Full text provided by www.sciencedirect.com

Agricultural input traits: past, present and future

Linda A Castle[1], Gusui Wu[1] and David McElroy[2]

For thousands of years farm practices have evolved as new innovations have become available. Farmers want more value per unit of land, clean fields, and high yields with less input. Plants with incorporated pest resistance and herbicide resistance help meet these needs through increased yield, reduced chemical use, and reduced soil impacts. Although researchers have developed useful traits for a wide variety of plant species, only a few traits are available commercially; however, global adoption of these traits has and continues to increase rapidly. Availability of future traits will be dependent on input not only from researchers, but from governments, interest groups, processors, distributors and ultimately consumers, in addition to the farmers that drive demand for transgenic seed.

Addresses
[1] Pioneer Hi-Bred International, Inc., 700A Bay Road, Redwood City, CA 94063, USA
[2] Pioneer Hi-Bred International, Inc., 7300 NW 62nd Avenue, Johnston, IA 50131, USA

Corresponding author: Castle, Linda A (linda.castle@pioneer.com)

Current Opinion in Biotechnology 2006, **17**:105–112

This review comes from a themed issue on
Plant biotechnology
Edited by Nam-Hai Chua and Scott V Tingey

Available online 17th February 2006

0958-1669/$ – see front matter

DOI 10.1016/j.copbio.2006.01.011

Introduction

Farm inputs encompass the operating resources used in the generation of crop products including seeds, fertilizers, irrigation, chemicals for crop protection and growth regulation, fuel, and electricity. Input traits, as defined here, cover transgenes that enhance or replace alternative farm inputs. These include herbicide, insect, and disease resistance traits that are able to substitute for pest-controlling crop protection chemicals. Input traits can be seen as just the latest step in a long history of production-enhancing technologies adopted in agriculture (Box 1).

In the 10 years since their first commercial introduction, transgenic crops containing input traits have been rapidly adopted in several important agricultural markets, and to date have been cumulatively grown on over 950 million acres (385 million hectares). In 2004 alone, 200 million acres (81 million hectares) of transgenic crops were grown across 17 countries, with an estimated market value of $4.7 billion [1]. Countries with the greatest number of biotech crop acres are (in millions of acres) the US (117.6), Argentina (40.0), Canada (13.3), Brazil (12.4), and China (9.1). Figure 1 details the 2004 global input trait adoption figures for the four major biotech crops. Global adoption rates for input traits have grown at 10% or more each year since 1996 and are projected to continue to grow at this rate [1] (see also Update).

Transgenic plant products generate economic benefit for farmers and retail consumers by lowering the financial and environmental costs of crop production. The cost savings to farmers associated with their use of input trait products can be readily calculated. A value-sharing mechanism, involving a distribution (between seed companies and technology providers) of the technology access fees or seed premiums collected from the farmer-producers is well established. Considering the distribution of farm input costs in US cotton production alone, since the introduction of input traits one can see that input (operating) costs did not increase significantly as a percentage of total production costs (Figure 2). However, there has been a significant increase in seed costs as transgenic input traits have been adopted throughout cotton production. At the same time, there has been a concomitant decline in chemical and chemical application costs as input traits have increasingly substituted for crop protection chemistry to control weeds and insects in US cotton production. Numerous studies have detailed the societal benefits of input trait products at both the environmental and economic level [2,3,4•].

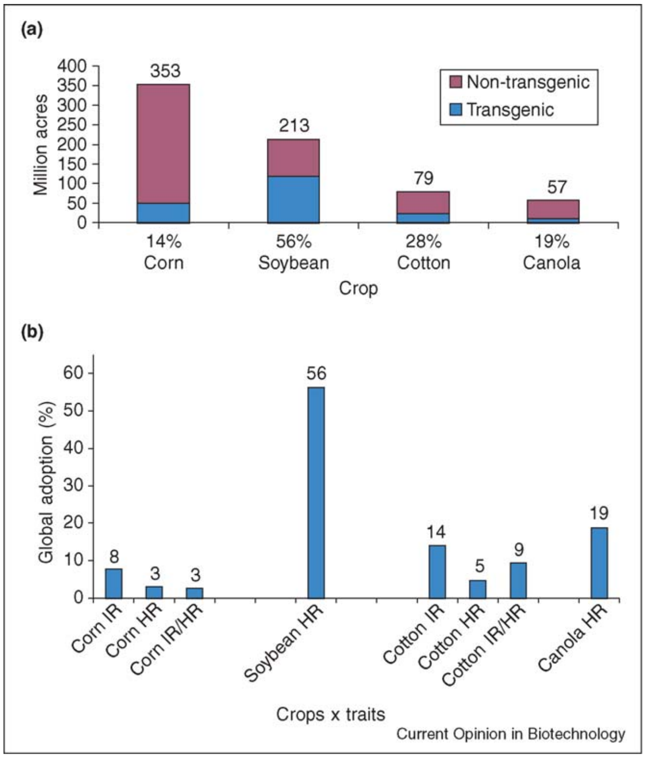
In this review, we discuss the current market for agricultural input traits, consider those traits that are poised to enter the market, and take a look at the research that could lead to novel input traits in the future. Within this context, we discuss why some traits are more successful than others. For detailed sources of information on other aspects of input traits, as well as details on the process of bringing transgenic traits to market, the reader is encouraged to pursue the following resources. An excellent collection of papers reviewing herbicide resistance traits can be found in *Pest Management Science* [5••]. Current and detailed data on all transgenic traits with regulatory approval in the US, Canada and elsewhere are maintained in a searchable database provided by Agbios (http://www.agbios.com/dbase.php). The PlantBiotech Projects database available for a fee from PJB Publications (http://www.pjbpubs.com/plantbiotech/index.htm) catalogs research phase projects as well as approved and marketed traits. Another rich source of information is the annual

