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Phytochemistry 62 (2003) 815–816

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

Editorial

Phytochemistry meets genome analysis, and beyond.........

Phytochemistry is entering a new era. In August 2001, the Phytochemical Society of North America held a meeting in Oklahoma City on the topic of "Phytochemistry in the Genomics and Post-Genomics Eras". A central theme of that meeting was the importance of phytochemical analysis in the new science of "functional genomics". Functional genomics is, in its simplest definition, the study of gene function on a large scale, i.e. the scale of the whole genome. This expansion of scale has been made possible by the recent advances in high throughput DNA sequencing that make sequencing of tens of thousands of expressed genes from cDNA libraries (EST sequencing), and even of whole genomes, routine procedures for laboratories that can afford the equipment. However, a large proportion of the gene sequences in plant EST and genomic sequence databases cannot be functionally annotated based on DNA sequence alone. Hence the need for functional genomics, which uses a variety of molecular and genetic approaches to address gene function by over-expressing, down-regulating or mutating genes in the plant of origin, or expressing genes in heterologous systems such as alternative plants, bacteria or yeast. Hopefully, the modified expression of the gene of interest will lead to a measurable phenotype that will give some hint as to the cellular function of the gene.

Plants are unique in the richness and diversity of their secondary metabolism leading to more than 200,000 secondary products, also called natural products. A significant proportion of plant genes (estimated at 25% for rice) encode enzymes of metabolism. Even among potential secondary metabolism genes that can be annotated into specific classes, there is much complexity. For example, in *Arabidopsis* and rice there are collectively more than 450 cytochrome P450s, 25 *O*-methyltransferases, 45 terpene synthases, 130 2-oxoglutarate dependent dioxygenases and 100 glucosyltransferases, the great proportion of which have no ascribed function. Disruption of secondary metabolism by functional genomics approaches will, in some cases, lead to a visible and therefore easily screenable phenotype (e.g. transparent testa mutants in *Arabidopsis* lacking flavonoid biosynthesis, photo-bleaching caused by loss of carotenoids, etc.). However, in many cases this will not be so. It is likely, however, that "hits" in a gene involved in natural product biosynthesis, or in partitioning between pathways of primary metabolism, will result in a biochemical phenotype that can be determined by careful profiling of metabolite levels. Such metabolite profiling is one of the major applications of phytochemical analysis to functional genomics. For this approach to be of value in genomics approaches that are random rather than targeted, metabolite profiling will have to be on large scale, preferably the scale of the "metabolome".

The term "metabolomics" has been used to describe analysis of metabolite composition of the cell determined at the same level of scale as analysis of the genome in genomics approaches. The term "metabolite profiling", also called "metabolic profiling", does not necessarily mean metabolomics, as its level of scale is not defined and can vary from relatively limited (e.g. analysis of flavonoid or soluble carbohydrate profiles) to much more global. The metabolome reflects the expression of the genome arising from the various transcriptional, translational and post-translational cellular events. Thus, surveying the complete metabolic status of a cell provides a snapshot of the end result of these processes, and changes in the metabolome provide strong clues as to the corresponding underlying changes in gene expression.

In addition to high throughput, "global" profiling for discovery of gene function, metabolite profiling is also finding important applications in biotechnology for the analysis of transgenic plants. How many other genes and metabolites/pathways are affected following modification of the expression of a single target gene? Does the transgenic plant show substantial equivalence to non-transgenic plants of the same species/variety? These are important questions in the debate over public acceptance of genetically modified organisms (GMOs) and, fortunately, phytochemistry, along with gene expression profiling, can provide the needed answers.

Cataloging of metabolites suffers in comparison to cataloging of genes from the fact that metabolites come

doi:10.1016/S0031-9422(02)00712-4

in all shapes and sizes, whereas genes consist only of permutations and combinations of four building blocks, the nucleoside triphosphates. However, the technologies for cataloging metabolites, usually consisting of extraction followed by a separation procedure (GC, HPLC, capillary electrophoreses, etc) and detection method (UV absorption, fluorescence, mass spectrometry, etc) will be familiar to most phytochemists. More rapid procedures that require no fractionation, such as FT-IR spectroscopy and FT-ICMS, are also being developed.

This issue presents a collection of papers submitted by colleagues working on various aspects of plant metabolite profiling. Their work demonstrates the value and importance of phytochemical analysis in genome research, transgenic technology (biotechnology), food science and chemical ecology, with examples of many of the above approaches. Traditionalists may argue that "metabolite profiling" is nothing new, and that terms like "metabolomics" are just further examples of molecular biology jargon. This view fails to appreciate the tremendous opportunities for discovery of new knowledge at the plant chemistry/genomics interface. True, the basic technologies themselves are not new, but the ways in which they are used, the scale of use, and the questions they can address, certainly are. The importance of the biological questions being addressed by the genomics/metabolomics approach will doubtless drive the development of ever more sophisticated tools for chemical analysis. The ultimate goals are improved throughput for massively parallel analyses and improved sensitivity for profiling large numbers of metabolites at the level of single cells. It is exciting to see phytochemistry play such a critical role in the plant genetic revolution.

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