Chapter 4

Plant biotechnology – connecting urban innovation and rural application

Humans began making genetic improvements to plants thousands of years before anyone even knew what a gene was. Starting circa 10,000 BCE, they initially began by selecting and domesticating crops from the natural biological diversity of plants. These crops differed from their wild predecessors through the propagation of carefully chosen specific plant materials, which were cultivated for human consumption and use.[1]

The techniques used to select and propagate crop varieties with desirable traits – known as cultivars – can generally be divided into three categories: the traditional, which began with domestication, the conventional and the modern. All three methods are in use today to varying degrees.

15,000,000 km²

Conventional breeding of new crop varieties and traits involves the sexual reproduction of two compatible crop varieties to produce a mutated offspring with the desired biological traits.[2] This method often requires many crosses to get to the right combination of genes to produce the desired crop. It also needs the crops to be sexually compatible.

Today, new crop varieties can be achieved by biotechnology. This modern technique relies on an understanding of a plant's genetic make-up and uses different methods of genetic engineering to make changes to its deoxyribonucleic acid (DNA), molecules of nucleotides which carry the genetic instructions for the development, functioning, growth and reproduction of all known organisms.

Biotechnology refers to "any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use."[3] It can also involve the implementation of advanced molecular and cellular technologies and techniques. In both the broader and narrower sense of its application, agricultural biotechnology relies on the discoveries and research tools of a relatively new science field.

It is changing the agriculture industry.[4] Advances have produced crops that are resistant to certain diseases, that result in higher yields than before, that can grow in extreme soil conditions, such as in arid and salty environments, and that are even infused with nutrients.[5]

Biotechnology innovation has the potential to increase agricultural productivity and quality, ultimately raising incomes for farmers across the world. It can also address environmental concerns about the use of chemical pesticides. Klümper and Qaim (2014) show that genetically modified technology had increased farmer profits worldwide by 68 percent, crop yields by 22 percent and reduced use of chemical pesticides by 37 percent. Brookes (2018) estimates that each extra U.S. dollar spent on transgenic soy seed – seed containing genes from another organism – relative to conventional seed raises a farmer's income by USD 3.88. The gains reflect higher yields and lower costs from using fewer pest and weed controls. Moreover, the technology is seen as a potential solution to global issues of hunger and poverty.

This chapter uses the case of agricultural biotechnology, specifically plant biotechnology, to illustrate the workings of a global innovation network.[6] It relies on information contained in patent documents and scientific publications to identify the actors and locations of innovation. It further exploits these two complementary measures of innovative activities to demonstrate how different innovation clusters link to one another.

The first section of this chapter describes the evolution of the plant biotechnology industry and identifies the factors that drive innovation. The second looks at how the industry's innovation landscape has evolved and how more countries are involved in innovation than ever before. The penultimate section examines the links between innovation centers in different parts of the world. The chapter concludes with how the plant biotechnology's global innovation landscape as well as the network may change due to new developments in the industry.

4.1 The rising importance of plant biotechnology

Plant biotechnology generally involves three areas of the farming industry: (i) plant breeding and seeds, (ii) soil health and fertility and (iii) pest control and pesticides.

The application of biotechnology in plant breeding and seeds refers to the development of new varieties and traits through hybridization, outcrossing (interbreeding), mutation, tissue culture, grafting and cloning of plants, genetic engineering and editing of the genome, which is the whole of the hereditary information encoded in a plant's DNA, to name a few. Most innovation is in this area.

For soil health and fertility, biotechnology involves using biofertilizers – the culturing and use of microbes for soil amendment and plant growth. Lastly, biotechnology for pest control and pesticides deals with biocontrol strategies, biopesticides, breeding and genetic engineering of pest resistance traits in crops, as well as mutation and genetic engineering for herbicide tolerance.

How biotechnology found its way into agriculture

The origin of agricultural biotechnology can be traced back to 1866 when an Augustinian friar, Gregor Mendel, postulated the fundamental laws of genetic inheritance, based on his work on pea plants. He laid the groundwork for scientific breeding and genetic engineering.

Subsequent breakthroughs and discoveries in the 1920s and 1930s on methods of chromosome and gene mutation, followed by the discovery of the double helix structure of DNA in 1953, at Cambridge and London in the United Kingdom (U.K.), led to an explosion in research in genetics – the study of genes, genetic variation and heredity in organisms.

However, it was the development of recombinant DNA (rDNA) technologies – the splicing together of strands of DNA from one organism to another – in bacteria in 1974 by researchers at Stanford University and the University of California, San Francisco, in the United States of America (U.S.), that cleared the way for genetic engineering to take place in plants and other organisms.

Table 4.1 lists a few breakthrough discoveries as well as innovations that form the basis of biotechnology methods and their application in plant biotechnology today.

The commercial application of biotechnology tools and techniques first found its way into the field of medicine in the mid-1970s; agricultural use began a few years later.[7] This was primarily because molecular biology was mainly developed in medical schools and universities, which were not much concerned with agriculture.[8]

However, as the use of biotechnology in medicine and for human health became more prominent, scientists began to apply biotechnology to veterinary science for animal health and then to plant breeding. Animals came first, because of their relative genetic proximity to humans.[9]

By the mid-1980s, the crop biotechnology industry had begun to grow. Several landmark legal decisions in the U.S. regarding whether living organisms may be patented led to the granting of patents on genetically engineered plants.[10] Toward the end of the decade, field trials of transgenic plants were underway in Australia, Canada, the U.S. and some European countries. Mexico, a developing economy, also began conducting field trials of transgenic crops around the same

A brief history of key scientific biotech advances

Table 4.1 Selected discoveries or scientific breakthroughs in crop biotechnology

Year	Discovery/scientific breakthrough	Affiliation
1974	Stanley Cohen and Herbert Boyer developed a technique – rDNA – that would splice together strands of DNA from more than one organism, paving the way for genetic engineering	Stanford University and University of California, San Francisco, California, U.S.
1977	DNA sequencing methods were independently devised by Walter Gilbert with graduate student Allan Maxam, and Frederick Sanger	Harvard University, Cambridge, Massachusetts, U.S., and Cambridge University, U.K.
1981	George Willems and Robert Schilperoort genetically engineered first plant (tobacco) using the bacterium Agrobacterium (see Box 4.1)	University of Leiden, Leiden, Netherlands
2000	Complete sequencing of Arabidopsis thaliana (a small plant) genome, published in 2000 as part of the Arabidopsis Genome Initiative	Consortium of universities as well as public research institutions in the U.S., Japan and Europe
2012	A new genome editing technique, CRISPR-Cas9, is developed	University of California, Berkeley, California, the U.S; and University of Vienna, Austria; Massachusetts Institute of Technology and Harvard, Cambridge, Massachusetts, the U.S.; Vilnius University, Lithuania

Source: Graff and Hamdan-Livramento (2019).

time.[11] Meanwhile, China became the first country to commercially farm a pest-resistant, transgenic tobacco plant in 1988. However, Chinese farmers stopped farming the plants in the mid-1990s as many tobacco-producing companies expressed concerns about using these genetically improved organisms (GIOs) in their products. In particular, consumers were apprehensive about consuming GIO cigarettes. These landmark events coincided with a rise in the number of specialized agricultural biotechnology startups, particularly in the U.S., during the 1980s and 1990s.

Figure 4.1 plots the rising global demand for patents for plant biotechnology inventions from 1970 to 2016. The red line shows the total number of patent applications in the field filed at different intellectual property (IP) offices worldwide.[12] By contrast, the dark red line represents the number of initial filings for new plant biotechnology patents, also known as *first filings*. The difference between the total number of patent filings and the first filings is referred to as the *subsequent filings*. The subsequent filings represent the number of applications filed in multiple countries, or jurisdictions, for the same inventions. The widening gap between the two lines from the 1980s onward shows how inventors increasingly requested patent protection for their inventions from competitors in more than one market. More importantly, it illustrates the growing commercial importance of plant biotechnology inventions globally.

What shapes innovation in the field?

Policies, rules and regulations shape and affect innovation in the plant biotechnology industry. They include the availability of IP rights as a mechanism for ensuring a return on investment in innovation, and regulations on health and safety and on protecting the environment, among others.

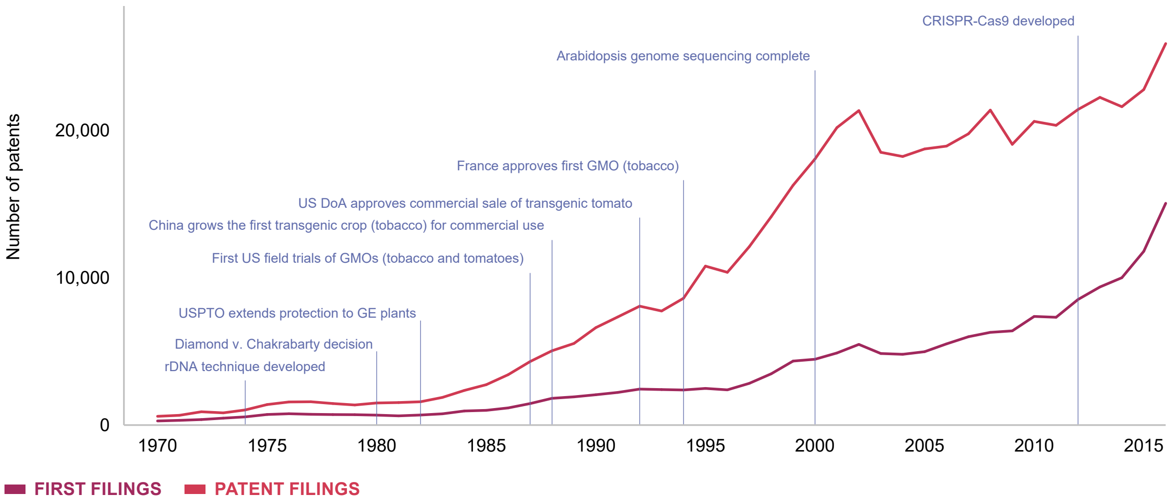
Appropriate returns on investments

Most jurisdictions do not allow for the patentability of things that exist in nature, including biological organisms. However, the lines have become blurred with new technological advances in biotechnology.[13]

Concerns with patentability on agricultural biotechnology innovation are similar to those expressed about patenting in the biotechnology field generally.[14] Granting exclusive rights on research tools may dampen follow-on innovation.[15] In crop biotechnology, patents could make it difficult for poorer economies to benefit from research that could alleviate poverty and address world hunger problems. In addition, critics have argued that most of the patents granted are too broad and are likely to infringe on other proprietary technology, resulting in the relatively high amount of litigation seen in the industry.