Box 1 A brief history of technology adoption in agriculture.

Time	Technology development
10 000 BC	Domestication of plants and animals
8000 BC	Domestication of wheat and barley
3000 BC	Development of wine production
1000 BC	Ox-drawn plow improved
	Development of irrigation systems
1000s	Cultivation and fallow rotation cycle developed
1300s	Initiation of common land enclosure for sheep production
1600s	Grain and legume rotation cycle developed
1700s	Selective breeding of livestock
	Application of limestone fertilizer for farm soils
Early 1800s	Improvement in farm cultivation and crop processing tools
	Deployment of on-farm steam power
	Sale of mixed chemical fertilizers
	Construction of road, rail and canal systems for delivery and distribution
Late 1800s	Selective breeding of plants
Early 1900s	Development of agricultural chemicals industry
	Development of rail- and ship-based refrigeration systems for distribution
1930s	Development of hybrid corn
1950s	Freeze drying and food irradiation
1980s	Development of transgenic crops

Many unrecognized technologies have contributed to modern agriculture. Since the initial domestication of plant species, genetic modification by selective breeding has provided the modern crop varieties into which specific input traits are added by biotechnology methods.

Figure 1



Global adoption of biotech crops in 2004. **(a)** Bars represent total acres for four crops grown globally with the percentage acreage devoted to biotech input traits listed below. (Figure adapted from [1]). **(b)** Bars represent the major crops and traits with the percentage global crop acreage devoted to that trait. Only insect resistance (IR) and herbicide resistance (HR) traits are available for these major crops.

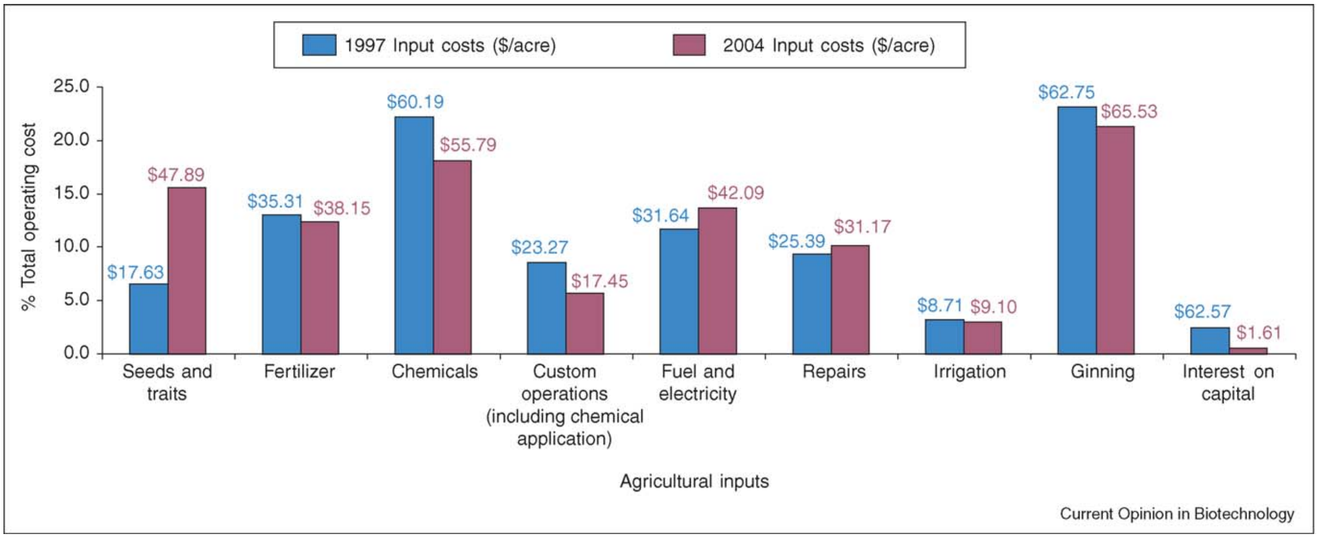
Global Status of Commercialized Biotech/GM Crops published each year as a brief from the International Service for the Acquisition of Agri-biotech Applications (ISAAA; http://www.isaaa.org). Interested readers can find links to sites addressing many aspects of plant biotechnology from these sites. Other recent reviews cover economic challenges [6], US regulatory requirements [7], intellectual property issues affecting trait commercialization [8], and global public perception issues [9] surrounding genetically modified crop plants as a whole.

