The Genetics of Quantitative Plant Pathology: *Botrytis cinerea* Genetic Control of Pathogen and Host Disease Phenotypes

By

NICOLE SOLTIS

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

Plant Biology

in the

OFFICE OF GRADUATE STUDIES

of the

UNIVERSITY OF CALIFORNIA

DAVIS

Approved:

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(Daniel Kliebenstein, Ph.D.), Chair

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(Takao Kasuga, Ph.D.)

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(Daniel Runcie, Ph.D.)

Committee in Charge

2019

Table of Contents

Acknowledgements ………………...………………………………………....…………………………..1

Abstract……………………………………………………………………………………………………3

CHAPTER 1: Natural variation of plant metabolism: genetic mechanisms, interpretive caveats, evolutionary and mechanistic insights …………………………………………………………………….

1.1 Manuscript ……………………………………………………..……………………………2

1.2 References ………………………………………………………………….……………….10

CHAPTER 2: Interactions of tomato and *Botrytis cinerea* genetic diversity: Parsing the contributions of host differentiation, domestication, and pathogen variation ………………………………………………

2.1 Manuscript ………………………………………………………..…………………………15

2.2 References ……………………….………………………………………….……………….44 2.3 Supplementary Documents ………………………………….………….………….………..71

CHAPTER 3: Pathogen genetic control of transcriptome variation in the *Arabidopsis thaliana* – *Botrytis cinerea* pathosystem ……………………………………………………………………………………….

3.1 Manuscript …………………………….…………………………..…………………………84

3.2 References …………………………...…………………………………….………………….X

3.3 Supplementary Documents ………………………………...………….…………….………..X

ACKNOWLEDGEMENTS

The decision of where to commit to a dissertation’s worth of research is a difficult one, and one I weighed heavily. I could not be happier with the choices I made, in finding a city, university, graduate group, and laboratory that I have been glad to call home. Those first few months were an abrupt transition in my training from ecology to genetics, quantitative biology, and developmental biology. I am grateful to the many wonderful instructors who made that transition seamless and interesting, particularly Dr. Judy Jernstedt, Dr. John Labavitch, Dr. Kentaro Inoue, and Dr. John Harada.

I am thankful for our group lab meetings, where I learned to listen closely, and began to build a context for how larger research paths of labs take shape. I’m particularly grateful to Dr. Katayoon Dehesh, Dr. Siobhan Brady, Dr. Allison Gaudinier, Dr. Gina Turco for the insight, encouragement, and advice they shared over the years.

The members of the Kliebenstein lab, who played many roles from mentor, to helper, to emotional support. To my advisor, Dr. Daniel Kliebenstein, for encouraging me to set my ambitions high, but helping me to understand both failures and successes at the appropriate (small) scale. Also, for somehow striking that elusive balance between offering a graduate student complete freedom to establish intellectual dependence yet directing me back to a productive track when I dig myself into a strange analytical hole. To the lab members who offered support, through words and lab work and hours spent sitting in quiet company analyzing data, especially Dr. Jason Corwin, Dr. Rachel Kerwin, Rachel Fordyce, Dr. Susanna Atwell, Dr. Gongjun Shi, Raoni Gwinner, Dr. Gongjun Shi, Dr. Wei Zhang. To the many undergraduate research assistants who helped with experiments, including

For the friends who worked beside me throughout the PhD process, and inspired me to be a better scientist. I’d particularly like to thank Michelle Tang, Kristin Lee, Dr. Mark Taylor, Dr. Geoff Benn, Dr. Alexander Wilson.

The friends and mentors who helped me stay positive and motivated through science communication. In particular I’d like to thank Shannon Albers, Dr. Jenna Gallegos, Dr. Gena Hoffman, Destiny Davis, Don Gibson, Sheila Montgomery.

My family members, for their unfailing belief in me and the many free dinners- my mother, stepfather, father, and sister.

ABSTRACT

Much of what is currently known in the genetic basis of plant disease comes from studies of large-effect loci for plant defense and pathogen virulence, which often evolve from reciprocal gene-for-gene adaptation in specialist plant pathogen systems. However, significant quantitative natural variation in disease interactions is controlled by numerous small-effect loci dispersed across the genome. Studies of natural variation of the plant side are elucidating the quantitative genetics of plant resistance through genome wide association (GWA). However, studies of the pathogen side of the interaction are relatively sparse, partially due to a lack of genetic resources. In fact, the majority of plant pathogen studies select a single pathogen genotype as the focus of research and strive to generalize findings to the diversity throughout a pathogen species. Particularly for diverse, generalist pathogen species, this restricted view may leave major gaps in our understanding of virulence genetics in pathogens, and hinder efforts to breed durable resistance in plant hosts.

