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**Publish or Patent?**  
**Knowledge Dissemination in Agricultural Biotechnology**

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## Contents

Abstract	v
1. Introduction	1
2. A Primer on Plant Transformation Technology	3
3. Patterns of Knowledge Dissemination in Transformation Technology	7
4. Conclusion and Future Challenges	13
Appendix: Supplementary Table	14
References	15

## **List of Tables**

1.	Research focus by plant species	9
2.	Types of affiliation of researchers	11
3.	Geographical distribution of research	12
A.1.	List of journals where patents are published	14

## **List of Figures**

1.	Schematic representation of <i>Agrobacterium</i> -mediated transformation of plant cells	4
2.	Trend of patent and journal publications since 1980	8
3.	<i>Agrobacterium</i> -mediated transformation method	10
4.	Changes in the composition of applied research in journal publications	10

## **ABSTRACT**

Plant transformation research has achieved outstanding progress in the development of transgenic crops over the past decades, and the research results have been spread through journal publications and patents. With the recent emergence of stronger intellectual property rights, investments in crop research and the landscape of plant transformation research have changed, along with the patterns of knowledge dissemination. In this paper, we discuss the recent trends in plant transformation research by examining patent and journal publication data during the last decade. The data analysis shows that there have been significant shifts toward applied research by developing countries and toward patenting as a means of knowledge dissemination during the past few decades, reflecting the increasing role of the private sector in developing countries in crop improvement research.

**Keywords:** biotechnology research, patent, crop improvement, journal publication



# 1. INTRODUCTION

Significant progress has been made over the past few decades in agricultural biotechnology, leading to the development of several transgenic crops worldwide. Advances in plant genetics technology such as bioinformatics, genomics, and proteomics have expanded the scope of research and generated a large body of knowledge. This stock of cumulative knowledge has traditionally been freely shared with the research community through journal articles, scientific databases, conferences, and other outlets. In the United States, for example, the public sector, including universities, has played a particularly important role in generating and disseminating knowledge in the area of agriculture, fostering an environment of free access and sharing (Wright et al. 2007).

However, as the commercial potential in biotechnology has increased through various legal and technological changes, private companies are increasingly involved in generating and privatizing scientific knowledge and technologies. The landmark *Diamond v. Chakrabarty* case in 1980, which allowed the patenting of living organisms, and subsequent rulings on patentability of plant and genes contributed to a rapid surge in biotechnology research by the private sector. Private companies have actively protected their technologies to capture the returns from their investment through intellectual property rights, such as patents and plant breeders' rights. Parallel to this trend of privatization, the public sector in the United States has also started to pursue intellectual property rights on its own research outputs, especially since the implementation of the 1980 Bayh-Dole Act, which allows universities and other public research institutes to patent and exclusively license their research results that were generated through federal funding (Jaffe 2000).

These changes in institutional environments led to a rapid surge in patenting worldwide in the late 1990s (Kortum and Lerner 1999). However, multiple patent claims in fundamental technologies and limited freedom to operate may slow down the utilization of these technologies and increase the transaction costs of developing new transgenic crops. Many of the core technologies in plant transformation have been patented and (exclusively) licensed through contracts, creating a thicket of overlapping patent claims. Heller and Eisenberg (1998) dubbed this phenomenon "tragedy of anticommons," where the proliferation of intellectual property rights in basic technologies may stifle subsequent improvements of the technologies and lead to fewer innovations. For example, Wright (1998) reports a case where University of California researchers had to abandon research on developing a transgenic tomato due to the inability to negotiate a licensing agreement on using patented technologies.

Continued accumulation of scientific knowledge and its dissemination to other sectors are today's seeds for tomorrow's innovations and agricultural improvements.<sup>1</sup> Traditionally, the dissemination of knowledge has taken the form of publication through journals or other outlets that ensure free access to the knowledge. The development of new technologies, together with changes in institutional environments toward privatization of research outputs, has given scientists different incentives to disseminate their research outputs. A detailed analysis of the patenting and publication patterns of research outputs can provide insights on how research outputs and scientific knowledge have been generated and disseminated with the changes in research environments.

In this paper, we will analyze recent patterns of knowledge generation and dissemination in agricultural biotechnology, in particular plant breeding, by using the example of the *Agrobacterium*-mediated transformation method. The *Agrobacterium*-mediated transformation method is one of the most widely adopted methods of developing transgenic crops, and active research is currently being performed to improve the technology. Recent developments in transgenic crops in both developed and developing countries largely used this technology, and timely adoption of this technology is critical to both traditional and transgenic crop improvement programs in developing countries.

By using the data on the journal publications and patents, this study examines the recent trend in *Agrobacterium*-mediated transformation technology, with a special emphasis on the types of technology

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<sup>1</sup> The continued importance of knowledge dissemination was also tucked away in the famous aphorism that Isaac Newton made in his letter to Hooke: "If I have seen further, it is by standing on the shoulders of giants."

(fundamental vs. applied) and their geographical distribution. The fundamental knowledge of this technology has mostly been generated by researchers in developed countries over the past few decades. An interesting research question is whether researchers in developing countries actively improve and apply the fundamental technology for local needs, or whether researchers in developed countries continue to improve the fundamental technology, and developing countries are simply early adapters of the applied technology. This analysis can evaluate the current research capacity of developing countries, and will provide useful information for policymakers to set resource allocation priorities for agricultural development. Furthermore, the increasing use of proprietary protection of research outputs may have a significant future impact on knowledge dissemination.