Available input traits

Herbicide resistance traits

Among the input traits offered to farmers, herbicide resistance has been the most widely adopted. Glyphosate-resistant soybeans were one of the earliest transgenic crops brought to market and they have experienced rapid adoption to the point that over 85% of US soybeans and 56% of soybeans globally are now glyphosate resistant. The use of glyphosate-resistant cotton, canola, and corn are also increasing at a rapid pace, especially when combined, or stacked, with insect resistance traits. Products commercially available in the US and other countries are listed in Table 1. Glyphosate resistance is achieved in Roundup Ready® brands (Monsanto, St. Louis, MO) by expression of a modified *Agrobacterium* gene coding for the herbicide insensitive enzyme CP4 enolpyruvyl-shikimate-3-phosphate synthase (CP4 EPSPS) that is targeted to the chloroplast [10]. In recent years, Monsanto licensed the trait to many seed companies allowing deep penetration of the trait into the global market. The GA21 trait for glyphosate-resistant maize relies on a modified maize *epsps* gene, but is largely being replaced by varieties with

Figure 2



Current Opinion in Biotechnology

A comparison of input costs in US cotton production between 1997 and 2004 represented as both a percentage of the total operating costs and in absolute cost/acre of cotton production. From 1997 to 2004 operating costs for cotton farms increased by about 14%. Seed and trait costs nearly tripled in that period, but were offset by decreasing chemical and chemical application costs. Sources: USDA Economic Research Service; http://www.ers.usda.gov/Data/CostsAndReturns/data/Forecast/cop_forecast.xls and National Cotton Council; http://risk.cotton.org/CotBudgets/us.htm.

the NK603 trait which has two copies of CP4 *epsps* with different promoters for better expression in the meristems. Glyphosate herbicides are relatively inexpensive and can be applied over-the-top of resistant seedling crops. Nearly all broadleaf and grass weeds are eliminated resulting in reduced competition, higher yields, and cleaner fields at harvest (Figure 3). Adoption of reduced and no-till practices, where dead vegetation is left in the field rather than plowed under, has been a significant unintended feature of herbicide-resistant crops, saving farmers money in fuel costs (Figure 2) and reducing soil erosion. Glyphosate resistance has become a must-have trait for major seed companies.

Traits for resistance to three other classes of herbicides have been developed, but have not reached the same level of popularity as glyphosate resistance. Resistance to oxynil herbicides conferred by the BXN nitrilase from *Klebsiella pneumoniae* (subspecies *ozaenae*) [11] was the first trait engineered in cotton (developed by Calgene, Davis, CA [now Monsanto]). Because glyphosate is less expensive and controls more weed species, interest in using the oxynil herbicides has waned and 2004 was the final year of BXN® cotton sales. BXN canola was commercialized by Rhone-Poulenc Canada (now Bayer CropScience, Monheim, Germany) and then discontinued. Phosphinothricin acetyltransferase (PAT or BAR) detoxifies phosphinothricin- or bialaphos-based herbicides (glufosinate). The *pat* gene is native to *Streptomyces viridichromogenes* and *bar* is from *S. hygroscopicus* where they act in both the biosynthesis and detoxification of the tripeptide bialaphos [12]. Like glyphosate, phosphinothricin herbicides control a broad spectrum of weed species and break down rapidly in the soil so that problems with residual activity and environmental impact are greatly reduced. Bayer CropScience markets this trait as LibertyLink® in several species (Table 1). The *pat* and *bar* genes are also popular plant transformation markers in the research community. Finally, BASF (Ludwigshafen, Germany) markets non-transgenic CLEARFIELD® imidazolinone-resistant canola, wheat, sunflowers, corn, lentils, and rice, while DuPont (Wilmington, DE) markets non-transgenic STS® soybeans with tolerance to sulfonylurea herbicides. A sulfonylurea-tolerant flax variety called CDC Triffid, developed by the University of Saskatchewan (Canada), was grown commercially in Canada in 2000 but is no longer offered. These crops all contain mutagenized versions of the acetohydroxyacid synthase, also called acetolactate synthase (ALS), which are not inhibited by imidazolinone and/or sulfonylurea herbicides [13]. Herbicides that inhibit ALS are considered low or very low use-rate herbicides with a good spectrum of weed control and are likely to remain an important part of weed resistance management programs.

Insect resistance traits

All current insect resistance traits have been developed using *cry*, or crystal, genes from the bacterium *Bacillus thuringiensis* (Bt). The crystal proteins produced by the bacteria are highly toxic to a broad range of insect pests, but are not harmful to mammals or other organisms [14–16]. Bt *cry* genes were a natural choice for an insect

Table 1

Examples of commercially available input traits.