Chapter 1 reviews the current literature in the quantitative genetics of metabolic and expression variation in the plant, including disease responses. Major findings include the separation of genetic mechanism from metabolic response by transport pathways, and the connection between organellar genetic variation and organismal metabolism.

Both chapters 2 and 3 utilize the resource of a resequenced population of 96 diverse *Botrytis cinerea* isolates collected from diverse host species and geographic origins. I use two methods and two genome alignments to correlate phenotypic diversity to SNP information across XX loci. As such, I identify candidate genes for the control of B. cinerea lesion size on tomato, and the control of gene expression in both host and pathogen for the A. thaliana x B. cinerea pathosystem. In whole, this research tests a matrix of XX phenotype – SNP connections and identifies XX loci in the pathogen genome of particular interest for virulence research.

Plant domestication is hypothesized to alter the interaction between plant and pathogen, potentially due to reduction of genetic diversity in the domestication bottleneck.

1. Combining quantitative genetics studies with metabolomics/metabolic profiling platforms, genomics, and transcriptomics is

creating significant progress in identifying the causal genes controlling natural variation in metabolite accumulations and

profiles. In this review, we discuss key mechanistic and evolutionary insights that are arising from these studies. This includes

the potential role of transport and other processes in leading to a separation of the site of mechanistic causation and metabolic

consequence. A reilluminated observation is the potential for genomic variation in the organelle to alter phenotypic variation

alone and in epistatic interaction with the nuclear genetic variation. These studies are also highlighting new aspects of metabolic

pleiotropy both in terms of the breadth of loci altering metabolic variation as well as the potential for broader effects on plant

defense regulation of the metabolic variation than has previously been predicted. We also illustrate caveats that can be

overlooked when translating quantitative genetics descriptors such as heritability and per-locus r2 to mechanistic or evolutionary

interpretations.

2. While the impacts of crop domestication on specialist pathogens are well known, less is

known about the interaction of crop variation and generalist pathogens. To study how

genetic variation within a crop affects plant resistance to generalist pathogens, we

infected a collection of wild and domesticated tomato accessions with a genetically

diverse population of the generalist pathogen *Botrytis cinerea*. We quantified variation in

lesion size of 97 *B. cinerea* genotypes (isolates) on six domesticated *Solanum*

*lycopersicum* and six wild *S. pimpinellifolium* genotypes. Lesion size was significantly

affected by large effects of the host and pathogen’s genotype, with a much smaller

contribution of domestication. This pathogen collection also enables genome-wide

association (GWA) mapping of *B. cinerea*. GWA mapping of the pathogen showed that

virulence is highly polygenic and involves a diversity of mechanisms. Breeding against

this pathogen would likely require the use of diverse isolates to capture all possible

mechanisms. Critically, we identified a subset of *B. cinerea* genes where allelic variation

was linked to altered virulence against wild versus domesticated tomato, as well as loci

that could handle both groups. This generalist pathogen already has a large collection

of allelic variation that must be considered when designing a breeding program.

**3.** A disease symptom arises from the interaction of the host and pathogen genomes. However, little is known about how genetic variation in the interaction leads to shifts in the transcriptomes, especially in polygenic interactions like those between generalist pathogens and their plant hosts. To elucidate how the *Botrytis cinerea* on *Arabidopsis thaliana* interaction is shaped by directional influences of genetic variation on pathogen virulence, we measured the co-transcriptome across a genotyped and genetically diverse collection of 96 *B. cinerea* isolates infected on the Arabidopsis wildtype, Col-0. Using the *B. cinerea* genomic variation, we performed genome-wide association (GWA) for each of 23,947 variable transcript expression profiles in the host, and 9,267 transcripts in the pathogen. This analysis identified mostly *trans*-eQTL in the pathogen and found eQTL hotspots dispersed across the pathogen genome affecting both the pathogen’s and the host’s transcriptomes. There was a relative absence of *cis*-eQTL that is likely explained by allelic heterogeneity and structural variants. The gene membership in the *trans-*eQTL hotspots suggests links to several known and many novel mechanisms of virulence in the plant-pathogen interaction. Genes annotated to these hotspots provide potential targets for blocking manipulation of the host response by this ubiquitous generalist pathogen. This shows that regulation of the co-transcriptome shows a polygenic nature that is similar to the virulence outcome in the *Botrytis cinerea* on *Arabidopsis thaliana* interaction.