The rise of genetic engineering coincided with an increase in subsequent patent filings

Figure 4.1 Total patent filings of plant biotechnology, 1970–2016



Source: WIPO based on PATSTAT and PCT data (see Technical Notes).

In the U.S., two changes related to IP policy in the 1980s played pivotal roles in shaping the agricultural biotechnology industry there. In particular, they led to the increasing reliance on IP as a way to ensure appropriate returns on investing in innovation.[16]

The first was the passing of the Bayh–Dole Act in 1980. The Bayh–Dole Act allows for the patenting of research from universities, even if it is funded by taxpayers. The second was the extension of patent protection to genetically modified organisms (GMOs) through a landmark case – *Diamond v. Chakrabarty* – decided by the U.S. Supreme Court of Justice, also in 1980.[17] By 1985, the U.S. Patent and Trademark Office (USPTO) had extended patent protection to genetically engineered plants. Europe and the rest of the world soon followed suit.

At the same time, the launch of the World Trade Organization (WTO) in 1995 included internationally binding rules for the protection of IP rights in signatory countries. This opened the way for many multinational companies (MNCs) to file for patent protection on their plant biotechnology inventions. But some developing economies, like Brazil, restrict the patenting of certain plant biotechnology products, particularly those that relate to seeds or new plant varieties. Instead, the private sector in Brazil relies on *sui generis* rights to protect their innovations.[18] Some file for patents on the development process itself, rather than the biotechnological result, or on complementary assets – infrastructure, capabilities or other inventions – that lead to the final crop biotechnology product.[19]

Protecting consumers and safeguarding the environment

The increasing potential commercial importance of plant biotechnology led government regulators and the public to question when and how to ensure that these purposely transformed, or transgenic, crops would not harm human health or the environment.

There are several layers of regulations on the use of plant biotechnology, at both the national and international levels.[20] They help ensure that GIOs meet biosafety, food safety and consumer protection standards. For example, at the international level, the United Nations' Codex Alimentarius sets the guidelines for food safety standards, the Cartagena Protocol on Biosafety, an international agreement, provides guidelines for biosafety regulations, and another international pact, the Aarhaus Convention, gives the general public a right to access information about policy decisions affecting the environment.[21]

At the national level, there are generally at least three regulatory processes before a new transgenic plant can be commercially farmed. They include:

Box 4.1 Key differences between breeding techniques

There are two ways to introduce desired traits into plants and they differ according to plant type. Dicots, or broad-leaved crops, such as cotton, soybean and tomato, rely on the transformation brought about by a bacterium known as *Agrobacterium tumefaciens*. In nature, this bacterium infects plants, inserting some of its own DNA directly into the DNA of the plant. By modifying the bacterium to exclude its unwanted traits and include the gene of interest, a crop may be transformed through bacterial infection. The cells containing the new gene subsequently can be identified and grown using plant cell-culture technology into a whole plant that now contains the new transgene incorporated into its DNA.

Monocots, or grass species, such as maize, wheat and rice, are transformed by physically shooting small tungsten balls coated with an external DNA into the plant's genome. Some of the DNA comes off and is incorporated into the DNA of the recipient plant. Those cells can also be identified and grown into a whole plant that contains the foreign DNA.

The differences between traditional and conventional breeding and their modern counterpart boil down to the control over the breeding process. The outcomes of plants bred through the traditional and conventional methods are often unpredictable. Breeders choose the parents with the desired traits to cross but the progeny may not carry the genotype with the desired traits or display it, the phenotype.

Modern breeding techniques, such as genetic engineering, allow for targeted transfer of desirable crop traits – the transgene – and the breeding of new transgenic plants in an efficient and fast manner. These transgenic crops are also known as GMOs. The modern techniques simplify the breeding process by bypassing the need for the sexual compatibility of the plants with the desired traits and allow for the selection of desirable traits from any living organism. The desired traits can come from the same species or a cross-species; they can even come from a modification of the expression of the plant's own genes. Targeting of the desired gene, tracking it and inserting it into a crop's DNA ensures a clean breed of the crop and excludes the potential for unwanted, ancillary traits, which are often a by-product of traditional and conventional breeding. Moreover, there is a faster turnaround in the development of new crop varieties in modern breeding techniques than its predecessors.

Source: FAO (2004). and Persley and Siedow (1999).

(i) approvals to conduct field tests, (ii) approvals to farm for commercial purposes and (iii) approval to sell and market to consumers. In the U.S., the agencies include the U.S. Department of Agriculture (USDA) and the U.S. Environmental Protection Agency (EPA) for field trial approval and the U.S. Food and Drug Administration (FDA) for commercial approval.

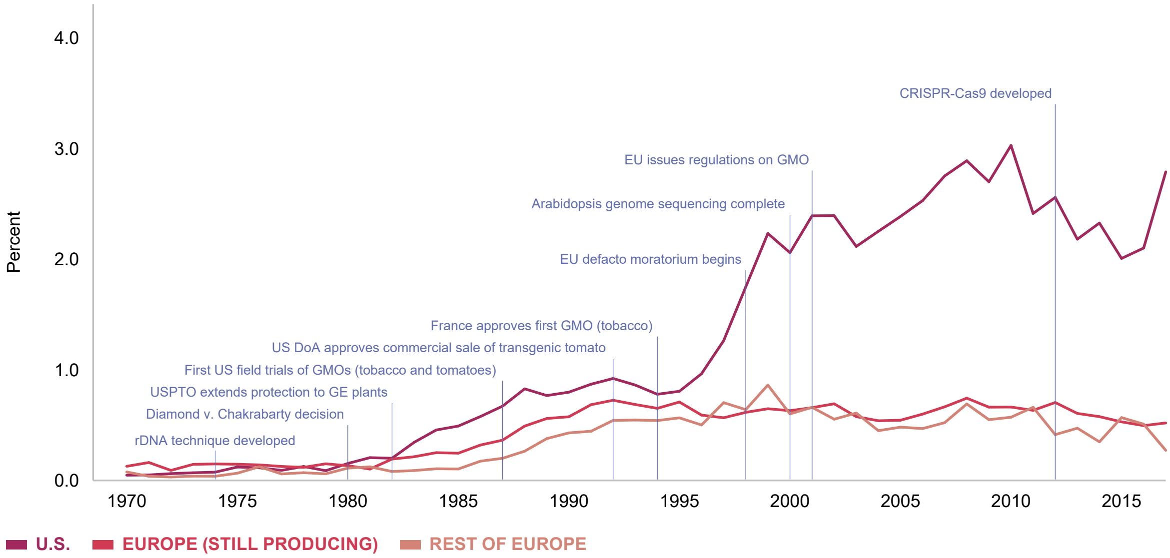
Europe was responsible for some important breakthroughs in plant biotechnology. In the early 1990s, Belgium, France and the U.K. were among the top five countries in the industry, which together accounted for nearly 95 percent of transgenic crops released – the other two were Canada and the U.S. However, by the turn of the century, European sentiment toward transgenic crops had changed significantly.[22]

Between 1998 and 2004, the European Commission (Commission), the European Union's executive arm, and five EU member states imposed a de facto moratorium on the approval of GMOs.[23] From 2003, the Commission then put in place several regulations and directives on GMOs.[24] During the moratorium, the Commission differentiated between plants whose genes had been edited with conventional breeding methods and those that had been genetically edited using biotechnology tools (see Box 4.1). The measures established specific requirements for conducting field tests and planting of transgenic crops, their import and use and the labeling of GMO products.

Several commercial explanations have been put forward for this change in the continent's attitude toward transgenic crops, besides the strong political campaigns against GMOs mounted by environmental and consumer groups. Graff and Zilberman (2007) argue that Europe's strong agrochemical businesses enjoyed a comparative advantage in chemistry and wanted to prevent their competitors from entering the market. Sheldon (2004) proposed that EU farmers saw the measures limiting the approval of genetically engineered plants as an opportunity to prevent agricultural commodities from the rest of the world from entering the market.

Crop biotechnology patent filings from the U.S. have grown faster than from Europe

Figure 4.2 Share of plant biotechnology filing over total patent filings by origin (%), 1970–2016



Source: WIPO based on PATSTAT and PCT data (see Technical Notes).

Regardless, the EU regulations have arguably had a cooling effect on research and development of agricultural biotechnology on the continent.

Figure 4.2 shows the share of patent filings by the U.S. (in dark red) and several European countries (in red and light red) of the total plant biotechnology filings worldwide.[25] Until the late 1990s, the share of plant biotechnology patents filed in the U.S. and the EU rose more or less in parallel. However, from 1997 onward there is a widening gap between patent filing growth rates in the U.S. and the EU. It is difficult to say conclusively if this is due to Europe's de facto moratorium. But since 1998, EU countries have been filing crop biotechnology patents at a relatively similar – if not slower – rate than the total patent filing rate.