Crop	Trait phenotype	Target trait gene(s)	Trait designation	Originating company	Year of first commercial sale	Trade name
Cotton	Resistance to lepidopteran insects	*cry1Ac*	MON531	Monsanto	1996	Bollgard®, Ingard®
		cry1Ac, cry2Ab2	MON15985	Monsanto	2003	Bollgard® II
		cry1Fa, cry1Ac, pat	281-24-236 x 3006-210-23	Dow AgroSciences	2005	WideStrike™
	Resistance to glyphosate herbicides	CP4 *epsps*	MON1445/1698	Monsanto	1996	Roundup Ready®
	Resistance to phosphinothricin herbicides	*bar*	LLCotton25	Bayer CropScience	2005	LibertyLink®
Corn	Resistance to European corn borer and other lepidopteran insects	*cry1Ab, pat*	Bt11	Northrup King (now Syngenta)	1996	YieldGard®, Attribute®
		cry1Ab	MON810	Monsanto	1997	YieldGard® Corn Borer
		cry1F, pat	TC1507	Dow AgroSciences; Pioneer Hi-Bred Intl	2003	Herculex® I
	Resistance to corn rootworm	*cry3Bb1*	MON863	Monsanto	2003	YieldGard® Rootworm
		cry1Ab, cry3Bb1	MON863 × MON810	Monsanto	2005	YieldGard® Plus
	Resistance to glyphosate herbicides	*Maize epsps*	GA21	DeKalb (now Monsanto)	1998	Roundup Ready®
		Two CP4 *epsps* expression cassettes	NK603	Monsanto	2001	Roundup Ready® Corn 2
	Resistance to phosphinothricin herbicides	*pat*	T14, T25	Aventis (now Bayer CropScience)	1996	LibertyLink®
Soybean	Resistance to glyphosate herbicides	CP4 *epsps*	GTS-40-3-2	Monsanto	1996	Roundup Ready®
Canola	Resistance to glyphosate herbicides	CP4 *epsps, gox v247*	GT73	Monsanto	1996	Roundup Ready®
	Resistance to phosphinothricin herbicides	*pat*	Topas 19/2	AgrEvo (now Bayer CropScience)	1995	LibertyLink®
Alfalfa	Resistance to glyphosate herbicides	CP4 *epsps*	J101, J163	Monsanto	2005	Roundup Ready®
Squash	Resistance to CMV, WMV2 and ZYMV	Coat protein genes of CMV, WMV2 and ZYMV	CZW3	Asgrow; Seminis Vegetable Seeds (now Monsanto)	1998	Destiny III, Conquerer III, Liberator III
	Resistance to WMV2 and ZYMV	Coat protein genes of WMV2 and ZYMV	ZW-20	Asgrow; Seminis Vegetable Seeds (now Monsanto)	1995	Prelude II, Patriot II, Declaration II, Independence II
Papaya	Resistance to PRSV	PRSV coat protein gene	55-1 63-1	Cornell University; University of Hawaii; USDA	1998	SunUp, Rainbow

Many insect resistance and herbicide resistance traits are also available in combinations as stacked traits. This table contains representative traits and is not an exhaustive list of all global commercial traits. Additional details on the genes and trait properties can be found at http://www.agbios.com/main.php and http://www.pjbpubs.com/plantbiotech/index.htm. Abbreviations: CMV, cucumber mosaic virus; PRSV, papaya ringspot virus; WMV2, watermelon mosaic virus; ZYMV, zucchini yellow mosaic virus.

protection trait, because crystal protein and spore fermentation products have been used successfully as sprayable insecticides for many years [15,16]. Transgenic varieties of cotton (Bollgard®, Monsanto) and corn (YieldGard®, Monsanto) transformed with the Bt genes have been on the market for nearly 10 years (Table 1). These products are effective in controlling lepidopteran insects, and have significantly reduced the field use of insecticides (Figure 2). Herculex® I (*cry1F, pat;* Dow AgroSciences [Indianapolis, IN] and Pioneer Hi-Bred International [Johnston, IA]) corn has broad-spectrum control that includes corn borers, black cutworm and other lepidopteran pests. The Chinese Academy of Agricultural Sciences has also developed and commercialized insect-resistant cotton varieties using the *cry1Ac* gene, alone or in combination with the cowpea trypsin inhibitor

Figure 3

Experimental field plots showing why herbicide-resistant soybeans are so desirable. Weed pressure in these plots makes it difficult to see the soybeans under the velvet leaf and grass weeds in untreated plots (back and right). Herbicide-resistant soybeans are kept free from weed competition resulting in higher yield when treated with herbicide (foreground). Non-transgenic control plants and weeds are killed by herbicide treatment (stakes at left center). (Photo courtesy of Pioneer Hi-Bred International, Inc.).

