

Innovation and Agricultural Biotechnology – Where's Canada's Future?

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Biotechnology and a Vision for Canada’s Agriculture and Food Industries

Biotechnology is a tool, a set of techniques and approaches that allow farmers and companies to achieve clearly identified objectives. In a little over a decade that tool has reshaped Canadian agriculture, providing new crop varieties and new ways to differentiate Canadian agricultural products, as well as higher yields, greater resilience and more sustainable management practices. It has increased profits, reduced costs and in some cases enhanced carbon sequestration and the potential for tradable carbon credits.

When we think about the future of biotechnology in Canada the questions we have to ask are “What is our vision for the future of Canadian agriculture and food?” “How can we use biotechnology to help achieve that vision?” “What policies and industry strategies will support our use of biotechnology?”

While a clear vision for Canadian agriculture has not been fully articulated, it appears to be implicitly assumed that “Canada will provide the world with innovative, high value food and industrial products produced in a sustainable manner”. The implications of such a vision for the industry are clear. We will produce both food and industrial products, including energy. We will continue to be a trading nation and we will endeavour to create and sell new dimensions of value both to export and domestic markets. The means that the industry will actively search for ways to differentiate Canadian products. We will do this in a way which respects the environment and looks for ways to minimize production impacts while maximizing the value and benefits to buyers and consumers. However, there will always be a large segment of Canadian agricultural production destined for commodity markets, so a focus on increasing productivity and reducing costs will also be important.

The Changing Environment for Agricultural Biotechnology

Over the last few years there have been several major changes that will affect the future of biotechnology in Canada.

1. Responding to global priorities – In recent years a number of global issues have become more urgent, including climate change and global warming, increasing demand for food due to population increases and changing consumption patterns, and increasing concerns over energy and human health.
Implications – The agri-food industry can be part of the solution to all of these problems and biotechnology will play a critical role in adapting to warming climates, increasing agricultural productivity and improving the ability of crops to deliver improved industrial or health properties.
2. Biotechnology has become a global technology – In spite of resistance to genetically modified foods in some markets, biotechnology has been a major success, spreading around the world and into new crops and markets. The companies behind them tend to be large multi-nationals, with the resources needed to manage global scale-up, distribution and regulatory requirements.

Implications – Canada should concentrate its resources on the crops and technologies where it has a natural advantage or can gain a competitive edge, working with multi-nationals to commercialize those crops where appropriate and to encourage more private R&D in Canada.

3. Traits in new crops are moving beyond the past focus on herbicide and insect resistance into drought and cold resistance, stacking multiple traits and improved output traits for food or industrial products. Appendix 1 summarizes some of the current developments in Canada.

Implications – Both the number and complexity of future biotechnology innovations will put pressure on Canada’s regulatory system.

4. New approaches for improving crop genetics – There have been many new developments in genomics and other methods to rapidly manipulate the genetic makeup of plants and animals. Many of these can accomplish significant modifications without employing trans-species gene insertion. Appendix 2 contains a brief description of the technologies which will play a role in the future of the industry.

Implications – The future will include many different sources of value in both food and industrial markets. To capture that value we will need to use the entire suite of technologies available for genetic enhancement. Biotechnology will be an important component but it will not be the only one.

5. The rapid development of the market for biofuels and bioproducts – The bioproduct industry is quickly becoming a major market for agricultural biomass and in the future the level of integration between industrial and agricultural biotechnology will continue to increase dramatically.

Implications - Industrial biotechnology represents a large, relatively untapped opportunity for Canadian agriculture but capitalizing on that opportunity will depend on creating the systems needed to support both industrial and food markets in Canada and abroad.

6. A bio-refinery approach to agricultural value – As markets for health and nutraceuticals and industrial products continue to develop, there will be more incentives to understand and capture all the different potential value streams from agricultural products.

Implications – As the industry develops new crop varieties and markets we will need to create systems to extract all of the components of value from the crops we produce.

In the past we have had a fairly linear view of biotechnology commercialization as a process driven by scientific discoveries which are transferred to the private sector, often through start-up companies, to be commercialized and marketed. While this model may hold for medical biotechnology, it rarely applies to agricultural or industrial biotechnology. Instead, new discoveries are either made in large biotechnology companies or are transferred from university or government laboratories to private companies with the resources necessary to commercialize the discoveries in major markets. It is extremely difficult for small agricultural biotechnology firms to attract the long term funding needed to commercialize their discoveries.