Industry has reported that the EU stance on transgenic crops has affected companies' business strategies. A study conducted by the USDA Foreign Agricultural Service showed that many European companies have shifted their research and development (R&D) outside of Europe, relocating to places such as the U.S. While public institutions and universities in Europe continue to conduct basic research into plant genetics, the likelihood of these outputs reaching the EU market is small. In addition, the report noted that many European biotechnology firms have shifted their focus away from agricultural uses toward medicinal and biofuel industrial applications.[26] One of the major European MNCs in the industry, BASF, a German chemical firm, halted the development and marketing of its transgenic crops for the EU in 2012.[27]

Who drives innovation?

Innovation in the plant biotechnology industry is driven by investments by both the public and private sectors.

Strong public sector push in agricultural research

The public sector plays a pivotal role in plant biotechnology research by funding and providing important infrastructure necessary for research. In Europe as well as the U.S., key policy documents and published reports underscore the importance of investing in genetic engineering research.[28]

Scientists and researchers in public research institutions have made important discoveries that paved the way to genetic engineering. The importance of basic science to innovation in the plant biotechnology field continues today. For example, fundamental advances in molecular biology and genetics have created more efficient ways to identify and target specific genotypes in organisms. Moreover, the development of CRISPR-Cas9, a gene editing technology, has significantly cut costs in the field of genetic engineering.[29]

Agricultural research centers and universities specializing in agricultural science play a pivotal role in adapting research and diffusing crop biotechnology innovations. These research centers are mandated to conduct and develop work that would improve agronomics and advance genetic improvements in crops and agricultural innovation in general. Moreover, support for their research work includes funding from governments, foundations and various intergovernmental and not-for-profit organizations and agencies. The strong mandate and financial support help ensure the continuity and importance of these institutions' work.

In the U.S., the 1862 Morrill Act established Land-Grant colleges by allocating 30,000 acres (nearly 121.5 km^2) of federal land across the country to build colleges and universities that would teach and promote the development of agriculture, among other things. The second Morrill Act, passed in 1890, ensured that these colleges had regular federal funding.

The success of Land-Grant colleges laid the foundation for establishing similar research centers in emerging economies.[30] The International Maize and Wheat Improvement Center (CIMMYT) in Mexico City, Mexico, and the International Rice Research Institute (IRRI) in Los Baños, the Philippines, were the first two such establishments. These two national agriculture research systems (NARS) would later become part of the Consultative Group for International Agricultural Research (CGIAR), an umbrella organization of 15 independent, non-profit research centers focused on innovation in agriculture. The CGIAR has shaped the historical evolution of innovation in agricultural biotechnology, particularly in crop genetic development.

Agriculture requires innovation to be adapted to different regional agro-ecological conditions, which include the combinations of soil, landform and climatic characteristics.[31] This means that transgenic crops should be bred with local cultivars and tested in local fields. In many developing countries these cultivars and germplasms – living genetic resources held for animal or plant breeding or preservation – are kept by public institutions, such as the NARS or international agriculture research centers (IARCs).[32]

Collaboration between public institutions is important, especially when trying to commercialize GIOs in less developed economies. Most of the transgenic crops planted in these economies during the late 1990s were locally adapted germplasms of their North American counterparts.[33] In poorer countries, IARCs can act as nodes in global networks of innovation by connecting agricultural scientists and breeders across many NARS, including agricultural research universities in the world.

Plant biotechnology innovation has the potential to address food scarcity and food security issues.[34] Thus, advances find strong support from the public sector, including intergovernmental organizations and not-for-profit institutions and agencies, to promote their diffusion to the rest of the world.[35]

Governments fund most of the agricultural research in many emerging economies. In a few cases, such as China, India and Brazil, public sector R&D spending in agriculture has increased rapidly. From 1990 to 2013, China's public sector agricultural R&D spending grew nearly tenfold, from USD 1 billion to more than USD 9 billion.[36] At the same time, India's spending tripled, from less than USD 1 billion to almost USD 3 billion and Brazil's almost doubled, from less than USD 2 billion to almost USD 3 billion. By contrast, public sector spending in agriculture in the U.S. grew only moderately from about USD 4 billion in 1990 and declined from 2003 onward.

But many emerging economies, especially those with limited capacities to innovate in plant biotechnology and/or those that lack the financial resources to conduct research in the field tend to rely on the work of NARS and/or IARCs.[37]

Incentives backed by market consolidation

Small, university-based startups initially dominated the plant biotechnology market in the early years. However, from the 1990s onward, MNCs bought many of them out. One study estimated that nearly 90 percent of all research and development agreements on agricultural biotechnology were between startups and large MNCs.[38]

At the same time, firms in the seed, chemical and fertilizer industries, both in richer and poorer countries, have experienced significant market concentration.[39] There are many reasons. The high fixed costs of commercializing transgenic plants require large financial resources, which many startup companies may not have. Second, the high fixed costs also necessitate increasing reliance on IP rights to ensure a return on investment. Accumulated proprietary technologies in plant biotechnology can be a barrier to innovation, as they are in the semiconductor industry. Firms that collaborate are less likely to infringe on one another's IP. For example, Monsanto, BASF, Dow, Bayer, DuPont and Syngenta cross-licensed one another's IP rights on transgenic crops.[40]

By 2001, 30 separate firms in the seeds and agrochemical industries had been reduced to six – Monsanto, DuPont, Swiss-based Syngenta, Bayer, Dow and BASF. The four biggest account for almost 60 percent of the agricultural biotechnology market. The major agrochemical-seed groups are: Bayer CropScience and BASF in Germany, Corteva Agriscience in the U.S. and ChemChina, which purchased Syngenta in 2017, in China.

This consolidation of crop biotechnology innovation in the hands of a few has not necessarily translated into a reduction of innovative activities in this field.[41]

Table 4.2 lists selected alliances, including mergers and acquisitions, of the multinational seed and agrochemical companies. It shows how the industry has become more concentrated since the 1990s.

Need for public–private collaboration

Zilberman *et al.* (1997) conducted a survey of plant biotechnology firms in the U.S. and found many cases of collaboration between the public and private sectors. In particular, they reported that in most patterns of plant biotechnology innovation the universities made the important discovery and the private sector then developed and commercialized the innovation. This pattern of collaboration between the private and public sectors continues.

Large chemical and seed MNCs commercialized and cultivated all of the major transgenic crops bred through genetic modifications in the early years.[42] The only exception was *Bacillus thuringiensis* (*Bt*) cotton, which was developed by a Chinese public research institution, the Biotechnology Research Center of the China Academy of Agricultural Sciences (CAAS) in Shenzhen. However, CAAS entered into a joint venture with U.S.

Industry has seen significant concentration

Table 4.2 Selected alliances in the industry, 1996–2016

Bayer [Germany] purchases Monsanto [U.S.] (2016)

Monstanto [U.S.] (merged with Pharmacia March, 2000; spun off entirely August, 2002)	Bayer (Bought Aventis Crop Sciences, 2001) [Germany]
Biotechnology • Agracetus [U.S.] (1995) • Calgene [U.S.] (1996) • Ecogen [U.S.] (2003) • Joint venture with Millennium Pharmaceuticals [U.S.] (1998) • Paradigm Genetics [U.S.] (2000), name changed to Icoria (2004) **Seeds** • DeKalb [U.S.] (1996) • Asgrow [U.S.] (1997) • Holden's Foundation Seeds [U.S.] (1997) • Cargill International Seeds, Plant Breeding International [U.S.] (1998) • Delta and Pineland [U.S.] (alliance, 1994; bought 2007) • Sensako [South Africa] (2002); Carnia [South Africa] (2002); later merged under DaKalb brand • Seminis [U.S.] (2005) • Emergent Genetics [U.S.] (2005) • Acquired De Ruiter [Netherlands] (2008); and Peotec Seeds S.r.l. [Italy] (2008) via Seminis	**Agricultural chemicals** • Hoechst [chemical, Germany] merged with Schering [pharmaceutical, Germany] to create Hoechst Schering AgrEvo (1994) [Dusseldorf, Germany] • Hoechst (Agrevo) and Rhône-Poulenc [pharmaceutical, France] merged (and their agrochemicals division became) to Aventis CropScience (1999); • Bayer buys Aventis CropSciences in August 2002 **Biotechnology** • Plant Genetics Systems (PGS) (acquired by AgrEvo in 1996; became part of Monsanto in 2002) [Belgium] • PlanTech [Japan] (1999) • Lion Biosciences (11.3%, 1999) • Limagrain (purchased the Canadian seeds activity; 2001) [France] **Seeds** • Nunhems [Netherlands], Vanderhave [Netherlands], Plant Genetic Systems [Belgium], Pioneer Vegetable Genetics, Sunseeds (1997) [U.S.] • Nunza (vegetables), Proagro (India) and two Brazilian seed companies (1999) • Fibermax (joint venture with Cotton Seed Inc. of Australia, 2000)

Notes:
a The corporate entities as they currently exist.
b The corporate entities as they had existed up to their latest merger, acquisition or takeover.
Source: Updated, based on Pray and Nassem (2003).