gene *CpT1* [17]. Potato varieties resistant to Colorado potato beetle were developed by Monsanto using the Bt gene *cry3A*. After receiving regulatory approval in 1995, insect-protected NewLeaf® potato varieties were sold in the US and Canada for several years. However, production of transgenic potatoes was discontinued in 2001 after a new effective insecticide was introduced and several major food processors announced that they would not use transgenic potato varieties (http://www.pjbpubs.com/plantbiotech/index.htm). StarLink® (*cry9C*) corn, developed by AgrEvo (now Bayer CropScience) and approved only for feed use, was grown commercially in 1999 and 2000, but was discontinued after the gene was found in food products. Bt-Xtra® (*cry1Ac*; DeKalb Genetics Corp., DeKalb, IL [now Monsanto]) and NaturGard®/KnockOut® (*cry1Ab*; Ciba Seeds [now Syngenta, Basel, Switzerland] in collaboration with Mycogen [now Dow AgroSciences]) corn varieties were also commercialized, but have since been replaced by newer products that offer increased insect protection throughout the growing season.

Second-generation products with input traits started entering the market in 2003 with the introduction of Bollgard II (*cry1Ac*, *cry2Ab2*) cotton by Monsanto. Features of second-generation products include stacked genes (e.g. combined traits of herbicide and insect resistance), two modes of action (e.g. two different Bt genes combined in one product) for improved insect resistance management, and enhanced performance of the traits (e.g. increased spectrum of target insects). For example, Widestrike™ (*cry1Fa*, *cry1Ac*; Dow AgroSciences) cotton and YieldGard Plus (*cry1Ab*, *cry3Bb1*; Monsanto) corn are newly released products with stacked Bt gene traits. Triple-stack traits — dual Bt genes combined with glyphosate or glufosinate resistance — are likely to replace many of the single trait products.

Disease resistance traits

Virus resistance is conferred through the expression of either viral coat protein or replicase genes in several transgenic products. Several squash varieties resistant to watermelon mosaic virus and zucchini yellow mosaic virus and also in combination with resistance to cucumber mosaic virus [18] were developed by Asgrow Seed Company (now Monsanto) and are sold commercially. Resistance to potato virus Y [19] and potato leafroll virus [20] was also developed by Monsanto and added to the (now discontinued) NewLeaf insect-resistant potato varieties. The most successful virus-resistant transgenic product available is papaya resistant to papaya ringspot virus (Table 1) developed by Cornell University (Ithaca, NY) in collaboration with The University of Hawaii and the United States Department of Agriculture (USDA). This single trait reversed the decimation of the papaya industry in Hawaii and has expanded the papaya growing area there since its introduction in 1997 [21].

Traits on the horizon

No herbicide traits with new modes of action are currently near commercialization. Roundup Ready Flex (Monsanto) was deregulated by the USDA in 2005 and initial commercial sale are anticipated in 2006. Flex cotton contains a second expression cassette of CP4 *epsps* with a meristem-active promoter, which allows an extended application window and higher glyphosate application rates. Roundup Ready wheat was deregulated and approved for sale, yet has not been sold owing to lack of support by the wheat industry. It will probably be sold when additional traits for disease resistance or nutritional quality are also available (http://www.monsanto.com). One Roundup Ready sugar beet trait was approved for sale in the US, but faced opposition from sugar refineries and food manufacturers. Another Roundup Ready sugarbeet has been deregulated in the US and, pending approval in major growth and export countries, might be marketed in 2007 (http://www.pjbpubs.com/plantbiotech/index.htm). Pending approval in the European Union, LibertyLink soybeans (Bayer Cropscience), first approved in the US in 1998, might soon be sold commercially.

Several insect-protected products are nearly commercial or are at the final stage of development. For example, Herculex RW (*cry34Ab1*, *cry35Ab1*, *pat*) and the broad spectrum, triple-stack Herculex XTRA (*cry1F*, *cry34Ab1*, *cry35Ab1*, *pat*) corn hybrid lines resistant to Liberty® herbicides, lepidopteran pests, and corn rootworm, co-developed by Dow AgroSciences and Pioneer Hi-Bred, will be available for commercial sales in 2006. Lepidopteran-resistant VipCot™ cotton products, with the unique Vip3A vegetative insecticidal protein from Bt [22], could also be introduced in the next couple of years by Syngenta in collaboration with Delta and Pine Land Company (Scott, MS). A second-generation Roundup Ready YieldGard RW corn product (CP4 *epsps*, *cry3Bb1*; Monsanto) tolerant to the corn rootworm but lacking the *nptII* antibiotic gene is in late-stage deregulation by USDA. Syngenta also has a corn rootworm product (modified *cry3A*) with regulatory approval pending. Internationally, anticipated new transgenic products include insect-resistant cotton hybrids in India [23] and insect-resistant rice in China [24] and Iran (see Update) all developed using Bt genes. Bio.org (http://www.bio.org/speeches/pubs/er/agri_products.asp) predicts that input traits headed for the market in the next six years include Roundup Ready lettuce and strawberries, LibertyLink rice, insect-protected soybeans, apples and additional corn products, disease-resistant bananas and canola, and drought-tolerant corn.

