value = 0.0007) (Figure 3). While this shows a general population behavior, we
332 used single-isolate ANOVAs to test if any specific pathogen genotypes had a significant
333 association with domestication. These general linear models included the fixed effects
334 of plant, domestication, and the random effect of experiment. After adjusting for multiple
335 testing, this identified two isolates (Fd2, Rose) with a significant effect of domestication
336 on lesion size ($p < 0.05$, FDR corrected) (Figure 1h), both of which are more virulent on
337 domesticated tomato (Supplemental Data Set 3).

338 To assess whether isolates could appear domestication-associated due to
339 random chance, we bootstrapped assignment of plant accessions to domestication
340 groups. 96 of the 100 bootstraps identified no isolates with domestication sensitivity,
341 and the other four bootstraps identified only 2 isolates showing significant domestication
342 association (FDR <0.01). Therefore, our individual isolate observations are in the 96th
343 percentile. While this is suggestive, a more precise estimate of isolate x domestication
344 interactions would require larger experiments using either more replication or additional
345 plant genotypes.

346

347 **Table 2. Rank order shifts of 97 *B. cinerea* isolates by lesion area across all of the**
348 **tomato accessions.**

349 Wilcoxon signed-rank test on comparing model-corrected mean *B. cinerea* lesion area
350 on tomato accessions. This tests for a change in the rank order of the 97 isolates
351 between each pair of tomato accessions. A significant p -value suggests that the relative
352 performance of individual isolates is altered from one host to the other. The lower left
353 corner of the chart includes B-H FDR-corrected p -values, the upper right corner
354 includes the test statistic (W). Bold text indicates significance at $p < 0.01$ after
355 correction, italicized text indicates suggestive p -values $0.01 < p < 0.1$. NS shows non-
356 significant interactions.

Wild						Domesticated					
LA1547	LA1589	LA1684	LA2093	LA2176	LA480	LA2706	LA3008	LA3475	LA410	LA4345	LA4355

			2978	3988	2927	1865	3008	1710	3460	1597	1135	3928	2944	
Wild	LA1589	LA1547	<0.001		5401	4699	3359	4662	3014	4918	2938	2340	5536	4454
	LA1684		NS	0.029		3709	2552	3690	2296	4004	2205	1690	4537	3571
	LA2093	LA2176	<0.001	NS	0.049		3013	4496	2732	4889	2588	1947	5534	4264
	LA480	LA2706	<0.001	0.004	<0.001	<0.001		5837	4029	6002	3963	3276	6706	5583
	LA3475	LA3008	<0.001	NS	0.044	NS	0.001		6143	4192	6286	6855	3575	4702
Domesticated	LA410	LA2706	<0.001	<0.001	<0.001	<0.001	NS	<0.001		6311	4523	3876	6917	5940
	LA4345	LA4355	0.009	NS	NS	NS	<0.001	NS	<0.001		2619	2082	5100	4049
	LA4355	LA410	<0.001	<0.001	<0.001	<0.001	NS	<0.001	NS	<0.001		3815	7088	5984
	LA4345		<0.001	<0.001	<0.001	<0.001	0.002	<0.001	NS	<0.001	NS		7567	6602
			0.16	0.011	NS	0.011	<0.001	0.021	<0.001	NS	<0.001	<0.001		3439
			<0.001	NS	0.02	NS	0.008	NS	<0.001	NS	<0.001	<0.001	<0.001	

358

359

360 Domestication and Lesion Size Variation

361 Existing literature predominantly reports that crop domestication decreases plant
 362 resistance to pathogens (Smale 1996, Rosenthal and Dirzo 1997, Couch, Fudal et al.
 363 2005, Dwivedi, Upadhyaya et al. 2008, Stukenbrock and McDonald 2008). While we did
 364 observe the expected decreased resistance (by 18%) in domesticated tomato (Figure 2
 365 and 3, Table 1), domestication was a minor player in controlling lesion size variation,
 366 with most of the plant genetic signature coming from variation within both the wild and
 367 domesticated tomato species, contributing 12-fold more variation in resistance than
 368 domestication alone (Table 1). Removing the two domestication-associated isolates
 369 (Fd2, Rose) from our population did not eliminate the effect of tomato domestication on
 370 lesion size, as it was still significant and *B. cinerea* was still more virulent on
 371 domesticated tomato by 17% (Supplemental Table 1). To test how this mild
 372 domestication effect might be sensitive to shifts in the collection of tomato genotypes,

373 we used the same bootstraps from above for the full model. Our observed
374 domestication effect was in the top 80th percentile across all bootstraps, suggesting that
375 while the domestication effect is small, it is relatively stable in response to shifts in the
376 genotypes. However, a larger sample of *S. lycopersicum* and *S. pimpinellifolium*
377 genotypes would be needed to develop a more precise estimate of any domestication
378 effect on lesion size.

379 In addition to altering trait means, domestication commonly decreases genetic
380 variation in comparison to wild germplasm due to bottlenecks, including for tomato
381 (Tanksley and McCouch 1997, Doebley, Gaut et al. 2006, Bai and Lindhout 2007). We
382 would expect this decreased genetic variation to limit phenotypic variation, including
383 disease phenotypes. Interestingly in this tomato population, we did not observe reduced
384 variation in lesion size in the domesticated tomato. The wild and domesticated tomato
385 genotypes showed similar variation in resistance (F -test, $F_{96,96}=1.39$, $p=0.11$) (Figure 3,
386 Supplemental Figure 2). Overall, there is a slight domestication impact on average
387 resistance to *B. cinerea*, and no evidence of a phenotypic bottleneck due to
388 domestication. This suggests that in the tomato-*B. cinerea* pathosystem, domestication
389 is not a major part of the variation.

390

391 Quantitative Genetics of Pathogen Virulence on Tomato

392 Genetic variation within *B. cinerea* had a large effect on virulence on tomato and
393 showed some evidence for interaction with tomato domestication (Table 1). This
394 suggests that there is genetic variation within the pathogen, in which some alleles
395 enhance, and other alleles decrease virulence depending upon the plant's genotype. To
396 identify variable pathogen genes controlling differential virulence across plant
397 genotypes, we conducted GWA mapping analysis within the pathogen, using 272,672
398 SNPs compared to the *B. cinerea* T4 reference genome (Supplemental Figure 1)
399 (Atwell, Corwin et al. 2018). Due to the large effect of plant genotype on resistance to *B.*
400 *cinerea*, we performed GWA using model-corrected least-squared mean virulence
401 measured on each tomato genotype as separate traits. We used a ridge-regression
402 approach (bigRR) to estimate the phenotypic effects across the genome (Shen, Alam et
403 al. 2013, Corwin, Copeland et al. 2016, Corwin, Subedy et al. 2016, Francisco, Joseph

404 et al. 2016, Atwell, Corwin et al. 2018). To determine significance of SNP effects under
405 GWA, we permuted phenotypes 1000 times to calculate 95, 99, and 99.9% effect size
406 thresholds within each plant host. At 1000 permutations, the 99.9% threshold is
407 imprecise, but we included this approximate threshold to identify conservative SNP
408 associations. GWA analysis showed that the genetic basis of *B. cinerea* virulence on
409 tomato is highly polygenic. Consistent with a polygenic structure of this trait in the
410 pathogen, GWA did not identify large-effect SNPs (Figure 4). The number of significant
411 *B. cinerea* virulence SNPs identified by this ridge-regression approach (bigRR) varied
412 by plant accession, from 1,284 to 25,421 SNPs on the 12 different host genotypes
413 (significance was determined by the SNP effect size estimate exceeding the 99% 1000-
414 permutation threshold).

415 At the SNP level, fewer loci contribute to virulence across all host genotypes. We
416 found five *B. cinerea* SNPs significantly linked to altered lesion size on all 12 tomato
417 accessions (Figure 4b). 215 SNPs were called in at least ten hosts, and 3,300 SNPs
418 were called in at least half of the hosts while 27% (46,000) of the significant SNPs were
419 linked to virulence on only a single host tomato genotype. These levels of overlap
420 exceed the expected overlap due to random chance (Figure 5a). While only a small
421 subset of these *B. cinerea* SNPs were linked to virulence on all the tomato genotypes,
422 we obtained better overlap across host genotypes by focusing on gene windows.

423 To focus on the small-effect genes linked to *B. cinerea* virulence, we classified a
424 gene as significantly associated if there was 1 SNP linked to a trait using a 2kb window
425 surrounding the start and stop codon for a given gene. This analysis identified 14 genes
426 linked to differential virulence in all 12 tomato accessions by bigRR (Figure 5b,
427 Supplemental Data Set 2a), as some SNPs within a gene had accession-specific
428 phenotypes (significant in <12 tomato accessions). A further 1045 genes were linked to
429 differential virulence on 7 to 11 of the tomato accessions by bigRR (Figure 5b,
430 Supplemental Data Set 2a).

431 Of the 14 genes with SNPs significantly associated with *B. cinerea* virulence on
432 all tomato genotypes by bigRR, most have not been formally linked to pathogen
433 virulence. However, SNPs within a pectinesterase gene (BcT4_6001, Bcin14g00870)
434 were associated to virulence across 11 tomato accessions. Pectinesterases are key

435 enzymes for attacking the host cell wall, suggesting that variation in this pectinesterase
436 locus and the other loci may influence pathogen virulence across all the tomato
437 genotypes (Valette-Collet, Cimerman et al. 2003). Therefore, as an example of a
438 virulence gene identified by our GWA methods, we looked for evidence of multiple
439 haplotypes in this locus linked to virulence by visualizing the SNP effects across the
440 pectinesterase gene. We plotted the effect sizes for all SNPs in this gene and
441 investigated the linkage disequilibrium amongst these SNPs (Figure 6). This showed
442 that the effect of SNPs across this gene vary in effect direction depending on tomato
443 host genotype (Figure 6a). We identified two haplotype blocks contributing to the
444 association of this gene to the virulence phenotype (Figure 6b). One block is associated
445 with SNPs in the 5' untranslated region in SNPs 5-11, and the second block is SNPs
446 that span the entirety of the gene in SNPs 13-26. Interestingly, there are only two SNPs
447 in the open reading frame of the associated gene (Figure 6). This suggests that the
448 major variation surrounding this locus is controlling the regulatory motifs for this
449 pectinesterase. Thus, there is significant genetic variation in *B. cinerea* virulence that is
450 dependent upon the host's genetic background. This suggests that the pathogen relies
451 on polygenic small effect loci, potentially allowing selection to customize virulence on
452 the different tomato hosts.

453

454

455 **Quantitative Genetics of Pathogen Response to Tomato Domestication**

456 The identification of two isolates that differed on wild and domesticated tomato
457 indicated that there may be some natural genetic variation in *B. cinerea* linked to this
458 phenotypic variation. To directly map *B. cinerea* genes that control differential virulence
459 on wild versus domesticated tomatoes, we used the least-squared mean virulence of
460 each isolate across all wild and all domesticated tomato genotypes as two traits. We
461 also calculated a domestication sensitivity trait; the relative difference in lesion size for
462 each isolate between domesticated and wild hosts. Using these three traits, we
463 conducted bigRR GWA within *B. cinerea* to map genes in the pathogen that respond to
464 domestication shifts in the plant. Using the mean lesion area of the *B. cinerea* isolates
465 on the wild or domesticated tomato hosts identified a complex, highly polygenic pattern

466 of significant SNPs, similar to the individual tomato accessions (Figure 4, Figure 7). The
467 significant SNP sets had a high degree of overlap between the wild phenotype and
468 domesticated phenotype. In contrast, Domestication Sensitivity identified a more limited
469 set of SNPs with less overlap to the mean lesion area on either Domesticated or Wild
470 tomato (Figure 7). To query the underlying gene functions for these *B. cinerea* loci, we
471 called genes as significant if there was one SNP within 2kb of the gene (Figure 7c).
472 Using all 1251 genes linked to domestication traits by bigRR for a functional enrichment
473 analysis found only 22 significantly overrepresented biological functions (Fisher exact
474 test, p<0.05, Supplemental Data Set 2b) when compared to the whole-genome T4 gene
475 annotation. The enrichments were largely surrounding enzyme and transport functions,
476 which are known to be key components of how the pathogen produces toxic metabolites
477 and conversely detoxifies plant defense compounds. Thus, there is an apparent subset
478 of *B. cinerea* genes that may be specific to the genetic changes that occurred in tomato
479 during domestication. Further work is needed to assess if and how variation in these
480 genes may link to altered virulence on domesticated and wild tomatoes.

481

482 **Discussion**

483 The genetics of plant resistance to generalist pathogens are mostly quantitative,
484 depend upon pathogen isolate, and rely on genetic variation in both signal perception
485 and direct defense genes (Kover and Schaal 2002, Parlevliet 2002, Glazebrook 2005,
486 Nomura, Melotto et al. 2005, Goss and Bergelson 2006, Tiffin and Moeller 2006, Rowe
487 and Kliebenstein 2008, Barrett, Kniskern et al. 2009, Corwin, Copeland et al. 2016,
488 Zhang, Corwin et al. 2017). Previous studies of tomato resistance to *B. cinerea* have
489 found a quantitative genetic architecture that varies between domesticated and wild
490 tomato species, with higher resistance in the wild species (Egashira, Kuwashima et al.
491 2000, Nicot, Moretti et al. 2002, Guimaraes, Chetelat et al. 2004, Finkers, van Heusden
492 et al. 2007, Ten Have, van Berloo et al. 2007, Finkers, Bai et al. 2008). However, it was
493 not known how the choice of *B. cinerea* isolate may change this plant-pathogen
494 interaction. To address these questions, we used genetic variation in wild and
495 domesticated tomato accessions in conjunction with a population of *B. cinerea* isolates.
496 *B. cinerea* virulence on tomato, as measured by lesion size, was significantly affected

497 by pathogen isolate, host genotype, and domestication status (Table 1). Pathogen
498 isolate and tomato genotype were the strongest determinants of the interaction with only
499 a slight but significant decrease in resistance to the pathogen associated with
500 domestication. Equally, there was no evidence of a domestication bottleneck, with
501 similar variance in resistance between the wild and domesticated tomato accessions
502 (Table 1, Figure 2). There was also little evidence in this *B. cinerea* population for
503 specialization to tomato, supporting the hypothesis that *B. cinerea* is a generalist at the
504 isolate and species level (Figure 1 c-h) (Giraud, Fortini et al. 1999, Martinez, Blancard
505 et al. 2003, Ma and Michailides 2005). GWA mapping within the pathogen showed that
506 the genetics underlying *B. cinerea* virulence on tomato are highly quantitative and vary
507 across tomato genotypes and domestication status (Figure 5, Figure 7). This analysis
508 identified a small subset of pathogen genes whose variation contributes to differential
509 virulence on most of the hosts tested, and a set of pathogen genes whose variation is
510 responsive to tomato domestication (Supplemental Data Set 2 b).

511

512 **Domestication and altered pathogen virulence genetics**

513 In biotrophic pathogens, host domestication has decreased the diversity of
514 resistance alleles because they are lost in the domestication bottleneck as found for
515 specialist pathogens (Tanksley and McCouch 1997, Doebley, Gaut et al. 2006, Hyten,
516 Song et al. 2006, Chaudhary 2013). Surprisingly, we did not find evidence for a
517 domestication bottleneck in the phenotypic resistance to *B. cinerea* (Figure 2, Figure 3).
518 This is in contrast to genomic studies that explicitly show a genotypic bottleneck within
519 tomato domestication (Miller and Tanksley 1990, Koenig, Jiménez-Gómez et al. 2013).
520 Previous work in *A. thaliana* with these isolates has shown that if plant defenses such
521 as jasmonic acid and salicylic acid signaling are non-functional, there is increased
522 variation in *B. cinerea* virulence (Zhang, Corwin et al. 2017). Thus, if these pathways
523 had large effect differences between wild and domesticated tomato we would expect to
524 see a wider range of *B. cinerea* virulence phenotypes in domesticated tomato (Zhang,
525 Corwin et al. 2017). The similarity in the variance suggests that any differences we are
526 seeing are not caused by large effect changes that abolish or greatly diminish specific
527 defense signaling networks (Figure 2 and 3). These patterns, of mild decrease in

528 resistance to *B. cinerea* due to plant domestication, and within-species plant variation
529 exceeding the contribution of domestication itself, may be unique to interactions
530 between *B. cinerea* and tomato, or more general. It is unclear whether this pattern is
531 unique to tomato, or if each domestication event is unique.

532

533 **Polygenic quantitative virulence and breeding complications**

534 Our results indicate a highly polygenic basis of quantitative virulence of the
535 generalist *B. cinerea* on tomato similar to the highly polygenic basis on the host side of
536 the interaction (Zhang, Corwin et al. 2017). The variation in lesion size is linked to
537 numerous *B. cinerea* SNPs, each with small effect sizes (Figure 4a). Importantly, the
538 tomato host accession greatly influenced which *B. cinerea* loci were significantly
539 associated to lesion size (Figure 5). Thus, it is possible that there is specialization at the
540 gene level, in which different alleles within the pathogen link to differential virulence on
541 specific host genotypes (Giraud, Fortini et al. 1999, Rowe and Kliebenstein 2007,
542 Blanco-Ulate, Morales-Cruz et al. 2014). This polygenic architecture of virulence is
543 different from virulence architecture in specialist pathogens that often have one or a few
544 large effect genes that control virulence (Keen 1992, De Feyter, Yang et al. 1993,
545 Abramovitch and Martin 2004, Boyd, Ridout et al. 2013, Vleeshouwers and Oliver
546 2014). Further studies are needed to compare how the host plant species may affect
547 this image of genetic variation in virulence.

548 These results indicate particular challenges for breeding durable resistance to *B.*
549 *cinerea*, and possibly other generalist pathogens. The highly polygenic variation in
550 virulence, combined with genomic sequencing showing that this pathogen is an inter-
551 breeding population, suggests that the pathogen is actively blending a large collection of
552 polymorphic virulence loci (Rowe and Kliebenstein 2007, Fekete, Fekete et al. 2012,
553 Atwell, Corwin et al. 2015, Atwell, Corwin et al. 2018). Thus, it is insufficient to breed
554 crop resistance against a single isolate of *B. cinerea*, as this resistance mechanism
555 would likely be rapidly overcome by new genotypes within the field population of *B.*
556 *cinerea*. In contrast, it is likely necessary to breed resistance using a population of the
557 pathogen, and to focus on plant loci that target entire virulence pathways or
558 mechanisms. The results in this study indicate that the specific genetics of the plant

559 host, the host's general domestication status, and the specific genetics of the pathogen
560 isolate will all combine to affect how the estimated breeding value inferred from any
561 experiment will translate to a field application (Table 1). As such, utilizing a single or
562 even a few pathogen isolates to guide resistance breeding in plants is unlikely to
563 translate to durable resistance against *B. cinerea* as a species. Further, the lack of
564 evidence for a domestication bottleneck on tomato resistance to *B. cinerea* suggests
565 that, at least for tomato, allelic variation in this generalist pathogen is sufficient to
566 overcome introgression of wild resistance genes or alleles into the domesticated crop.