ChemChina [China] purchases Syngenta [Switzerland] (2017)

Syngenta [Switzerland]

Agricultural chemicals
- Ciba-Geigy and Sandoz merged to form Novartis [Switzerland] (1996)
- Novartis [Switzerland] buys Merck's pesticide business for USD 910 million (1997)
- Merger of Novartis agriculture division [Switzerland] and AstraZeneca's Ag. Chemicals [U.K.] to form Syngenta [Switzerland] (1999)

Biotechnology
- Zeneca Ag. [U.K.] bought Moden International N.V. [Netherlands] (1997)
- Alliance with Japan Tobacco [Japan] on rice (1999)
- Alliance with Diversa [U.S.] (2003)
- Zeneca [pharmaceutical, U.K.] buys PSA Genetics (via Garst subsidiary, 1999)

Seeds
- Merger between Northrup-King and Ciba Seeds brings together S&G Seeds, Hilleshog and Rogers Seed Co. under one umbrella (1997)
- ICI (Imperial Chemical Industries, pharmaceuticals and agrochemcials) [U.K.] splits into Zeneca (inclduing ICI seeds) and ICI PLC (1993)
- Garst [U.S.] reborn as a Zeneca company (1996)
- Zeneca [U.K.] via Garst [U.S.] buys Agripro Seeds [U.S.] (1998), Gutwein Seeds (2000)

Corteva Agriscience [U.S.] spinoff created in (2019), result of DuPont and Dow merger (2015)

Dow Chemicals [U.S.]; Dow AgroSciences [US]

Agricultural chemicals
- Dow purchases Eli Lilly's [U.S.] 40% share of Dow Elanco for USD 900 million (1997)
- Rohm and Hass Ag. Chem [U.S.] (2001)

Biotechnology
- Mycogen (1996) [U.S.]
- Ribozyme Pharmaceuticals Inc. [U.S.] (1999)
- Contract with Proteome Systems Limited [Australia] (1999)

Seeds
- Mycogen buys Agrigenetics [U.S.] (1992)
- United AgriSeeds [U.S.] becomes part of Mycogen (1996)
- Joint venture of Mycogen [U.S.] with Boswell [U.S.] on cotton seed to form Phytogen (1998)
- Joint venture with Danisco Seeds [Denmark] (1999)
- Agreement with Illinois Foundation Seed [U.S.] (1999)
- Cargill Hybrid Seeds [U.S.] (2000)

DuPont [U.S.]

Agricultural chemicals
- Hoechst [chemical, Germany] merged with Schering [pharmaceutical, Germany] to create Hoechst Schering AgrEvo (1994) [Dusseldorf, Germany]
- Hoechst (Agrevo) and Rhône-Poulenc [pharmaceutical, France] merged (and their agrochemicals division became) to Aventis CropScience (1999);
- Bayer buys Aventis CropSciences in August 2002

Biotechnology
- Alliances with Human Genome Sciences [U.S.] (1996)
- Alliance with Curagen [U.S.] (1997)
- Purchased Verdia from Maxygen [U.S.] for USD 65 million (2004)

Seeds
- Pioneer [U.S.] (1997, 20%)
- Hybrinova [France] (1999)

BASF [Germany]

Agricultural chemicals
- Bought corn herbicide business from Sandoz [Switzerland] (1996)
- American Cyanamid [U.S.], crop protection subsidiary from American Home Products for USD 3.8 billion (2000)

Biotechnology
- Joint venture with Institute of Plant Genetics and Crop Plant Research [Germany] to create SunGene [Germany] (1998)
- Joint venture with Max Planck Institute [Germany] and Metanomics [Germany] (1997)

Seeds
- Bought 40% of Savlöf Weibell [Sweden] (1999)

firms, Monsanto and Delta and Pineland, and China's Heibei Provincial Seed to bring *Bt* cotton to market. The transgenic crop was made available to Chinese farmers in 1997.[43]

The need for access to complementary assets in innovating in agricultural biotechnology necessitates collaboration between innovators. Commercialization of research work from universities, or public research institutions, both in developed and developing economies, may require further assistance from the private sector. This was the case for the Chinese *Bt* cotton and continues to be the case for many joint research projects between university research labs and private companies.

In many developing economies, there are a few instances of collaboration between the NARS and large MNCs to develop transgenic crops adapted to the region.[44] These public institutions may need access to proprietary biotechnological research tools to conduct their research work, and thus would need the collaboration of the IP owners. One such example is through licensing in proprietary technologies held by private companies.[45] Another is through purchasing the technology at an agreed cost. The firm may be paid by funds raised by donor countries. Collaboration between the IARC and the private firm may be made available royalty-free to developing economies or on reasonable royalty terms.[46] For example, the International Potato Center (IPC) in Peru made arrangements with Plant Genetics Systems, a Belgian firm later acquired by Bayer CropScience, to use *Bt* genes to test its line of genetically engineered potatoes.[47]

Private firms may collaborate with NARS or IARCs on research in return for exclusive commercial rights on any resulting technology in developed markets. Developing economies would be entitled to the resulting technology at a preferential rate. There could also be a hybrid approach to IP, with the private company applying for patents in developed markets only.

Collaborations have also been initiated by the private sector. For example, large life sciences firms may need access to different pools of germplasms administered by various IARCs and NARS for further innovation. CGIAR has a collection of germplasm which it has committed to keep in the public domain. Access to this pool of germplasm could help in cultivating various different versions of transgenic crops for use in many parts of the world.

The increasing need for collaboration between the private and public sectors implies some changes to the use of IP. Research institutions in many emerging economies used to shy away from relying on the IP system and focused instead on ensuring that knowledge could be easily shared. This view has changed. Collaboration between the two sectors – either to help with commercialization (for the research institutions) or as sources of germplasms and cultivars (for the private sector) – necessitates a hybrid approach to IP use.

Evidence collected from patent documents shows that the number of collaborations between the private and public sectors is on the rise. On average, only 18 percent of plant biotechnology patents are inventions with co-applications.[48] However, this underestimates collaboration activities. Not all collaborations lead to patented inventions and the number does not accurately capture collaborations between subsidiaries of large MNCs in different locations, because, typically, only the headquarters appears as the applicant on many MNC patent applications. Moreover, some of the public–private collaborations take place during the commercialization stage, such as during field trials, and these are not generally captured by either patent or scientific publication data.

Figure 4.3 plots the number of co-applications involving the private and public sectors. The trend shows an increase in the share of patents filed with at least one public-sector applicant since 1999.

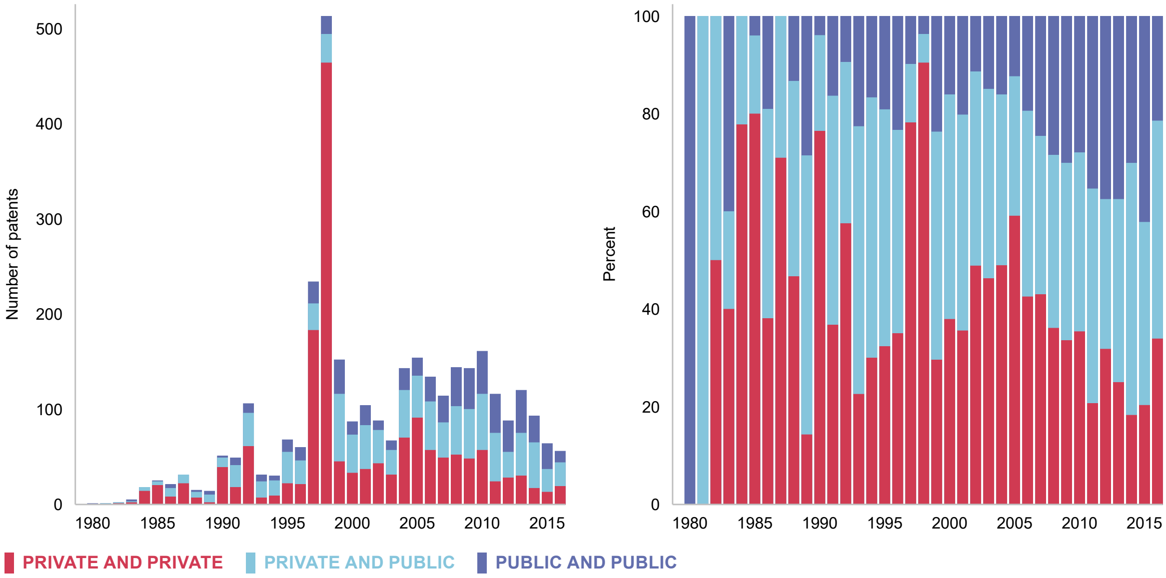
4.2 The innovation landscape of plant biotechnology

The global innovation landscape of plant biotechnology is spread relatively widely across the globe. Figure 4.4 plots the innovation landscape using two proxies for innovative activities – patents and scientific publication in the form of articles and conference proceedings (see Chapters 1 and 2) – for two time periods, 1998–2007 (top) and 2008–2017 (bottom).

It shows the evolution of innovative regions in the industry and illustrates how patenting and publication tend to mirror one another, at least for the top plant biotechnology clusters. The four top countries for innovation activities in plant biotechnology are China, Germany, Japan and the U.S., with Switzerland joining them in the top five for patenting and France for scientific publication.

Innovation by the private sector is the main driver of agricultural biotechnology innovation, but public–private and public–public collaborations are on the rise

Figure 4.3 Trend in patent co-application type by number (left) and share (right), 1980–2016



Source: WIPO based on PATSTAT and PCT data (see Technical Notes).

In addition, Figure 4.4 also shows how some regions lean more toward patenting, while others toward scientific publication. The U.S., Europe, Japan and China show more patenting, while developing countries generally have more regions featuring scientific publication work.[49]

The difference in innovative output as captured by Figure 4.4 for patents and scientific publication can be quite significant for plant biotechnology. There are two reasons for this.

First, patenting of plant biotechnology inventions is subject to different criteria across jurisdictions. Hence, using patenting as the sole indicator of crop biotechnology innovation may miss important research work carried out by scientists in countries where patenting possibilities are limited.