The analysis of the technology in journal and patent publications requires a certain level of knowledge underlying the research output, and Section 2 provides a brief introduction of the technology on *Agrobacterium*-mediated transformation method. This section helps distinguish the fundamental knowledge from applied technology in the data analysis, and explains the current level of technological progress. Readers with background knowledge of the technology can skip this section. Section 3 analyzes the detailed data on patents and publications, such as the current trend in plant transformation research, its research focus, and the geographical distribution of research outputs. The conclusion follows in Section 4.



## 2. A PRIMER ON PLANT TRANSFORMATION TECHNOLOGY

### Overview of Plant Transformation Technologies

Developing a new transgenic crop involves the transfer of genes with desired traits to other cells, and gene transformation technology is one of the main research focuses in crop improvements. Understanding the technical process involved in crop improvement is prerequisite to evaluating the recent technological developments in plant transformation methods published in journals or patents. This section briefly reviews the key technical steps in the process of plant transformation.

Although the first successful experimental transfer of individual genes to a plant was described only a few decades ago (Herrera-Estrella et al. 1983; DeBlock et al. 1984; Horsch et al. 1984), the gene transfer mechanism itself is an old natural phenomenon. In their natural environment, organisms can transfer genetic information in a vertical way from parent to progeny or in a horizontal way from one organism to the other. *Vertical* gene transfer through sexual reproduction induces genetic variations in the progeny through crossover and natural mutagenesis. Scientists and farmers often cross closely related species in order to produce new varieties with particular traits, and this approach has played an important role in natural selection and crop improvement since agriculture started millenniums ago.

On the other hand, *horizontal* gene transfer between different species has been applied in agriculture only recently. The possibility started with the discovery that genetic information can be transferred from one bacterium to another through DNA, and it was confirmed with the discovery of the DNA structure by Watson and Crick in the 1950s. Rapid technological advances in genetic engineering during the last few decades enabled scientists to create new plants with specific traits by incorporating genes from other species. In 1994, the first transgenic crop, the FlavrSavr tomato, with a prolonged shelf life, developed by Calgene, was approved for sale in the United States. Several other transgenic crops have been developed and commercially released since then. Most genetically modified crops are either herbicide tolerant, such as Roundup Ready soybeans and canola, or insect resistant, such as Bt corn or Bt cotton.<sup>2</sup> Many other types of crops are currently being developed with such traits as disease and pest resistance, drought and cold tolerance, and improved protein content, product quality, and vitamin enrichment.

The process of developing these transgenic crops involves the transfer of genes across species (called “transformation”), and several transformation technologies can be used to transfer genes into plant cells. One method, known as particle bombardment or biolistics, is a mechanical cell-disruption approach in which gold particles coated with DNA are “bombarded” into plant cells under high pressure. The transferred DNA molecules can then be incorporated into the target plant genome. This method has successfully been applied to monocots like wheat or maize, for which the *Agrobacterium*-mediated transformation is less effective. This technology of using “gene guns” was developed by scientists at Cornell University in the 1980s, and was licensed to DuPont in 1990. The problem with this method is that it often damages the cellular tissue. Another method, called “electroporation,” uses electrical impulses to make the plant cell membrane permeable, so that DNA molecules are transferred directly into the cell. Though this technique can be applicable to nearly all cells and species types, it often causes cell damage, and the transport of material is often nonspecific (Weaver 1995).

The most widely applied method in developing transgenic crops is the *Agrobacterium*-mediated transformation method (Tzfira et al. 2004; Valentine 2003). This method uses the natural process of the soil-borne bacterium *Agrobacterium tumefaciens*, which causes crown gall disease in plants by transferring some of its own DNA molecules into the plant cells (Hooykaas and Schilperpoort, 1992; Van Montagu, 2003; Van Larebeke et al. 1975). *Agrobacterium* was identified by Smith and Townsend in 1907, but the gene transfer capacity of *Agrobacterium* was only understood in the 1970s and 1980s.

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<sup>2</sup> Insect resistance in crops can be obtained by introducing a gene from the *Bacillus thuringiensis* (Bt) bacteria. The Bt protein that is produced in Bt transgenic plants is toxic to insects but harmless to higher animal and humans.

Initially, this method was believed to be applicable to only dicotyledonous plants<sup>3</sup>, but recent advances made its application to monocotyledonous plants (e.g., most cereals) possible. However, the transformation of some legumes and woody species is still limited due to the low efficiency of transformation and unstable transgenic expression.<sup>4</sup>

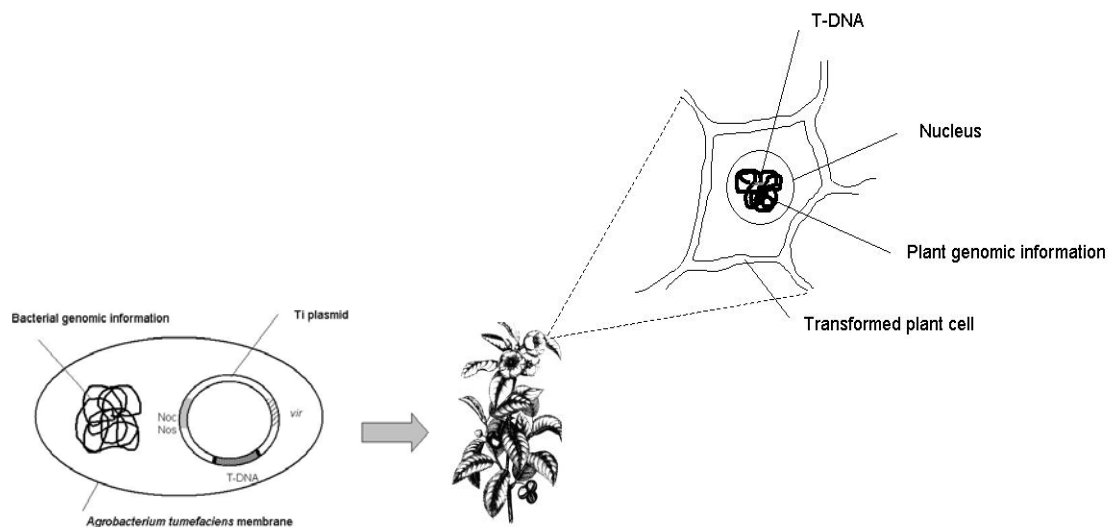
The efficiency of *Agrobacterium*-mediated plant transformation varies not only by plant species but also by plant tissues. A majority of transformation protocols have been based on *in vitro* modification of cotyledons, callus cells, embryonic tissue, leaves, shoot apices, roots, pollen, or hypocotyl tissue. Recently, *in planta* transformation methods—in which scientists dip the flowers in *Agrobacterium* solution to mediate gene transfer without prior isolation and sterilization of plant tissue—have been developed, avoiding the need for *in vitro* culturing. Although the *in planta* transformation methods would facilitate high throughput transformation and reduce the overall transformation time and costs, they cannot be applied routinely to all agriculturally important crops (Clough and Bent 1998).