567 This study examined the contributions of host and pathogen natural genetic
568 variation to the quantitative interaction in the tomato-*B. cinerea* pathosystem. *B. cinerea*
569 has a highly quantitative genetic basis of virulence on tomato, which is dominated by
570 pathogen effects but also sensitive to genetic variation linked to tomato domestication.
571 Future studies are necessary to test if this pattern of domestication responses in tomato
572 is similar to patterns in other crops. Because this population of *B. cinerea* can infect a
573 wide range of hosts, it will be possible to directly conduct this study. By extending future
574 work to additional domestication events, it may be possible to test whether independent
575 crop domestication events have a consistent underlying genetic signal of *B. cinerea*
576 adaptation to plant domestication.

577

578 **Methods**

579 **Tomato genetic resources**

580 We obtained seeds for 12 selected tomato genotypes in consultation with the UC
581 Davis Tomato Genetics Resource Center. These include a diverse sample of 6
582 genotypes of domesticated tomato's closest wild relative (*S. pimpinellifolium*) sampling
583 across its major geographic regions (Peru, Ecuador) and 6 heritage and modern
584 varieties of *S. lycopersicum*, focusing on mid- to late-20th century improved varieties
585 (Lin, Zhu et al. 2014, Blanca, Montero-Pau et al. 2015). While genetic data is not
586 available for all of our *S. pimpinellifolium* accessions, 9 of the 12 accessions have been
587 genotyped and span the mappable diversity in domesticated tomato and its close
588 relatives (Sim, Durstewitz et al. 2012) (Supplemental Figure 2). We bulked all
589 genotypes in long-day (16h photoperiod) greenhouse conditions at UC Davis in fall

590 2014. We grew plants under metal-halide lamps using day/night temperatures at
591 25°C/18°C in 4" pots filled with standard potting soil (Sunshine mix #1, Sun Gro
592 Horticulture). Plants were watered once daily and pruned and staked to maintain upright
593 growth. Fruits were collected at maturity and stored at 4°C in dry paper bags until seed
594 cleaning. To clean the seeds, we incubated seeds and locule contents at 24°C in 1%
595 protease solution (Rapidase C80 Max) for 2h, then rinsed them in deionized water and
596 air-dried. We then stored seeds in a cool, dry, dark location until use.

597 To grow plants for detached leaf assays, we bleach-sterilized all seeds and
598 germinated them on paper in the growth chamber using flats covered with humidity
599 domes. At 7 days we transferred seedlings to soil (SunGro Horticulture, Agawam, MA)
600 and grew all plants in growth chambers in 20°C, short-day (10h photoperiod) conditions
601 with 180-190 uM light intensity and 60% RH. We bottom-watered with deionized water
602 every two days for two weeks, and at week 3 watered every two days with added
603 nutrient solution (0.5% N-P-K fertilizer in a 2-1- 2 ratio; Grow More 4-18-38). The plants
604 were used for detached leaf assays 6 weeks after transferring seedlings to soil.
605 Flowering in this system did not occur until minimally 9 weeks of age for any accession,
606 and as such we were sampling midway between the juvenile/adult transition and any
607 flowering time decision. This window has been successful to minimize any major
608 ontogenetic effects on the pathogen/host interaction in other systems (Corwin,
609 Copeland et al. 2016).

610

611 **B. cinerea genetic resources**

612 We utilized a previously described collection of *B. cinerea* isolates that were
613 isolated as single spores from natural infections of fruit and vegetable tissues collected
614 in California and internationally (Atwell, Corwin et al. 2015, Zhang, Corwin et al. 2017, Atwell,
615 Corwin et al. 2018). This included five isolates obtained from natural infections of tomato.
616 We maintained *B. cinerea* isolates as conidial suspensions in 30% glycerol for long-term
617 storage at -80°C. For regrowth, we diluted spore solutions to 10% concentration in filter-
618 sterilized 50% grape juice, and then inoculated onto 39g/L potato dextrose agar (PDA)
619 media. We grew isolates at 25°C in 12h light and propagated every 2 weeks.
620 Sequencing failed for 6 out of our 97 phenotyped isolates. For bigRR GWA mapping

621 with the 91 isolates genotyped in this study, we utilized a total of 272,672 SNPs against
622 the *B. cinerea* T4 genome with minor allele frequency (MAF) 0.20 or greater, and less
623 than 10% missing calls across the isolates (SNP calls in at least 82/ 91 isolates) (Atwell,
624 Corwin et al. 2018).

625

626 **Detached leaf assay**

627 To study the effect of genetic variation in host and pathogen on lesion formation,
628 we infected detached leaves of 12 diverse tomato varieties with the above 97 *B. cinerea*
629 isolates. We used a randomized complete block design for a total of 6 replicates across
630 2 experiments. In each experiment, this included a total of 10 plants per genotype
631 randomized in 12 flats in 3 growth chambers. Each growth chamber block corresponded
632 with a replicate of the detached leaf assay, such that growth chamber and replicate
633 shared the same environmental block. At 6 weeks of age, we selected 5 leaves per
634 plant (expanded leaves from second true leaf or younger), and 2 leaflet pairs per leaf.
635 We randomized the order of leaves from each plant, and the leaflets were placed on 1%
636 phytoagar in planting flats, with humidity domes. Our inoculation protocol followed
637 previously described methods (Denby, Kumar et al. 2004, Kliebenstein, Rowe et al.
638 2005). Spores were collected from mature *B. cinerea* cultures grown on canned peach
639 plates and diluted to 10 spores/ μ L in filter-sterilized 50% organic grape juice. Spores in
640 grape juice were maintained in 4°C refrigeration or on ice from the time of collection, to
641 inhibit germination prior to inoculation. The diluted spore suspensions were
642 homogenized by agitation continuously during the entire process of applying the spores
643 to all samples. This maintains the spores in the suspension and ensures even
644 application across samples, then 4 μ l droplets were placed onto the detached leaflets at
645 room temperature. The entire inoculation took approximately 2 hours of time per
646 experiment. Mock-inoculated control leaves were treated with 4 μ L of 50% organic grape
647 juice without spores. Digital photos were taken of all leaflets at 24, 48, and 72 hours
648 post inoculation and automated image analysis was used to measure lesion size.

649

650 **Automated Image Analysis**

651 Lesion area was digitally measured using the EBImage and CRIImage packages
652 (Pau, Fuchs et al. 2010, Failmezger, Yuan et al. 2012) in the R statistical environment
653 (R Development Core Team 2008), as previously described (Corwin, Copeland et al.
654 2016, Corwin, Subedy et al. 2016). Leaflets were identified as objects with green hue,
655 and lesions were identified as low-saturation objects within leaves. Images masks were
656 generated for both the leaf and lesion, then manually refined by a technician to ensure
657 accurate object calling. The area of these leaves and lesions were then automatically
658 measured as pixels per lesion and converted to area using a 1 cm reference within each
659 image.

660

661 **Data analysis**

662 We analyzed lesion areas using general linear models for the full experiment to
663 determine the contributions of plant and pathogen genotype(R lme4 package; (Bates,
664 Maechler et al. 2015))Two of our 97 isolates that did not have replication across 2
665 experiments were dropped at this stage of analysis. We used the following linear
666 models throughout our analyses.

667 Main mixed-effect model of lesion size variation

668 $Y = I + D/P + I:D + I:D/P + W_R/L/A + E_R + E_R:I$

669 Within-plant accession mixed-effect model of lesion size

670 $Y = I + W_R/L/A + E_R + E_R:I$

671 Within-isolate mixed-effect model of lesion size

672 $Y = D/P + E_R$

673

674 Where I represents fungal genotype (isolate), P represents plant genotype
675 (accession), D represents domestication status, E represents experiment, W represents
676 whole plant, L represents leaf, A represents leaflet position. Factors with the subscript R
677 are included in the analysis as random effects.

678 The within-plant accession model was used to calculate the significance of each
679 factor and to obtain the least-squared means of lesion size for each *B. cinerea* isolate x
680 tomato accession as well as for each *B. cinerea* isolate x domesticated/ wild tomato. We
681 also calculated a domestication sensitivity phenotype, Sensitivity = (Domesticated lesion
682 size – Wild lesion size) / Domesticated lesion size.

683 We bootstrapped assignment of plant accessions to domestication groups in
684 order to assess the robustness of our observed domestication effects. We randomly
685 drew three genotypes from the domesticated and wild groupings and assigned them to
686 a new pseudo-wild grouping. The other six genotypes were assigned as a pseudo-
687 domesticated grouping and the model was rerun. This bootstrapping was repeated 100
688 times with each representing a random draw. We used these to repeat the full model
689 and to repeat the individual isolate models, as a test of the robustness of the tomato
690 domestication effect.

691 Using tomato sequence data from the SolCAP diversity panel that contained 9 of
692 our 12 accessions, we determined pairwise genetic distances between our accessions
693 (Sim, Durstewitz et al. 2012). We calculated pairwise Euclidean distances between 426
694 wild and domesticated tomato accessions from Infinium SNP genotyping at 7,720 loci
695 using the R adegenet package (Jombart , Sim, Durstewitz et al. 2012). Clustering is by
696 R hclust (in the stats package) default UPGMA method (R Development Core Team
697 2008).

698 We used several methods to examine host specialization to tomato within *B.*
699 *cinerea*. First, we split our *B. cinerea* population into isolates collected from tomato
700 tissue vs. other hosts. We compared these groups by t-test for virulence on
701 domesticated tomato genotypes, wild tomato genotypes, or all tomato genotypes. Next,
702 we used a Wilcoxon signed-rank test to compare the rank order distribution of model-
703 adjusted lesion sizes across paired tomato genotypes. Also, to examine host
704 specialization to tomato domestication within *B. cinerea*, we used a Wilcoxon signed-
705 rank test to compare the rank order of model-adjusted lesion sizes across all
706 domesticated vs. all wild tomato genotypes. Finally, we conducted single-isolate
707 ANOVAs with FDR correction on general linear models to identify isolates with a
708 significant response to plant genotype or domestication status.

709 The model means and Domestication Sensitivity were used as the phenotypic
710 input for GWA using bigRR, a heteroskedastic ridge regression method that
711 incorporates SNP-specific shrinkage (Shen, Alam et al. 2013). This approach has
712 previously had a high validation rate (Ober, Huang et al. 2015, Corwin, Copeland et al.
713 2016, Francisco, Joseph et al. 2016, Kooke, Kruijer et al. 2016). The *B. cinerea* bigRR

714 GWA used 272,672 SNPs at MAF 0.20 or greater and <10% missing SNP calls as
715 described above (Atwell, Corwin et al. 2018). Because bigRR provides an estimated
716 effect size, but not a p-value, significance was estimated using 1000 permutations to
717 determine effect significance at 95%, 99%, and (approximately) 99.9% thresholds
718 (Doerge and Churchill 1996, Shen, Alam et al. 2013, Corwin, Copeland et al. 2016).
719 SNPs were annotated by custom R scripts with gene transfer format file construction
720 from the T4 gene models for genomic DNA by linking the SNP to genes within a 2kbp
721 window (<http://www.broadinstitute.org>, (Staats and van Kan 2012)). Functional
722 annotations are based on the T4 gene models for genomic DNA
723 (<http://www.broadinstitute.org>, *B. cinerea*; (Staats and van Kan 2012)). Additional genes
724 of interest, based on a broad literature search of known virulence loci, were taken from
725 NCBI (<https://www.ncbi.nlm.nih.gov/>) and included by mapping sequence to the T4
726 reference using MUMmer v3.0 (Kurtz, Phillippy et al. 2004).

727 To predict expected overlap of significant SNPs across plant genotypes, we used
728 the average number of significant SNPs per each of the 12 plant genotypes (14,000
729 SNPs) and calculated expected overlap between those 12 lists using binomial
730 coefficients. Functional annotations of the gene lists are based on the T4 gene models
731 for genomic DNA (<http://www.broadinstitute.org>, *B. cinerea*; (Staats and van Kan 2012)).
732

733 **Supplemental Data Files**

734 Supplemental Data Set 1. Mean \pm SE of *B. cinerea* lesion size of all isolates across all
735 tomato accessions.

736 Supplemental Data Set 2. Gene and Function Annotation from T4 GWA Results

737 Supplemental Data Set 3. Results of single-isolate ANOVA on mixed effect model

738 Supplemental Table 1. Results of ANOVA following removal of domestication-
739 associated isolates

740 Supplemental Figure 1. Allele frequency spectrum of *B. cinerea* SNPs.

741 Supplemental Figure 2. Genetic distance between selected tomato accessions

742 Supplemental Figure 3. Correlation between *B. cinerea* lesion size on tomato and on *A.*
743 *thaliana*

744 Supplemental Figure 4. Rank order plot of *B. cinerea* lesion size on two tomato
745 genotypes

746

747

748 **Figure Legends**

749

750 **Figure 1. *Botrytis cinerea* x tomato diversity in detached leaf assay and digital
751 image analysis.** a) Individual tomato leaflets of 6 *S. lycopersicum* genotypes and 6 *S. pum
752 pinellifolium* genotypes are in randomized rows, spore droplets of individual *B.
753 cinerea* isolates are in randomized columns. Digital images are collected 72 hours post
754 inoculation. Single droplets of 40 *B. cinerea* spores are infected on randomized leaflets
755 using randomized isolates, and digital images are taken 72 hours post inoculation.
756 b) Digital masking of leaf and lesion is followed by automated measurement of area for
757 each lesion.

758 c-h) Variation in lesion size resulting of the interaction of *B. cinerea* and diverse tomato
759 genotypes.

760 c) Average lesion size of single *B. cinerea* isolates (line traces) across tomato host
761 genotypes grouped by domestication status.

762 d) Highlight of the common reference *B. cinerea* isolate B05.10.

763 e) Highlight of the ten highest-virulence isolates, as estimated by mean virulence across
764 all tomato genotypes.

765 f) Highlight of the ten most saprophytic, or low virulence, isolates, as estimated by mean
766 virulence across all genotypes.

767 g) Highlight of the five isolates collected from tomato tissue.

768 h) Highlight of the two isolates with significant domestication sensitivity.

769

770 **Figure 2. Distribution of tomato genotype susceptibility to infection with 97
771 genetically diverse *B. cinerea* isolates.**

772 Violin plots show the distribution of lesion size caused by *B. cinerea* isolates on each
773 tomato host genotype. Individual points are mean lesion size for each of the 97 different
774 isolate-host pairs. The boxes show the 75th percentile distribution, and the horizontal
775 line shows the mean resistance of the specific host genotype. The tomato genotypes
776 are grouped based on their status as wild or domesticated germplasm.

777

778 **Figure 3. Distribution of *B. cinerea* virulence by tomato domestication status.**

779 The violin plots show the mean virulence of each *B. cinerea* isolate on the tomato
780 genotypes, grouped as wild or domesticated germplasm. The domestication effect on
781 lesion size is significant (Table 1 ANOVA, p=0.0006). The interaction plot between the
782 two violin plots connects the average lesion size of a single *B. cinerea* isolate between
783 the wild and domesticated germplasm.

784

785 **Figure 4. GWA of *B. cinerea* lesion size on individual tomato genotypes.**

786 Botrytis cinerea chromosomes are differentiated by shading, alternating light and dark
787 grey.

788 a) Manhattan plot of estimated SNP effect sizes from bigRR for *B. cinerea* lesion size
789 using a single tomato accession, LA2093. Permutation-derived thresholds are shown in
790 horizontal dashed lines.

791 b) The number of tomato accessions for which a *B. cinerea* SNP was significantly linked
792 to lesion development by bigRR using the 99% permutation threshold. Frequency is
793 number of phenotypes in which the SNP exceeds the threshold. Vertical dotted lines
794 identify regions with overlap between the top 100 large-effect SNPs for LA2093 and
795 significance across the majority (≥ 6) of tomato genotypes tested.

796

797 **Figure 5. Frequency of overlap in *B. cinerea* GWA significance across tomato
798 accessions.**

799 a) The frequency with which the *B. cinerea* SNPs significantly associate with lesion size
800 on the 12 tomato accessions using bigRR and the 99% permutation threshold. The
801 black line indicates the expected frequency of random overlap, given the number of
802 significant SNPs per plant genotype and size of total SNP set. The inset zooms in on
803 the distribution for overlapping SNPs above 6 plant genotypes for easier visualization.
804 There were no SNPs expected to overlap by random chance in the inset.

805 b) The frequency with which *B. cinerea* genes significantly associated with lesion size
806 on the 12 tomato accessions. Genes were called as significant if there was one
807 significant SNP called at the 99% permutation threshold within the gene body, or within
808 2kb of the gene body.

809

810 **Figure 6. Host specificity of significant SNPs linked to the gene BcT4_6001
811 (Bcin14g00870).**

812 a) SNPs with effects estimates above the 99% permutation threshold are colored by
813 trait (plant accession in which the effect was estimated). Wild accessions are oranges
814 (yellow to red shades) and domesticated accessions are blues (green to purple
815 shades). BcT4_6001 (Bcin14g00870) is a pectinesterase gene linked to at least one
816 significant SNP on all 12 of the tested tomato accessions by bigRR. The annotated
817 exons are depicted as turquoise rectangles, with the start codon marked with an arrow
818 indicating the direction of transcription. Red rectangles indicate corresponding linkage
819 disequilibrium blocks from Figure 6b.

820 b) Linkage disequilibrium plot, including all pairwise comparisons of SNPs in the 2kb
821 region surrounding Bcin14g00870. The color scheme for each SNP pair is D'/LOD:
822 white if LOD <2 and D' <1, bright red for LOD ≥ 2 and D'=1, intermediate shades for
823 LOD ≥ 2 and D'<1.

824

825 **Figure 7. GWA analysis of domestication sensitivity in *B. cinerea*.**

826 Domestication sensitivity of each isolate was estimated using the average virulence on
827 the wild and domesticated tomato germplasm and using calculated Sensitivity. This was
828 then utilized for GWA mapping by bigRR.

