TIMELINE

Biotechnology in the 1930s: the development of hybrid maize

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Hybrid maize was one of the first examples of genetic theory successfully applied to food production. When first introduced, it seemed almost miraculous; sturdy hybrids convinced sceptical farmers that 'the professors' and their arcane science could do them some good. Strangely, the genetic basis of heterosis (hybrid vigour) was and still is unknown. But to this day, newer hybrids continue to outyield their predecessors; they do so because they are tougher and healthier.

Hybrid maize (*Zea mays*) is not new, but the biological and sociological bases on which it was built are now considered as new — and disturbing — by some segments of the public.

When hybrid maize was invented and presented to US farmers in the first decades of the twentieth century, it was based on two new operations, one biological and the other socio-economic. First, strange manipulations (forced inbreeding and controlled hybridization) produced biological products that had never before existed in nature. Second, farmers gave up their time-honoured practice of saving their own varieties of seed in favour of annual purchases of hybrid maize seed.

These two actions are deplored today by some elements of society as the undesired and potentially dangerous consequences of the application of biotechnology (especially, of genetic transformation) to plant breeding[1,2]. (The term 'biotechnology' has many definitions, but is used here to refer to the branch of molecular biology that uses recombinant DNA technology to study, categorize and manipulate genetic materials. Genetic transformation, also called genetic engineering, is one kind of biotechnology.)

Why were similar concerns not expressed 70 years ago when maize hybrids were bred and released rapidly and on a large scale in the heart of the United States 'Corn Belt'? I will consider these questions in the light of the following account of the origins and development of hybrid maize.

Darwin, maize and hybrid vigour

Charles Darwin did many experiments to test his theory on the origin of species[3]. One of them involved a comparison of inbred and cross-pollinated maize. He noted that the progeny of cross-pollinated maize plants were 25% taller than the progeny of self-pollinated plants and had greater tolerance to cooler growing conditions. From these experiments, he concluded in 1876 that, as a general rule, cross-pollinated (hybrid) plants have "greater height, weight, and fertility" as compared with their self-pollinated counterparts because of their "greater innate constitutional vigour"[4].

In the United States, William Beal at Michigan State College was encouraged by Darwin's observations on hybrid vigour and hybridized pairs of open-pollinated varieties of maize. Beal observed increased vigour and grain yield in the hybrids of different varieties and, in 1880, he encouraged the use of this method[5–7]. However, because the results of further experiments were unpredictable[5], hybridization seemed to have no future as a way to improve maize yields and general performance. But other methods were in the process of development.

New breeding methods

Improved varieties. Around the turn of the twentieth century, farmers in the United States began to look harder than before for ways to increase maize yields. Urban populations were increasing rapidly with a concomitant increase in the demand for meat, which in turn increased demand for feed grains. As new lands were no longer available for exploitation, increased production needed to come from higher yields. The use of plant breeding to produce new and/or improved, higher-yielding varieties of maize looked like a promising option. Those farmers and scientists who selected new breeding varieties rose to the challenge.

Disappointingly, the use of 'improved varieties' did not produce substantial increases in yield. Average maize yields in the midwestern Corn Belt state of Iowa, for example, were essentially unchanged during the first three decades of the twentieth century[8].

With hindsight, we know that the primary reason for lack of success in variety improvement by either farmers or scientists was that their selection methods were not very powerful, as judged by modern standards of statistical design and genetic theory[9].

Inbred-hybrid method. Meanwhile, two young scientists laid the foundations for a new method of maize breeding[5,10]. George Harrison Shull and Edward Murray East, working well away from the midwestern Corn Belt at two separate institutions on the Atlantic seaboard (East worked in Connecticut, Shull on Long Island in New York.), independently rediscovered the phenomenon of inbreeding depression and hybrid vigour in maize, and reported their results independently in 1908 (REFS. 11,12). They went further than Darwin did, by self-pollinating several generations to produce essentially homozygous (pure-breeding) inbred lines that were then crossed to produce hybrids. Shull coined the term "heterosis" to describe hybrid vigour.

Both men recognized the potential of the 'inbred-hybrid method' for producing high-yielding maize hybrids that, once identified, could be reproduced without change year after year. Hybrid seed could be made on a large, farm-field scale (as opposed to labour-intensive hand pollination) by removing the tassels (detasselling) from one inbred and allowing it to be pollinated by a second inbred planted in adjacent blocks (FIG. 1). Maize is unique among the cereal crops in that male and female flowers are borne on separate organs — tassel and ear shoot, respectively — and it is wind-pollinated. No other crop is so well suited by nature to large-scale hybridization.

But neither East nor Shull believed that farmers could grow hybrids profitably. The inbreds developed by Shull and East were so weak and low yielding that seed yields were very low or absent (BOX 1). Seed production costs — and therefore seed prices — would be too high; the extra expense for annually purchased seed would be greater than the value of the extra yield of the hybrid. And freshly made hybrid seed was needed each season, for yields dropped precipitously (15% or more) if seed saved from the hybrid plants was replanted.

The inbred-hybrid idea did not die, however. A few years after the 1908 announcements, one of East's students, Donald F. Jones in Connecticut, came up with a solution to the problem of seed cost[13]. 'Double cross hybrids' could be made, by crossing two 'single cross hybrids'. (A single cross is a cross of two inbred lines; see BOX 1.) The double cross, although perhaps lower yielding than the best single crosses, nevertheless, would be much better than the best open-pollinated varieties. Seed production on high-yielding single cross parents would bring seed prices down to a level that farmers could afford. This news, published in 1918, electrified a small group of scientists and maize-breeding enthusiasts.

