**Introduction**

* For generalist necrotrophs, virulence & susceptibility are quantitative traits
  + Most plant immunity studies on large-effect genes (qual-R)
* genetics of Botrytis virulence
  + virulence loci on tomato
  + Quantitative genetics of resistance in Arabidopsis – Jason’s GWAS
* Domestication in pathogen resistance
  + Theory: loss of resistance alleles in domestication & cultivation
    - Email JRI for assumptions in maize genomics
  + Assumptions
    - domestication model holds for disease resistance
    - Resistance is low across all domesticated varieties
    - applies to plants domesticated for fruit
* Approach: detached-leaf GWAS using genetics of Botrytis
  + Work with variation in pathogen
  + Can expand to additional host species - generalist
* Questions
  + Does domestication give us a strong hypothesis about susceptibility?
    - Is this dependent on: pathogen genotype, host genotype
  + Genetic basis of virulence in Botrytis
    - Do the same loci confer virulence across host genotypes?
* Summary of major findings
  + Contributions of host, domestication, isolate and interactions
  + Highly quantitative: Number of SNPs/genes associated with phenotype
  + GO terms associated with multi-host candidate genes

Paragraph 1.

Pathogen virulence and host susceptibility are highly complex traits. Virulence and susceptibility can be viewed as the cumulative outcome of the interaction between host pathways and pathogen pathways. Specialist pathogens are only pathogenic (and therefore exhibit virulence) on a narrow range of hosts. Suitable hosts may be limited to a single species or genus. As such, coevolution between host and pathogen can lead to crosstalk between genes contributing to pathogen virulence and host susceptibility. Generalist pathogens, in contrast, can affect diverse hosts across taxa. They may be less sensitive to variation in host phenotypes, including some resistance strategies.

The simplest genetic basis of plant resistance involves R-gene mediated resistance, in which alleles at a single plant resistance locus (R-gene) and a single pathogen avirulence locus determine susceptibility. The plant R gene has specific recognition of the pathogen Avr locus, causing a qualitative resistance phenotype. The R gene strategy often induces programmed cell death, a strategy which is effective against biotrophic pathogens feeding on living tissue {Glazebrook 2005}. It is unclear what effect domestication of host plants would have on R-gene mediated resistance. Domestication may lead to loss of some R-genes, or reduce diversity at those loci.

Most known genes for plant resistance to pathogens confer qualitative resistance through plant innate immunity. Pattern recognition receptors in plants induce defense pathways following sensing of a conserved pathogen signal, such as cell-wall polymers or flagellin. R genes evolve to recognize specific pathogen effectors.

Gene-for-gene resistance depends upon specific recognition, and requires close coevolution between host and pathogen. Specialist pathogens infect a single host species or taxon, and thus host and pathogen act as reciprocal selective pressures. Generalist pathogens evolve to infect a broad host range. As such, generalists respond to evolutionary pressures from many host species, making the evolution of gene-for-gene resistance unlikely.

Domestication is expected to affect the path of coevolution between host and pathogen. Domestication poses a strong genetic bottleneck for many species. This may also reduce genetic variation contributing to pathogen resistance, particularly if pathogen pressures are reduced in cultivation. In contrast, persistent pathogen pressures throughout cultivation could select for resistance loci. [something about specialists vs. generalists?]

Paragraph 2.

In plants, most naturally variable genes for generalist pathogen resistance likely contribute to quantitative, rather than qualitative, resistance. There are no known naturally variable large-effect resistance loci for plant defense against generalist pathogens. Further, there are no known naturally variable large-effect virulence loci in generalist pathogens.

Studies of plant resistance have identified several mechanisms contributing to quantitative plant resistance and pathogen virulence. The Botrytis cinerea toxins botrydial and botrynalide [+ botycnic acid] increase virulence XXXXXXX. VELVET is necessary for oxalic acid production and B. cinerea mutants exhibit reduced virulence {Schumacher 2012}.

Further, virulence phenotypes and the underlying genetics are highly variable between B. cinerea isolates.

[Inter-isolate variation. Quantitative variation in virulence mechanisms and resistance mechanisms. HCR JA paper, JAC paper]

[Fusarium oxysporum. Generalist species- broad host. But each isolate is ~specialized to narrow host lineages] [botrytis: specific isolate has extreme host range]

A few genes are known to contribute to quantitative plant resistance to pathogens. Genes involved in secondary metabolite biosynthesis regulate quantitative resistance {Ferrari 2007}. Additional transporters and kinases contribute to resistance.

To identify the genomic basis of resistance to generalist and necrotrophic pathogens, we must work with genetic variation within pathogens and their plant hosts.

To look at the interactions between genetic variation in plants and pathogens and the role of evolutionary processes (lineage, domestication) we focus on Botrytis cinerea. [why botrytis. Cite papers w Bc virulence genes.] [expand on quantitative variation here]

[why tomato w botrytis… botrytis resistance a quantitative trait. Agronomic effects.

Domesticated and wild varieties available. Samir and Maloof clock genes papers: domestication drives traits which may affect resistance. Cite papers with tomato virulence genes.]

Domestication paragraph.

[result summary]

Scraps and bits:

*Botrytis cinerea* is one such generalist necrotroph, with a sequenced genome and over 200 host plants {Elad 2007}, including nearly all eudicots. Previous experiments found evidence of quantitative resistance in the response of *Arabidopsis thaliana* to *B. cinerea*, due to an interaction between plant host genotype and isolate genotype {Corwin 2016}. Additional evidence for isolate-dependent resistance comes from the fact that candidate genes for *A. thaliana* quantitative resistance were largely unique to each of the 4 *B. cinerea* isolates tested. The plant response likely varies depending on molecular patterns perceived from individual pathogen genotypes. [add more about specific genes in Botrytis/ Arabidopsis interactions?]

Genes contributing to botrytis virulence {ADD CITATIONS} and

[known virulence loci on tomato]

[lead in to domestication in pathogen resistance… how?]

Much of what we know about pathogen resistance comes from the Arabidopsis model. Something about Arabidopsis genetic diversity- weedy but selfing?

For domesticated plants, in theory the population bottleneck of plant breeding has led to a reduction in genetic diversity genome-wide, including regions contributing to pathogen resistance. [evidence from maize]

Breeding durable resistance necessitates a quantitative genetic approach.

These assumptions are also applied to species domesticated for fruit and leaf traits.

If the domestication bottleneck did indeed reduce genetic diversity genome-wide, it is expected to reduce genetic diversity for pathogen resistance loci as well. This would likely lead to reduced pathogen defense, and reduced variation for defense, in domesticated hosts compared to wild relatives. However, these assumptions are untested, particularly in relation to different pathogen life histories.

For genes in Botrytis/host, simply put together a list of citations on genes in Botrytis and genes in Tomato/Arabidopsis.

Say that they affect a diversity of processes.

Then say that most of these studies do not look at which genes function in diverse roles across the pathogen genotypes or how they interact with diverse hosts.

Then talk briefly about Jason’s paper and how there is isolate x host interactions.

Then the Botrytis velvet paper and Botrytdial papers talk about genetic variation in Botrytis genes.

Then finish off saying that there is a need for genome wide analysis in the pathogen to understand how the host broadly handles host variation.

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Thought: We know relatively little about how genetic variation in a generalist pathogen impacts its ability to infect diverse hosts.

Notes on virulence loci

BAK1 – quantitative immunity. Cell death, bak1 necrotroph sensitive. Arabidopsis

BIK1 – interacts with FLS2 and BAK1

How does Botrytis evade/ survive non-host resistance in such diverse species?