829 a) The top 1000 SNPs that significantly affect lesion size across domesticated tomato,
830 wild tomato or domestication sensitivity are shown. Significance is called as crossing
831 the 99% permutation threshold.

832 b) Venn diagram of overlapping SNPs identified as crossing the 99% permutation
833 threshold for each trait.

834 c) Venn diagram of overlapping genes identified as crossing the 99% permutation
835 threshold for each trait. Genes were called as significant if there was one significant
836 SNP within the gene body or within 2kb of the gene body.

837

838

839 Acknowledgements

840 Financial support for this work was provided by the National Research Foundation DNRF grant
841 99, US NSF grants IOS 1339125, MCB 1330337 and IOS 1021861, and the USDA National
842 Institute of Food and Agriculture, Hatch project number CA-D-PLS-7033-H.

843

844 References

- 845 Abramovitch, R. B. and G. B. Martin (2004). "Strategies used by bacterial pathogens to suppress plant
846 defenses." *Current opinion in plant biology* **7**(4): 356-364.
- 847 AbuQamar, S., M.-F. Chai, H. Luo, F. Song and T. Mengiste (2008). "Tomato protein kinase 1b mediates
848 signaling of plant responses to necrotrophic fungi and insect herbivory." *The Plant Cell* **20**(7): 1964-1983.
- 849 Atwell, S., J. Corwin, N. Soltis and D. Kliebenstein (2018). "Resequencing and association mapping of the
850 generalist pathogen *Botrytis cinerea*." *bioRxiv*.
- 851 Atwell, S., J. Corwin, N. Soltis, A. Subedy, K. Denby and D. J. Kliebenstein (2015). "Whole genome
852 resequencing of *Botrytis cinerea* isolates identifies high levels of standing diversity." *Frontiers in
853 microbiology* **6**: 996.
- 854 Bai, Y. and P. Lindhout (2007). "Domestication and breeding of tomatoes: what have we gained and
855 what can we gain in the future?" *Annals of botany* **100**(5): 1085-1094.
- 856 Ballaré, C. L. and R. Pierik (2017). "The shade-avoidance syndrome: multiple signals and ecological
857 consequences." *Plant, cell & environment* **40**(11): 2530-2543.
- 858 Barrett, L. G. and M. Heil (2012). "Unifying concepts and mechanisms in the specificity of plant–enemy
859 interactions." *Trends in plant science* **17**(5): 282-292.
- 860 Barrett, L. G., J. M. Kniskern, N. Bodenhausen, W. Zhang and J. Bergelson (2009). "Continua of specificity
861 and virulence in plant host–pathogen interactions: causes and consequences." *New Phytologist* **183**(3):
862 513-529.
- 863 Bartoli, C. and F. Roux (2017). "Genome-Wide Association Studies In Plant Pathosystems: Toward an
864 Ecological Genomics Approach." *Frontiers in plant science* **8**.
- 865 Bates, D., M. Maechler, B. Bolker and S. Walker (2015). "Fitting Linear Mixed-Effects Models Using
866 lme4." *Journal of Statistical Software* **67**(1): 1-48.
- 867 Bergougnoux, V. (2014). "The history of tomato: from domestication to biopharming." *Biotechnology
868 advances* **32**(1): 170-189.
- 869 Bhardwaj, V., S. Meier, L. N. Petersen, R. A. Ingle and L. C. Roden (2011). "Defence responses of
870 *Arabidopsis thaliana* to infection by *Pseudomonas syringae* are regulated by the circadian clock." *PloS
871 one* **6**(10): e26968.
- 872 Bittel, P. and S. Robatzek (2007). "Microbe-associated molecular patterns (MAMPs) probe plant
873 immunity." *Current opinion in plant biology* **10**(4): 335-341.
- 874 Blanca, J., J. Montero-Pau, C. Sauvage, G. Bauchet, E. Illa, M. J. Díez, D. Francis, M. Causse, E. van der
875 Knaap and J. Cañizares (2015). "Genomic variation in tomato, from wild ancestors to contemporary
876 breeding accessions." *BMC genomics* **16**(1): 257.
- 877 Blanco-Ulate, B., A. Morales-Cruz, K. C. Amrine, J. M. Labavitch, A. L. Powell and D. Cantu (2014).
878 "Genome-wide transcriptional profiling of *Botrytis cinerea* genes targeting plant cell walls during
879 infections of different hosts." *Frontiers in plant science* **5**.

- 880 Boller, T. and S. Y. He (2009). "Innate immunity in plants: an arms race between pattern recognition
881 receptors in plants and effectors in microbial pathogens." *Science* **324**(5928): 742-744.
- 882 Boyd, L. A., C. Ridout, D. M. O'Sullivan, J. E. Leach and H. Leung (2013). "Plant-pathogen interactions:
883 disease resistance in modern agriculture." *Trends in genetics* **29**(4): 233-240.
- 884 Campos, M. L., Y. Yoshida, I. T. Major, D. de Oliveira Ferreira, S. M. Weraduwage, J. E. Froehlich, B. F.
885 Johnson, D. M. Kramer, G. Jander and T. D. Sharkey (2016). "Rewiring of jasmonate and phytochrome B
886 signalling uncouples plant growth-defense tradeoffs." *Nature communications* **7**: 12570.
- 887 Cerveny, L., A. Straskova, V. Dankova, A. Hartlova, M. Ceckova, F. Staud and J. Stulik (2013).
888 "Tetratricopeptide repeat motifs in the world of bacterial pathogens: role in virulence mechanisms."
889 *Infection and immunity* **81**(3): 629-635.
- 890 Chaudhary, B. (2013). "Plant domestication and resistance to herbivory." *International journal of plant
891 genomics* **2013**.
- 892 Choquer, M., E. Fournier, C. Kunz, C. Levis, J.-M. Pradier, A. Simon and M. Viaud (2007). "Botrytis cinerea
893 virulence factors: new insights into a necrotrophic and polyphagous pathogen." *FEMS microbiology
894 letters* **277**(1): 1-10.
- 895 Corwin, J. A., D. Copeland, J. Feusier, A. Subedy, R. Eshbaugh, C. Palmer, J. Maloof and D. J. Kliebenstein
896 (2016). "The quantitative basis of the Arabidopsis innate immune system to endemic pathogens
897 depends on pathogen genetics." *PLoS Genet* **12**(2): e1005789.
- 898 Corwin, J. A., A. Subedy, R. Eshbaugh and D. J. Kliebenstein (2016). "Expansive phenotypic landscape of
899 Botrytis cinerea shows differential contribution of genetic diversity and plasticity." *Molecular Plant-
900 Microbe Interactions* **29**(4): 287-298.
- 901 Couch, B. C., I. Fudal, M.-H. Lebrun, D. Tharreau, B. Valent, P. Van Kim, J.-L. Nottéghem and L. M. Kohn
902 (2005). "Origins of host-specific populations of the blast pathogen Magnaporthe oryzae in crop
903 domestication with subsequent expansion of pandemic clones on rice and weeds of rice." *Genetics
904* **170**(2): 613-630.
- 905 Dalmais, B., J. Schumacher, J. Moraga, P. Le Pecheur, B. Tudzynski, I. G. Collado and M. Viaud (2011).
906 "The Botrytis cinerea phytotoxin botcinic acid requires two polyketide synthases for production and has
907 a redundant role in virulence with botrydial." *Molecular plant pathology* **12**(6): 564-579.
- 908 Dalman, K., K. Himmelstrand, Å. Olson, M. Lind, M. Brandström-Durling and J. Stenlid (2013). "A
909 genome-wide association study identifies genomic regions for virulence in the non-model organism
910 Heterobasidion annosum ss." *PLoS One* **8**(1): e53525.
- 911 Dangl, J. L. and J. D. Jones (2001). "Plant pathogens and integrated defence responses to infection."
912 *nature* **411**(6839): 826-833.
- 913 De Feyter, R., Y. Yang and D. W. Gabriel (1993). "Gene-for-genes interactions between cotton R genes
914 and Xanthomonas campestris pv. malvacearum avr genes." *Molecular plant-microbe interactions: MPMI
915* **6**(2): 225-237.
- 916 Dean, R., J. A. Van Kan, Z. A. Pretorius, K. E. Hammond-Kosack, A. Di Pietro, P. D. Spanu, J. J. Rudd, M.
917 Dickman, R. Kahmann and J. Ellis (2012). "The Top 10 fungal pathogens in molecular plant pathology."
918 *Molecular plant pathology* **13**(4): 414-430.
- 919 Deighton, N., I. Muckenschnabel, A. J. Colmenares, I. G. Collado and B. Williamson (2001). "Botrydial is
920 produced in plant tissues infected by Botrytis cinerea." *Phytochemistry* **57**(5): 689-692.
- 921 Denby, K. J., P. Kumar and D. J. Kliebenstein (2004). "Identification of Botrytis cinerea susceptibility loci
922 in Arabidopsis thaliana." *The Plant Journal* **38**(3): 473-486.
- 923 Desjardins, C. A., K. A. Cohen, V. Munsamy, T. Abeel, K. Maharaj, B. J. Walker, T. P. Shea, D. V. Almeida,
924 A. L. Manson and A. Salazar (2016). "Genomic and functional analyses of Mycobacterium tuberculosis
925 strains implicate ald in D-cycloserine resistance." *Nature genetics* **48**(5): 544-551.
- 926 Diaz, J., A. ten Have and J. A. van Kan (2002). "The role of ethylene and wound signaling in resistance of
927 tomato to Botrytis cinerea." *Plant physiology* **129**(3): 1341-1351.

- 928 Dodds, P. N. and J. P. Rathjen (2010). "Plant immunity: towards an integrated view of plant-pathogen
929 interactions." *Nature Reviews Genetics* **11**(8): 539-548.
- 930 Doebley, J. F., B. S. Gaut and B. D. Smith (2006). "The molecular genetics of crop domestication." *Cell*
931 **127**(7): 1309-1321.
- 932 Doerge, R. W. and G. A. Churchill (1996). "Permutation tests for multiple loci affecting a quantitative
933 character." *Genetics* **142**(1): 285-294.
- 934 Dwivedi, S. L., H. D. Upadhyaya, H. T. Stalker, M. W. Blair, D. J. Bertioli, S. Nielsen and R. Ortiz (2008).
935 "Enhancing crop gene pools with beneficial traits using wild relatives." *Plant Breeding Reviews* **30**: 179.
- 936 Egashira, H., A. Kuwashima, H. Ishiguro, K. Fukushima, T. Kaya and S. Imanishi (2000). "Screening of wild
937 accessions resistant to gray mold (*Botrytis cinerea* Pers.) in *Lycopersicon*." *Acta physiologiae plantarum*
938 **22**(3): 324-326.
- 939 Elad, Y., B. Williamson, P. Tudzynski and N. Delen (2007). *Botrytis spp. and diseases they cause in*
940 *agricultural systems—an introduction. Botrytis: Biology, pathology and control*, Springer: 1-8.
- 941 Failmezger, H., Y. Yuan, O. Rueda, F. Markowetz and M. H. Failmezger (2012). "CRImage: CRImage a
942 package to classify cells and calculate tumour cellularity." *R package version 1.24.0*.
- 943 Farhat, M. R., B. J. Shapiro, K. J. Kieser, R. Sultana, K. R. Jacobson, T. C. Victor, R. M. Warren, E. M.
944 Streicher, A. Calver and A. Sloutsky (2013). "Genomic analysis identifies targets of convergent positive
945 selection in drug-resistant *Mycobacterium tuberculosis*." *Nature genetics* **45**(10): 1183-1189.
- 946 Fekete, É., E. Fekete, L. Irinyi, L. Karaffa, M. Árnyasi, M. Asadollahi and E. Sándor (2012). "Genetic
947 diversity of a *Botrytis cinerea* cryptic species complex in Hungary." *Microbiological Research* **167**(5): 283-
948 291.
- 949 Ferrari, S., R. Galletti, C. Denoux, G. De Lorenzo, F. M. Ausubel and J. Dewdney (2007). "Resistance to
950 *Botrytis cinerea* induced in *Arabidopsis* by elicitors is independent of salicylic acid, ethylene, or
951 jasmonate signaling but requires PHYTOALEXIN DEFICIENT3." *Plant physiology* **144**(1): 367-379.
- 952 Ferrari, S., J. M. Plotnikova, G. De Lorenzo and F. M. Ausubel (2003). "Arabidopsis local resistance to
953 *Botrytis cinerea* involves salicylic acid and camalexin and requires EDS4 and PAD2, but not SID2, EDS5 or
954 PAD4." *The Plant Journal* **35**(2): 193-205.
- 955 Fillinger, S. and Y. Elad (2015). *Botrytis-the Fungus, the Pathogen and Its Management in Agricultural*
956 *Systems*, Springer.
- 957 Finkers, R., Y. Bai, P. van den Berg, R. van Berloo, F. Meijer-Dekens, A. Ten Have, J. van Kan, P. Lindhout
958 and A. W. van Heusden (2008). "Quantitative resistance to *Botrytis cinerea* from *Solanum neorickii*."
959 *Euphytica* **159**(1-2): 83-92.
- 960 Finkers, R., A. W. van Heusden, F. Meijer-Dekens, J. A. van Kan, P. Maris and P. Lindhout (2007). "The
961 construction of a *Solanum habrochaites* LYC4 introgression line population and the identification of QTLs
962 for resistance to *Botrytis cinerea*." *Theoretical and Applied Genetics* **114**(6): 1071-1080.
- 963 Fordyce, R., N. Soltis, C. Caseys, G. Gwinne, J. Corwin, S. Atwell, D. Copeland, J. Feusier, A. Subedy, R.
964 Eshbaugh and D. Kliebenstein (2018). "Combining Digital Imaging and GWA Mapping to Dissect Visual
965 Traits in Plant/Pathogen Interactions." *Plant Physiology*.
- 966 Francisco, M., B. Joseph, H. Caligagan, B. Li, J. A. Corwin, C. Lin, R. E. Kerwin, M. Burow and D. J.
967 Kliebenstein (2016). "Genome wide association mapping in *Arabidopsis thaliana* identifies novel genes
968 involved in linking allyl glucosinolate to altered biomass and defense." *Frontiers in plant science* **7**.
- 969 Gao, Y., Z. Liu, J. D. Faris, J. Richards, R. S. Brueggeman, X. Li, R. P. Oliver, B. A. McDonald and T. L.
970 Friesen (2016). "Validation of genome-wide association studies as a tool to identify virulence factors in
971 *Parastagonospora nodorum*." *Phytopathology* **106**(10): 1177-1185.
- 972 Giraud, T., D. Fortini, C. Levis, C. Lamarque, P. Leroux, K. LoBuglio and Y. Bryggo (1999). "Two sibling
973 species of the *Botrytis cinerea* complex, transposa and vacuma, are found in sympatry on numerous
974 host plants." *Phytopathology* **89**(10): 967-973.

- 975 Glazebrook, J. (2005). "Contrasting mechanisms of defense against biotrophic and necrotrophic
976 pathogens." *Annu. Rev. Phytopathol.* **43**: 205-227.
- 977 Goss, E. M. and J. Bergelson (2006). "Variation in resistance and virulence in the interaction between
978 *Arabidopsis thaliana* and a bacterial pathogen." *Evolution* **60**(8): 1562-1573.
- 979 Guimaraes, R. L., R. T. Chetelat and H. U. Stotz (2004). "Resistance to *Botrytis cinerea* in *Solanum*
980 *lycopersicoides* is dominant in hybrids with tomato, and involves induced hyphal death." *European*
981 *journal of plant pathology* **110**(1): 13-23.
- 982 Hacquard, S., B. Kracher, T. Maekawa, S. Vernaldi, P. Schulze-Lefert and E. V. L. van Themaat (2013).
983 "Mosaic genome structure of the barley powdery mildew pathogen and conservation of transcriptional
984 programs in divergent hosts." *Proceedings of the National Academy of Sciences* **110**(24): E2219-E2228.
- 985 Hahn, M. (2014). "The rising threat of fungicide resistance in plant pathogenic fungi: *Botrytis* as a case
986 study." *Journal of chemical biology* **7**(4): 133-141.
- 987 Hevia, M. A., P. Canessa, H. Müller-Esparza and L. F. Larrondo (2015). "A circadian oscillator in the
988 fungus *Botrytis cinerea* regulates virulence when infecting *Arabidopsis thaliana*." *Proceedings of the*
989 *National Academy of Sciences* **112**(28): 8744-8749.
- 990 Hyten, D. L., Q. Song, Y. Zhu, I.-Y. Choi, R. L. Nelson, J. M. Costa, J. E. Specht, R. C. Shoemaker and P. B.
991 Cregan (2006). "Impacts of genetic bottlenecks on soybean genome diversity." *Proceedings of the*
992 *National Academy of Sciences* **103**(45): 16666-16671.
- 993 Izquierdo-Bueno, I., V. E. González-Rodríguez, A. Simon, B. Dalmais, J. M. Pradier, P. Le Pêcheur, A.
994 Mercier, A. S. Walker, C. Garrido and I. G. Collado (2018). "Biosynthesis of abscisic acid in fungi:
995 Identification of a sesquiterpene cyclase as the key enzyme in *Botrytis cinerea*." *Environmental*
996 *microbiology*.
- 997 Jombart, T. (2008). "adegenet: a R package for the multivariate analysis of genetic markers."
998 *Bioinformatics* **24**(11): 1403-1405.
- 999 Jones, J. D. and J. L. Dangl (2006). "The plant immune system." *Nature* **444**(7117): 323-329.
- 1000 Katan, T. (1999). "Current status of vegetative compatibility groups in *Fusarium oxysporum*."
1001 *Phytoparasitica* **27**(1): 51-64.
- 1002 Keen, N. (1992). "The molecular biology of disease resistance." *Plant molecular biology* **19**(1): 109-122.
- 1003 Kliebenstein, D. J., H. C. Rowe and K. J. Denby (2005). "Secondary metabolites influence
1004 *Arabidopsis*/Botrytis interactions: variation in host production and pathogen sensitivity." *The Plant*
1005 *Journal* **44**(1): 25-36.
- 1006 Koenig, D., J. M. Jiménez-Gómez, S. Kimura, D. Fulop, D. H. Chitwood, L. R. Headland, R. Kumar, M. F.
1007 Covington, U. K. Devisetty and A. V. Tat (2013). "Comparative transcriptomics reveals patterns of
1008 selection in domesticated and wild tomato." *Proceedings of the National Academy of Sciences* **110**(28):
1009 E2655-E2662.
- 1010 Kooke, R., W. Kruijer, R. Bours, F. F. Becker, A. Kuhn, J. Buntjer, T. Doeswijk, J. Guerra, H. J. Bouwmeester
1011 and D. Vreugdenhil (2016). "Genome-wide association mapping and genomic prediction elucidate the
1012 genetic architecture of morphological traits in *Arabidopsis thaliana*." *Plant Physiology*: pp. 00997.02015.
- 1013 Kover, P. X. and B. A. Schaal (2002). "Genetic variation for disease resistance and tolerance among
1014 *Arabidopsis thaliana* accessions." *Proceedings of the National Academy of Sciences* **99**(17): 11270-
1015 11274.
- 1016 Kretschmer, M. and M. Hahn (2008). "Fungicide resistance and genetic diversity of *Botrytis cinerea*
1017 isolates from a vineyard in Germany." *Journal of Plant Diseases and Protection*: 214-219.
- 1018 Kurtz, S., A. Phillippy, A. L. Delcher, M. Smoot, M. Shumway, C. Antonescu and S. L. Salzberg (2004).
1019 "Versatile and open software for comparing large genomes." *Genome biology* **5**(2): R12.
- 1020 Lin, T., G. Zhu, J. Zhang, X. Xu, Q. Yu, Z. Zheng, Z. Zhang, Y. Lun, S. Li and X. Wang (2014). "Genomic
1021 analyses provide insights into the history of tomato breeding." *Nature genetics* **46**(11): 1220.

