

# Plant biotechnology From genome projects to molecular breeding

## Editorial overview

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Csaba's research focuses on the functional analysis of regulatory genes in sugar, stress and steroid hormone signaling using genetic and biochemical approaches in *Arabidopsis*.

Upon completion of the *Arabidopsis* and rice genome sequences and following the collection of vast amounts of expressed sequence tags (ESTs) from crops, medicinal plants and trees, plant science has entered into a qualitatively new development phase. Researchers in this post-genomic era are convinced that the characterization of function and regulation of all conserved plant genes will be achieved by 2010. The ultimate goal is to gain an integrated knowledge on the temporal and spatial regulation of transcription, translation, protein interactions, proteolysis, metabolism, transport and so on, and to learn how these pathways control all events through the plants life-cycle. Plant science thus moves from analytical to integrative multi-disciplinary approaches. This also means that new powerful technologies and accumulating knowledge are becoming equally accessible to plant breeders, geneticists, physiologists, anatomists, ecologists, pharmacologists and botanists. As illustrated by this issue, there are many intriguing developments in progress that exploit the results of genome projects leading to the gradual conversion from classical breeding to molecular breeding.

One of the new research fields is metabolomics, which employs sensitive analytical tools such as combinations of gas or liquid chromatography with mass spectrometry, nuclear magnetic resonance, and Fourier transformation mass spectrometry to determine metabolic changes caused by gene mutations or the expression of foreign genes. As discussed by Stitt and Fernie, these technologies are being exploited in breeding programs. They are being used to screen for the overproduction of specific metabolites, to study the temporal and spatial regulation of metabolic pathways and fluxes, to characterize metabolic profiles of different species producing rare bioactive compounds, and to control the quality of seed stocks and food products. By developing proper sampling, cell fractionation and laser microdissection procedures, these tools can also be used to monitor the tissue- and cell-type specific distribution of metabolites. Technologies based on fluorescence resonance energy transfer allow facile detection of interactions between ligands and their transporters or receptors. In addition, metabolomics can be applied to monitoring stress-induced metabolic changes, to identify rate-limiting steps in metabolic pathways, to determine the metabolic effects of knockout mutations or to perform simple agronomical tasks (e.g. the measurement of levels of minerals, fertilizers, etc). Metabolic profiling data are evaluated and collected in central databases using hierarchical cluster and principal component analyses in order to assist the computer modeling of various pathways.

It has been demonstrated during the past decade that plants can be successfully used as cell factories to produce bioactive animal proteins, including antibodies and biopharmaceuticals (e.g. anticoagulants, growth

hormones, antimicrobial agents, etc). These developments led to the remarkable discovery that, upon digestion, mammals can produce antibodies against proteins expressed in plants (e.g. human immunodeficiency virus-1, foot-and-mouth disease virus VP-1 and Norwalk virus capsid epitopes). Walmsley and Arntzen review recent advances in the use of plants for oral and nasal vaccination. The authors critically discuss the results of laboratory and clinical trials, safety regulations, potential limitations, and recent improvements in chloroplast and seed-specific expression of stable antigens of multi-component vaccines.

Morant and colleagues introduce us into the wonderful world of medicinal plants, which provide the active components of 25% of currently used pharmaceutical products. It has been known for a while that cytochrome P450s play a distinguished role not only in the biosynthesis of many anticancer drugs, alkaloids, phytoosteroids, antioxidants, and antimicrobial compounds, but also in the detoxification of xenobiotics (e.g. herbicides and pesticides). So far, 1052 plant cytochrome P450s have been identified and the task to determine their precise biochemical functions is vast. With the advances of metabolic profiling, gene knockout, yeast and jasmonate-inducible plant expression technologies, P450 researchers have made significant progress in the characterization of several enzymes. These include P450s that control the biosynthesis of the antimitotic drug taxol, terpene indole alkaloids with antineoplastic and antiarrhythmic activities (e.g. vinblastine), caffeic acid derivatives, and several antioxidants. Readers of this chapter will also find interesting information on the synthesis of flower scents, the harmfulness of the genistein-rich Asian diet, the breeding of better *Cassava* by elimination of bitter cyanogenic glucosides, the use of P450s in the degradation of agrochemicals, and the application of capsidiol and dhurrin as defense compounds against herbivores and pathogens.

