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EDITORIAL: REFLECTIONS ON *THE PLANT CELL* CLASSICS

Questionomics: Using Big Data to Ask and Answer Big Questions[OPEN]

Genomics and the myriad other "-omics" that have arisen over the past decades have created a dramatic—almost frenetic—boost in the ability to generate data. This has amplified with the invention of new technologies that are thrashing the imperative of parsing between model and nonmodel study systems. This frenetic pace has led to the characterization of genomics as a descriptive science, a collector of parts, incapable of asking or answering essential questions. A contrasting difficulty with genomics is that these massive data sets on complex biology are often combined with myriad filters to identify a single gene or mechanism. This frequently leaves a puzzling aftertaste of how much has been truly learned about a complex system if it is collapsed to a single gene. This can lead to a cynical view of genomics as either pure description or an extensive exercise in oversimplification.

As a postdoctoral researcher at the Max Planck Institute for Chemical Ecology and a new, undented hire at the University of California, Davis, there were two sibling articles in *The Plant Cell* that showed me why this cynical view is unnecessary and how genomics data can be used to directly ask large-scale biological questions. Philippe Reymond and Edward Farmer along with colleagues published two articles on plant-biotic interactions that showed how genomics could be used to ask and answer sweeping biological questions **(Reymond et al., 2000, 2004)**. These articles used genomics to ask fundamental questions that lay at the base of all mechanistic gene-centric articles that followed. Is mechanical wounding similar to Lepidopteran herbivory (Reymond et al., 2000)? And similarly, does the plant distinctly perceive different herbivores (Reymond et al., 2004)? In both cases, the genomics data gave unequivocal answers that even today are not fully appreciated.

In the comparison between mechanical wounding and Lepidopteran herbivory, the genomics showed that there were clear differences and that wounding is not a great approximation of herbivory (Reymond et al., 2000). The study also showed how asking big questions with genomics has the added benefit of being able to then dive into additional questions. For example, the study showed that there were genes uniquely induced by the herbivore but not in response to mechanical wounding. They further interrogated the genomic patterns and showed that the wound responses are decreased during attack by the herbivore. They postulated that the herbivore may have mechanisms to dampen or antagonize responses linked to mechanical wounding. For me, this was highly significant, as it was a genomics-derived insight that directly fused with ecology and evolutionary theory by linking to the coevolutionary battles between organisms that work to confuse each other.

They then tested if plants perceive generalist and specialist Lepidopteran herbivores differently (Reymond et al., 2004). Generalists are herbivores that have a wide potential host range; in contrast, specialists have a limited host range and are considered to have coevolved to defeat their host's defense mechanisms. The transcriptomics showed that Arabidopsis (*Arabidopsis thaliana*) perceived the two attackers similarly, leading to a highly comparable response. However, there were defense responses elevated in comparison with one or the other Lepidopteran herbivore. This analysis fundamentally answered the question about generalists and specialist Lepidopteran defense by showing that the plant has a highly similar response to the two organisms. Thus, the inherent difference in generalist versus specialist herbivore likely has more to do about discerning insects than about the plant.

This concept that genomics can be used directly to ask and answer large questions is at the core of a developing trend in genomics that is working to address large-scale topics without overly simplifying. For example, there are efforts to develop whole-genome models that describe how the entire transcriptome is temporally regulated in response to a single biotic or abiotic event (Windram et al., 2012; Gaudinier et al., 2018). Other studies are working to ask similarly simple large-scale questions, like does a plant recognize biotic attackers as members of a species or as individuals (Zhang et al., 2017)? In my career, the two *Plant Cell* articles by Reymond, Farmer, and colleagues were the first that helped to form my own conception of how genomics can be used to ask direct big questions. They showed how it was possible to derive information from the entirety of the results without simply describing the patterns or reducing the complexity to a single interesting gene. It will be exciting to see how, in the next 30 years, genomics and high-throughput biology might build on this potential and begin testing complex biological systems with equally complex data systems to derive ground truths that we would never have contemplated asking based on our molecular biology beginnings.

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*References highlighted for the 30th anniversary of *The Plant Cell.*