- 1022 Liu, B., Y.-B. Hong, Y.-F. Zhang, X.-H. Li, L. Huang, H.-J. Zhang, D.-Y. Li and F.-M. Song (2014). "Tomato
1023 WRKY transcriptional factor SIDRW1 is required for disease resistance against Botrytis cinerea and
1024 tolerance to oxidative stress." *Plant Science* **227**: 145-156.
- 1025 Lo Presti, L., C. López Díaz, D. Turrà, A. Di Pietro, M. Hampel, K. Heimel and R. Kahmann (2016). "A
1026 conserved co-chaperone is required for virulence in fungal plant pathogens." *New Phytologist* **209**(3):
1027 1135-1148.
- 1028 Loxdale, H. D., G. Lushai and J. A. Harvey (2011). "The evolutionary improbability of 'generalism' in
1029 nature, with special reference to insects." *Biological Journal of the Linnean Society* **103**(1): 1-18.
- 1030 Ma, Z. and T. J. Michailides (2005). "Genetic structure of Botrytis cinerea populations from different host
1031 plants in California." *Plant disease* **89**(10): 1083-1089.
- 1032 Martinez, F., D. Blanckard, P. Lecomte, C. Levis, B. Dubos and M. Fermaud (2003). "Phenotypic differences
1033 between vacuma and transposa subpopulations of Botrytis cinerea." *European Journal of Plant
1034 Pathology* **109**(5): 479-488.
- 1035 Miller, J. and S. Tanksley (1990). "RFLP analysis of phylogenetic relationships and genetic variation in the
1036 genus *Lycopersicon*." *TAG Theoretical and Applied Genetics* **80**(4): 437-448.
- 1037 Müller, N. A., C. L. Wijnen, A. Srinivasan, M. Ryngajillo, I. Ofner, T. Lin, A. Ranjan, D. West, J. N. Maloof
1038 and N. R. Sinha (2016). "Domestication selected for deceleration of the circadian clock in cultivated
1039 tomato." *Nature genetics* **48**(1): 89-93.
- 1040 Nicot, P., A. Moretti, C. Romiti, M. Bardin, C. Caranta and H. Ferriere (2002). "Differences in
1041 susceptibility of pruning wounds and leaves to infection by Botrytis cinerea among wild tomato
1042 accessions." *TGC Report* **52**: 24-26.
- 1043 Nicot, P. C. and A. Baille (1996). Integrated control of Botrytis cinerea on greenhouse tomatoes. *Aerial
1044 Plant Surface Microbiology*, Springer: 169-189.
- 1045 Nomura, K., M. Melotto and S.-Y. He (2005). "Suppression of host defense in compatible plant–
1046 *Pseudomonas syringae* interactions." *Current opinion in plant biology* **8**(4): 361-368.
- 1047 Ober, U., W. Huang, M. Magwire, M. Schlather, H. Simianer and T. F. Mackay (2015). "Accounting for
1048 genetic architecture improves sequence based genomic prediction for a *Drosophila* fitness trait." *PLoS
1049 One* **10**(5): e0126880.
- 1050 Ormond, E. L., A. P. Thomas, P. J. Pugh, J. K. Pell and H. E. Roy (2010). "A fungal pathogen in time and
1051 space: the population dynamics of *Beauveria bassiana* in a conifer forest." *FEMS microbiology ecology*
1052 **74**(1): 146-154.
- 1053 Panthee, D. R. and F. Chen (2010). "Genomics of fungal disease resistance in tomato." *Current genomics*
1054 **11**(1): 30-39.
- 1055 Parlevliet, J. E. (2002). "Durability of resistance against fungal, bacterial and viral pathogens; present
1056 situation." *Euphytica* **124**(2): 147-156.
- 1057 Pau, G., F. Fuchs, O. Sklyar, M. Boutros and W. Huber (2010). "EBImage—an R package for image
1058 processing with applications to cellular phenotypes." *Bioinformatics* **26**(7): 979-981.
- 1059 Pedras, M. S. C. and P. W. Ahiahonu (2005). "Metabolism and detoxification of phytoalexins and analogs
1060 by phytopathogenic fungi." *Phytochemistry* **66**(4): 391-411.
- 1061 Pedras, M. S. C., S. Hossain and R. B. Snitinsky (2011). "Detoxification of cruciferous phytoalexins in
1062 *Botrytis cinerea*: Spontaneous dimerization of a camalexin metabolite." *Phytochemistry* **72**(2): 199-206.
- 1063 Peralta, I., D. Spooner and S. Knapp (2008). "The taxonomy of tomatoes: a revision of wild tomatoes
1064 (*Solanum* section *Lycopersicon*) and their outgroup relatives in sections *Juglandifolium* and
1065 *Lycopersicoides*." *Syst Bot Monogr* **84**: 1-186.
- 1066 Persoons, A., E. Morin, C. Delaruelle, T. Payen, F. Halkett, P. Frey, S. De Mita and S. Duplessis (2014).
1067 "Patterns of genomic variation in the poplar rust fungus *Melampsora larici-populina* identify
1068 pathogenesis-related factors." *Frontiers in plant science* **5**.

- 1069 Pieterse, C. M., D. Van der Does, C. Zamioudis, A. Leon-Reyes and S. C. Van Wees (2012). "Hormonal
1070 modulation of plant immunity." *Annual review of cell and developmental biology* **28**: 489-521.
- 1071 Poland, J. A., P. J. Balint-Kurti, R. J. Wisser, R. C. Pratt and R. J. Nelson (2009). "Shades of gray: the world
1072 of quantitative disease resistance." *Trends in plant science* **14**(1): 21-29.
- 1073 Power, R. A., J. Parkhill and T. de Oliveira (2017). "Microbial genome-wide association studies: lessons
1074 from human GWAS." *Nature Reviews Genetics* **18**(1): 41-50.
- 1075 Quidde, T., P. Büttner and P. Tudzynski (1999). "Evidence for three different specific saponin-detoxifying
1076 activities in *Botrytis cinerea* and cloning and functional analysis of a gene coding for a putative
1077 avenacinase." *European Journal of Plant Pathology* **105**(3): 273-283.
- 1078 Quidde, T., A. Osbourn and P. Tudzynski (1998). "Detoxification of α-tomatine by *Botrytis cinerea*."
1079 *Physiological and Molecular Plant Pathology* **52**(3): 151-165.
- 1080 R Development Core Team (2008). "R: A language and environment for statistical computing." *R*
1081 *Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0.*
- 1082 Romanazzi, G. and S. Droby (2016). Control Strategies for Postharvest Grey Mould on Fruit Crops.
1083 *Botrytis—the Fungus, the Pathogen and its Management in Agricultural Systems*, Springer: 217-228.
- 1084 Rosenthal, J. P. and R. Dirzo (1997). "Effects of life history, domestication and agronomic selection on
1085 plant defence against insects: evidence from maizes and wild relatives." *Evolutionary Ecology* **11**(3): 337-
1086 355.
- 1087 Rowe, H. C. and D. J. Kliebenstein (2007). "Elevated genetic variation within virulence-associated *Botrytis*
1088 *cinerea* polygalacturonase loci." *Molecular Plant-Microbe Interactions* **20**(9): 1126-1137.
- 1089 Rowe, H. C. and D. J. Kliebenstein (2008). "Complex genetics control natural variation in *Arabidopsis*
1090 *thaliana* resistance to *Botrytis cinerea*." *Genetics* **180**(4): 2237-2250.
- 1091 Rowe, H. C., J. W. Walley, J. Corwin, E. K.-F. Chan, K. Dehesh and D. J. Kliebenstein (2010). "Deficiencies
1092 in jasmonate-mediated plant defense reveal quantitative variation in *Botrytis cinerea* pathogenesis."
1093 *PLoS Pathog* **6**(4): e1000861.
- 1094 Samuel, S., T. Veloukas, A. Papavasileiou and G. S. Karaoglanidis (2012). "Differences in frequency of
1095 transposable elements presence in *Botrytis cinerea* populations from several hosts in Greece." *Plant*
1096 *disease* **96**(9): 1286-1290.
- 1097 Sauerbrunn, N. and N. L. Schlaich (2004). "PCC1: a merging point for pathogen defence and circadian
1098 signalling in *Arabidopsis*." *Planta* **218**(4): 552-561.
- 1099 Schumacher, J., J.-M. Pradier, A. Simon, S. Traeger, J. Moraga, I. G. Collado, M. Viaud and B. Tudzynski
1100 (2012). "Natural variation in the VELVET gene bcvel1 affects virulence and light-dependent
1101 differentiation in *Botrytis cinerea*." *PLoS One* **7**(10): e47840.
- 1102 Shen, X., M. Alam, F. Fikse and L. Rönnegård (2013). "A novel generalized ridge regression method for
1103 quantitative genetics." *Genetics* **193**(4): 1255-1268.
- 1104 Siewers, V., M. Viaud, D. Jimenez-Teja, I. G. Collado, C. S. Gronover, J.-M. Pradier, B. Tudzynsk and P.
1105 Tudzynski (2005). "Functional analysis of the cytochrome P450 monooxygenase gene bcbot1 of *Botrytis*
1106 *cinerea* indicates that botrydial is a strain-specific virulence factor." *Molecular plant-microbe*
1107 *interactions* **18**(6): 602-612.
- 1108 Sim, S.-C., G. Durstewitz, J. Plieske, R. Wieseke, M. W. Ganal, A. Van Deynze, J. P. Hamilton, C. R. Buell,
1109 M. Causse and S. Wijeratne (2012). "Development of a large SNP genotyping array and generation of
1110 high-density genetic maps in tomato." *PloS one* **7**(7): e40563.
- 1111 Smale, M. (1996). "Understanding global trends in the use of wheat diversity and international flows of
1112 wheat genetic resources."
- 1113 Staats, M. and J. A. van Kan (2012). "Genome update of *Botrytis cinerea* strains B05. 10 and T4."
1114 *Eukaryotic cell* **11**(11): 1413-1414.

- 1115 Stefanato, F. L., E. Abou-Mansour, A. Buchala, M. Kretschmer, A. Mosbach, M. Hahn, C. G. Bochet, J. P.
1116 Métraux and H. j. Schoonbeek (2009). "The ABC transporter BcatrB from Botrytis cinerea exports
1117 camalexin and is a virulence factor on Arabidopsis thaliana." *The Plant Journal* **58**(3): 499-510.
1118 Stukenbrock, E. H. and B. A. McDonald (2008). "The origins of plant pathogens in agro-ecosystems."
1119 *Annu. Rev. Phytopathol.* **46**: 75-100.
1120 Talas, F., R. Kalih, T. Miedaner and B. A. McDonald (2016). "Genome-wide association study identifies
1121 novel candidate genes for aggressiveness, deoxynivalenol production, and azole sensitivity in natural
1122 field populations of Fusarium graminearum." *Molecular Plant-Microbe Interactions* **29**(5): 417-430.
1123 Tanksley, S. D. (2004). "The genetic, developmental, and molecular bases of fruit size and shape
1124 variation in tomato." *The plant cell* **16**(suppl 1): S181-S189.
1125 Tanksley, S. D. and S. R. McCouch (1997). "Seed banks and molecular maps: unlocking genetic potential
1126 from the wild." *Science* **277**(5329): 1063-1066.
1127 ten Have, A., W. Mulder, J. Visser and J. A. van Kan (1998). "The endopolygalacturonase gene Bcpg1 is
1128 required for full virulence of Botrytis cinerea." *Molecular Plant-Microbe Interactions* **11**(10): 1009-1016.
1129 Ten Have, A., R. van Berloo, P. Lindhout and J. A. van Kan (2007). "Partial stem and leaf resistance
1130 against the fungal pathogen Botrytis cinerea in wild relatives of tomato." *European journal of plant
1131 pathology* **117**(2): 153-166.
1132 Tiffin, P. and D. A. Moeller (2006). "Molecular evolution of plant immune system genes." *Trends in
1133 genetics* **22**(12): 662-670.
1134 Upadhyaya, N. M., D. P. Garnica, H. Karaoglu, J. Sperschneider, A. Nemri, B. Xu, R. Mago, C. A. Cuomo, J.
1135 P. Rathjen and R. F. Park (2014). "Comparative genomics of Australian isolates of the wheat stem rust
1136 pathogen Puccinia graminis f. sp. tritici reveals extensive polymorphism in candidate effector genes."
1137 *Frontiers in plant science* **5**.
1138 Valette-Collet, O., A. Cimerman, P. Reignault, C. Levis and M. Boccardo (2003). "Disruption of Botrytis
1139 cinerea pectin methylesterase gene Bcpme1 reduces virulence on several host plants." *Molecular Plant-
1140 Microbe Interactions* **16**(4): 360-367.
1141 Viaud, M., A.-F. Adam-Blondon, J. Amselem, P. Bally, A. Cimerman, B. Dalmais-Lenaers, N. Lapalu, M.-H.
1142 Lebrun, B. Poinsot and J. M. Pradier (2012). "Le génome de Botrytis décrypté." *Revue des oenologues
1143 et des techniques vitivinicoles et oenologiques*(142): 9-11.
1144 Vleeshouwers, V. G. and R. P. Oliver (2014). "Effectors as tools in disease resistance breeding against
1145 biotrophic, hemibiotrophic, and necrotrophic plant pathogens." *Molecular plant-microbe interactions*
1146 **27**(3): 196-206.
1147 Weyman, P. D., Z. Pan, Q. Feng, D. G. Gilchrist and R. M. Bostock (2006). "A circadian rhythm-regulated
1148 tomato gene is induced by arachidonic acid and Phytophthora infestans infection." *Plant physiology*
1149 **140**(1): 235-248.
1150 Wicker, T., S. Oberhaensli, F. Parlange, J. P. Buchmann, M. Shatalina, S. Roffler, R. Ben-David, J. Doležel,
1151 H. Šimková and P. Schulze-Lefert (2013). "The wheat powdery mildew genome shows the unique
1152 evolution of an obligate biotroph." *Nature Genetics* **45**(9): 1092-1096.
1153 Wu, J. Q., S. Sakthikumar, C. Dong, P. Zhang, C. A. Cuomo and R. F. Park (2017). "Comparative genomics
1154 integrated with association analysis identifies candidate effector genes corresponding to Lr20 in
1155 phenotype-paired Puccinia triticina isolates from Australia." *Frontiers in plant science* **8**.
1156 Zerbino, D. R., P. Achuthan, W. Akanni, M. R. Amode, D. Barrell, J. Bhai, K. Billis, C. Cummins, A. Gall and
1157 C. G. Girón (2017). "Ensembl 2018." *Nucleic acids research* **46**(D1): D754-D761.
1158 Zhang, L., A. Khan, D. Nino-Liu and M. Foolad (2002). "A molecular linkage map of tomato displaying
1159 chromosomal locations of resistance gene analogs based on a Lycopersicon esculentum× Lycopersicon
1160 hirsutum cross." *Genome* **45**(1): 133-146.