Second, while both patented inventions and scientific publication are used to measure innovative activities, there are important differences. For example, inventions disclosed under patenting requirements may be closer to the commercialization stage than research published in scientific publications, which may be more "upstream" and science related.[50] Moreover, most innovative activities in the U.S. are carried out by the private sector, which tends to rely on patents, while in China, universities and public institutions are the main sources of such activities.

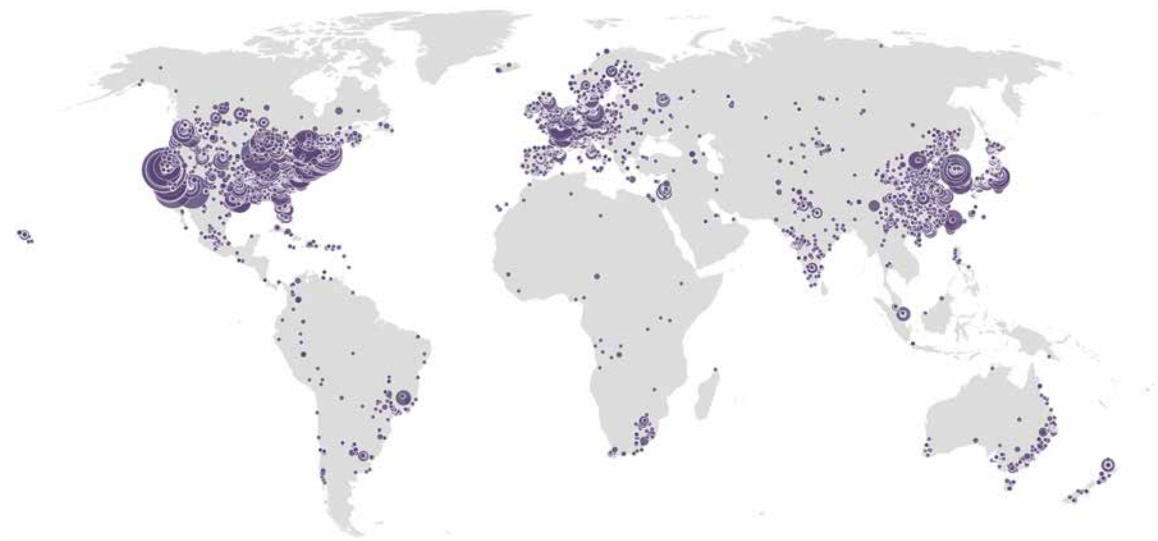
Figure 4.5 maps the international and national clusters of crop biotechnology across the world. These clusters are determined by the relative significant co-location of inventors and authors of plant biotechnology outputs across countries (international clusters) and within countries (national clusters).

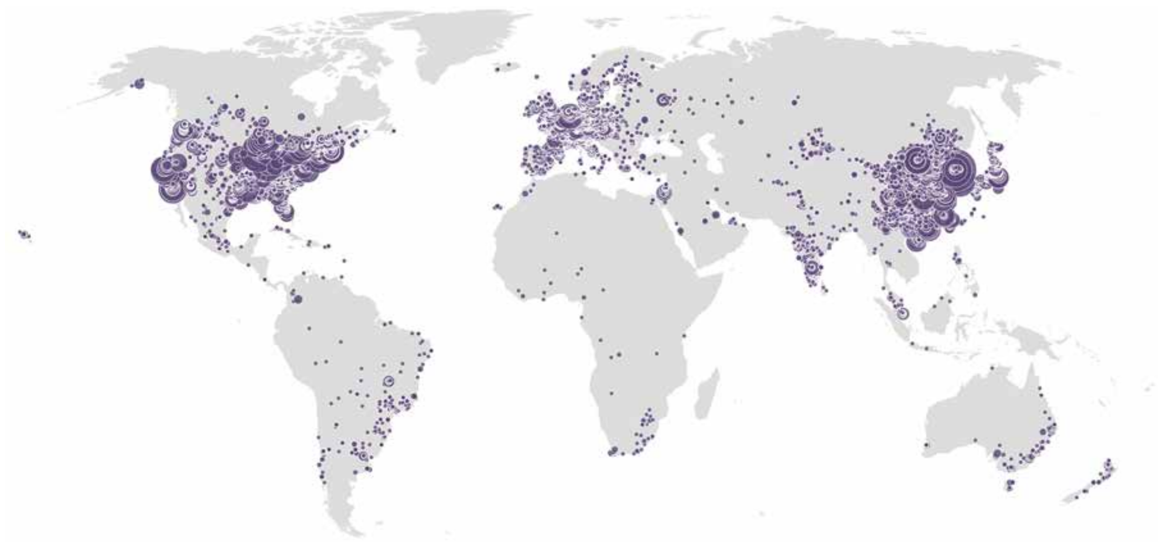
Box 4.2 highlights the method used to identify these clusters. It emphasizes how only international plant biotechnology clusters are comparable across countries, while national clusters are only comparable across regions in one country.

The international clusters of plant biotechnology show how geographically diverse is its innovation landscape. The clusters include the three main corridors of innovation, namely the U.S., Europe and East Asian countries, Japan and the Republic of Korea. They further include India, Israel, China and Singapore in Asia, Australia in Oceania, and Argentina and Mexico in Latin America and the Caribbean. But at the same

The distribution of agricultural biotech innovation has been relatively wide since the 2000s

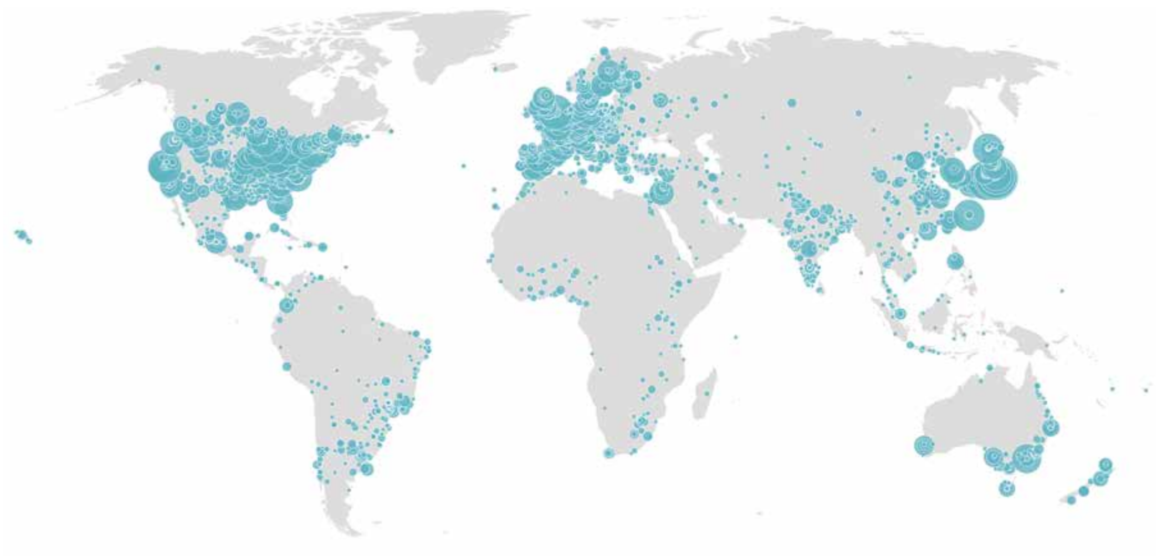
Figure 4.4 Distribution of plant biotechnology innovation centers by patent filings (left) and publication (right), 1998–2007 (top) and 2008–2017 (bottom)