Today, over 12 000 alkaloid structures are known, yet only a few dozen compounds are used as pharmaceuticals and only 30 genes involved in alkaloid biosynthesis from amino acids and adenine nucleotides have been characterized. Hashimoto and Yamada call our attention to recent developments that led to the reconstruction of the caffeine biosynthesis pathway from 7-methylxanthoside *in vitro* and the identification of enzymes in the morphine and berberine biosynthesis routes. Biochemists now capitalize on the finding that genes controlling the biosynthesis of several alkaloids are induced by the stress hormone jasmonate and can thus be identified by comparative transcript profiling or differential display analysis of jasmonate-induced and non-induced mRNAs. Studies of alkaloid metabolism and transport also provide interesting insights into the evolution of plant interactions with pathogens that use alkaloid transporters and degradation enzymes to inactivate plant antimicrobial

compounds. Remarkably, some plants 'learned' how to defend themselves better by producing inhibitors of bacterial multidrug resistance pumps that function as alkaloid transporters.

Degenhardt and co-workers teach us how plants use the production of volatile C6-alcohols, aldehydes, monoterpenes and sesquiterpenes to invite carnivores and parasites of their attacking herbivorous insects. This exciting chapter shows how teams of molecular and population geneticists, protein biochemists, ecologists, plant breeders and entomologists have successfully worked together on the exploitation of natural plant protection systems. They have uncovered the modes of regulation of genes and pathways involved in the biosynthesis and metabolism of plant volatiles and studied the perception, metabolism and physiological effects of these compounds in insects.

The astonishing speed in deciphering regulatory pathways of plant-pathogen communications is illustrated by the review of Hammond-Kosack and Parker. Genetic dissection of signaling functions has started to reveal an intricate cross-talk between several pathways that control plant resistance responses to pathogens. Studies of non-race-specific resistance genes and receptors that recognize, for example, common pathogen-associated molecular patterns have identified novel principles of regulation and revealed similarities between mechanisms of plant and animal pathogenesis. This chapter excellently documents how previous strategies, focusing on the engineering of single genes for improving resistance responses, will change to the well-designed modification of entire pathways. These new trends will soon show whether breeding can generate durable resistance against plant pathogens through a full understanding of the regulation of race-specific, basal and systemic resistance responses.

Plants are destined to cope not only with attacks of pathogens and insects, but also with environmental extremities, including drought, salinity and cold stress. Functional genomics and proteomics projects using *Arabidopsis* and rice as models have started to reveal many exciting details of environmental stress responses, including canonical signaling pathways, transcription factors and target genes. As reviewed by Seki and colleagues, these studies demonstrate that breeding plants to withstand cold and salt stress can be realistically achieved by targeted alteration of either the expression or function of regulatory genes with or without using transgenic plants.

Weidner, Pühler and Küster provide an overview of the current status of genome projects on legumes and their nitrogen-fixing symbiotic partners. Recently, these projects reported the genome sequences of *Mesorhizobium* and *Sinorhizobium* species, including their Sym-plasmids, and produced several hundred thousand ESTs from

*Medicago truncatula*, *Lotus corniculatus* and soybean. Whereas work to sequence the *M. truncatula* genome progresses with full-speed, functional dissection of signaling pathways controlling legume symbiosis with mycorrhiza and nitrogen-fixing bacteria is aided by the availability of a genetic map for alfalfa, T-DNA insertion mutants in *Lotus* and both T-DNA and transposon tagging systems in *M. truncatula*. Recently, the power of genetics was documented by the long-awaited identification of an alfalfa receptor that is required for the recognition of bacterial nodulation signals, the so-called NOD factors.

Forest biotechnology is another stronghold that collects and exploits EST information from poplar, pine, birch, spruce, radiata pine and eucalyptus. The devastation of natural forests provides a sufficiently sad motivation to invest significantly in tree genome projects that aim at mapping quantitative trait loci (QTL) to identify genes controlling perenniality, developmental phase changes, herbivore interactions, growth, stress responses, and the synthesis of secondary metabolites, lignin and cellulose. Bhalerao, Nilsson and Sandberg provide a detailed insight into exploitation of the poplar model system by high-

lighting recent results in the analysis of hormonal pathways and genes controlling wood formation. The authors also discuss various approaches to induce early flowering, which represents a major bottleneck in tree genetics.

Morgante and Salamini discuss several strategies as to how the tools and knowledge derived from genome projects can be best applied to current breeding practices. Their review focuses on new approaches that exploit the measurement of linkage disequilibrium in natural populations to map QTL and identify the corresponding genes using modern technologies, such as detection of single nucleotide polymorphisms. The authors refer to Fischer's infinitesimal model, suggesting that molecular tools might not be very helpful in the modification of potentially endless allelic combinations that contribute to the regulation of quantitative traits. This 'dark side', as it is referred to by the authors, is fortunately illuminated by the fact that many of the so far characterized QTLs code for well-defined regulatory factors. At the end, the reader can, thus, optimistically look forward to further exciting applications emerging from the use of genomics tools in molecular breeding.