Although much of the basic research and findings that led to *Agrobacterium*-mediated transformation was done in public institutions, the private sector now holds many of the key patent positions. The patents were obtained by the private sector either from internal research and development or from public institutions in the form of a license, or occasionally, as the assignee. Thus, the science and the patent positions are of high interest to both public and commercial sectors (Roa-Rodriguez and Nottenburg 2003). The limited availability of methods for transforming plants might indicate some degree of patent holdup on plant transformation technologies (Schimmelpfennig 2004).

### Steps for Plant Transformation with *Agrobacterium*

*Agrobacterium*-mediated plant transformation is a very labor-intensive and complex process, requiring well-trained personnel, specific equipment, and various technologies in each stage. A schematic representation of *Agrobacterium*-mediated plant transformation method is illustrated in Figure 1.

**Figure 1. Schematic representation of *Agrobacterium*-mediated transformation of plant cells**



Source: \* This figure was prepared by the authors.

<sup>3</sup> *Agrobacterium* was initially believed to be restricted to the transformation of certain dicotyledonous plants (flowering plants with two cotyledons in their seeds and broad leaves with reticulated veins), such as potatoes, tomatoes, beans, tobacco, and so forth, but nowadays transformation of monocotyledonous plants (flowering plants with one cotyledon in their seeds and narrow leaves with parallel veins), such as maize and rice, is routinely performed (Roa-Rodriguez and Nottenburg 2003).

<sup>4</sup> The transformation efficiency and time influence the overall costs, benefits, and risks of transgenic crop development.

### *Plasmid Preparation*

The first step in the transformation process is the preparation of the tumor-inducing plasmid, also called Ti-plasmid. It is a circular nongenomic DNA molecule that is present in *Agrobacterium* cells. The ability of *Agrobacterium* to transfer genes into the target plant cells is controlled by this large Ti-plasmid that contains three essential regions: the transferred-DNA (T-DNA) region, the *Nos/Noc* region, and the virulence genes (*vir*) region (Figure 1). The *Nos/Noc* region contains the genes for nopaline synthesis and catabolism as energy sources for the bacterium. The *vir* region contains the genes required for the excision, transfer, and integration of the T-DNA fragment. The gene of interest (e.g., herbicide-tolerance gene, male-sterility gene) is inserted into the T-DNA region. To enable specific selection of the cells containing the gene of interest at a later stage, a selectable marker gene (mostly antibiotic-resistance genes inducing kanamycine or hygromycine resistance) is also added to the T-DNA region. The T-DNA region also contains regulatory sequences such as promoter and terminator sequences to regulate the expression of selectable markers and transgenes (Figure 1). Lots of research has focused on developing many of these tools (e.g., markers, promoters, genes), and most of them are protected through patents. Obtaining licensing agreements to use these basic tools is important in developing transgenic crops, and holdups in obtaining licenses are often observed (Heller and Eisenberg 1998).

### *Gene Transfer*

After the preparation of plasmid, the T-DNA with the gene of interest is transferred and integrated into the genomic DNA of the target plant cell. For gene transfer, both *Agrobacterium* bacteria (containing T-DNA in Ti-plasmid) and plant cells are cocultivated *in vitro* for about 24 hours and then transferred to growth medium. High levels of hormones in the growth medium initiate cell proliferation and induce the growth of unorganized cell masses, called *callus*. Some of the transformed cells in the callus contain the gene of interest. The efficiency of this process is species-dependent and affected by tissue quality, concentration of *Agrobacterium* cells, length of T-DNA region, type of Ti-plasmid, and other environmental factors. Researchers have optimized this procedure for different types of species.

### *Selection of Transgenic Cells*

Not only do the transformed plant cells containing the T-DNA region proliferate in the cell cultures, but the neighboring cells that do not harbor the T-DNA (including the gene of interest) also form callus. Therefore, the presence of the selectable marker gene (antibiotic resistance gene) in the T-DNA region is necessary to distinguish the successfully transformed plant cells from the cells without T-DNA. During the selection of cell cultures, antibiotics are added to the growth medium to inhibit growth of plant cells without T-DNA. Only those cells that contain the selectable marker gene (along with the transgene in the T-DNA region) will show resistance to the antibiotics in the medium and will survive the selection conditions. A repetition of the selection steps may be required to specifically select transgenic cells.