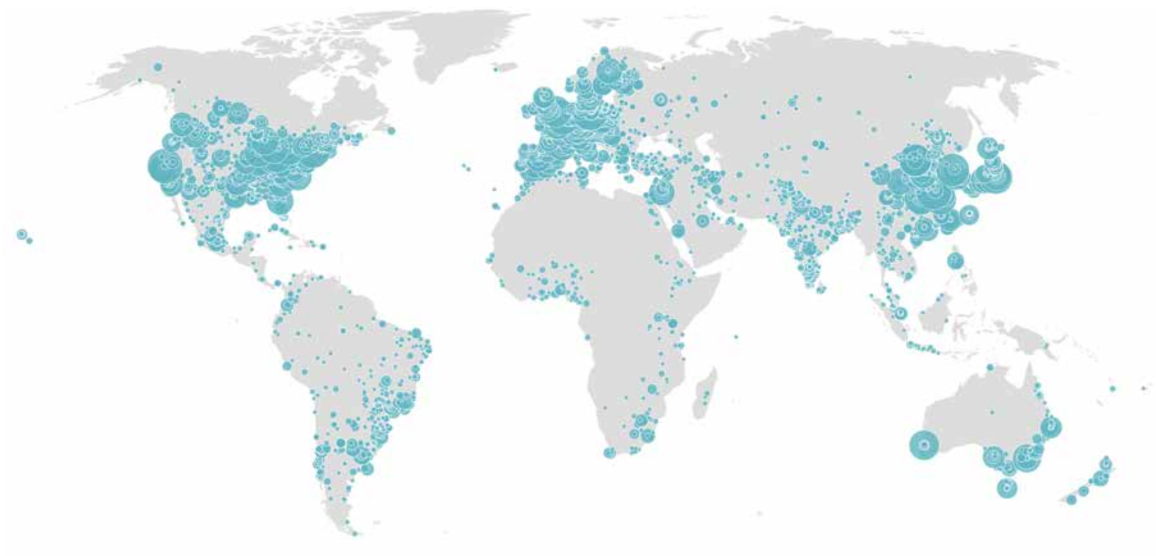




PATENTS SCIENTIFIC PUBLICATIONS

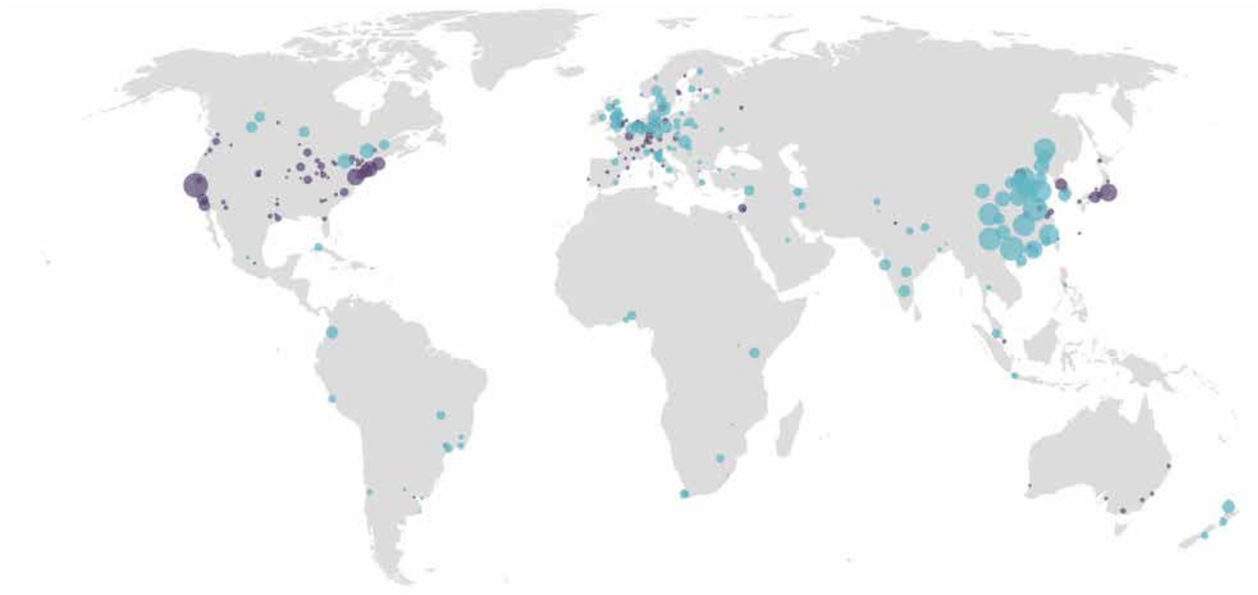
Source: WIPO based on PATSTAT, PCT and Web of Science data (see Technical Notes).
Note: Size of bubbles corresponds to the relative volume of patent and scientific publications, respectively.





Agricultural biotechnology clusters are spread across the globe

Figure 4.5 Global distribution of plant biotechnology innovation clusters, 1970–2017



INTERNATIONAL PLANT BIOTECH CLUSTERS NATIONAL PLANT BIOTECH CLUSTERS

Source: WIPO based on PATSTAT, PCT and Web of Science data (see Technical Notes).

time, these international plant biotechnology clusters mirror their related biotechnology field clusters.

Not all countries with significant innovative activities have international clusters. Brazil, for example, is a leading developing economy with important innovative activities in the field, but with no international cluster. The main reason for this is that its innovative activities in plant biotechnology are spread across seven different regions that individually do not reach volume thresholds for the production of patents and scientific articles (see Box 4.2). The Brazilian Agricultural Research Corporation (EMBRAPA), its NARS, mandates that its research activities should be scattered across its different research campuses and not just concentrated in its main office in Brasilia.

There are two notable insights from the global mapping of plant biotechnology's international and national clusters. First, there is an urban–rural divide between the location of innovation centers and the farming the innovation is aimed at.[51] Most innovation in the plant biotechnology industry is conceptualized, researched and developed in urban areas rather than in farming areas. However, field trials are conducted in rural areas, which may require some innovative activities to adapt the genetically engineered crop to local agro-ecological conditions – to the local combinations of soil, landform and climatic characteristics.[52]

Figure 4.6 maps the international and national crop biotechnology clusters against the crop areas (shaded green) of the world for four regions: North America, Europe, Asia and Latin America. Most of the international clusters tend to be in urban areas. In the U.S., for example, they are in such places as San Jose, Boston and New York City.

However, there are some clusters that are adjacent to crop areas. The location of these clusters is not an accident. Most of these clusters are located in major agriculture-related universities, for example the U.S. Land-Grant colleges already mentioned. One notable example is Des Moines, Iowa, which is both a farming area and an international plant biotechnology cluster. Des Moines is home to Iowa State University, a Land-Grant university, and Pioneer Hi-Bred, one of the first startups specializing in agriculture biotechnology.

Box 4.2 Identifying the international and national clusters of crop biotechnology

Identifying international and national clusters of agricultural biotechnology involves at least three steps.

Step 1: Identify plant biotechnology patents and scientific publication
Patents: use a combination of two international technological classification schemes, the International Patent Classification (IPC) and the Cooperative Patent Classification (CPC) codes, and keywords to arrive at crop-specific agricultural biotechnology (see Technical Notes for the complete list of codes and keywords used in the search strategy). The categories for crop patents include: (i) crops' genetic improvement; (ii) pest control in crops; (iii) soil fertility; and (iv) climate change.

Scientific publication: use a combination of well-known top journals in agricultural biotechnology, combined with relevant plant biotechnology-specific keywords (see Technical Notes for details).

Step 2: Geocoding the addresses of inventors and authors
The addresses of authors of patented inventions and scientific articles related to plant biotechnology are geocoded and mapped. Inventors' resident addresses, as listed in the patented documents, are used, while for scientific publication, the authors' addresses are usually not disclosed. Instead, the location of the authors' affiliation is employed.

Step 3: Differentiating between national and international clusters
Once the location of both patented inventions and scientific publications are mapped out, two different thresholds are used to identify international and national clusters. For international clusters, only foreign-oriented patent families are considered, in combination with published scientific articles. These patents must be either filed in an IP office different from the applicant's residence or in at least one foreign IP office, for example, at a national IP office and a foreign IP office. Patents filed at an international patent office, such as the European Patent Office or through the Patent Cooperation Treaty (PCT), are also considered as foreign-oriented patent families.

For national clusters, all patent families, along with scientific publication, are used. The patent families include singletons, which are patents filed in the same IP office as the applicant's residence and nowhere else.

Classification as an international cluster is based on a global threshold combining foreign-oriented patents and scientific publication. National clusters are based only on a country-specific threshold.

Therefore, international clusters differ from national clusters in two main ways. First, international clusters are calculated by only considering foreign-oriented patent families. National clusters, by contrast, are based on all patents filed by the residents of a country, including both singletons and foreign-oriented patents. Second, the threshold criterion determined at the international level is based on the average volume of patents and scientific articles attributed to one region, across the globe. The threshold at the national level is measured by the average volume of patents and scientific publication attributed to one region in a country.

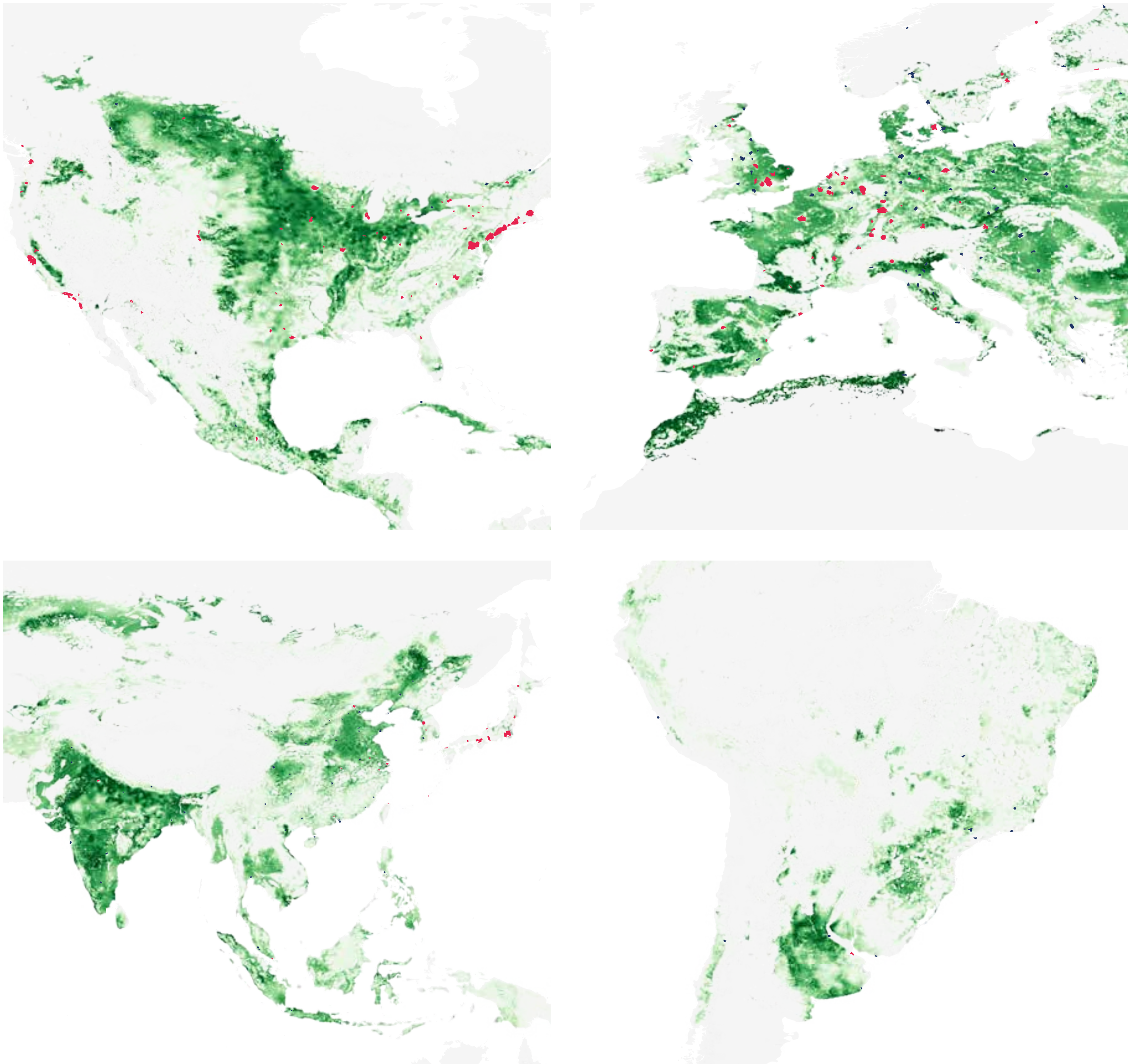
Only the international clusters are comparable across countries.