- 1161 Zhang, W., J. A. Corwin, D. Copeland, J. Feusier, R. Eshbaugh, F. Chen, S. Atwell and D. J. Kliebenstein
1162 (2017). "Plastic transcriptomes stabilize immunity to pathogen diversity: the jasmonic acid and salicylic
1163 acid networks within the *Arabidopsis*/*Botrytis* pathosystem." *The Plant Cell*: tpc. 00348.02017.
1164 Zhou, X. and M. Stephens (2012). "Genome-wide efficient mixed-model analysis for association studies."
1165 *Nature genetics* **44**(7): 821.
1166 Zipfel, C., S. Robatzek, L. Navarro and E. J. Oakeley (2004). "Bacterial disease resistance in *Arabidopsis*
1167 through flagellin perception." *Nature* **428**(6984): 764.
1168 Züst, T. and A. A. Agrawal (2017). "Trade-offs between plant growth and defense against insect
1169 herbivory: an emerging mechanistic synthesis." *Annual review of plant biology* **68**: 513-534.
1170

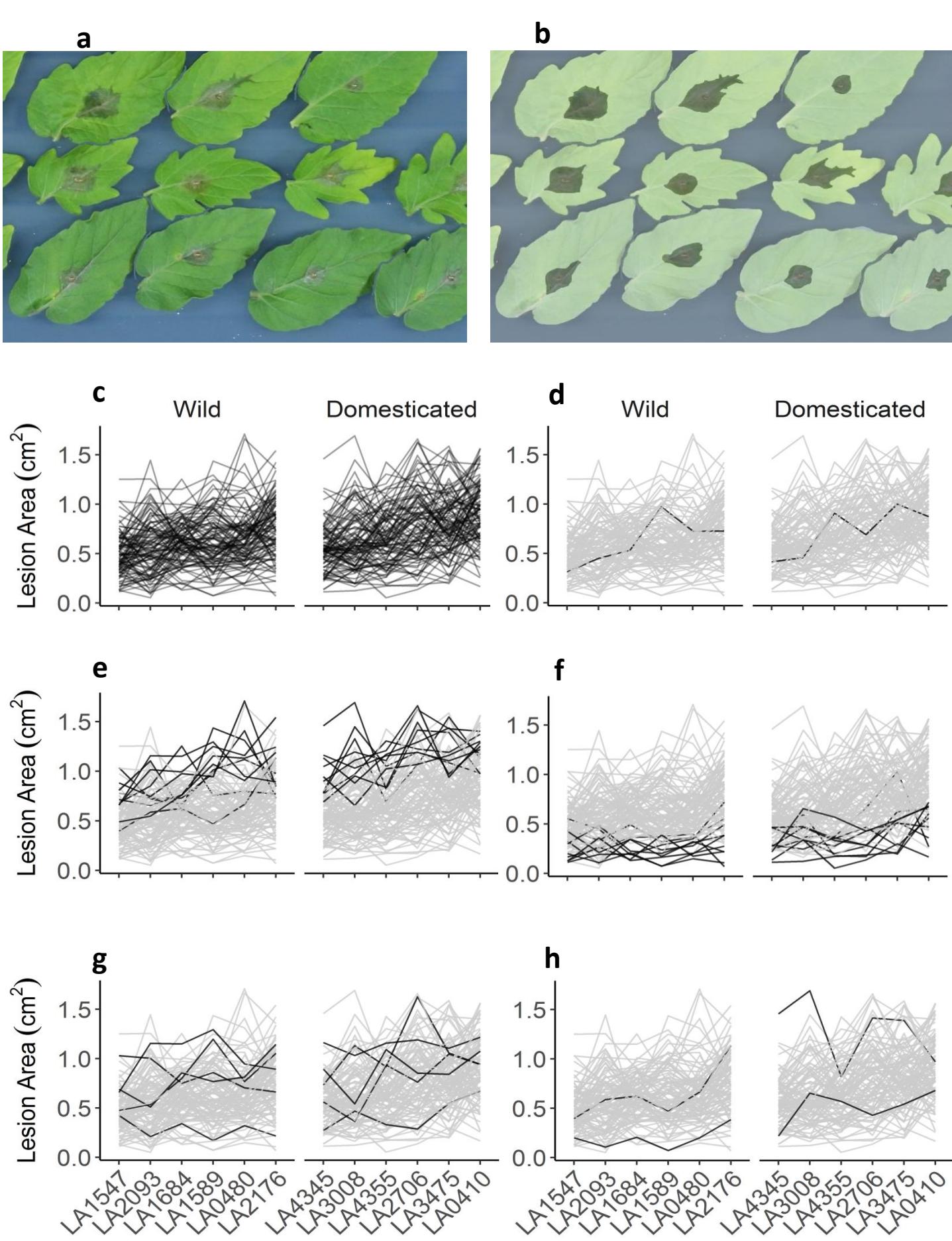


Figure 1. *Botrytis cinerea* x tomato diversity in detached leaf assay and digital image analysis. a) Individual tomato leaflets of 6 *S. lycopersicum* genotypes and 6 *S. pimpinellifolium* genotypes are in randomized rows, spore droplets of individual *B. cinerea* isolates are in randomized columns. Digital images are collected 72 hours post inoculation. Single droplets of 40 *B. cinerea* spores are infected on randomized leaflets using randomized isolates, and digital images are taken 72 hours post inoculation.

- b) Digital masking of leaf and lesion is followed by automated measurement of area for each lesion.
- c-h) Variation in lesion size resulting of the interaction of *B. cinerea* and diverse tomato genotypes.
- c) Average lesion size of single *B. cinerea* isolates (line traces) across tomato host genotypes grouped by domestication status.
- d) Highlight of the common reference *B. cinerea* isolate B05.10.
- e) Highlight of the ten highest-virulence isolates, as estimated by mean virulence across all tomato genotypes.
- f) Highlight of the ten most saprophytic, or low virulence, isolates, as estimated by mean virulence across all genotypes.
- g) Highlight of the five isolates collected from tomato tissue.
- h) Highlight of the two isolates with significant domestication sensitivity.

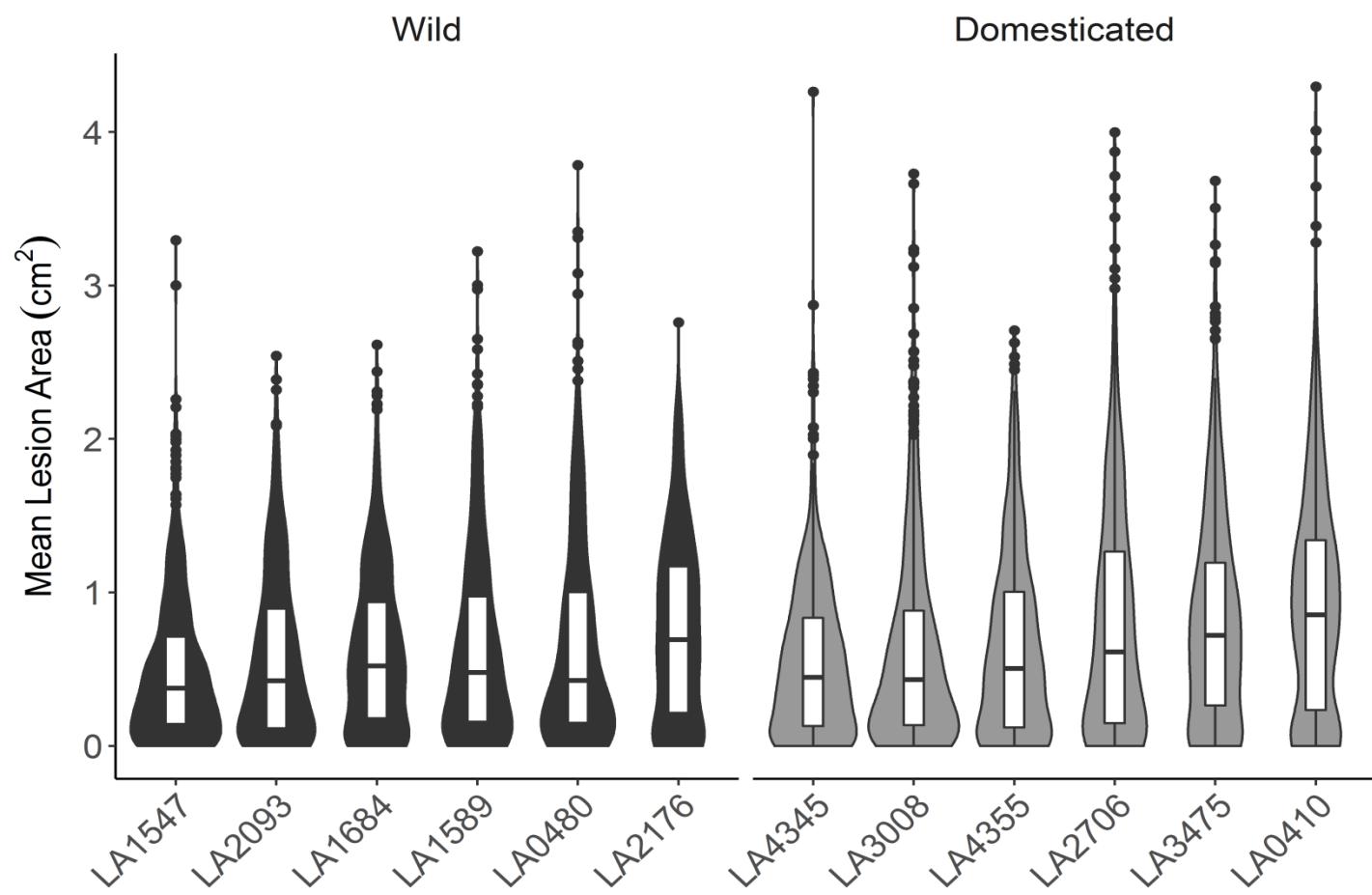


Figure 2. Distribution of tomato genotype susceptibility to infection with 97 genetically diverse *B. cinerea* isolates.

Violin plots show the distribution of lesion size caused by *B. cinerea* isolates on each tomato host genotype. Individual points are mean lesion size for each of the 97 different isolate-host pairs. The boxes show the 75th percentile distribution, and the horizontal line shows the mean resistance of the specific host genotype. The tomato genotypes are grouped based on their status as wild or domesticated germplasm.

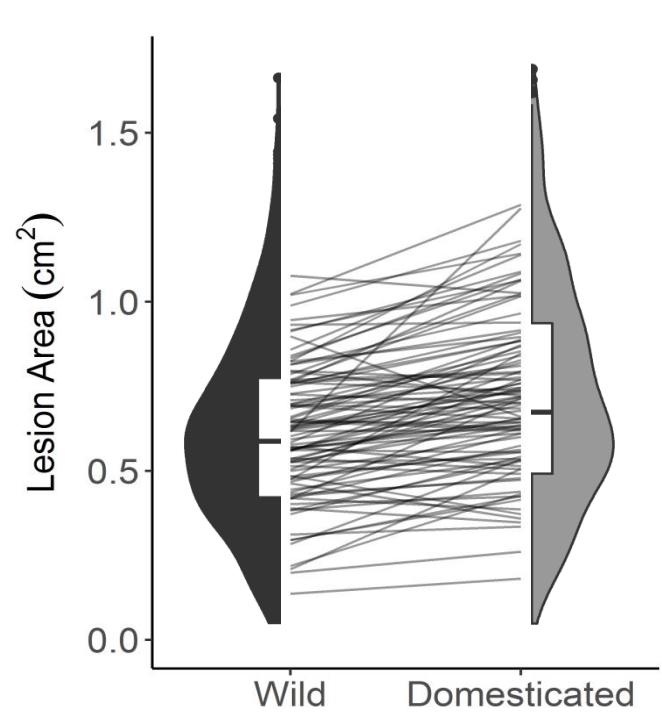
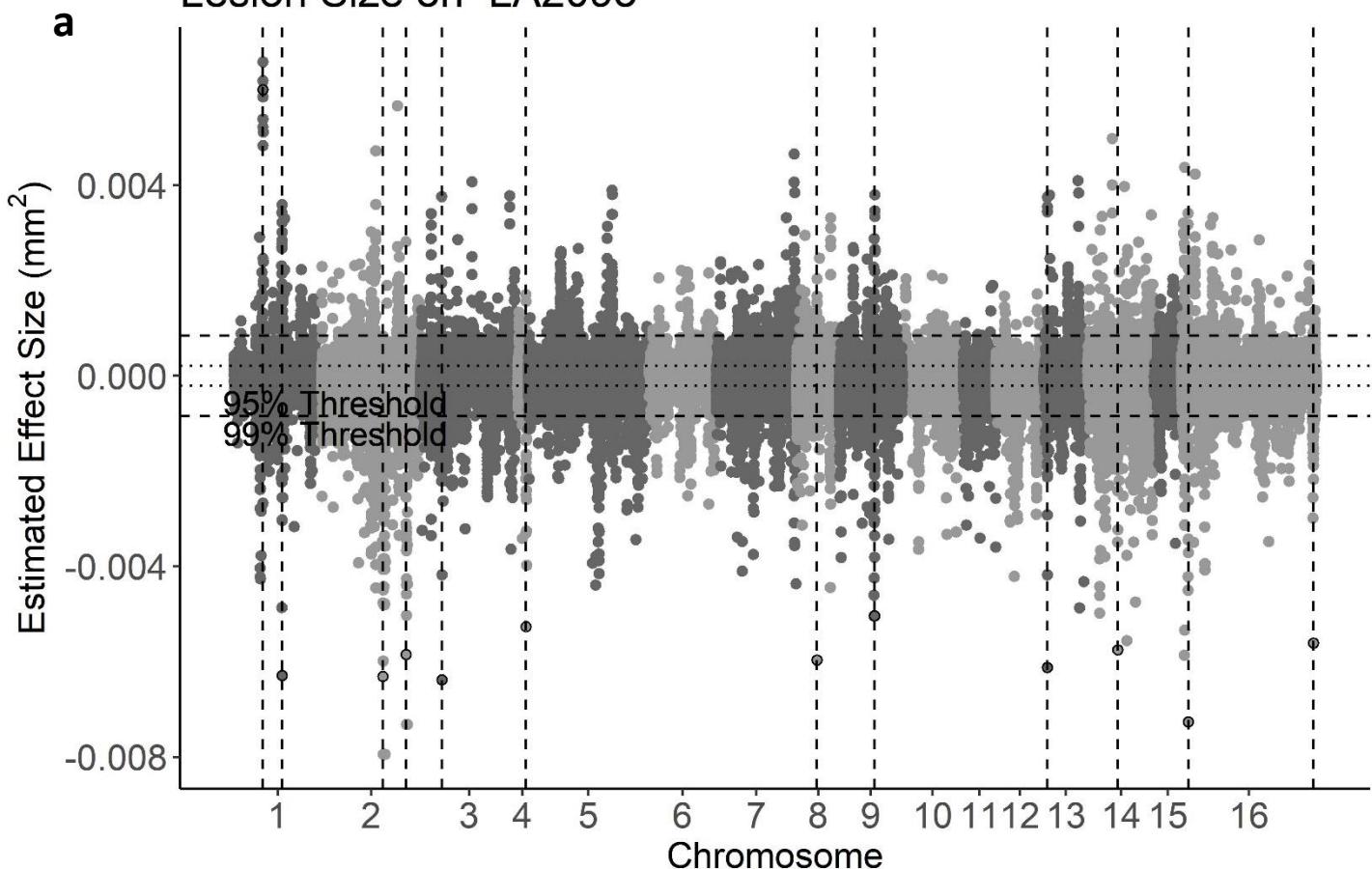


Figure 3. Distribution of *B. cinerea* virulence by tomato domestication status.

The violin plots show the mean virulence of each *B. cinerea* isolate on the tomato genotypes, grouped as wild or domesticated germplasm. The domestication effect on lesion size is significant (Table 1 ANOVA, $p < 2e-16$). The interaction plot between the two violin plots connects the average lesion size of a single *B. cinerea* isolate between the wild and domesticated germplasm.

Lesion Size on LA2093



b

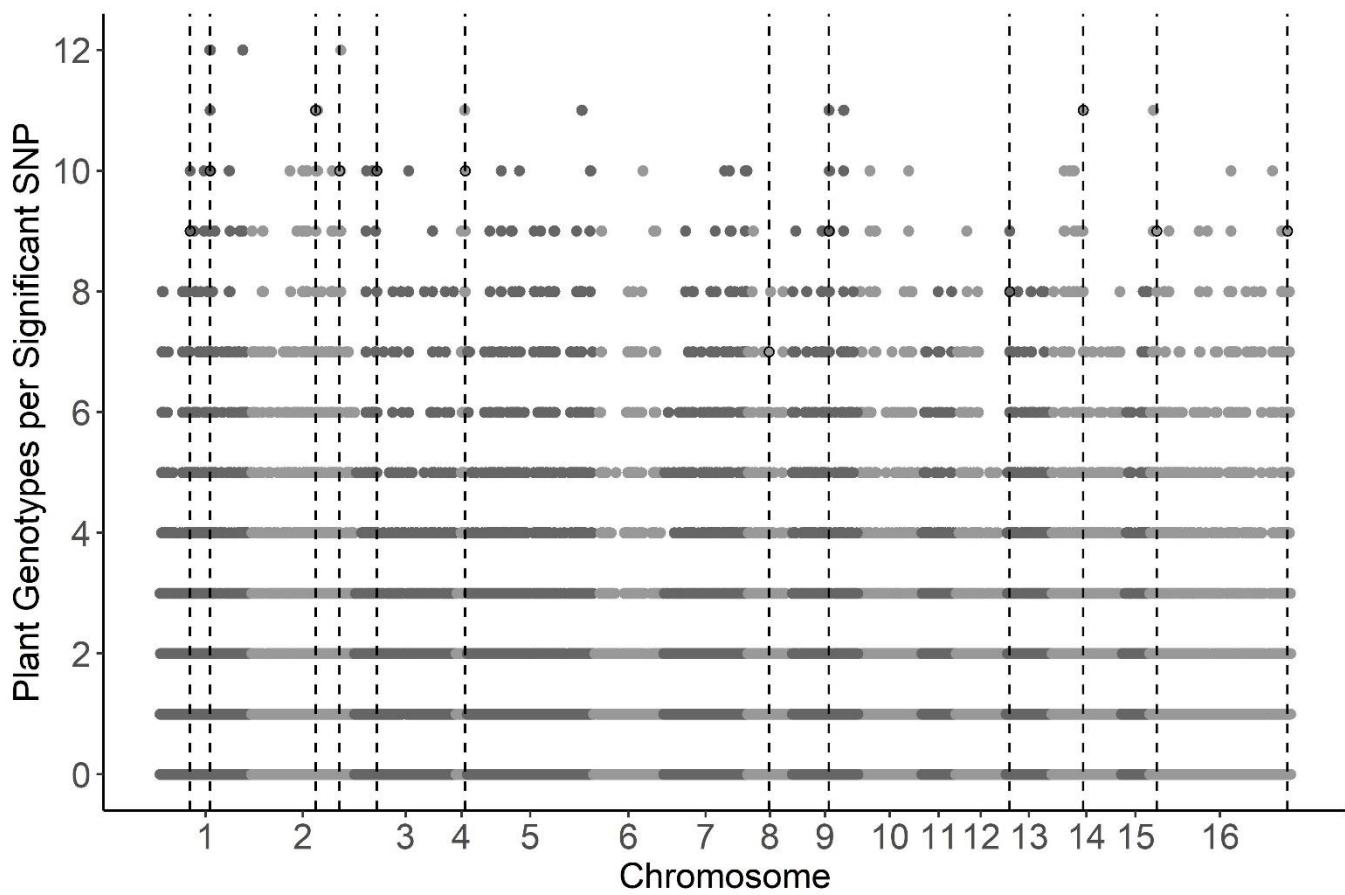


Figure 4. GWA of *B. cinerea* lesion size on individual tomato genotypes.

Botrytis cinerea chromosomes are differentiated by shading, alternating light and dark grey.

- a) Manhattan plot of estimated SNP effect sizes from bigRR for *B. cinerea* lesion size using a single tomato accession, LA2093. Permutation-derived thresholds are shown in horizontal dashed lines.
- b) The number of tomato accessions for which a *B. cinerea* SNP was significantly linked to lesion development by bigRR using the 99% permutation threshold. Frequency is number of phenotypes in which the SNP exceeds the threshold. Vertical dotted lines identify regions with overlap between the top 100 large-effect SNPs for LA2093 and significance across the majority (≥ 6) of tomato genotypes tested.