### *Regeneration of Plants*

Once plant cells that successfully incorporate the gene of interest are selected, they are transferred to the regeneration medium to induce plant development. Unlike most animal cells, plant cells are totipotent, and entire plants can be regenerated from a single cell. The first step in this regeneration process is to transfer the selected cells to an appropriate growth medium to induce the development of shoots. When shoots are formed, the cells are transferred to a second regeneration medium for root development. When both shoot and root structures are developed, the small plantlets are transferred to larger *in vitro* containers for further growth.

### *Further Screening*

The selection process with markers in the previous stage is not perfect, and some plantlets without the transgene can survive the antibiotic selection. To further screen for cells that contain the gene of interest,

DNA samples of the plantlets are subjected to polymerase chain reaction (PCR) testing and Southern blot analysis. Since the presence of the targeted gene does not guarantee the expression of the transgene, the expression level of the transgene (i.e., the transcription of transgenic DNA into transgenic mRNA) is measured using the quantitative real time PCR or Southern blot analysis. Finally, the presence of the trait protein or enzyme (i.e., the translation of transgenic mRNA into transgenic protein) should be verified by the Western blot analysis or ELISA technology. This selection process is very time-consuming and labor-intensive, but it is necessary to reduce the cost of transgenic plant multiplication in the next stage.

### *Transfer to the Greenhouse*

After the final screening, the selected plantlets are carefully transplanted from *in vitro* culture medium to soil and transferred to the greenhouse to further grow into mature plants. At this stage, the transgenic plants are subjected to phenotypic analysis, that is, they are tested for the presence of desired traits such as herbicide tolerance, fruit quality, production yield, or insect resistance. The regeneration and multiplication process often requires a few weeks to several months for most species, but may take up to several years for woody species.

### 3. PATTERNS OF KNOWLEDGE DISSEMINATION IN TRANSFORMATION TECHNOLOGY

#### Data on Patent and Journal Publications

To analyze the recent trend of knowledge generation and dissemination in the agricultural biotechnology area, this study uses the development of *Agrobacterium*-mediated transformation technology as a case study. We collected patent and peer-reviewed journal publications that are related to *Agrobacterium*-mediated transformation in agriculture. For patent information, we collected global patent data from the patent database esp@cenet, version 3 (<http://be.espacenet.com>). This patent database, which is managed by the European Patent Office, covers about 50 million patents from 71 countries as of February 2005. For journal publication data, we used the literature database National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/Literature>), which is managed by the National Library of Medicine and the National Institutes of Health in the United States. The PubMed archive in this database contains more than 1.1 million full-text journal articles and 15 million citations from over 340 biomedical and life sciences journals worldwide.

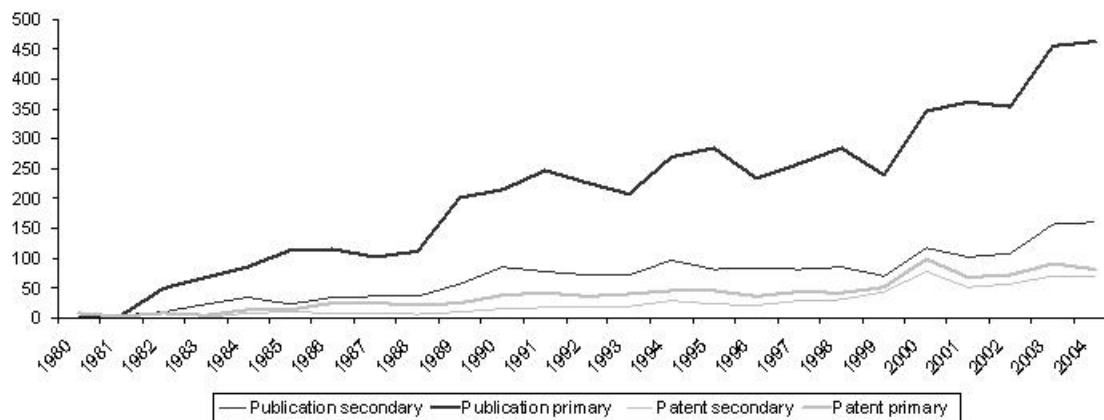
To obtain the relevant data on *Agrobacterium*-mediated transformation from both sources in a consistent manner, we adopted the keyword search strategy rather than relying on the built-in classification codes in the database (e.g., international patent classification code for the esp@cenet patent database). In the first stage, we searched for the keywords *Agrobacterium* and *transformation* in the fields of titles, abstracts, and main texts from both patents and journals that were published since 1980. In the second stage, we manually read all abstracts of the first-cut data to screen out those that were not directly related to the *Agrobacterium*-mediated plant transformation method in crop improvement. This two-step search process resulted in a total of 612 patent observations and 1,692 journal articles that were published during 1980–2004 (Figure 2).<sup>5</sup>

For more detailed, in-depth analysis of the changing trend of research activity, we choose in the following analysis the data for three discrete years (1996, 2000, and 2004) that are considered to cover the period of major research developments in the area of plant transformation. In this process, we also eliminated duplicative patents that were obtained in different countries from the same technology or innovation. An innovator often applies for patents in different countries even though the underlying innovation is the same (often called a *patent family*). These patents can be identified with the priority date information and are counted as a single innovation in the following analysis.

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<sup>5</sup>The lists of journals included in the data observations are summarized in Appendix Tables A1. The countries or institutes of data sources for patent data include Australia; Belgium; Canada; Switzerland; China; Germany; Eurasian Patent Office; European Patent Office; Spain; Finland; France; United Kingdom; Greece; Israel; Italy; Japan; Korea; Luxembourg; Mexico; Netherlands; New Zealand; Russia; Taiwan; United States; World Intellectual Property Organization; Ukraine; South Africa..