Note: See Box 2.1 and Box 2.2 of Chapter 2. See also the glossary list in the annex of WIPO (2018).

For many developing economies, the relevant international and national clusters of plant biotechnology are close to their respective NARS, which tend to be located in farming areas. The CIMMYT in Texcoco is approximately one hour away from Mexico City, while Buenos Aires is home to the National Agricultural Technology Institute (INTA) of Argentina. The International Crops Research Institute for the Semi-Arid Tropics, a CGIAR institute, is located in Patancheru, close to Hyderabad, in India, while the IRRI in Los Baños, the Philippines, is around one hour from Dasmarinas City. In Brazil, the national clusters coincide with the locations of EMBRAPA centers. All of these NARS are within a 50-km radius of national crop biotechnology clusters.

Innovation takes place far away from cropland

Figure 4.6 Location of plant biotechnology innovation centers and croplands



INTERNATIONAL PLANT BIOTECH CLUSTERS   NATIONAL PLANT BIOTECH CLUSTERS

Source: WIPO based on PATSTAT, PCT and Web of Science data (see Technical Notes). Cropland data from Ramankutty *et al*. (2008).
Note: Green areas represent croplands and pastures circa 2000.

The presence of these agricultural institutions is likely to create regional ecosystems that are conducive to startups as well as R&D facilities of companies in the industry. Samad and Graff (2020) show that the single most important determinant of the number of inventions to come from a given region is the number of inventions that have come from that region in the past. This relationship represents the "sticky" nature of fixed investments in regional knowledge infrastructure and human capital – the fact that knowledge, as opposed to information, does not transfer that easily between locations – as well as the localized nature of knowledge spillovers (see Chapter 1).

Second, as noted, most of the international plant biotechnology clusters are concentrated in metropolitan areas. Figure 4.7 plots the location of these international clusters alongside global innovation

Innovative activities tend to cluster, particularly in metropolitan areas

Figure 4.7 Worldwide distribution of innovation (GIHs, SNCs and international plant biotechnology clusters)

Source: WIPO based on PATSTAT, PCT and Web of Science data (see Technical Notes).

hotspots (GIHs) and specialized niche clusters (SNCs), as defined in Chapter 2 of this report.

Strong agglomerating forces determine where the innovative regions of plant biotechnology are located. By co-locating in regions where there are strong innovative activities, whether plant biotechnology specific or not, researchers in both public and private sectors are able to benefit from the knowledge spillover (see Chapter 2). For example, they can profit from the presence of other related innovating industries and specialized skilled workers, some of which could be relevant and useful and facilitate new technological advances in the crop biotechnology industry.[53]

4.3 The innovation network of plant biotechnology

The main innovation clusters in agricultural biotechnology are found, not surprisingly, in the leading countries that invest in agricultural R&D.

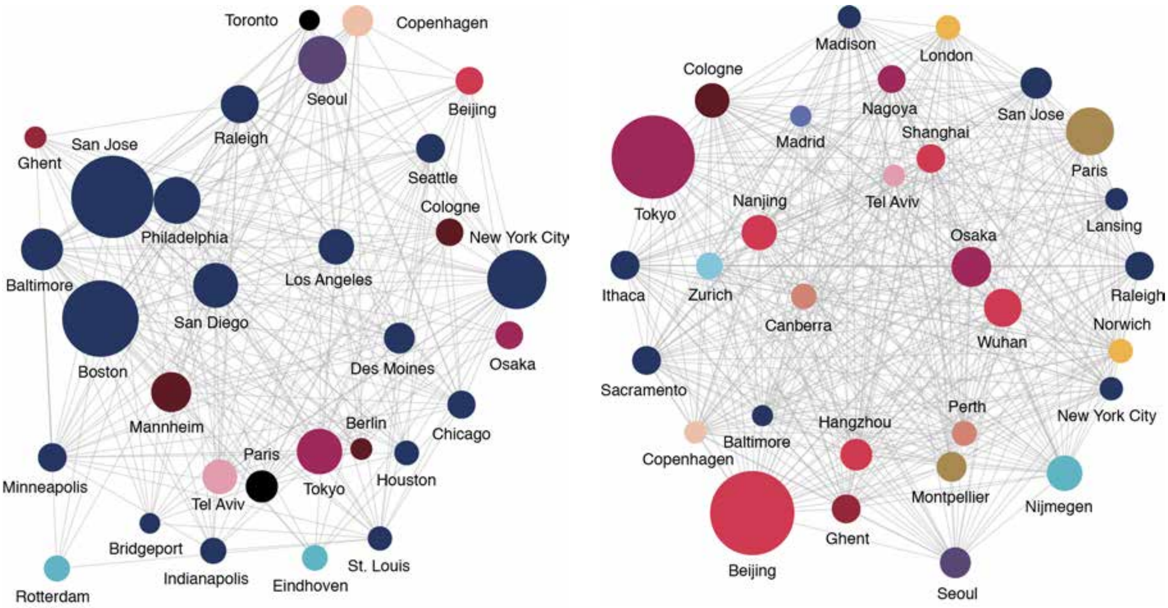
Figure 4.8 provides rough illustrations of how the top 30 international clusters connect to one another, based on patented inventions (left) and scientific publication (right) for 2010–2017. These links are based on co-inventorship and co-authorship across regions. The size of the bubbles in the figure represents the volume of patented inventions (or scientific publication) in that particular cluster, while the thickness of the lines represents the frequency of the interactions between them. The colors of the bubbles indicate the countries to which the clusters belong.

The U.S., Canada, Europe, particularly Germany, France, Netherlands, Denmark and the U.K., and countries in East Asia (Japan, the Republic of Korea and China) are home to most of the international clusters for patented innovation in crop biotechnology.[54] As in the case of biotechnology, distance is not necessarily the main criterion for connecting to clusters.

For example, inventors in the two largest international clusters, San Jose and New York City (nearly 4,724 km apart), interact more frequently than San Jose with San Diego (approximately 739 km apart). Inventors in Rotterdam, the Netherlands, co-invent more frequently with inventors in San Diego than with their compatriots in Eindhoven.

More openness in scientific publications than patenting? Collaboration between plant biotechnology clusters are more frequent and denser in scientific publications than in patenting activities

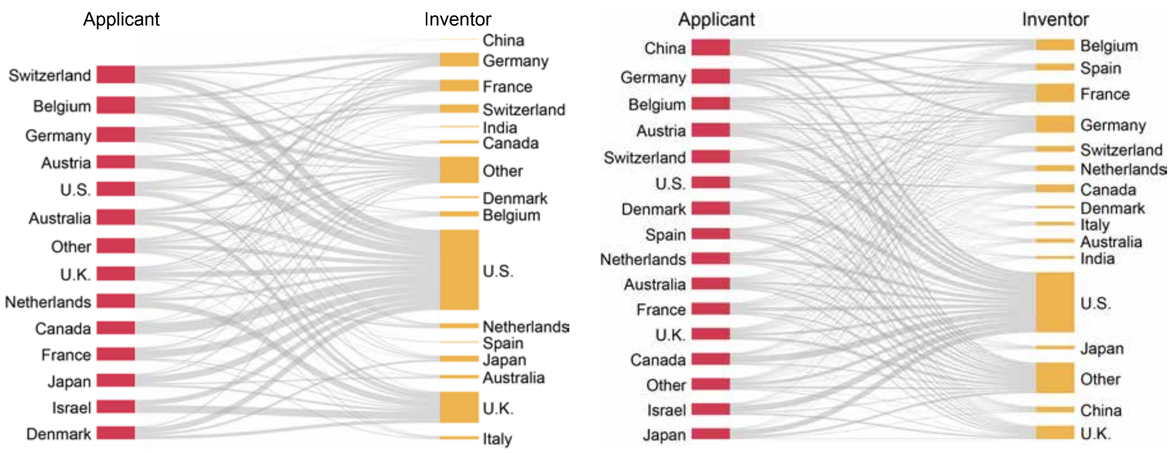
Figure 4.8 Linkages between the top 30 international biotechnology clusters based on patent filings (left) and scientific publications (right), 2010–2017



Source: WIPO based on PATSTAT, PCT and Web of Science data (see Technical Notes).
Note: Size of the bubbles corresponds to the relative volume of patent and scientific publications, respectively.

Specialized researchers in agricultural biotechnology tend to come from the U.S.