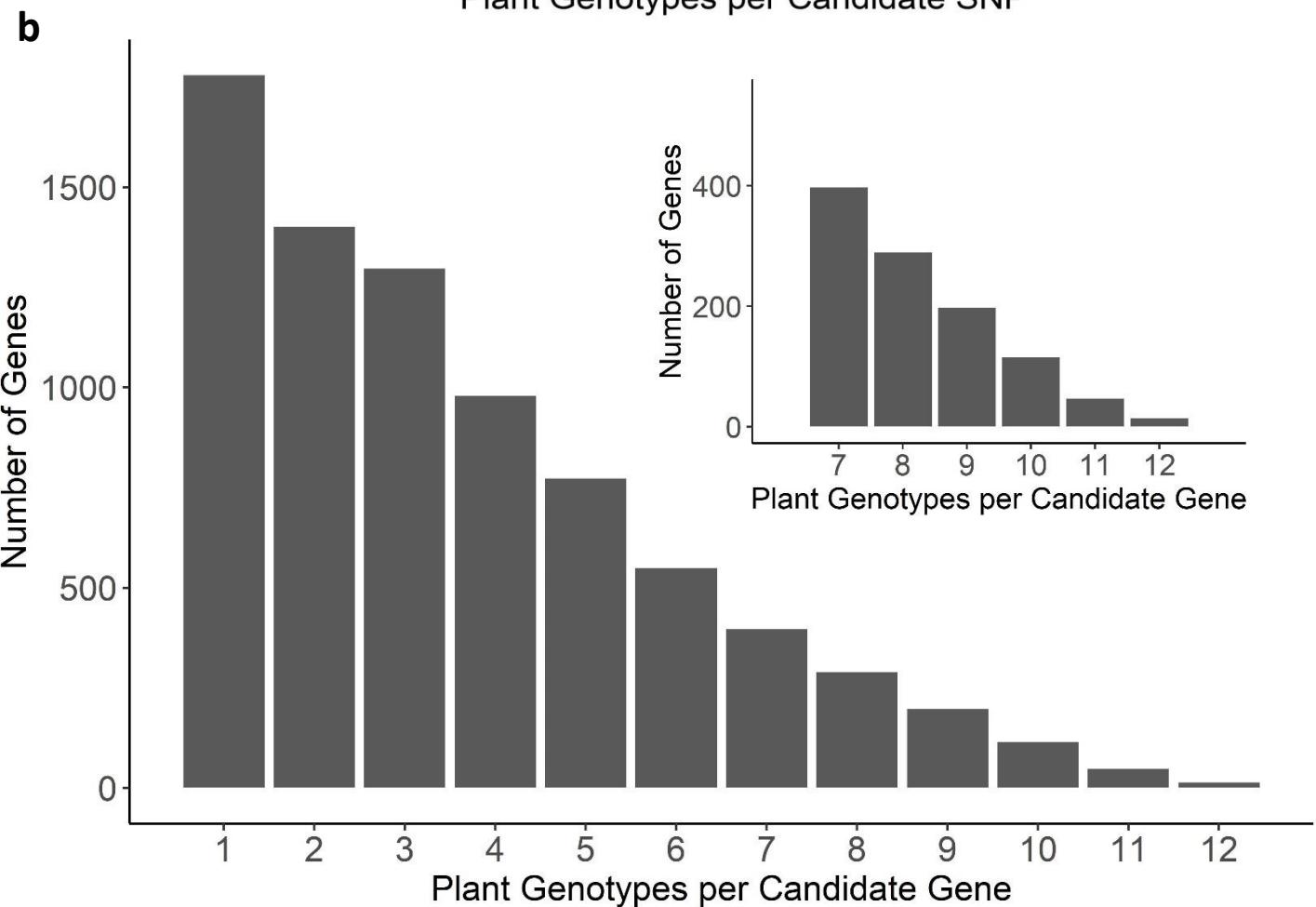
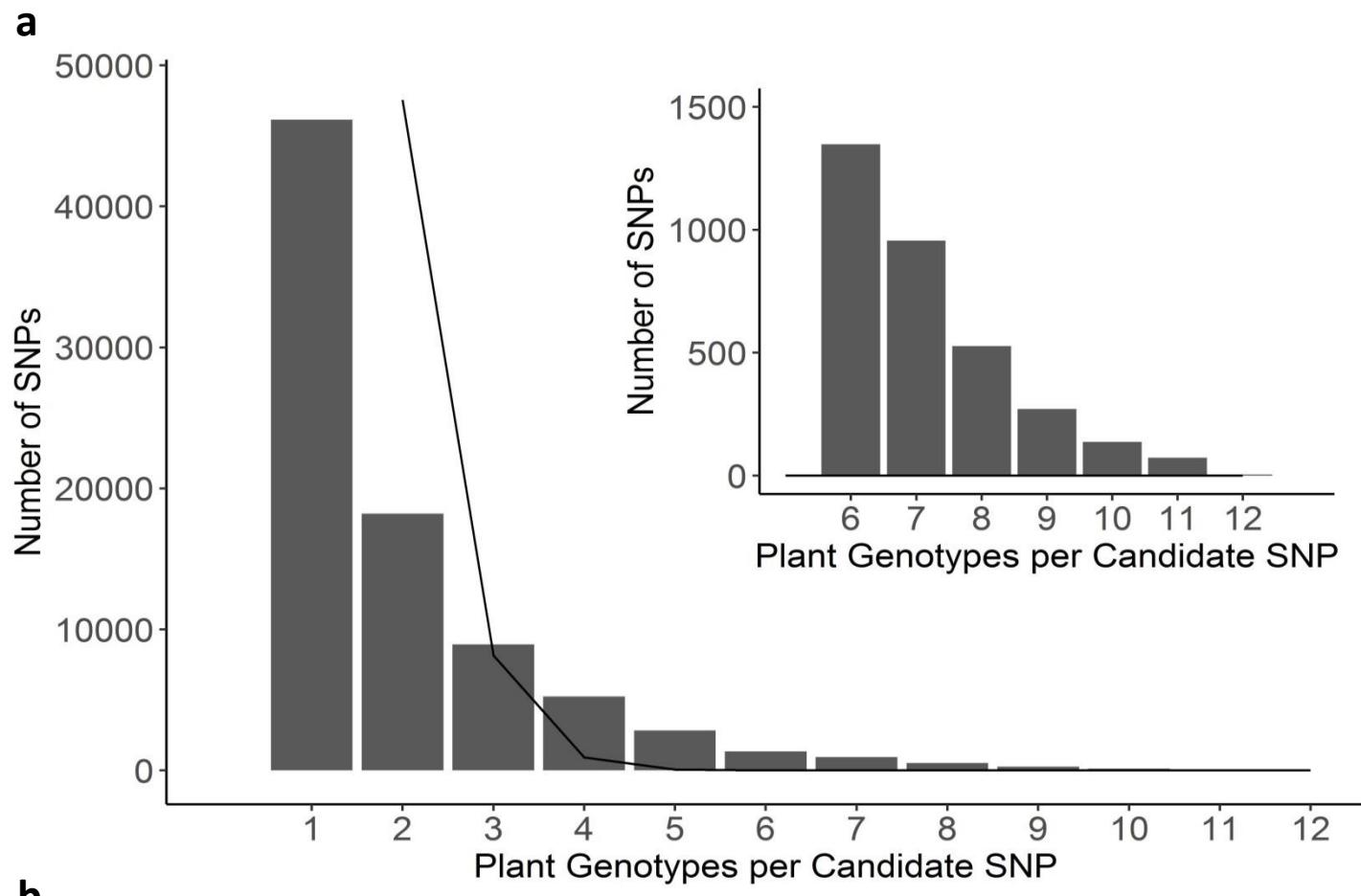
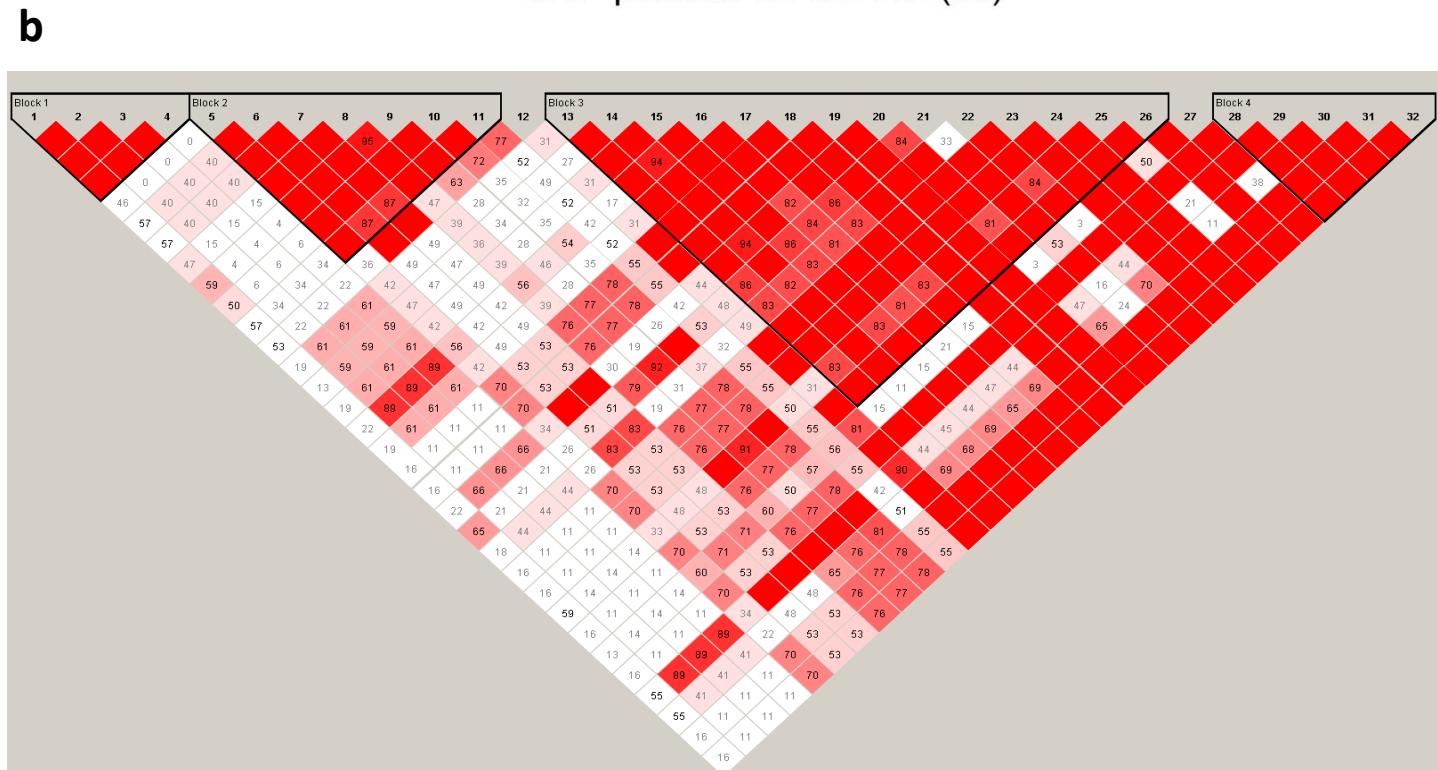
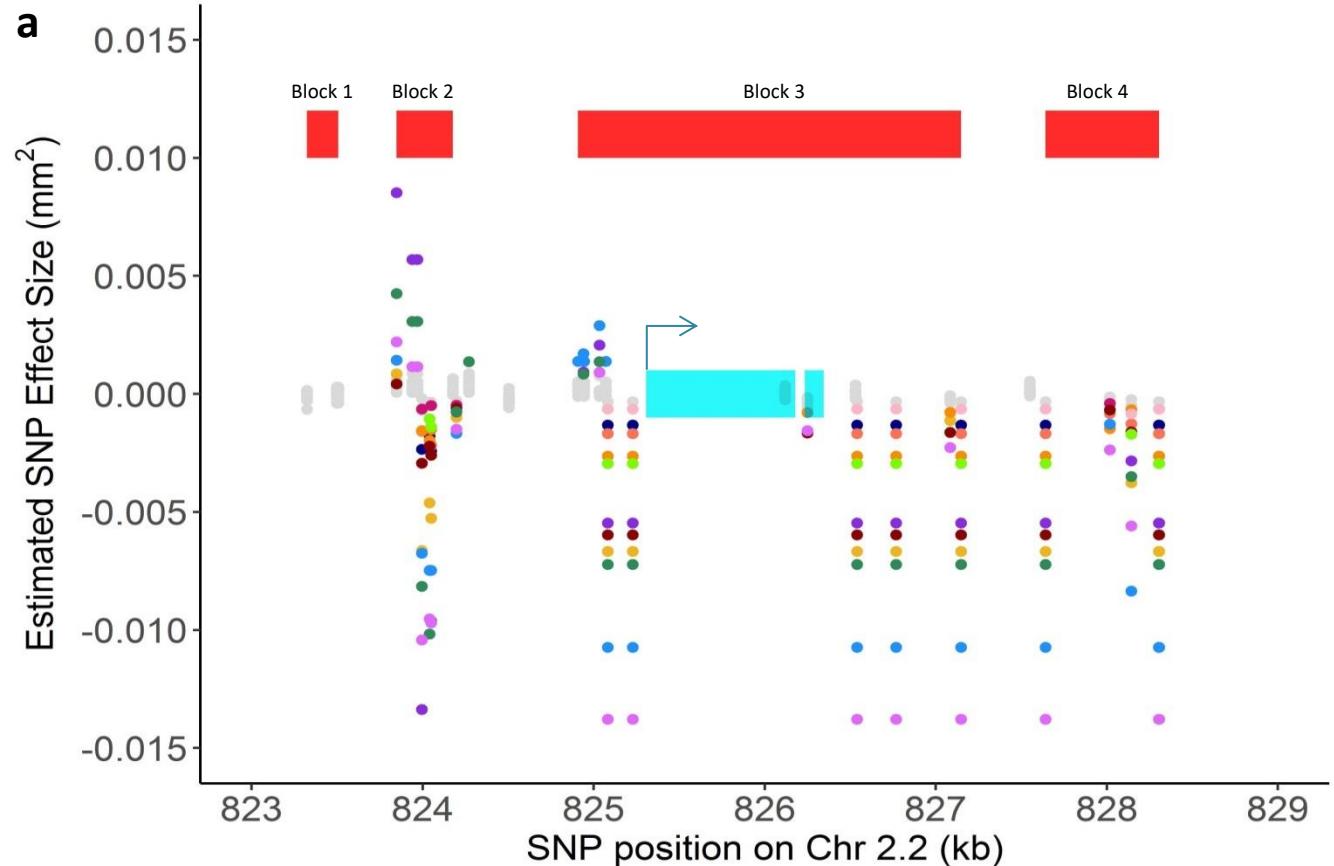


Figure 5. Frequency of overlap in *B. cinerea* GWA significance across tomato accessions.

- a) The frequency with which the *B. cinerea* SNPs significantly associate with lesion size on the 12 tomato accessions using bigRR and the 99% permutation threshold. The black line indicates the expected frequency of random overlap, given the number of significant SNPs per plant genotype and size of total SNP set. The inset zooms in on the distribution for overlapping SNPs above 6 plant genotypes for easier visualization. There were no SNPs expected to overlap by random chance in the inset.
- b) The frequency with which *B. cinerea* genes significantly associated with lesion size on the 12 tomato accessions. Genes were called as significant if there was one significant SNP called at the 99% permutation threshold within the gene body, or within 2kb of the gene body.