**Figure 2. Trend of patent and journal publications since 1980**



## Knowledge Generation and Dissemination: Patent versus Journal Publication

### Recent Trends in Plant Transformation Research

Figure 2 shows recent trends in the research on *Agrobacterium*-mediated plant transformation methodology in terms of the number of worldwide patent and journal publications from 1980 through 2004. The primary data series are those that pass the first screening process, and the secondary series are the ones garnered through a more refined screening process. Though there was an upward, steady trend in the number of journal publications during the last few decades, the number of patents has increased sharply since the late 1990s. Technological breakthroughs in the areas of genomics and bioinformatics since the 1980s might have contributed to the overall increase in research activities, which is reflected in the overall increase in the number of both journal and patent publications.

In terms of the relative surge in patents compared to journal publications in recent years, institutional changes since the 1980s might have contributed to the upward trend. Since the 1980s, a series of institutional changes in intellectual property rights protection have provided pro-patent environments both in the United States (see Kortum and Lerner 1999 for examples) and worldwide (see Harhoff 2006 for examples in Europe). Recent surges in the number of patents in most areas somewhat reflect these global institutional changes. Though it is difficult to make a concrete judgment with the current data, we can argue that both technological and institutional changes have contributed to the recent increases in patents in the *Agrobacterium*-mediated plant transformation technology.

### Research Focus by Plant Species

Though the *Agrobacterium*-mediated transformation method is widely adopted in transgenic crop development, its efficiency varies greatly by crop species, as discussed in Section 2. For many dicotyledonous plant species such as tobacco, *Medicago*, *Arabidopsis*, and petunia, the efficient transformation protocols with *Agrobacterium* have been well established over the past decades. However, *Agrobacterium*-mediated transformation of monocot plants has encountered technical difficulties, and its efficiencies were very low in the early years of transformation attempts. Alternative transformation methods, such as particle bombardment or the gene-gun method, were more commonly used for this type of plant in the 1980s and 1990s. Since the first successful transformations of rice and corn plants with *Agrobacterium* in the mid-1990s, however, research on the transformation of other monocot plants has rapidly increased.

Table 1 shows the number and share of patent and journal publications on *Agrobacterium*-mediated transformation research in 1996, 2000, and 2004 by types of target species. While the number of journal publications during the three sample years is stable at around 80, the number of patents has dramatically increased from 21 in 1996 to 70 in 2004, reflecting the recent surge in patenting in the biotechnology area. In terms of the types of species, the share of patent and journal publications reporting monocot plant transformation has substantially increased in the early part of this decade. In addition, it should be noted that the share of monocot plants in patents is higher than in journal publications in the early part of this decade (i.e., 20 percent vs. 12 percent). Most commercially valuable cereals are monocots, and they attract more patent applications to capitalize the commercial market.

**Table 1. Research focus by plant species**

	Total		1996	2000	2004
	Number	Share			
	(count)	(percent)		(count)	
<b>Journal</b>					
Monocot <sup>a</sup>	31	12	3	12	16
Dicot <sup>b</sup>	141	54	37	45	59
Both	88	34	43	33	12
Other <sup>c</sup>	1	0	0	0	1
Subtotal	261	100	83	90	88
<b>Patent</b>					
Monocot	32	20	3	19	10
Dicot	57	36	11	22	24
Both	65	41	7	24	34
Other	5	3	0	3	2
Subtotal	159	100	21	68	70

Notes: a. Monocot (monocotyledonous) plants contain one embryonic leaf, and most cereals belong to this group.

b. Dicot (dicotyledonous) plants, including tobacco and legumes, typically contain two leaves.

c. Other includes gymnosperm plants, whose seeds are not enclosed, such as some trees and seed corn.

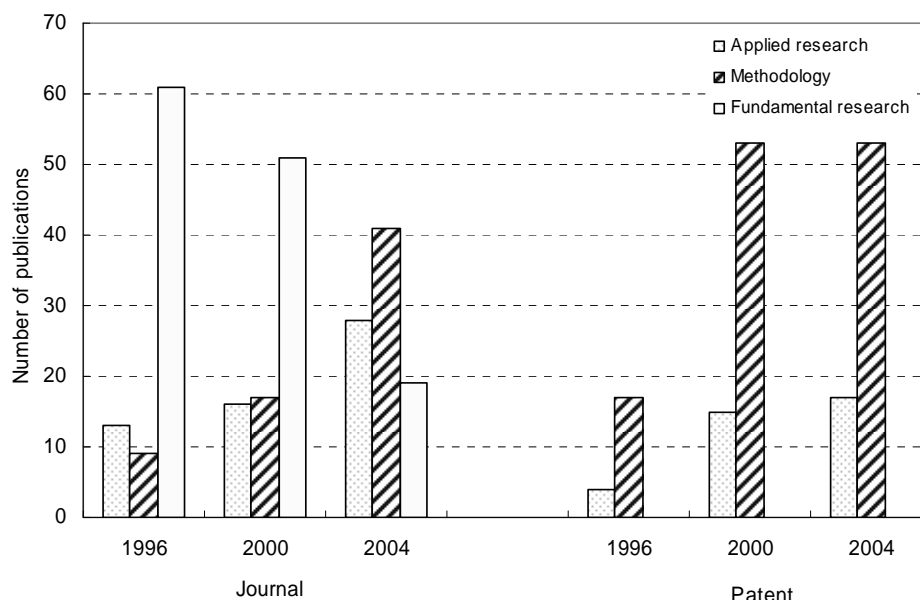
### *Nature of Research: Fundamental versus Applied Research*

Figure 3 illustrates how the nature of research has changed over time. *Agrobacterium*-mediated transformation research can be methodological, applied, or fundamental in nature. Methodological research focuses on the specific steps of a transformation protocol for a specific plant species, and applied research analyzes the development of specific transformation procedures and their applications to biotic and abiotic stress resistance, product quality, modified nutrient quality, and crops as biofactories. On the other hand, fundamental research examines gene-transfer mechanisms without direct reference to industrial applications and includes plant physiological and ecological studies and research on plant–microbe interaction and symbiosis. Patents, by definition, report research outputs with industrial applicability, so the patent data are classified only as either applied or methodological research.

