**DISCUSSION**

1. Patterns of few cis and many trans eQTL
2. Patterns of cross-species trans eQTL
   1. How does this connect to the research from the intro/ previous cross-species trans eQTL studies?
3. Connect triangle of interaction: phenotype / expression / genotype
   1. Jason: virulence to host DNA
   2. Virulence to pathogen DNA
   3. Vivian: host expression variation, link to virulence
   4. Vivian: pathogen expression variation, link to virulence
   5. My work: expression variation to pathogen DNA
      1. And virulence to expression variation to pathogen DNA
4. Interpretation of correlation interactions
   1. Host 🡪 Pathogen
      1. Pathogen response to host environment
      2. Host defenses
   2. Pathogen 🡪 Host
      1. Pathogen virulence mechanisms
      2. Pathogen detection and defense by host
      3. Compensatory host response to infection
5. Pathogen control of both sides of interaction to affect phenotypes
   1. Hotspots: regulators/ modulators?

From Guo et al. 2017

* DNA 🡪 RNA 🡪 phenotype (refs for this in Guo)
  + DNA polymorphisms alter protein structure, causing phenotypic effects. This can include the trait of gene expression.
  + Gene expression variation alters phenotype.
  + We can trace causality from polymorphism to expression variation to phenotypic outcomes.
  + This reveals mechanism in the relationship between genotype and phenotype.
* Future directions
  + Additional analyses: infer regulatory networks between pathogen and host
  + For genes in *A. thaliana* regulated by *B. cinerea*; are the homologs in other species differentially expressed in infection? Could look up a tomato / B. cinerea RNAseq study?
  + When a similar infection experiment was repeated in tomato, the differentially expressed host genes were enriched for homologs of the eQTL-identified Medicago genes (Guo, Fudali et al. 2017).
* Polygenicity in B. cinerea eQTL for A. thaliana transcripts: are most genes only linked to one SNP/ locus? Or multiple?
  + For Medicago and nematode, host host expression profiles were explained by only a single major-effect pathogen locus (Guo, Fudali et al. 2017)
  + In interspecific trans-eQTL, the affected plant genes are dispersed across the genome, but only a few of the parasite linkage groups contain these eQTL loci (Guo, Fudali et al. 2017).
  + Variation in plant gene expression was most often explained by a single major-effect parasite eQTL (Guo, Fudali et al. 2017).
* Cross-species trans-eQTL hotspots
  + From Guo, can use the term Host Expression Modulator (HEM) for these loci
* Could add gene ontology/ host atlas gene expression for A. thaliana genes under Bc eQTL hotspots

From Wu et al. 2015

* Terminology
  + (trans-species) ts-eQTL analysis (Wu, Cai et al. 2015)
  + I-chromosomes: the ones in the parasite that interact with the host genome.
* Number of interactions between host gene expression and controlling parasite loci: 6957. For 208 parasite loci and 1054 host genes.
* eQTL clustering
  + Clustering of eQTL to only a few parasite chromosomes
  + And eQTL mostly in subteleomeric regions
* Genes from the same host network often shared eQTL in the pathogen (Wu, Cai et al. 2015)
* Interpretation of mRNA change: could be expression level or could be change in cell populations!
* Novel receptors and adaptors in pattern recognition and signal transduction

From Zhang 2017

* Expression is more sensitive to isolate x host interactions than lesion size
* SA and JA canalize lesion development by choosing between alternate molecular pathways for isolate defense. We have some insight into the B. cinerea modulation of these genetic pathways here…
  + Both pathways provide some defense against B. cinerea {Zhang 2017}
* Polygenicity: both host and pathogen draw from extensive genetic variation to determine disease outcomes
* Future directions
  + Expand this work to examine the B. cinerea control of plant and pathogen gene expression with the host immune knockouts. Explore that interaction term in the genetic control of host and pathogen gene expression: how do the B. cinerea eQTL change in response to host immune pathways? Can we parse out what in the B. cinerea genetics is active/ insensitive to host immune pathway, and what is more conditional or responsive?
    - Flip side to this: how do plant defense pathways XX against the diverse B. cinerea genotypes— genotype specific hotspots (present in knockouts but NOT wildtype) are potential targets of plant defenses in the B. cinerea genome
* Network overlaps
  + Network IV: nuclear photosynthesis genes, PS reaction centers in the chloroplast: change to photosynthetic function during infection.
  + Network I: the transcriptome response of this network at 16 HPI predicts resistance at 72 HPI. The direction of the interaction, however, is dependent upon host genetics. Here we have a strong link to complete the connection from genetic change in the pathogen, to expression pathway responses, to phenotypes of virulence.

Guo, Y., S. Fudali, J. Gimeno, P. DiGennaro, S. Chang, V. M. Williamson, D. M. Bird and D. M. Nielsen (2017). "Networks underpinning symbiosis revealed through cross-species eQTL mapping." Genetics: genetics. 117.202531.

Wu, J., B. Cai, W. Sun, R. Huang, X. Liu, M. Lin, S. Pattaradilokrat, S. Martin, Y. Qi and S. C. Nair (2015). "Genome-wide analysis of host-Plasmodium yoelii interactions reveals regulators of the type I interferon response." Cell reports **12**(4): 661-672.