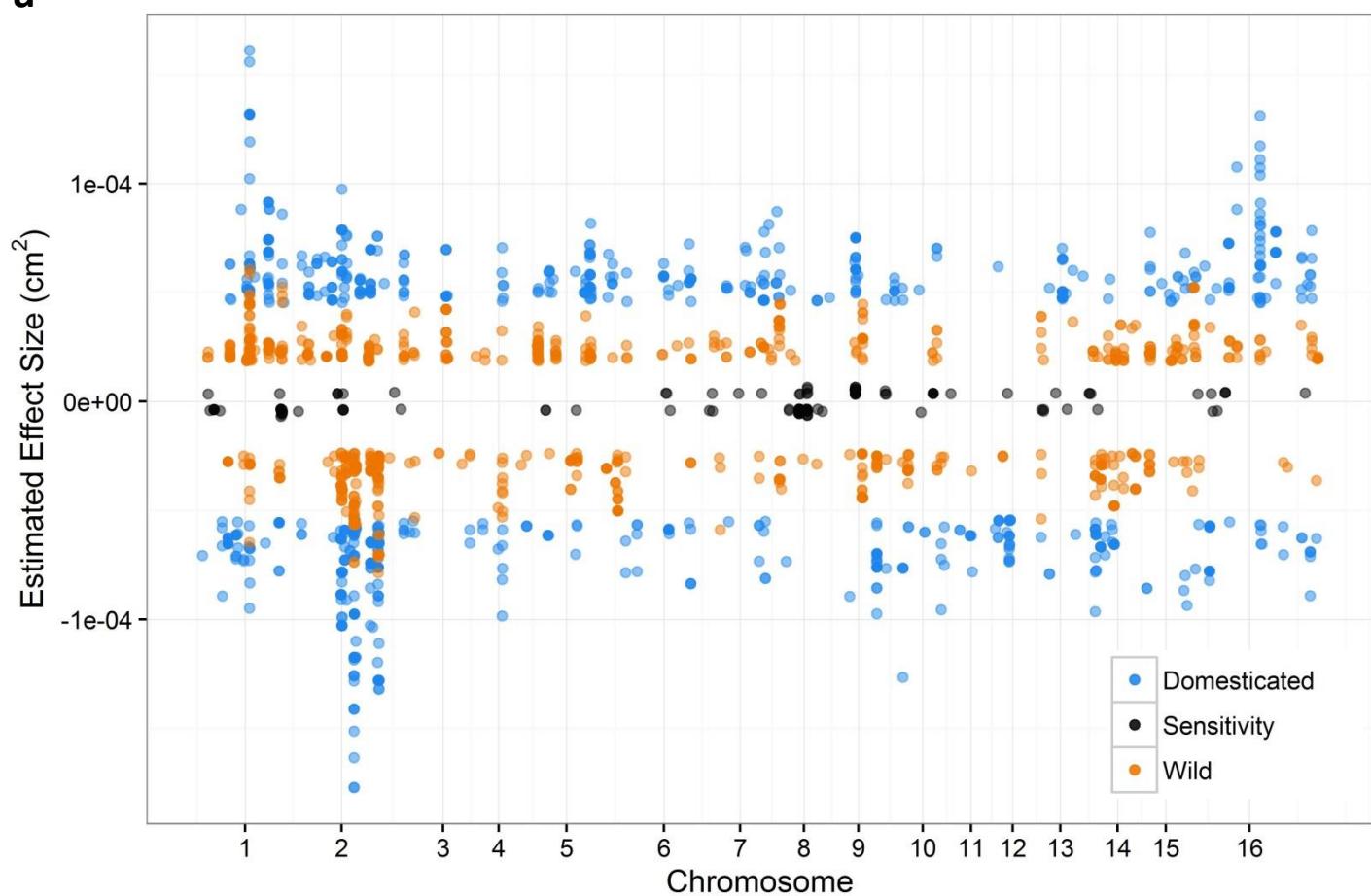
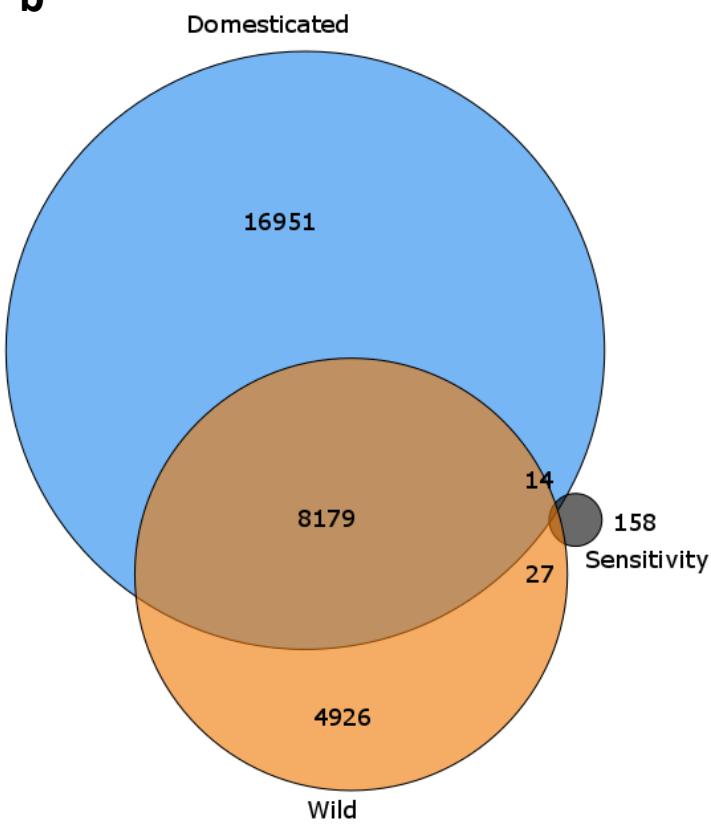
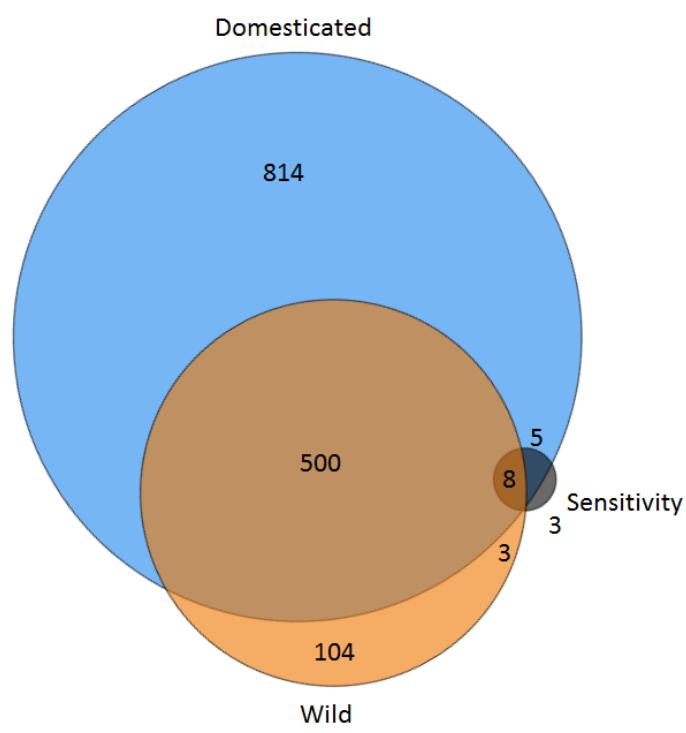
a**b****c**

Figure 7. GWA analysis of domestication sensitivity in *B. cinerea*.

Domestication sensitivity of each isolate was estimated using the average virulence on the wild and domesticated tomato germplasm and using calculated Sensitivity. This was then utilized for GWA mapping by bigRR.

- a) The top 1000 SNPs that significantly affect lesion size across domesticated tomato, wild tomato or domestication sensitivity are shown. Significance is called as crossing the 99% permutation threshold.
- b) Venn diagram of overlapping SNPs identified as crossing the 99% permutation threshold for each trait.
- c) Venn diagram of overlapping genes identified as crossing the 99% permutation threshold for each trait. Genes were called as significant if there was one significant SNP within the gene body or within 2kb of the gene body.

Parsed Citations

Abramovitch, R. B. and G. B. Martin (2004). "Strategies used by bacterial pathogens to suppress plant defenses." *Current opinion in plant biology* 7(4): 356-364.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

AbuQamar, S., M.-F. Chai, H. Luo, F. Song and T. Mengiste (2008). "Tomato protein kinase 1b mediates signaling of plant responses to necrotrophic fungi and insect herbivory." *The Plant Cell* 20(7): 1964-1983.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Atwell, S., J. Corwin, N. Soltis and D. Kliebenstein (2018). "Resequencing and association mapping of the generalist pathogen *Botrytis cinerea*." *bioRxiv*.

Atwell, S., J. Corwin, N. Soltis, A. Subedy, K. Denby and D. J. Kliebenstein (2015). "Whole genome resequencing of *Botrytis cinerea* isolates identifies high levels of standing diversity." *Frontiers in microbiology* 6: 996.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Bai, Y. and P. Lindhout (2007). "Domestication and breeding of tomatoes: what have we gained and what can we gain in the future?" *Annals of botany* 100(5): 1085-1094.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Ballaré, C. L. and R. Pierik (2017). "The shade-avoidance syndrome: multiple signals and ecological consequences." *Plant, cell & environment* 40(11): 2530-2543.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Barrett, L. G. and M. Heil (2012). "Unifying concepts and mechanisms in the specificity of plant–enemy interactions." *Trends in plant science* 17(5): 282-292.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Barrett, L. G., J. M. Kniskern, N. Bodenhausen, W. Zhang and J. Bergelson (2009). "Continua of specificity and virulence in plant host–pathogen interactions: causes and consequences." *New Phytologist* 183(3): 513-529.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Bartoli, C. and F. Roux (2017). "Genome-Wide Association Studies In Plant Pathosystems: Toward an Ecological Genomics Approach." *Frontiers in plant science* 8.

Bates, D., M. Maechler, B. Bolker and S. Walker (2015). "Fitting Linear Mixed-Effects Models Using lme4." *Journal of Statistical Software* 67(1): 1-48.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Bergougnoux, V. (2014). "The history of tomato: from domestication to biopharming." *Biotechnology advances* 32(1): 170-189.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Bhardwaj, V., S. Meier, L. N. Petersen, R. A. Ingle and L. C. Roden (2011). "Defence responses of *Arabidopsis thaliana* to infection by *Pseudomonas syringae* are regulated by the circadian clock." *PLoS one* 6(10): e26968.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Bittel, P. and S. Robatzek (2007). "Microbe-associated molecular patterns (MAMPs) probe plant immunity." *Current opinion in plant biology* 10(4): 335-341.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Blanca, J., J. Montero-Pau, C. Sauvage, G. Bauchet, E. Illa, M. J. Díez, D. Francis, M. Causse, E. van der Knaap and J. Cañizares (2015). "Genomic variation in tomato, from wild ancestors to contemporary breeding accessions." *BMC genomics* 16(1): 257.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Blanco-Ulate, B., A. Morales-Cruz, K. C. Amrine, J. M. Labavitch, A. L. Powell and D. Cantu (2014). "Genome-wide transcriptional profiling of *Botrytis cinerea* genes targeting plant cell walls during infections of different hosts." *Frontiers in plant science* 5.

Boller, T. and S. Y. He (2009). "Innate immunity in plants: an arms race between pattern recognition receptors in plants and effectors in microbial pathogens." *Science* 324(5928): 742-744.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Boyd, L. A., C. Ridout, D. M. O'Sullivan, J. E. Leach and H. Leung (2013). "Plant-pathogen interactions: disease resistance in modern agriculture." *Trends in genetics* 29(4): 233-240.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Campos, M. L., Y. Yoshida, I. T. Major, D. de Oliveira Ferreira, S. M. Weraduwage, J. E. Froehlich, B. F. Johnson, D. M. Kramer, G. Jander and T. D. Sharkey (2016). "Rewiring of jasmonate and phytochrome B signalling uncouples plant growth-defense tradeoffs." *Nature communications* 7: 12570.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Cerveny, L., A. Straskova, V. Dankova, A. Hartlova, M. Ceckova, F. Staud and J. Stulik (2013). "Tetratricopeptide repeat motifs in the world of bacterial pathogens: role in virulence mechanisms." *Infection and immunity* 81(3): 629-635.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Chaudhary, B. (2013). "Plant domestication and resistance to herbivory." *International journal of plant genomics* 2013.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Choquer, M., E. Fournier, C. Kunz, C. Levis, J.-M. Pradier, A. Simon and M. Viaud (2007). "Botrytis cinerea virulence factors: new insights into a necrotrophic and polyphagous pathogen." *FEMS microbiology letters* 277(1): 1-10.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Corwin, J. A., D. Copeland, J. Feusier, A. Subedy, R. Eshbaugh, C. Palmer, J. Maloof and D. J. Kliebenstein (2016). "The quantitative basis of the *Arabidopsis* innate immune system to endemic pathogens depends on pathogen genetics." *PLoS Genet* 12(2): e1005789.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Corwin, J. A., A. Subedy, R. Eshbaugh and D. J. Kliebenstein (2016). "Expansive phenotypic landscape of *Botrytis cinerea* shows differential contribution of genetic diversity and plasticity." *Molecular Plant-Microbe Interactions* 29(4): 287-298.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Couch, B. C., I. Fudal, M.-H. Lebrun, D. Tharreau, B. Valent, P. Van Kim, J.-L. Nottéghem and L. M. Kohn (2005). "Origins of host-specific populations of the blast pathogen *Magnaporthe oryzae* in crop domestication with subsequent expansion of pandemic clones on rice and weeds of rice." *Genetics* 170(2): 613-630.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Dalmais, B., J. Schumacher, J. Moraga, P. Le Pecheur, B. Tudzynski, I. G. Collado and M. Viaud (2011). "The *Botrytis cinerea* phytotoxin botcinic acid requires two polyketide synthases for production and has a redundant role in virulence with botrydial." *Molecular plant pathology* 12(6): 564-579.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Dalman, K., K. Himmelstrand, Å Olson, M. Lind, M. Brandström-Durling and J. Stenlid (2013). "A genome-wide association study identifies genomic regions for virulence in the non-model organism *Heterobasidion annosum* ss." *PLoS One* 8(1): e53525.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Dangl, J. L. and J. D. Jones (2001). "Plant pathogens and integrated defence responses to infection." *nature* 411(6839): 826-833.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

De Feyter, R., Y. Yang and D. W. Gabriel (1993). "Gene-for-genes interactions between cotton R genes and *Xanthomonas campestris* pv. *malvacearum* avr genes." *Molecular plant-microbe interactions: MPMI* 6(2): 225-237.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Dean, R., J. A. Van Kan, Z A Pretorius, K. E. Hammond-Kosack, A Di Pietro, P. D. Spanu, J. J. Rudd, M. Dickman, R. Kahmann and J. Ellis (2012). "The Top 10 fungal pathogens in molecular plant pathology." *Molecular plant pathology* 13(4): 414-430.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Deighton, N., I. Muckenschabel, A. J. Colmenares, I. G. Collado and B. Williamson (2001). "Botrydial is produced in plant tissues infected by *Botrytis cinerea*." *Phytochemistry* 57(5): 689-692.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Denby, K. J., P. Kumar and D. J. Kliebenstein (2004). "Identification of *Botrytis cinerea* susceptibility loci in *Arabidopsis thaliana*." *The Plant Journal* 38(3): 473-486.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Desjardins, C. A., K. A. Cohen, V. Munsamy, T. Abeel, K. Maharaj, B. J. Walker, T. P. Shea, D. V. Almeida, A. L. Manson and A. Salazar (2016). "Genomic and functional analyses of *Mycobacterium tuberculosis* strains implicate *ald* in D-cycloserine resistance." *Nature genetics* 48(5): 544-551.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Diaz, J., A ten Have and J. A. van Kan (2002). "The role of ethylene and wound signaling in resistance of tomato to *Botrytis cinerea*." *Plant physiology* 129(3): 1341-1351.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Dodds, P. N. and J. P. Rathjen (2010). "Plant immunity: towards an integrated view of plant-pathogen interactions." *Nature Reviews Genetics* 11(8): 539-548.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Doebley, J. F., B. S. Gaut and B. D. Smith (2006). "The molecular genetics of crop domestication." *Cell* 127(7): 1309-1321.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Doerge, R. W. and G. A. Churchill (1996). "Permutation tests for multiple loci affecting a quantitative character." *Genetics* 142(1): 285-294.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Dwivedi, S. L., H. D. Upadhyaya, H. T. Stalker, M. W. Blair, D. J. Bertioli, S. Nielsen and R. Ortiz (2008). "Enhancing crop gene pools with beneficial traits using wild relatives." *Plant Breeding Reviews* 30: 179.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Egashira, H., A. Kuwashima, H. Ishiguro, K. Fukushima, T. Kaya and S. Imanishi (2000). "Screening of wild accessions resistant to gray mold (*Botrytis cinerea* Pers.) in *Lycopersicon*." *Acta physiologiae plantarum* 22(3): 324-326.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Elad, Y., B. Williamson, P. Tudzynski and N. Delen (2007). *Botrytis spp. and diseases they cause in agricultural systems—an introduction. Botryotis: Biology, pathology and control*, Springer: 1-8.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Failmezger, H., Y. Yuan, O. Rueda, F. Markowetz and M. H. Failmezger (2012). "CRImage: CRImage a package to classify cells and calculate tumour cellularity." *R package version 1.24.0*.

Farhat, M. R., B. J. Shapiro, K. J. Kieser, R. Sultana, K. R. Jacobson, T. C. Victor, R. M. Warren, E. M. Streicher, A. Calver and A. Sloutsky (2013). "Genomic analysis identifies targets of convergent positive selection in drug-resistant *Mycobacterium tuberculosis*." *Nature genetics* 45(10): 1183-1189.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Fekete, É., E. Fekete, L. Irinyi, L. Karaffa, M. Árnyasi, M. Asadollahi and E. Sándor (2012). "Genetic diversity of a *Botrytis cinerea* cryptic species complex in Hungary." *Microbiological Research* 167(5): 283-291.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Ferrari, S., R. Galletti, C. Denoux, G. De Lorenzo, F. M. Ausubel and J. Dewdney (2007). "Resistance to *Botrytis cinerea* induced in *Arabidopsis* by elicitors is independent of salicylic acid, ethylene, or jasmonate signaling but requires PHYTOALEXIN DEFICIENT3." *Plant physiology* 144(1): 367-379.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Ferrari, S., J. M. Plotnikova, G. De Lorenzo and F. M. Ausubel (2003). "Arabidopsis local resistance to *Botrytis cinerea* involves salicylic acid and camalexin and requires EDS4 and PAD2, but not SID2, EDS5 or PAD4." *The Plant Journal* 35(2): 193-205.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Fillinger, S. and Y. Elad (2015). *Botrytis-the Fungus, the Pathogen and Its Management in Agricultural Systems*, Springer.

Finkers, R., Y. Bai, P. van den Berg, R. van Berloo, F. Meijer-Dekens, A. Ten Have, J. van Kan, P. Lindhout and A. W. van Heusden (2008). "Quantitative resistance to *Botrytis cinerea* from *Solanum neorickii*." *Euphytica* 159(1-2): 83-92.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Finkers, R., A. W. van Heusden, F. Meijer-Dekens, J. A. van Kan, P. Maris and P. Lindhout (2007). "The construction of a *Solanum*

habrochaites LYC4 introgression line population and the identification of QTLs for resistance to *Botrytis cinerea*." Theoretical and Applied Genetics 114(6): 1071-1080.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Fordyce, R., N. Soltis, C. Caseys, G. Gwinner, J. Corwin, S. Atwell, D. Copeland, J. Feusier, A. Subedy, R. Eshbaugh and D. Kliebenstein (2018). "Combining Digital Imaging and GWA Mapping to Dissect Visual Traits in Plant/Pathogen Interactions." *Plant Physiology*.

Francisco, M., B. Joseph, H. Caligagan, B. Li, J. A. Corwin, C. Lin, R. E. Kerwin, M. Burow and D. J. Kliebenstein (2016). "Genome wide association mapping in *Arabidopsis thaliana* identifies novel genes involved in linking allyl glucosinolate to altered biomass and defense." *Frontiers in plant science* 7.