Figure 3 also shows that there has been a significant shift in recent years from fundamental toward applied research projects in terms of journal publication. While the majority of the published journal papers (nearly 73 percent) were fundamental in nature in 1996, only 21 percent of papers published in 2004 discussed fundamental research problems. The process of technological development in general evolves from fundamental to applied focus as the research progresses, but the shift was more

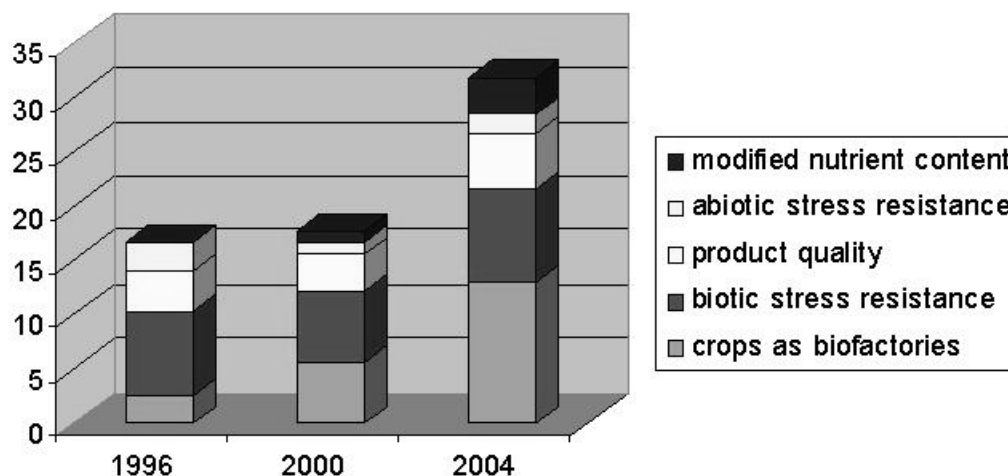
drastic in the area of plant transformation research. The increased patentability of research outputs because of various court rulings and changes in law (e.g., the 1980 Bayh-Dole Act in the United States) and the growth of commercial markets for crop varieties might have encouraged the shift of research focus.

**Figure 3. *Agrobacterium*-mediated transformation method**



In the field of applied research, the main application has been to develop transgenic crops with resistance to biotic stress, such as insect, bacterial, viral, and fungal resistance (Cohen 2005). Over the past few years, there has been an increasing interest in developing crops for use as biofactories (Figure 4). The first recombinant plant-derived pharmaceutical protein was human serum albumin, initially produced in 1990 in transgenic potato and tobacco plants (Sijmons et al. 1990). The focus was later shifted to industrial applications, and several drugs, such as antibodies, growth factors, blood products, cytokines, and human enzymes, are currently produced in plants (Twyman et al. 2005).

**Figure 4. Changes in the composition of applied research in journal publications**





## Who is Paying the Research Bill?

Table 2 categorizes the number of journal and patent publications by the affiliation of researchers. Though somewhat arbitrary, we classified all universities and research institutes as public sector (some may be privately operated). In terms of journal publication, the majority (93 percent) of articles have been published by researchers in the public sector, especially in universities. This trend hasn't changed much during the past decade: nearly 91 percent of all journal publications were still lodged by the public sector in 2004, down by only 3 percent compared to 1996.

**Table 2. Types of affiliation of researchers**

	Total		1996	2000 (count)	2004
	Number (count)	Share (percent)			
Journal					
Public	244	93	78	86	80
University	189	72	62	66	61
Research institute	55	21	16	20	19
Private company	17	7	5	4	8
Subtotal	261	100	83	90	88
Patent					
Public	72	45	6	30	36
University	39	25	4	14	21
Research institute	33	21	2	16	15
Private company	87	55	15	38	34
Subtotal	159	101	21	68	70

However, the trend is very different in the case of patents. During the study period, the majority of patents (55 percent) on the *Agrobacterium*-mediated transformation method were owned by the private sector, but its share has been rapidly decreasing, from 71 percent in 1996 to 49 percent in 2004. Many universities have adopted various measures to encourage researchers to apply for patents, which can explain the increased role of university patents from 19 percent to 30 percent during the same period. Overall, the public sector still accounts for about 45 percent of all patents in the area of agricultural biotechnology, unlike some other industries, where the private sector dominates the number of patent applications.

## Geographical Distribution of Research

Though most of the research activities in biotechnology are found in Organization for Economic Co-operation and Development (OECD) countries (89 percent for all journal articles and 84 percent for patents), the rapid growth of research activities in some developing countries during the past decade is noteworthy (Table 3). In particular, China has been very active in plant transformation research in recent years, with policy commitments toward transgenic crop research and development, and a similar trend can be found for India. In terms of journal publications, OECD countries' share of published articles dropped from 95 percent in 1996 to 83 percent in 2004. However, for patents, the drop is much more significant—from 95 percent to 68 percent during the same period—indicating the active role of China. Both patent and journal publication data show that some developing countries actively improve fundamental

knowledge to fit their environment, instead of passively receiving fully applied technology from developed countries.