The framework shown in Figure 1 can be used to consider the process of agricultural biotechnology innovation, the factors driving or constraining the process and the policy tools available to facilitate the development and adoption of biotechnology in the industry. The framework distinguishes between the production system, where production attributes sought by farmers are the predominant focus, and the consumption system, where the focus is on product attributes, although those attributes may also include how the product was produced. It also recognizes the expanding role of agricultural biotechnology's in the bioeconomy, using biomass to replace oil (and other inputs) to reduce production costs and environmental impact.

What's worked for Canada?

Canada has made significant public investments in biotechnology and reaped many of the rewards. Canada's approval and adoption system worked well during the introduction of agricultural biotechnology. Canada was an early adopter and a biotechnology innovator in soybeans, corn and canola. Canadian farmers were the primary beneficiaries, both financially and with easier management practices. Canola, in particular, has been a national success (see box).

The Canola Success Story

Canola is a Canadian invention that is transforming farming in Western Canada. Developed and refined by Canadian scientists canola is now Canada's largest crop with adoption of herbicide resistant canola now making up roughly 98% of Canadian plantings. Canola oil is also an important element in shifting to healthier oils to reduce chronic disease.

The impacts:

Capturing economic value - Canola currently contributes over \$16 billion in economic activity to the Canadian economy. Canola production, transportation to export, crushing, refining and inclusion in panoply of foods generates over 214,000 jobs in Canada. A 2006 study found that every \$100 million of additional demand for canola generates an additional \$83 million in Canadian GDP and more than 730 jobs in value-added industries including crushing, processing and food production (NRC, Key Sector Plan in Agriculture, 2009).

Capturing R&D investment - Saskatoon is now the world centre for Canola research and development and global companies like Dow and Bayer are choosing to move a major portion of their canola research to Saskatoon to be part of the canola research cluster. A significant proportion of Canadian field trials are dedicated to canola attributes (Appendix 1).

What challenges has the industry faced?

Market acceptance – The biggest challenge for Canada has been the reluctance of some major markets like the E.U. and Japan to consume GM foods although they do accept GM crops for feed and biofuels. This has created a market opportunity for Canada in non-GM food grade soybeans but has stalled the use of biotechnology as a means of improving the performance of Canadian wheat and resulted in lagging

productivity and reduced market share relative to crops like canola. There is pressure from industry to reopen the debate around the use of biotechnology in wheat.

Regulation – Although value chain approaches like the Canola Council of Canada Export Ready system are in place and functioning well, the speed of regulatory approvals for new traits and the apparent challenges around finding effective risk-based models for managing new technologies are concerns for the industry.

The lack of predictability and uncertainty around how new products would be addressed has resulted in some companies moving their research to other countries or, in some cases, going out of business. Another aspect of the regulatory challenges is the number of organizations involved in agri-food biotechnology regulation. Depending on the innovation or its intended market a company may have to deal with CFIA, AAFC and/or Health Canada. Companies need help navigating the regulatory process. There may be merit in exploring the option of a single agency to help guide them through the process. A recent AAFC innovation, the Food Regulatory Issues Division, is an example of a step in the right direction. The Division works with companies and Health Canada to help each understand the needs and requirements of the other in order to speed up approvals for health related food innovations.

Funding – Several factors have combined to make funding a significant challenge for developers of Canadian biotechnologies. The long time to market, due in part to regulatory approvals, challenges around intellectual property and the relatively unsexy nature of agriculture to investors have all contributed to a dearth of venture capital for the industry.

Management of biotechnology research and production systems – The recent situation with flax, where a research strain of GM flax has contaminated much of the flax crop and resulted in a European ban on Canadian flax, is just the most recent and high profile example of challenges in managing biotechnology research and production systems. This situation underscores the necessity of low level presence policies in Canada and globally.

Succeeding in a more complex future

We have barely scratched the surface of what biotechnology can and will do to change agricultural production and products. Our ability to manipulate genes will continually become faster, cheaper and more accurate. The science of biotechnology will converge with genomics, bioinformatics, and nanotechnology. The innovations will encompass all three elements of sustainability – economy, environment and society. Some innovations will be focused on production, others on reducing environmental impact and still others on health. Traits will be stacked and intellectual property will be mixed in many ways. Most of our agricultural and food products will be novel in some way. In this exciting but more complex future we will have to manage not only the science but also its interaction with the environment and societies in Canada and around the world. Canadian success will depend on getting the entire system right, from research through to domestic and foreign markets – implementing policies and programs to support the new opportunities, systems to make sure that it is safe while removing unnecessary barriers. Elements of that system include:

Continued funding for research and development – We have already shown that Canada can be a world leader in biotechnology but only in carefully selected crops or traits. Multi-national companies will continue to lead research in global crops, with some of that done in Canada. We should attempt to attract and

support more of that private research into Canada while focusing public research on crops or traits that will translate into a national advantage. Research will also be required to continue to develop the tools that scientists need to advance their efforts in biotechnology and other methods for genetic improvement. Support for research and development needs to extend beyond the walls of government facilities and laboratories to ensure relevance to industry and future uptake in the market.