The future of input traits

Given that weeds, insects, bacteria, viruses, nematodes, and fungi will not go away, new and different traits will always be needed to combat future pests. The first alternate mode of action trait for glyphosate resistance, detoxification by glyphosate *N*-acetyltransferase, is being developed by Pioneer Hi-Bred [25] and is slated to be offered in combination with resistance to sulfonylurea herbicides (http://www.pioneer.com/usa/research/pipeline/index.htm. Dual herbicide resistance products will offer all the advantages of glyphosate resistance with the additional benefits of two modes of action for resistant weed management. Other herbicide traits with new modes of action are currently in the research phase. Recent publications describe herbicide resistance using glutathione conjugation [26], *p*-hydroxyphenylpyruvate dioxygenase-inhibiting herbicide resistance [27], protoporphyrinogen oxidase-inhibiting herbicide resistance [28], and broad-range herbicide resistance owing to P450-catalyzed detoxification [29]. Detoxification of dicamba herbicides could translate to herbicide-tolerant plants as well [30].

When the major lepidopteran and coleopteran pests are controlled, secondary pests such as nematodes and the sucking and chewing bugs emerge as the next targets for pest resistance traits. Novel Bt crystal proteins could provide some protection, but new modes of action are needed not only for controlling new insect targets but also for insect resistance management of the current targets. The vegetative insecticidal proteins produced by Bt are unrelated to Bt crystal proteins and represent a new source of active insecticidal agents [22]. Protein TcdA isolated from *Photorhabdus luminescens*, a symbiotic bacterium associated with soil nematodes, is another example of a non-Bt insecticidal protein shown to confer insect resistance [31]. With the impending ban on methyl bromide soil fumigation owing to environmental concerns, nematode control will be an emerging market that has not been previously addressed by transgenes.

Newly emerging RNAi technology may provide additional traits such as virus resistance with broad-spectrum control and potentially enhanced durability [32]. Significant progress has been made in the past decade in understanding the molecular mechanisms of plant resistance to diseases. From the picture of extremely complex plant–pathogen relationships, several potential approaches for developing disease control traits are emerging [33•,34]. The recent example of combining marker-assisted selection with genetic transformation to develop blast and bacterial blight resistance in rice [35•] illustrates how transgenic traits can be stacked with native resistance genes for broad-spectrum disease resistance.

As other nutrition, quality, yield, and biopharming (end-use or output) traits are introduced, they are likely to be stacked with herbicide, insect, and pest resistance traits. Acceptance of new pest- and herbicide-resistant rice varieties could enable the nutritional traits to reach many countries facing growing and hungry populations [36]. Current and new traits may be deregulated in minor crops and local varieties, especially in regions with specific variety and pest control needs. Reaching into marginal lands and the need to manage nutrient availability, especially in developing countries, is driving the development of traits to address water and fertilizer inputs. Promising drought tolerance research is covered elsewhere in this issue [37] and genes with the potential to alter nitrogen metabolism in crops are reviewed elsewhere [38].

A wide array of major and minor crop and tree species have been transformed with pest resistance traits, including virus resistance, disease resistance, nematode and insect resistance, and herbicide resistance (http://www.pjbpubs.com/plantbiotech/index.htm). The future picture for the expansion of all transgenic traits into new countries and crops will depend on the acceptance scenario that plays out globally over the next five to ten years [39].

Conclusions

The first herbicide and insect resistance input traits are heading into their second decade of adoption. The acreage planted with input traits continues to increase for corn, soy, canola, and cotton in the US and globally. Relatively few genes have been approved and the major crops dominate due to the high costs of bringing the traits to market. The current herbicide, insect, and virus resistance traits meet the major needs of farmers in developed nations. New diversity in modes of action toward the major target pests and herbicides will help prolong the usefulness of these traits. The scientific capabilities to develop useful crop traits and the desire of growers to use them is high. Nevertheless, several outstanding questions remain that could affect the future use of input traits. How will future products fare against public opinion and the challenges of the current regulatory systems? Will there be regional or global markets for these products that can justify their development expenses? Will acceptance of consumer oriented traits facilitate acceptance of future input traits in Europe? Grower demands for transgenic traits may be high, but in global agriculture the (seed buying) customer must also deal with the input from governments and society in determining the availability of crop traits. Future expansion in this area will depend strongly on the answers to some of these issues.

Update

Data for 2005 statistics of transgenic/GM crops around the world were published in January 2006 [40••]. The growth trends continued as in 2004. There was an 11% increase in GM acres grown globally and four new countries grew GM crops. Glyphosate and Bt-mediated insect resistance remained the top traits. In addition to the major row crops, 2005 marked the first year of commercial sales of GM insect resistant (*cry1Ab*) rice.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. James C: **Global status of commercialized biotech/GM crops: 2004**. *ISAAA Briefs* 2004. No. 32.

2. Gianessi LP, Silvers CS, Sankula S, Carpenter JE: **Plant biotechnology: current and potential impact for improving pest management in US agriculture, an analysis of 40 case studies** Washington, DC: National Center for Food & Agricultural Policy; 2002 http://www.ncfap.org/40casestudies.htm.