Gao, Y., Z. Liu, J. D. Faris, J. Richards, R. S. Brueggeman, X. Li, R. P. Oliver, B. A. McDonald and T. L. Friesen (2016). "Validation of genome-wide association studies as a tool to identify virulence factors in *Parastagonospora nodorum*." *Phytopathology* 106(10): 1177-1185.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Giraud, T., D. Fortini, C. Levis, C. Lamarque, P. Leroux, K. LoBuglio and Y. Brygoo (1999). "Two sibling species of the *Botrytis cinerea* complex, *transposa* and *vacuma*, are found in sympatry on numerous host plants." *Phytopathology* 89(10): 967-973.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Glazebrook, J. (2005). "Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens." *Annu. Rev. Phytopathol.* 43: 205-227.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Goss, E. M. and J. Bergelson (2006). "Variation in resistance and virulence in the interaction between *Arabidopsis thaliana* and a bacterial pathogen." *Evolution* 60(8): 1562-1573.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Guimaraes, R. L., R. T. Chetelat and H. U. Stotz (2004). "Resistance to *Botrytis cinerea* in *Solanum lycopersicoides* is dominant in hybrids with tomato, and involves induced hyphal death." *European journal of plant pathology* 110(1): 13-23.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Hacquard, S., B. Kracher, T. Maekawa, S. Vernaldi, P. Schulze-Lefert and E. V. L. van Themaat (2013). "Mosaic genome structure of the barley powdery mildew pathogen and conservation of transcriptional programs in divergent hosts." *Proceedings of the National Academy of Sciences* 110(24): E2219-E2228.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Hahn, M. (2014). "The rising threat of fungicide resistance in plant pathogenic fungi: *Botrytis* as a case study." *Journal of chemical biology* 7(4): 133-141.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Hevia, M. A., P. Canessa, H. Müller-Esparza and L. F. Larrondo (2015). "A circadian oscillator in the fungus *Botrytis cinerea* regulates virulence when infecting *Arabidopsis thaliana*." *Proceedings of the National Academy of Sciences* 112(28): 8744-8749.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Hyten, D. L., Q. Song, Y. Zhu, I.-Y. Choi, R. L. Nelson, J. M. Costa, J. E. Specht, R. C. Shoemaker and P. B. Cregan (2006). "Impacts of genetic bottlenecks on soybean genome diversity." *Proceedings of the National Academy of Sciences* 103(45): 16666-16671.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Izquierdo-Bueno, I., V. E. González-Rodríguez, A. Simon, B. Dalmais, J. M. Pradier, P. Le Pêcheur, A. Mercier, A. S. Walker, C. Garrido and I. G. Collado (2018). "Biosynthesis of abscisic acid in fungi: Identification of a sesquiterpene cyclase as the key enzyme in *Botrytis cinerea*." *Environmental microbiology*.

Jombart, T. (2008). "adegenet: a R package for the multivariate analysis of genetic markers." *Bioinformatics* 24(11): 1403-1405.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Jones, J. D. and J. L. Dangl (2006). "The plant immune system." *Nature* 444(7117): 323-329.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Katan, T. (1999). "Current status of vegetative compatibility groups in *Fusarium oxysporum*." *Phytoparasitica* 27(1): 51-64.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Keen, N. (1992). "The molecular biology of disease resistance." Plant molecular biology 19(1): 109-122.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Kliebenstein, D. J., H. C. Rowe and K. J. Denby (2005). "Secondary metabolites influence Arabidopsis/Botrytis interactions: variation in host production and pathogen sensitivity." The Plant Journal 44(1): 25-36.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Koenig, D., J. M. Jiménez-Gómez, S. Kimura, D. Fulop, D. H. Chitwood, L. R. Headland, R. Kumar, M. F. Covington, U. K. Devisetty and A. V. Tat (2013). "Comparative transcriptomics reveals patterns of selection in domesticated and wild tomato." Proceedings of the National Academy of Sciences 110(28): E2655-E2662.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Kooke, R., W. Kruijer, R. Bours, F. F. Becker, A. Kuhn, J. Buntjer, T. Doeswijk, J. Guerra, H. J. Bouwmeester and D. Vreugdenhil (2016). "Genome-wide association mapping and genomic prediction elucidate the genetic architecture of morphological traits in Arabidopsis thaliana." Plant Physiology: pp. 00997.02015.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Kover, P. X. and B. A. Schaal (2002). "Genetic variation for disease resistance and tolerance among Arabidopsis thaliana accessions." Proceedings of the National Academy of Sciences 99(17): 11270-11274.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Kretschmer, M. and M. Hahn (2008). "Fungicide resistance and genetic diversity of Botrytis cinerea isolates from a vineyard in Germany." Journal of Plant Diseases and Protection: 214-219.

Kurtz, S., A. Phillippe, A. L. Delcher, M. Smoot, M. Shumway, C. Antonescu and S. L. Salzberg (2004). "Versatile and open software for comparing large genomes." Genome biology 5(2): R12.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Lin, T., G. Zhu, J. Zhang, X. Xu, Q. Yu, Z. Zheng, Z. Zhang, Y. Lun, S. Li and X. Wang (2014). "Genomic analyses provide insights into the history of tomato breeding." Nature genetics 46(11): 1220.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Liu, B., Y.-B. Hong, Y.-F. Zhang, X.-H. Li, L. Huang, H.-J. Zhang, D.-Y. Li and F.-M. Song (2014). "Tomato WRKY transcriptional factor SIDRW1 is required for disease resistance against Botrytis cinerea and tolerance to oxidative stress." Plant Science 227: 145-156.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Lo Presti, L., C. López Díaz, D. Turrà, A. Di Pietro, M. Hampel, K. Heimel and R. Kahmann (2016). "A conserved co-chaperone is required for virulence in fungal plant pathogens." New Phytologist 209(3): 1135-1148.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Loxdale, H. D., G. Lushai and J. A. Harvey (2011). "The evolutionary improbability of 'generalism' in nature, with special reference to insects." Biological Journal of the Linnean Society 103(1): 1-18.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Ma, Z. and T. J. Michailides (2005). "Genetic structure of Botrytis cinerea populations from different host plants in California." Plant disease 89(10): 1083-1089.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Martinez, F., D. Blancard, P. Lecomte, C. Levis, B. Dubos and M. Fermaud (2003). "Phenotypic differences between vacuma and transposa subpopulations of Botrytis cinerea." European Journal of Plant Pathology 109(5): 479-488.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Miller, J. and S. Tanksley (1990). "RFLP analysis of phylogenetic relationships and genetic variation in the genus Lycopersicon." TAG Theoretical and Applied Genetics 80(4): 437-448.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Müller, N. A., C. L. Wijnen, A. Srinivasan, M. Ryngajlo, I. Ofner, T. Lin, A. Ranjan, D. West, J. N. Maloof and N. R. Sinha (2016). "Domestication selected for deceleration of the circadian clock in cultivated tomato." Nature genetics 48(1): 89-93.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Nicot, P., A. Moretti, C. Romiti, M. Bardin, C. Caranta and H. Ferriere (2002). "Differences in susceptibility of pruning wounds and

leaves to infection by *Botrytis cinerea* among wild tomato accessions." TGC Report 52: 24-26.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Nicot, P. C. and A. Baille (1996). Integrated control of *Botrytis cinerea* on greenhouse tomatoes. *Aerial Plant Surface Microbiology*, Springer: 169-189.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Nomura, K., M. Melotto and S.-Y. He (2005). "Suppression of host defense in compatible plant–*Pseudomonas syringae* interactions." *Current opinion in plant biology* 8(4): 361-368.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Ober, U., W. Huang, M. Magwire, M. Schlather, H. Simianer and T. F. Mackay (2015). "Accounting for genetic architecture improves sequence based genomic prediction for a *Drosophila* fitness trait." *PLoS One* 10(5): e0126880.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Ormond, E. L., A. P. Thomas, P. J. Pugh, J. K. Pell and H. E. Roy (2010). "A fungal pathogen in time and space: the population dynamics of *Beauveria bassiana* in a conifer forest." *FEMS microbiology ecology* 74(1): 146-154.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Panthee, D. R. and F. Chen (2010). "Genomics of fungal disease resistance in tomato." *Current genomics* 11(1): 30-39.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Parlevliet, J. E. (2002). "Durability of resistance against fungal, bacterial and viral pathogens; present situation." *Euphytica* 124(2): 147-156.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Pau, G., F. Fuchs, O. Sklyar, M. Boutros and W. Huber (2010). "EBImage-an R package for image processing with applications to cellular phenotypes." *Bioinformatics* 26(7): 979-981.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Pedras, M. S. C. and P. W. Ahiahou (2005). "Metabolism and detoxification of phytoalexins and analogs by phytopathogenic fungi." *Phytochemistry* 66(4): 391-411.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Pedras, M. S. C., S. Hossain and R. B. Snitinsky (2011). "Detoxification of cruciferous phytoalexins in *Botrytis cinerea*: Spontaneous dimerization of a camalexin metabolite." *Phytochemistry* 72(2): 199-206.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Peralta, I., D. Spooner and S. Knapp (2008). "The taxonomy of tomatoes: a revision of wild tomatoes (*Solanum section Lycopersicon*) and their outgroup relatives in sections *Juglandifolium* and *Lycopersicoides*." *Syst Bot Monogr* 84: 1-186.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Persoons, A., E. Morin, C. Delaruelle, T. Payen, F. Halkett, P. Frey, S. De Mita and S. Duplessis (2014). "Patterns of genomic variation in the poplar rust fungus *Melampsora larici-populina* identify pathogenesis-related factors." *Frontiers in plant science* 5.

Pieterse, C. M., D. Van der Does, C. Zamioudis, A. Leon-Reyes and S. C. Van Wees (2012). "Hormonal modulation of plant immunity." *Annual review of cell and developmental biology* 28: 489-521.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Poland, J. A., P. J. Balint-Kurti, R. J. Wisser, R. C. Pratt and R. J. Nelson (2009). "Shades of gray: the world of quantitative disease resistance." *Trends in plant science* 14(1): 21-29.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Power, R. A., J. Parkhill and T. de Oliveira (2017). "Microbial genome-wide association studies: lessons from human GWAS." *Nature Reviews Genetics* 18(1): 41-50.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Quidde, T., P. Büttner and P. Tudzynski (1999). "Evidence for three different specific saponin-detoxifying activities in *Botrytis cinerea* and cloning and functional analysis of a gene coding for a putative avenacinase." *European Journal of Plant Pathology* 105(3): 273-283.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Quidde, T., A. Osbourn and P. Tudzynski (1998). "Detoxification of α -tomatine by *Botrytis cinerea*." *Physiological and Molecular Plant Pathology* 52(3): 151-165.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

R Development Core Team (2008). "R: A language and environment for statistical computing." R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Romanazzi, G. and S. Droby (2016). Control Strategies for Postharvest Grey Mould on Fruit Crops. *Botrytis—the Fungus, the Pathogen and its Management in Agricultural Systems*, Springer: 217-228.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Rosenthal, J. P. and R. Dirzo (1997). "Effects of life history, domestication and agronomic selection on plant defence against insects: evidence from maizes and wild relatives." *Evolutionary Ecology* 11(3): 337-355.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Rowe, H. C. and D. J. Kliebenstein (2007). "Elevated genetic variation within virulence-associated *Botrytis cinerea* polygalacturonase loci." *Molecular Plant-Microbe Interactions* 20(9): 1126-1137.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Rowe, H. C. and D. J. Kliebenstein (2008). "Complex genetics control natural variation in *Arabidopsis thaliana* resistance to *Botrytis cinerea*." *Genetics* 180(4): 2237-2250.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Rowe, H. C., J. W. Walley, J. Corwin, E. K.-F. Chan, K. Dehesh and D. J. Kliebenstein (2010). "Deficiencies in jasmonate-mediated plant defense reveal quantitative variation in *Botrytis cinerea* pathogenesis." *PLoS Pathog* 6(4): e1000861.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Samuel, S., T. Veloukas, A. Papavasileiou and G. S. Karaoglanidis (2012). "Differences in frequency of transposable elements presence in *Botrytis cinerea* populations from several hosts in Greece." *Plant disease* 96(9): 1286-1290.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Sauerbrunn, N. and N. L. Schlaich (2004). "PCC1: a merging point for pathogen defence and circadian signalling in *Arabidopsis*." *Planta* 218(4): 552-561.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Schumacher, J., J.-M. Pradier, A. Simon, S. Traeger, J. Moraga, I. G. Collado, M. Viaud and B. Tudzynski (2012). "Natural variation in the VELVET gene bcvel1 affects virulence and light-dependent differentiation in *Botrytis cinerea*." *PLoS One* 7(10): e47840.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Shen, X., M. Alam, F. Fikse and L. Rönnegård (2013). "A novel generalized ridge regression method for quantitative genetics." *Genetics* 193(4): 1255-1268.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Siewers, V., M. Viaud, D. Jimenez-Teja, I. G. Collado, C. S. Gronover, J.-M. Pradier, B. Tudzynski and P. Tudzynski (2005). "Functional analysis of the cytochrome P450 monooxygenase gene bcbot1 of *Botrytis cinerea* indicates that botrydial is a strain-specific virulence factor." *Molecular plant-microbe interactions* 18(6): 602-612.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Sim, S.-C., G. Durstewitz, J. Plieske, R. Wieseke, M. W. Ganal, A. Van Deynze, J. P. Hamilton, C. R. Buell, M. Causse and S. Wijeratne (2012). "Development of a large SNP genotyping array and generation of high-density genetic maps in tomato." *PloS one* 7(7): e40563.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Smale, M. (1996). "Understanding global trends in the use of wheat diversity and international flows of wheat genetic resources."

Staats, M. and J. A. van Kan (2012). "Genome update of *Botrytis cinerea* strains B05. 10 and T4." *Eukaryotic cell* 11(11): 1413-1414.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Stefanato, F. L., E. Abou-Mansour, A. Buchala, M. Kretschmer, A. Mosbach, M. Hahn, C. G. Bochet, J. P. Métraux and H. j. Schoonbeek (2009). "The ABC transporter BcatrB from *Botrytis cinerea* exports camalexin and is a virulence factor on *Arabidopsis thaliana*." The

Plant Journal 58(3): 499-510.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Stukenbrock, E. H. and B. A. McDonald (2008). "The origins of plant pathogens in agro-ecosystems." Annu. Rev. Phytopathol. 46: 75-100.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Talas, F., R. Kalih, T. Miedaner and B. A. McDonald (2016). "Genome-wide association study identifies novel candidate genes for aggressiveness, deoxynivalenol production, andazole sensitivity in natural field populations of *Fusarium graminearum*." Molecular Plant-Microbe Interactions 29(5): 417-430.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Tanksley, S. D. (2004). "The genetic, developmental, and molecular bases of fruit size and shape variation in tomato." The plant cell 16(suppl 1): S181-S189.

Tanksley, S. D. and S. R. McCouch (1997). "Seed banks and molecular maps: unlocking genetic potential from the wild." Science 277(5329): 1063-1066.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

ten Have, A., W. Mulder, J. Visser and J. A. van Kan (1998). "The endopolygalacturonase gene Bcpg1 is required for full virulence of *Botrytis cinerea*." Molecular Plant-Microbe Interactions 11(10): 1009-1016.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Ten Have, A., R. van Berloo, P. Lindhout and J. A. van Kan (2007). "Partial stem and leaf resistance against the fungal pathogen *Botrytis cinerea* in wild relatives of tomato." European journal of plant pathology 117(2): 153-166.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Tiffin, P. and D. A. Moeller (2006). "Molecular evolution of plant immune system genes." Trends in genetics 22(12): 662-670.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Upadhyaya, N. M., D. P. Garnica, H. Karaoglu, J. Sperschneider, A. Nemri, B. Xu, R. Mago, C. A. Cuomo, J. P. Rathjen and R. F. Park (2014). "Comparative genomics of Australian isolates of the wheat stem rust pathogen *Puccinia graminis* f. sp. tritici reveals extensive polymorphism in candidate effector genes." Frontiers in plant science 5.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Valette-Collet, O., A. Cimerman, P. Reignault, C. Levis and M. Boccardo (2003). "Disruption of *Botrytis cinerea* pectin methylesterase gene Bcpme1 reduces virulence on several host plants." Molecular Plant-Microbe Interactions 16(4): 360-367.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Viaud, M., A-F. Adam-Blondon, J. Amselem, P. Bally, A. Cimerman, B. Dalmais-Lenaers, N. Lapalu, M.-H. Lebrun, B. Poinssot and J. M. Pradier (2012). "Le génome de *Botrytis* décrypté." Revue des oenologues et des techniques vitivinicoles et oenologiques(142): 9-11.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Vleeshouwers, V. G. and R. P. Oliver (2014). "Effectors as tools in disease resistance breeding against biotrophic, hemibiotrophic, and necrotrophic plant pathogens." Molecular plant-microbe interactions 27(3): 196-206.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Weyman, P. D., Z. Pan, Q. Feng, D. G. Gilchrist and R. M. Bostock (2006). "A circadian rhythm-regulated tomato gene is induced by arachidonic acid and *Phytophthora infestans* infection." Plant physiology 140(1): 235-248.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Wicker, T., S. Oberhaensli, F. Parlange, J. P. Buchmann, M. Shatalina, S. Roffler, R. Ben-David, J. Doležel, H. Šimková and P. Schulze-Lefert (2013). "The wheat powdery mildew genome shows the unique evolution of an obligate biotroph." Nature Genetics 45(9): 1092-1096.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only Title Only Author and Title](#)

Wu, J. Q., S. Sakthikumar, C. Dong, P. Zhang, C. A. Cuomo and R. F. Park (2017). "Comparative genomics integrated with association analysis identifies candidate effector genes corresponding to Lr20 in phenotype-paired *Puccinia triticina* isolates from Australia." Frontiers in plant science 8.

Zerbino, D. R., P. Achuthan, W. Akanni, M. R. Amode, D. Barrell, J. Bhai, K. Billis, C. Cummins, A. Gall and C. G. Girón (2017). "Ensembl

2018." Nucleic acids research 46(D1): D754-D761.

Zhang, L., A. Khan, D. Nino-Liu and M. Foolad (2002). "A molecular linkage map of tomato displaying chromosomal locations of resistance gene analogs based on a *Lycopersicon esculentum*×*Lycopersicon hirsutum* cross." Genome 45(1): 133-146.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Zhang, W., J. A. Corwin, D. Copeland, J. Feusier, R. Eshbaugh, F. Chen, S. Atwell and D. J. Kliebenstein (2017). "Plastic transcriptomes stabilize immunity to pathogen diversity: the jasmonic acid and salicylic acid networks within the *Arabidopsis*/*Botrytis* pathosystem." The Plant Cell: tpc. 00348.02017.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Zhou, X. and M. Stephens (2012). "Genome-wide efficient mixed-model analysis for association studies." Nature genetics 44(7): 821.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Zipfel, C., S. Robatzek, L. Navarro and E. J. Oakeley (2004). "Bacterial disease resistance in *Arabidopsis* through flagellin perception." Nature 428(6984): 764.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)

Züst, T. and A. A. Agrawal (2017). "Trade-offs between plant growth and defense against insect herbivory: an emerging mechanistic synthesis." Annual review of plant biology 68: 513-534.

Pubmed: [Author and Title](#)

Google Scholar: [Author Only](#) [Title Only](#) [Author and Title](#)