**Table 3. Geographical distribution of research**

	Total		1996	2000 (count)	2004
	Number (count)	Share (percent)			
<b>Journal</b>					
<i>OECD country</i>	233	89	79	81	73
USA	96	37	44	30	22
Japan	25	10	4	10	11
UK	20	8	8	8	4
Others	92	35	23	33	36
<i>Non-OECD country</i>	28	11	4	9	15
China	10	4	2	2	6
India	7	3	1	4	2
Others	11	4	1	3	7
Subtotal	261	100	83	90	88
<b>Patent</b>					
<i>OECD country</i>	133	84	20	65	48
USA	63	40	10	26	27
Japan	23	14	1	13	9
Netherlands	8	5	0	6	2
Others	39	25	9	20	10
<i>Non-OECD country</i>	26	16	1	3	22
China	11	7	1	0	10
Russia	6	4	0	0	6
Others	9	6	0	3	6
Subtotal	159	100	21	68	70

Among the OECD countries, the United States accounts for nearly half of all journal publications and patenting activities in the *Agrobacterium*-mediated transformation research, followed by Japan. However, the share of U.S. research activity gradually decreased from 1996 to 2004, while OECD countries' share of research activity has been gradually increasing. We can argue that the knowledge base of agricultural biotechnology has globally spread out during the past decade.

## 4. CONCLUSION AND FUTURE CHALLENGES

Economic development and technological progress depend on continued generation of new knowledge and innovations and their wide dissemination to society. The right balance of these two is one of the main objectives in innovation policy. While new innovations can be readily generated by assigning proprietary rights, the patent itself can limit the dissemination of research outputs. On the other hand, although new innovations and knowledge may be disseminated widely through publication in journals, there may be less incentive to develop new innovations if the return on investment is not secured. Historically, innovation policy has shifted between these two considerations, and recently it has been moving toward an increasingly protected research environment. As policy shifts from one direction toward another, the research environment and reaction of the scientific community changes accordingly. Using patent and journal publication data on plant transformation technology, this paper analyzed how researchers' incentives in disseminating research outputs have changed in response to the institutional changes in the research environment.

We found that the research focus in the last decade, in the area of plant transformation, has shifted from fundamental to applied research, and from journal publication to patents. We also found a rapid rise of the role of developing countries (e.g., China and India) in applied research in crop improvement, which reflects significant knowledge dissemination from developed to developing countries.

The increasing shift toward patenting of research outputs is an important trend observed in this analysis, but this trend poses several challenges. First, patents tend to limit access to the technology, since they require users to obtain a licensing agreement with the patent holder. Several rights holders (Bayer CropScience, Monsanto, and the Max Planck Society) recently agreed to cross license their *Agrobacterium*-mediated transformation technologies. This allows them to access each other's patented technologies free of charge (press release February 2005, <http://www.mpg.de/>). This agreement may limit technology access for other companies who want to apply these methods, and might slow down the overall technological progress, though the opposite argument exists (Binenbaum et al. 2003). The significant knowledge dissemination achieved during the past few decades may not continue in the future.

Second, public sector institutes, which use others' proprietary technologies without acquiring formal license, are increasingly vulnerable to patent infringement claims (Eisenberg 2003). Public sector researchers have assumed that they could easily resort to the statutory "research exemption," which allows free access to patented technologies for noncommercial and/or research applications of an invention. A survey reported that most of the international research centers of the CGIAR used patented technologies without formal approval of the patentees (Cohen, Flack-Zepeda, and Komen 2004), and most university researchers rarely seek a license when using proprietary technologies. However, a recent ruling (*Mady v. Duke*, 307 F.3d 1351, October 3, 2002) showed that the research exemption can be very narrowly interpreted, and the public sector should not be complacent with this exemption clause. Public research institutes are now in a difficult situation where they should make their research outputs available to the public without restriction, but they have to get licenses for using others' technologies.

Third, there has been a small movement toward open access to technology in the biotechnology area, similar to open-source projects in the software industry. An example is the Biological Innovation for Open Society (BIOS) initiative—recently launched by CAMBIA, a non-profit research institute in Australia—which aims to forge a new commons in fundamental technologies for biological innovation (Broothaerts et al. 2005). Frustrated by the complex patent maze and by the enormous financial and bureaucratic barriers to obtain licenses, this initiative intends to create a common pool of technologies that are made freely available to scientists who could otherwise not afford them. The success of the open-source movement depends on the incentive structure of the providers of technologies, but the role of the public research community is critical.

## APPENDIX: SUPPLEMENTARY TABLE

**Table A.1. List of journals where patents are published**

Annu Rev Microbiol	J Plant Res
Annu Rev Plant Physiol Plant Mol Biol	Journal of Zhejiang University Science
Appl Environ Microbiol	Lett Appl Microbiol
Biochem Soc Trans	Membr Cell Biol
Ann Bot (Lond)	Methods
Ann N Y Acad Sci	Methods Mol Biol
Appl Biochem Biotechnol	Microbiology
Appl Environ Microbiol	Mol Biotechnol
Arch Biochem Biophys	Mol Cell Biol
Arch Insect Biochem Physiol	Mol Cells
Biosci Biotechnol Biochem	Mol Ecol
Biotechniques	Mol Gen Genet
Biotechnol Appl Biochem	Mol Microbiol
Biotechnol Lett	Mol Plant Microbe Interact
Cell	Nat Biotechnol
Cell Mol Biol Lett	Nature
Cell Res	Nucleic Acids Res
Chem Biol	Pest Manag Sci
Chin J Biotechnol	Plant Biol (Stuttg)
Chromosoma	Plant Cell
Curr Biol	Plant J
Curr Genet	Plant Mol Biol
Curr Infect Dis Rep	Plant Physiol
Curr Opin Microbiol	Plant Sci
FEBS Lett	Planta
FEMS Microbiol Lett	Planta Med
Funct Integr Genomics	Proc Natl Acad Sci U S A
Gene	Protein Expr Purif
Genetics	Science
Indian J Exp Biol	Shi Yan Sheng Wu Xue Bao
Int Arch Allergy Immunol	Theoretical and Applied Genetics
J Am Coll Nutr	The EMBO Journal
J Bacteriol	Transgenic Res
J Biol Chem	Tree Physiol
J Biotechnol	Trends Genet
J Exp Bot	Trends Microbiol
J Med Virol	Virology
J Nat Prod	Virus Res
J Nutr	Yi Chuan Xue Bao
J Plant Physiol	