3. Marra MC, Pardey PG, Alston JM: **The payoffs to transgenic field crops: an assessment of the evidence**. *AgBioForum* 2002, **5**:43-50.

4. • Brookes G, Barfoot P: **GM crops: the global socioeconomic and environmental impact – the first nine years 1996-2004** UK: PG Economics Ltd; 2005 http://www.pgeconomics.co.uk.

A new summary of the impact of transgenic crops worldwide. This review addresses both economic and environmental impact resulting from widespread adoption of GM crops. It is filled with figures and tables of detailed data for all countries.

5. •• *Pest Management Science*. **Special issue: Herbicide-resistant crops from biotechnology**. John Wiley & Sons, Vol 61, Issue 3; 2005.

This issue contains articles contributed from the American Chemical Society symposium organized by Stephen O Duke and Nancy N Ragsdale held in March 2004. It covers the past, present and future of herbicide resistance traits.

6. McElroy D: **Sustaining agbiotechnology through lean times**. *Nat Biotechnol* 2003, **21**:996-1002.

7. *Pew Initiative on Food and Biotechnology*: **Issues in the regulation of genetically engineered plants and animals**. Washington DC; 2004, http://pewagbiotech.org/research/regulation/.

8. Graff GD, Rausser GC, Small AA: **Agricultural biotechnology's complementary intellectual assets**. *Rev Econ Stats* 2003, **85**:349-363.

9. Fischhoff B, Fischhoff I: **Publics' opinions about biotechnologies**. *AgBioForum* 2001, **4**:155-162.

10. Padgette SR, Re DB, Barry GF, Eichholtz DE, Delannay X, Fuchs RL, Kishore GM, Fraley RT: **New weed control opportunities: development of soybeans with a Roundup Ready® gene**. In *Herbicide-Resistant Crops: Agricultural, Economic, Environmental, Regulatory and Technological Aspects.* Edited by Duke SO. Lewis Publishers; 1996:53-84.

11. Stalker DM, McBride KE, Malyj LD: **Herbicide resistance in transgenic plants expressing a bacterial detoxification gene**. *Science* 1988, **242**:419-423.

12. De Block M, Botterman J, Vandewiele M, Dockx J, Thoen C, Gossele V, Movva NR, Thompson C, Van Montagu M, Leemans J: **Engineering herbicide resistance in plants by expression of a detoxifying enzyme**. *EMBO J* 1987, **6**:2513-2518.

13. Devine MD, Preston C: **The molecular basis of herbicide resistance**. In *Herbicides and their Mechanisms of Action.* Edited by Cobb AH, Kirkwood RC. Sheffield Academic Press; 2000:72-104.

14. de Maagd RA, Bravo A, Berry C, Crickmore N, Schnepf HE: **Structure, diversity, and evolution of protein toxins from spore-forming entomopathogenic bacteria**. *Annu Rev Genet* 2003, **37**:409-433.

15. Whalon ME, Wingerd BA: **Bt: mode of action and use**. *Arch Insect Biochem Physiol* 2003, **54**:200-211.

16. Federici BA: **Insecticidal bacteria: an overwhelming success for invertebrate pathology**. *J Invertebr Pathol* 2005, **89**:30-38.

17. Wu KM, Guo YY: **The evolution of cotton pest management practices in China**. *Annu Rev Entomol* 2005, **50**:31-52.

18. Tricoli DM, Carney KJ, Russell PF, McMaster JR, Groff DW, Hadden KC, Himmel PT, Hubbard JP, Boeshore ML, Quemada HD: **Field evaluation of transgenic squash containing single or multiple virus coat protein gene constructs for resistance to cucumber mosaic virus, watermelon mosaic virus 2, and zucchini yellow mosaic virus**. *Biol/Technology* 1995, **13**:1458-1465.

19. Lawson C, Kaniewski W, Haley L, Rozman R, Newell C, Sanders P, Tumer NE: **Engineering resistance to mixed virus infection in a commercial potato cultivar: resistance to potato virus X and potato virus Y in transgenic Russet Burbank**. *Biotechnology (NY)* 1990, **8**:127-134.

20. Thomas PE, Lawson EC, Zalewski JC, Reed GL, Kaniewski WK: **Extreme resistance to *Potato leafroll virus* in potato cv. Russet Burbank mediated by the viral replicase gene**. *Virus Res* 2000, **71**:49-62.

21. Ferreira SA, Pitz KY, Manshardt R, Zee F, Fitch M, Gonsalves D: **Virus coat protein transgenic papaya provides practical control of *Papaya ringspot virus* in Hawaii**. *Plant Dis* 2002, **86**:101-105.

22. Estruch JJ, Warren GW, Mullins MA, Nye GJ, Craig JA, Koziel MG: **Vip3A, a novel *Bacillus thuringiensis* vegetative insecticidal protein with a wide spectrum of activities against lepidopteran insects**. *Proc Natl Acad Sci USA* 1996, **93**:5389-5394.

