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Integrating plant 'omics'

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Although the *Arabidopsis* and rice genomes have been sequenced, the [complex gene-to-metabolite networks](#) that produce what we know as these plants have been difficult to discern. In the June 15 [Proceedings of the National Academy of Sciences USA](#), Masami Hirai and colleagues report a solution that involves mathematically combining transcriptomics and metabolomics, thus allowing the analysis of sulfur and nitrogen gene-to-metabolite networks in *Arabidopsis* (*Proc Natl Acad Sci USA* 2004, DOI:10.1073/pnas.0403218101).

"Understanding... network behavior through a combination of analytical and mathematical approaches has great potential for deepening our understanding of metabolic regulation," said Alisdair Fernie, from the Max Planck Institute, Golm, Germany, who was not involved the study.

After 10 years of studying sulfur metabolism at the individual gene and enzyme levels, Kazuki Saito, from Chiba University in Japan and senior author of the new study, said that he realized this approach was not sufficient to understand global network responses in plants. "In the post-genome era, drawing a holistic picture of cellular process is absolutely necessary for the understanding of gene-to-metabolite networks," Saito said.

Therefore, Saito, lead author Masami Hirai, and their colleagues decided to integrate gene expression analysis (transcriptomics) and non-targeted metabolite profiling (metabolomics) to better understand sulfur and nitrogen metabolism in *Arabidopsis*.

Using plants grown under sulfur- and/or nitrogen-deficient conditions, the authors determined the expression profiles of about 13,000 expression sequence tags with cDNA arrays. On the same samples, they also determined metabolic profiles of about 3,000 mass peaks with Fourier transform-ion cyclotron mass spectrometry. Mathematical integration of this data, using principal component analysis and batch-learning self-organizing map analysis, was then used to discern gene-to-metabolite networks potentially involved in sulfur and nitrogen metabolism.

"We could show the presence of general responses to sulfur and nitrogen deficiencies in the transcriptome and metabolome. In addition, a specific pathway, glucosinolate metabolism, among all metabolic pathways, is coordinately modulated by nutritional stresses of sulfur and nitrogen," Saito told us.

"Saito's group has done an exceptional job in integrating data and this publication represents one of the first of its kind," said [Lloyd Sumner](#), from the Samuel Roberts Noble Foundation, Ardmore, Okla., who was not involved in the study.

Such integrated studies will have important implications for our understanding of biological questions, Sumner said. "It amazes me how little is known about the interaction of metabolic pathways on a more global scale. I believe that gene-to-metabolite networks offer a great mechanism for interrelating components," he told us.

Sumner cautioned that such 'omics' technologies are relatively new and it remains unclear how much relevant information is being gleaned from such studies. "[For example], although we can differentiate a

large number of genes, proteins, and metabolites, only a limited portion of these can be qualitatively identified," he said.

Saito suggested that the development of both improved bioinformatics and technology for metabolomics will thus be required for further progress, adding that "actually, metabolomics technology is currently far behind those of genomics, transcriptomics, and proteomics, because no single automated analytical method has been established."

"Despite these caveats, network behavior is undoubtedly a hot topic and one that will develop very rapidly," said Fernie. "In doing so, [you] give an elevated chance of success in the rational manipulation of metabolism. This could be envisaged to have major benefits in both plant and microbe biotechnology and the biomedical sciences."

For example, the integration of transcriptomics and metabolomics could provide the potential to predict the function of unknown genes or new metabolites as well as uncover new metabolic pathways, Saito said. "Plants can synthesize more than 200,000 compounds," he said, making such information quite important for the future use of plant metabolites in various industries.

Thus, the mathematical combination of such global approaches is likely to expand as a technique. "If you can integrate the evaluation of biological activity of complex plant metabolites together with 'omics,' it will be a new approach of drug discovery from plant cells," Saito said.

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