## REFERENCES

- Binenbaum, E., C. Nottenburg, P. Pardey, B. Wright, and P. Zambrano. 2003. South-north trade, intellectual property jurisdictions and freedom to operate in agricultural research on staple crops. *Economic Development and Cultural Exchange* 51:309–335.
- Broothaerts, W., H. Mitchell, B. Weir, S. Kaines, L. Smith, W. Yang, J. Mayer, C. Roa-Rodriguez, and R. Jefferson. 2005. Gene transfer to plants by diverse species of bacteria. *Nature* 433:629–33.
- Clough, S., and A. Bent. 1998. Floral dip: A simplified method for *Agrobacterium*-mediated transformation of *Arabidopsis thaliana*. *Plant Journal* 16:735–43.
- Cohen, J. 2005. Poorer nations turn to publicly developed GM crops. *Nature Biotechnology* 23:27–33.
- Cohen, J., J. Falck Zepeda, and J. Komen. 2004. National agricultural biotechnology research capacity in developing countries. ESA working paper 04-14.
- DeBlock, M., L. Herrera-Estrella, M. Van Montagu, J. Schell, and P. Zambryski. 1984. Expression of foreign genes in regenerated plants and in their progeny. *EMBO Journal* 3:1681–89.
- Eisenberg, R. 2003. Patent swords and shields. *Science* 299:1018–19.
- Harhoff, D. 2006. Intellectual property rights in Europe: Where do we stand and where should we go? Helsinki. Prime Minister's Office, Economic Council of Finland.
- Heller, M.A., and R.S. Eisenberg. 1998. Can patents deter innovation? The anticommons in biomedical research. *Science* 280:698–701.
- Herrera-Estrella, L., A. Depicker, M. Van Montagu, and J. Schell. 1983. Expression of chimeric genes transferred into plant cells using a Ti-plasmid derived vector. *Nature* 303:209–11.
- Hooykaas, P., and R. Schilperpoort. 1992. *Agrobacterium* and plant genetic engineering. *Plant Molecular Biology* 19:15–38.
- Horsch, R., R. Fraley, S. Rogers, P. Sanders, A. Lloyd, and N. Hoffmann. 1984. Inheritance of functional foreign genes in plants. *Science* 223:496–98.
- Jaffe, A. B. 2000. The U.S. patent system in transition: Policy innovation and the innovation process. *Research Policy* 29:531–57.
- Kortum, S., and J. Lerner. 1999. What is behind the recent surge in patenting? *Research Policy* 28:1–22.
- Roa-Rodriguez, C., and C. Nottenburg. 2003. *Agrobacterium*-mediated transformation of plants. CAMBIA White paper. Available at <http://www.bios.net/daisy/bios/81/version/live/part/4>.
- Schimmelpfennig, D. 2004. Agricultural patents: Are they developing bad habits? *Choices* 1<sup>st</sup> quarter, 19–23.
- Sijmons, P., B. Dekker, B. Schrammeijer, T. Verwoerd, P. Van den Elzen, and A. Hoekema. 1990. Production of correctly processed human serum albumin in transgenic plants. *Biotechnology* 8:217–21.
- Twyman, R., E. Stoger, S. Schillberg, P. Christou, and R. Fischer. 2005. Transgenic plants in the biopharmaceutical market. *Expert Opinion on Emerging Drugs* 10:185–218.
- Tzfira, T., J. Li, B. Lacroix, and V. Citovsky. 2004. *Agrobacterium* T-DNA integration: Molecules and models. *Trends in Genetics* 20:375–83.
- Valentine, L. 2003. *Agrobacterium tumefaciens* and the plant: The David and the Goliath of modern genetics. *Plant Physiology* 133:948–55.
- Van Larebeke, N., C. Genetello, J. Schell, R. Schilperpoort, A. Hermans, M. Van Montagu, and J. Hernalsteens. 1975. Acquisition of tumor-inducing ability by non-oncogenic *agrobacteria* as a result of plasmid transfer. *Nature* 26:742–43.
- Van Montagu, M. 2003. Jeff Schell (1935-2003): Steering *Agrobacterium*-mediated plant gene engineering. *Trends in Plant Science* 8:353–54.

- Weaver J.C. 1995. Electroporation theory: Concepts and mechanisms. In *Electroporation protocols for microorganisms*, ed: J.A. Nickoloff, 1–26. Totowa, NJ: Humana Press.
- Wright, B.D. 1998. Public germplasm development at a crossroads: Biotechnology and intellectual property. *California Agriculture* 52 (6) (November/December): 8–13.
- Wright, Brian D., Philip G. Pardey, Carol Nottenburg, and Bonwoo Koo. 2007. Agricultural innovation: Investments and incentives. In *Handbook of agricultural economics*, vol. 3, ed. Robert Evenson and Prabhu Pingali. North Holland, Elsevier.

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