Figure 4.9 Comparison of top 10 percent applicant–inventor ties of foreign-oriented patents, 1970–1999 (left) and 2000–2017 (right)



Source: WIPO based on PATSTAT, PCT and Web of Science data (see Technical Notes).
Note: Only patent families with foreign-orientation are shown. In addition, applicant-inventor ties where the applicant has a different residence than the inventor are displayed.

The picture for international clusters based on published scientific articles follows a similar pattern. However, the size of the clusters and their interactions with one another are more diverse and denser. The two biggest clusters based on publication are Beijing and Tokyo. U.S. clusters do not figure as prominently as they do for patenting.

Nevertheless, the U.S. has by far the most international clusters based on both measures of innovation: 16 clusters using patents and eight using scientific publication. It is followed by Germany with three international clusters, as measured by patents, and China with six international clusters, as measured by scientific publication.

Both measures of internationally comparable crop biotechnology clusters point to the U.S. as central to innovation in plant biotechnology. One reason for the U.S.'s importance in international clusters of plant biotechnology is the quantity and quality of its specialized inventors and researchers. When looking at where most inventors reside, especially when it is different to that of the patent applicant, we see the overwhelming centrality of the U.S. as the place to find crop biotechnology researchers.

Figure 4.9 illustrates the location of researchers in plant biotechnology by exploiting the different locations of the applicant (left) and the inventor (right) of a particular patent. The left panel provides the links between applicant–inventor pairs in the years 1970–1999, while the right panel paints the picture for the years 2000–2017. The lines connecting the applicant to the inventor are proxies for the strength of the relationship: the thicker the line the more frequent the interaction.

In both periods, many patent applicants outside the U.S. search for U.S. researchers and scientists. The fact that many of the important discoveries in agricultural biotechnology came from U.S. universities and public institutions is one reason why U.S. scientists and researchers are highly sought after. Another explanation is that private companies in the U.S. were often the first to invest strategically in the exploration of commercial applications of biotechnology in plants. These factors combine to increase the weight of the U.S. in the crop biotechnology innovation network.

4.4 Future of plant biotechnology

Three new developments in plant biotechnology could transform the current global innovation network. Recent breakthroughs in molecular biology are opening new research avenues and hence applications for plant biotechnology. The adaptation of CRISPR-Cas9 is likely to reinvigorate research on the genetic improvement of crops and livestock. Moreover, as this technology becomes more affordable, it has the potential to "democratize" innovation in agricultural biotechnology. [55] Combined with the rising role of developing economies in such innovation, this latest advance could lead to the global innovation network being more evenly dispersed. Clusters in different parts of the world could soon be making important contributions that will enhance food security in an efficient and sustainable manner.

In addition, new applications of sensors and artificial intelligence to systematize the quantification of an organism's phenotype and physical traits could enable much more powerful and precise connections to be drawn between genotype, genetic traits and phenotype than was previously possible. With the combined abilities to "read," "write" and "edit" nucleotide sequences, new technological opportunities are possible for the genetic improvement of crops and livestock.

The second development that may change the global innovation landscape and improve developing economies' participation in the global innovation network is the recent shift in CGIAR's stance on IP rights.[56] In the past, CGIAR had been committed to ensuring that its members' work could be shared and would be easily accessible to all; it had shied away from the exclusionary properties of IP rights. This stance has changed. The CGIAR has recognized the importance of collaborating with the private sector and has begun using IP rights as an incentive for such collaboration and partnerships and to encourage innovation.

Finally, in July 2018, the European Court of Justice (ECJ) ruled that plants engineered using gene-editing technologies, such as CRISPR-Cas9, would be subject to the same regulations as those applied to GMOs. The CRISPR-Cas9 technique changes a plant's make-up, its DNA, but without introducing any foreign material, and arguably might have been exempt from the regulations. However, the ECJ ruled that the technique was still subject to the European Commission directive. Scientists and researchers argue that the ruling could result in a further exodus of plant biotech R&D outside Europe. If proven true, then the ruling will further change the innovation landscape and networks of plant biotechnology.

Notes

1 This chapter draws on Graff and Hamdan-Livramento (2019).
2 Other traditional ways include hybridization as well as grafting.
3 The United Nations Convention on Biodiversity (CBD) definition. It differs slightly from that of the Biotechnology Innovation Organization (BIO), a major industry association. BIO defines biotechnology as "technology based on biology – [it] harnesses cellular and biomolecular processes to develop technologies and products that help improve our lives and the health of our planet" (www.bio.org/what-biotechnology).
4 Graff *et al*. (2003).
5 FAO (2003).
6 The term "agricultural biotechnology" differs from "plant biotechnology" in that the former refers to the general industry, while the latter applies to a particular field of agricultural biotechnology. "Plant biotechnology" is used interchangeably with "crop biotechnology."
7 The first licensed drug using rDNA technology was the human insulin drug, produced by Genetech and licensed to Eli Lilly and Company (Johnson, 1983).
8 Kenny (1988).
9 The proximity between humans and animals. Humans fall under the category of mammals in the animal kingdom, which allows for easier transition between human and animal health.
10 Carrer *et al*. (2010). The terms genetically engineered-, genetically modified- and genetically improved-organisms are used interchangeably throughout this chapter. Another term that is used alongside these is transgenic crops.
11 See Alvarez-Morales (2000).
12 Patents are territorial in nature. This means that a patent granted in one country or jurisdiction is not necessarily enforceable in another. Inventors who want to ensure that their invention is protected from imitation across countries would have to file patent applications for the same invention in those jurisdictions.
13 Other forms of IP protection on plants are plant varieties and plant patents (specific to the U.S.). However, these two IP instruments are outside the scope of this chapter and not addressed here.
14 Barton (2000).
15 See Eisenberg (1996) and Heller and Eisenberg (1998).
16 Barton and Berger (2001).
17 Brennan (1980).
18 Another instrument which protects innovation in plants is the International Union for the Protection of New Varieties of Plants (UPOV) system of plant varieties rights. This chapter does not touch on this right.
19 Figueiredo *et al*. (2019). See Teece (1986) and Rothaermel (2001) for importance of complementary assets.
20 See Eckerstorfer *et al*. (2019) for an overview of the different existing regulatory frameworks.
21 See Glowka (2003) and Komen (2012).
22 See Graff and Hamdan-Livramento (2019), and Brenner and Komen (1994).
23 See WTO dispute settlement case DS291: European Communities — Measures Affecting the Approval and Marketing of Biotech Products (www.wto.org/english/traptop_e/dispu_e/cases/e/ds291_e.htm).
24 For the list of regulations and directive on GMOs visit ec.europa.eu/food/plant/gmo/legislation_en
25 The European countries included in the figure are: EU-28 (except for missing data from Malta, Bulgaria and Poland). Portugal, Spain and the U.K. are included in the list of countries in Europe still farming transgenic crops.
26 USDA Foreign Agricultural Service (2018).
27 ISAAA (2017). In 2012, BASF announced that it was closing its SunGene, its main plant biotechnology activity in Gatersleben, Germany, to concentrate on the North and South American markets by 2013. Visit www.sungene.de
28 See European Commission (2004, 2009); National Research Council (1987, 1998); FAO (2003, 2004).
29 "CRISPR" stands for clustered regularly interspaced short palindromic repeats while "Cas9" refers to CRISPR-associated protein 9.
30 Wright (2012). See Alston *et al*. (2010) and Olmstead and Rhode (2011) on how these Land-Grant colleges have been useful for the agriculture industry in the U.S.
31 See Chapter 2 of FAO (1996) for further details on agro-ecological conditions.
32 Byerlee and Fischer (2002) and FAO (2004).
33 Barry and Hosch (2000).
34 See FAO (2004), and Serageldin and Persley (2000).
35 Bijman and Tait (2002).
36 Clancy *et al*. (2016).
37 Komen and Persley (1993), Persley (2000) and Fukuda-Parr (2006).
38 Kalaitzandonakes and Bjornson (1997) calculated the number of mergers, acquisitions and

strategic alliances between startups and MNCs at 167 between 1981 and 1985, and 801 mergers between 1991 and 1996.

39 See Kalaitzandonakes (2000); Fulton and Giannakas (2001); Tait *et al*. (2002); and OECD (2018).

40 Howard (2015).

41 See OECD (2018) and Fuglie *et al*. (2012). The OECD (2018, p. 104) reviewed the empirical literature on concentration in the seed industry and impact on innovation. The study concludes that there is little evidence for the adverse impact of concentration on innovation based on historical data.

42 Fukuda-Parr (2006).

43 Huang *et al*. (2002).

44 Byerlee and Fischer (2002).

45 See Barton and Berger (2001).

46 Pinstrup-Andersen and Cohen (2003).

47 See International Potato Center (1995).

48 Co-applications refer to patent applications where there are at least two listed applicants on the document.

49 It is plausible that there are more regions that should be included rather than those displayed in this chapter. In other words, the regions covered by scientific publication may be an underestimate. This is because identifying articles on plant biotechnology is sensitive to the method used. Here it is based on the top journals in plant biotechnology. Other journals that are not as well known, but which may have equally relevant contributions, are excluded.

50 See Griliches (1990).

51 Samad and Graff (2020) also find this urban–rural divide when looking at the innovation centers of agriculture biotechnology regions in the U.S.

52 See Graff and Hamdan-Livramento (2019) for more information on the procedure for farming transgenic crops.

53 Hermans *et al*. (2008).

54 See annex in Graff and Hamdan-Livramento (2019) for a detailed list of the top 30 clusters by patents and scientific articles published, respectively.

55 See Mahfouz *et al*. (2014) and Shwartz (2018).

56 See CGIAR (2006, 2013).

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Innovation is becoming more collaborative as technology becomes more complex. For large multi-skilled teams to thrive, knowledge needs to be able to flow freely across borders.