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Dear Editor,

We would like to respectfully submit our manuscript entitled “Crop domestication and pathogen virulence: Interactions of tomato and *Botrytis* genetic diversity” for possible inclusion into *Nature Genetics*.

This manuscript empirically tests how tomato domestication has altered resistance to the common generalist fungal pathogen, *Botrytis cinerea*. Research into the genetic basis of the plant immune response has given us a clear picture of how interactions between plant hosts and specialist pathogens cause simple disease outcomes. For example, when a specialist pathogen attacks a host plant, disease or defense can be determined by interactions between a single plant gene and a single corresponding pathogen gene. Thus, variation within a small number of genes causes large, binary changes to the disease phenotype. Many of these genes are well characterized through molecular and functional studies in plant pathology. This has generated a model in which domestication leads to decreased resistance to pathogens and lower genetic variation in resistance via a bottleneck.

In contrast, we understand less clearly how complex genetics in the host and pathogen control complex disease phenotypes with continuous variation. These quantitative interactions are common between generalist pathogens and their varied plant targets and involve loci of unknown effect sizes or numbers. Even more, there is almost nothing known about how crop domestication may influence resistance to generalist pathogens.

In this paper, we directly tested how tomato domestication influenced resistance to a genome sequenced collection of 97 *Botrytis* isolates. This allowed us to directly quantify the effects of tomato domestication on resistance to a species wide collection of a generalist pathogen.

Using the genome polymorphism data within the pathogen, we conducted a genomic analysis of genes controlling virulence. This showed that, like quantitative resistance in the host, quantitative virulence in the pathogen is controlled by a polygenic architecture with large numbers of loci with small effects. This work also allowed us to directly identify loci within the pathogen that were responsive to the shifts in tomato resistance caused by crop domestication.

We feel that this work is well suited to the interests of *Nature Genetics*. In this paper we focus on genome-wide variation associated with a complex disease that is common across a multitude of plants, including many species of agricultural importance. We also ask how domestication has shaped the evolution of plant defenses and the virulence of their pathogens. This research has helped to deepen our understanding of plant immunity, and has implications for agricultural control of generalist plant pathogens.

Sincerely,

A handwritten signature in black ink that reads "Dan Kliebenstein". The signature is written in a cursive, slightly slanted style.

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