A broad based approach to innovation using all of the tools available, including biotechnology, to help Canada's agri-food products and companies compete in global markets.

Support for biotechnology commercialization and adoption – Canada will continue to experience challenges attracting venture capital. Public private partnerships may be more realistic given Canada's small scale on the global stage. Programs like the Agri-Opportunities Fund and Sustainable Development Technology Canada, which funds green technology development, will continue to be needed to help develop Canadian solutions to market opportunities. These programs should provide funding and support but should accomplish this with the minimum overhead needed to ensure that funds are used appropriately. Complaints over current excessive reporting requirements and lag in project approval are common among innovating companies.

Support for developing the science and business skills needed to capitalize on Canada's biotechnology opportunity.

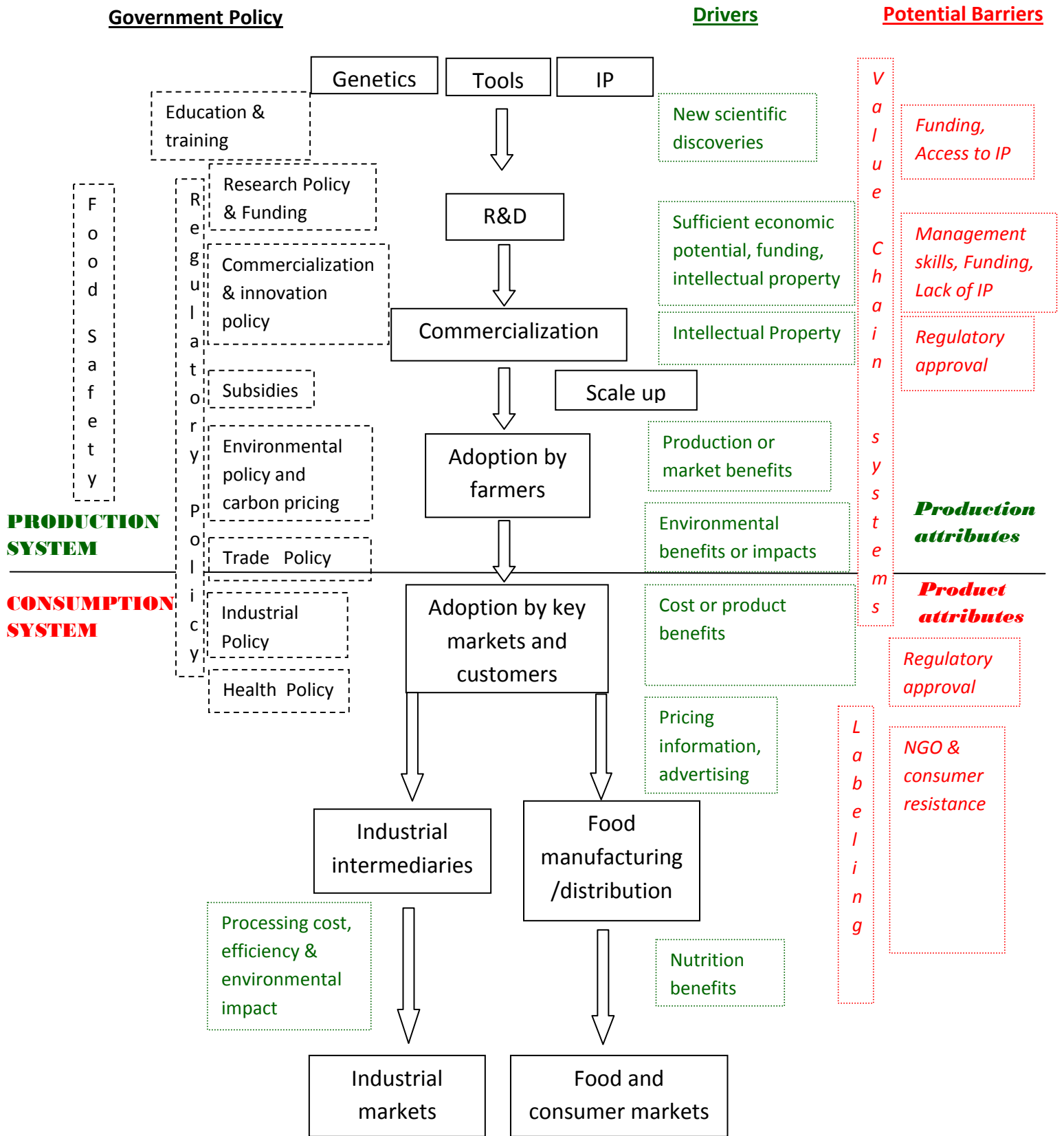
Improved coordination between industrial and agricultural biotechnology and applications – Canada has real opportunities in the bioeconomy with its significant agricultural and forestry biomass. We should continue to focus research and resources on this opportunity.

