Dear Editors,

Thank you for considering this work for publication in *PNAS*. Our manuscript, "Mapping of genotype-by-environment interactions in phenology identifies two cues for flowering in switchgrass (*Panicum virgatum*)" is suitable for publication in *PNAS* for three reasons.

Our work makes use of a key methodological development to improve our understanding of the genetics of genotype-by-environment interactions, or GxE. Just as different populations can exhibit different responses to the environment, it seems clear that different genes and genetic variants can exhibit different responses to the environment. Yet current statistical models to test for GxE don't have robust frameworks to specify and compete different models of GxE effects. Here, we use multivariate adaptive shrinkage (mash, Urbut et al Nat. Gen 2019) to determine the regions of the switchgrass genome with effects on phenological dates that covary with several weather-based 'cues'. To do this, we use a recently developed genome-wide association mapping panel of clonally replicated switchgrass genotypes grown at common gardens across the native latitudinal range of switchgrass. This panel contains two deeply diverged genetic subpopulations of switchgrass. Using mash, we find that these two subpopulations are segregating for SNPs with effects on flowering date that covary with two distinct weather-based environmental cues.

Second, to our knowledge, this work is the first to use a statistically unbiased test to detect the relative frequencies of two important types of GxE: antagonistic pleiotropy, or a change in sign of effects between environments, and differential sensitivity, or a change in magnitude of effects between environments. Previous work has had a statistical bias against detecting antagonistic pleiotropy, and to date very few instances of antagonistic pleiotropy have been mapped to small genetic intervals. We use this test to find thousands of genetic effects with antagonistic pleiotropy for one of our phenological measures, green-up, or the start of above-ground spring growth for switchgrass.

Finally, with current advances in high-throughput measurement, and the increased resources devoted to experiments in natural and semi-natural environments, we must consider how to share information across these experiments and how to associate natural variation in genomes with natural variation in complex field environments. Advances in methods to find the environmental cues that matter should allow researchers to determine the adaptations important to responses to the natural environment, and how the importance of these genetic mechanisms changes as the environment itself changes. Our manuscript should be of broad interest to *PNAS* readership for the insights it provides into these important issues.

We suggest that Douglas Schemske, Hopi Hoekstra, and Qifa Zhang would be good Editorial Board members for this manuscript. All would be able to provide strong insights into mapping the genetic basis of adaptive and ecologically relevant traits in a field experimental context.

We suggest that Johanna Schmitt, Trudy Mackay, and Detlef Weigel would be excellent editors for this manuscript. Dr. Schmitt has done extensive work in *Arabidopsis thaliana* and other plant species unravelling the genetic mechanisms involved in responses to the natural environment. Dr. Mackay has extensive experience mapping the genetics of complex traits and genotype-by-environment interactions. Dr. Weigel has done extensive work understanding genetic diversity in *A. thaliana* including extensive work on floral induction cues.

All the best,

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