23. Bhat SR, Chopra VL: **Transgenic crops: priorities and strategies for India**. *Curr Sci* 2005, **88**:886-889.

24. Huang J, Hu R, Rozelle S, Pray C: **Insect-resistant GM rice in farmers' fields: assessing productivity and health effects in China**. *Science* 2005, **308**:688-690.

25. Castle LA, Siehl DL, Gorton R, Patten PA, Chen YH, Bertain S, Cho HJ, Duck N, Wong J, Liu D, Lassner MW: **Discovery and directed evolution of a glyphosate tolerance gene**. *Science* 2004, **304**:1151-1154.

26. Skipsey M, Cummins I, Andrews CJ, Jepson I, Edwards R: **Manipulation of plant tolerance to herbicides through coordinated metabolic engineering of a detoxifying glutathione transferase and thiol cosubstrate**. *Plant Biotechnol J* 2005, **3**:409-420.

27. Matringe M, Sailland A, Pelissier B, Rolland A, Zink O: ***p*-Hydroxyphenylpyruvate dioxygenase inhibitor-resistant plants**. *Pest Manag Sci* 2005, **61**:269-276.

28. Li X, Nicholl D: **Development of PPO inhibitor-resistant cultures and crops**. *Pest Manag Sci* 2005, **61**:277-285.

29. Hirose S, Kawahigashi H, Ozawa K, Shiota N, Inui H, Ohkawa H, Ohkawa Y: **Transgenic rice containing human CYP2B6 detoxifies various classes of herbicides**. *J Agric Food Chem* 2005, **53**:3461-3467.

30. Herman PL, Behrens M, Chakraborty S, Chrastil BM, Barycki J, Weeks DP: **A three-component dicamba *o*-demethylase from *Pseudomonas maltophilia*, strain DI-6**. *J Biol Chem* 2005, **280**:24759-24767.

31. Liu D, Burton S, Glancy T, Li ZS, Hampton R, Meade T, Merlo DJ: **Insect resistance conferred by 283-kDa *Photorhabdus luminescens* protein TcdA in *Arabidopsis thaliana***. *Nat Biotechnol* 2003, **21**:1222-1228.

32. Prins M: **Broad virus resistance in transgenic plants**. *Trends Biotechnol* 2003, **21**:373-375.

33. • Hammond-Kosack KE, Parker JE: **Deciphering plant–pathogen communication: fresh perspectives for molecular resistance breeding**. *Curr Opin Biotechnol* 2003, **14**:177-193.

A comprehensive review of the current knowledge of plant resistance genes, pathogenic factors and components involved in host defense pathways. Some emerging technologies and tools for studying plant–pathogen interactions and for developing resistance are highlighted. The authors discuss several approaches to develop durable disease resistance traits using genetic transformation and molecular breeding.

34. Gurr SJ, Rushton PJ: **Engineering plants with increased disease resistance: what are we going to express?** *Trends Biotechnol* 2005, **23**:275-282.

35. • Narayanan NN, Baisakh N, Oliva NP, VeraCruz CM, Gnanamanickam SS, Datta K, Datta SK: **Molecular breeding: marker-assisted selection combined with biolistic transformation for blast and bacterial blight resistance in Indica rice (cv. CO39)**. *Mol Breed* 2004, **14**:61-71.

Marker-assisted selection was used to breed populations of rice carrying the major genes *Pi-1 and Piz-5* conferring resistance to the blast pathogen *Magnaporthe grisea*. The blast-resistant pyramids were subsequently transformed with *Xa21*, a broad-spectrum resistance gene for bacterial blight caused by *Xanthomonas oryzae pv. oryzae.* The paper underscores the value of combining the two different approaches of molecular breeding.

36. Brookes G, Barfoot P: **GM rice: will this lead the way for global acceptance of GM crop technology?** *ISAAA Briefs* 2003. No. 28.

37. Umezawa T, Fujita M, Fujita Y, Yamaguchi-Shinozaki K, Shinozaki K: **Engineering drought tolerance in plants: discovering and tailoring genes to unlock the future.** *Curr Opin Biotechnol* 2005: in this issue.

38. Good AG, Shrawat AK, Muench DG: **Can less yield more? Is reducing nutrient input into the environment compatible with maintaining crop production?**. *Trends Plant Sci* 2004, **9**:597-605.

39. Advisory USDA: Committee on Biotechnology and 21st Century Agriculture: **Preparing for the future**. *AC21 Consensus Report* 2005; http://w3.usda.gov/agencies/biotech/ac21/reports/scenarios-4-5-05final.pdf.

This concise brief contains a wealth of data on where GM crops are grown, what traits are grown, which countries are growing GM crops, and an analysis of the trends.

40. •• James C: **Global status of commercialized biotech/GM crops: 2005**. *ISAAA Briefs* 2005. No. 34.

This concise brief contains a wealth of data on where GM crops are grown, what traits are grown, which countries are growing GM crops, and an analysis of the trends.