Development of rigorous biotechnology value chain systems – As we move into more crop production for industrial applications and for pharmaceuticals and nutraceuticals, we will need strong identity preservation systems to protect the value in the products and to eliminate issues related to product contamination. Currently, AAFC's value chain round tables do not include bioproduct value chains but this will have to change in the future as these take on larger roles in the industry.

Flexibility and adaptability in the regulatory system – As the sciences of biotechnology, genomics and advanced breeding continue to progress the industry will have the ability to develop new traits and characteristics more rapidly than in the past¹. Canada's regulatory system is already struggling to keep up and will be even more challenged in the future. We will need an effective regulatory system that adapts to new technologies and market opportunities and develops risk-based solutions to new biotechnology innovations.

¹ CropLife International states that 30 biotech events approved globally to date with a total of 90 events globally by 2015.

Figure 1 A Framework for Agricultural Biotechnology Commercialization



Appendix 1 Agricultural Biotechnologies under Development and Review

From CFIA – Plants with novel traits awaiting approval - retrieved May 20, 2010:

Submission Title	Developer	Review to begin after
Soybean FG72 which has been genetically modified for tolerance to glyphosate and HPPD inhibitor herbicides.	MS Technologies LLC and Bayer CropScience Inc.	2010-05-22
Corn (DAS-40278-9) which has been genetically modified for herbicide tolerance	Dow AgroSciences Canada Inc.	2010-03-26
Soybean (MON 87705) which has been genetically modified for oil with enhanced stability and nutrition and herbicide tolerance	Monsanto Canada Inc.	2010-03-26
Soybean (MON 87769) which has been genetically modified to produce an omega-3 fatty acid	Monsanto Canada Inc.	2009-11-17
Soybean (MON 87701) which has been genetically modified for insect resistance	Monsanto Canada Inc.	2009-10-16
Soybean (CV 127) which has been genetically modified for imidazolinone herbicide tolerance	BASF Canada Inc.	2009-07-09
Cotton (T304-40 x GHB119) which has been genetically engineered for lepidopteran insect resistance and glufosinate-ammonium herbicide tolerance	Bayer CropScience Inc.	2009-06-29
Corn (MON 87460) which has been genetically modified for drought tolerance	Monsanto Canada Inc.	2009-05-22
Helianthus annuus, which has been developed for herbicide tolerance using mutagenesis and conventional breeding	BASF Canada Inc.	2009-04-18

Field trials from spring 2009 (not a complete list – only numbers of interest)

Crop	No. of trials completed	Objective: selectable market	Obj: herbicide tolerance	Obj: insect resistance	Obj: increase yield	Obj: stress tolerance
Camelina	20		4		20	
Canola	661	99	558		214	385
Corn	15		25	4		1
Soybeans	114		86		74	
Total for all crops	818					

Notes of interest – one trial was conducted with tobacco under the breeding objective of commercial enzyme production. Camelina is an oil crop that is said to have opportunity in the bioproducts/biofuel markets.

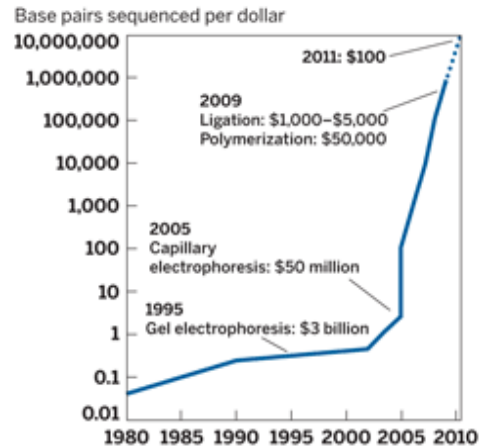
Appendix 2 Technology Platforms

Next-Generation Sequencing – DNA sequencing is a core technology required for plant and agricultural biotechnology, as well as a number of other basic and applied fields of research. DNA sequencing is the determination of the order of the nucleotide base units in a molecule of DNA, which is unique to each organism. In agriculture, DNA sequencing allows the identification of genes or markers related to important agronomic traits such as increased stress tolerance or seed quality.

New platforms such as the Roche 454 Genome Sequencer FLX™ and the Illumina Genome Analyzer (both recently adopted at PBI) are relatively new platforms that increase dramatically the amount of sequencing that can be done in a short timeframe and decrease the costs of that sequencing as well. The figure on the right demonstrates the increase in amount of sequencing that can be done for a lower cost over the last 30 years. These instruments also allow the researcher to analyze many other things besides only the sequence – for instance we can determine relative expression of particular genes in comparative studies to determine whether a gene of interest is up- or down-regulated under certain conditions (ie. drought).

A NEW 'MOORE'S LAW'

Improvements in DNA sequencing are driving down the cost of whole genomes



NOTE: Dollar figures refer to reagent costs.
SOURCE: George Church, Harvard University

Bioinformatics – Next-generation sequencing is a vital tool for plant biotechnology, however, the vast amounts of data produced introduce new challenges to the research community. Bioinformatics is the use of computers and advanced software to deal with these “data dumps” more efficiently. The Bioinformatics Lab at NRC-PBI (and those groups elsewhere) develops tools and infrastructure for the storage, analysis, and exploration of biological research data to enable researchers to extract knowledge from biological data.

Molecular Markers is a term used to describe a DNA fragment that can be used to identify a particular sequence of DNA to determine presence or absence of genetic material. In breeding, markers can be developed to identify whether or not a gene or trait is present in a particular individual for selection. Markers have been developed for many types of traits including sex (in animal breeding), disease resistance, cold tolerance, etc. Markers speed the development process by several years compared to the conventional breeding method.

Gene Stacking is simply a term to describe the insertion of more than one gene (or trait) into an organism. This technology is becoming an important tool in plant breeding as it enables companies to develop new varieties that have multiple commercial applications; for example, increased yield, herbicide-tolerance, and drought-resistance could all be incorporated in one variety for crop production.

TILLING is a molecular biology approach that allows directed mutations in a specific gene to produce a “library” of mutations that can be screened for novel functions. It is viewed as a non-GM approach for plant breeding, offering many possibilities to researchers, breeders and companies.

Targeted mutagenesis refers to the practice of modifying an organism’s DNA through site-directed individual changes in the host DNA. This can be done via multiple technologies, though many of them are proprietary to different companies. One example of this type of modification is Cibus’ Rapid Trait Development System™

(RTDS), a new gene repair technology being deployed to develop new and useful traits in crops.

RTDS is based on altering a targeted gene by utilizing the cell's own gene repair system to specifically modify the gene sequence in situ and not insert foreign DNA and gene expression control sequences. This procedure effects a precise change in the genetic sequence while the rest of the genome is left unaltered. In contrast to conventional transgenic GMOs, there is no integration of foreign genetic material, nor is any foreign genetic material left in the plant. The changes in the genetic sequence introduced by RTDS are targeted and precise. Finally, since affected genes remain in their native location, no random, uncontrolled or adverse pattern of expression occurs. (www.cibus.com)

Mass Spectrometry can be used to analyze compounds ranging from plant metabolites and other small molecules (**metabolomics**) to proteins and other biopolymers (**proteomics**). The analysis of metabolites and proteins provide the knowledge to understand gene function and linking the analytes (or chemicals) to relevant traits. Some examples of services that can be provided through mass spectrometry include:

- quantitative analysis of specific compounds or proteins
- metabolite profiling
- identification and characterization of natural products
- protein identification

Plant Hormone Profiling – Plant hormones regulate gene expression through complicated signaling networks. Hormone profiling is an important tool to understand plant development and response to stress. Hormone profiles can be integrated with genomic, proteomic and metabolomic information to obtain a global view of plant biological processes.

At NRC-PBI, we provide plant hormone profiling on a service or collaborative basis to plant biologists. The analytical approach enables the quantification of multiple plant signaling molecules in a single plant sample, using labeled internal standards. The compounds targeted include biologically active hormones, their precursors and inactive metabolites, all of which together provide information on the hormone status of the plant.

Plant Phenomics – The evaluation of plant phenotypes may be referred to as phenomics. In order to allow for rapid screening of several prototypes or events before going to the field, Plant Phenotyping Facilities are a recent infrastructure and technical development. The screening is based on sophisticated and automated tools using imaging and bioinformatics. More information on these kinds of facilities can be found at www.lemnatec.com.