The public and private sectors

Even before Jones' announcement of the double cross method, several young scientists that were working in the public sector had begun to inbreed maize, with no knowledge of the precise method that would be followed to make hybrids. After Jones' announcement, the initial group was joined by a few more researchers, raising their total to about one dozen. This diverse group included agricultural scientists, a farmer and a magazine editor. They worked at several institutions, such as the United States Department of Agriculture (USDA), agricultural colleges and (a few) private companies. Despite their diversity, they were united in their belief that the inbred-hybrid method would succeed where other breeding methods had failed. Their confidence was based on two premises: first, that hybrid vigour gives extra yield; and second, that individual hybrids can be precisely reproduced year after year. The hybrids can be precisely reproduced because they are crosses of uniform inbred lines that, in turn, can be precisely reproduced by self-pollination.

The technique was simple: develop inbred lines, find their best combination in hybrids by running replicated yield trials of the different combinations, produce the seed of selected hybrids and deliver it to farmers.

In reality, there were several complications, but the basic method was so simple that, in the early years, anyone with energy, time and ability could learn to apply it. One other item was not exactly a problem but rather a mystery. No one knew the genetic basis for heterosis — hybrid vigour. If this were known, breeding could be more precise and hybrid yields presumably could be advanced further than by using 'cut and try' (empirical) methods. To this end, theories were proposed and experiments conducted

Box 1 | How to make a double cross hybrid

To make a double cross hybrid, four inbreds are crossed pairwise, making two single crosses: B × A and C × D. The two single crosses are crossed, giving a double cross: (B × A) × (C × D). Hybridization is effected on a field scale by planting alternating blocks of the two lines to be crossed (such as inbreds A and B), then detasselling one block (such as inbred B). Inbred B therefore is pollinated exclusively by inbred A, and all seed on inbred B is hybrid, B ×A.

Breeding by farmers produced several popular open-pollinated varieties, such as Reid's Yellow Dent and Krug's Yellow Dent. Mr. Reid started with a mixture of a New England Flint variety (too early) and a Southern Dent variety (too late) and developed a high-yielding variety of the right maturity for central Illinois. Further gains were more difficult. Modern geneticists say that neither the breeding protocols used by farmers or the earliest scientific breeding programmes were designed to give sharp and continuing increases in performance. Experiments were not replicated a sufficient number of times, and there was too little control over the source of the pollen used to fertilize the selected ears. Breeding designs based on current genetic theory enable breeders to improve open-pollinated varieties at about the same rate as that achieved by breeders of hybrid maize, but this knowledge was not available in the nineteenth and early twentieth centuries. It is now thought that, even using modern designs, the best hybrids will always outdo the best open-pollinated varieties. Open-pollinated varieties are a diverse collection of hybrid plants and the performance of a variety is equal to the average of all of its plants, from best to worst. Therefore the best hybrid, developed and dependably reproduced with the inbred-hybrid breeding method, will always be superior to the best open-pollinated variety, even though it may not be superior to the very best plants in that variety.

This illustration, from a farm magazine in the 1930s, shows how to make seed of a double cross maize hybrid. Note the difference in size between inbred and hybrid ears. Education and advertising were combined then, as they are now.

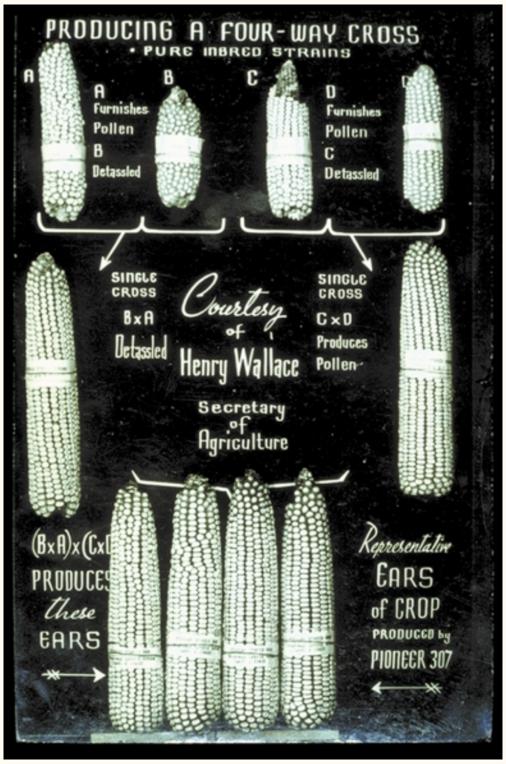


Image courtesy of Pioneer Hi-Bred International, Inc.

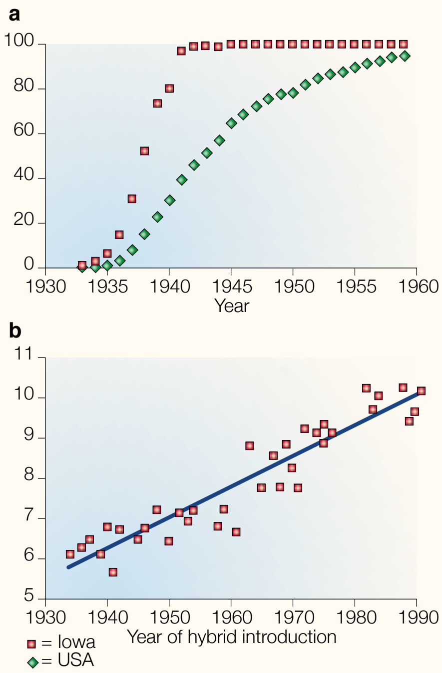
Figure 1 | **Detasselling maize plants** Detasselling — pulling tassels — is vital for the production of hybrid maize. The detasselled plants are called 'females'; they will bear the hybrid seed. In the early years, men on foot did the detasselling, as in this photo from the 1930s. In later years, high school boys and girls were recruited to do the job, also on foot. Today, youths are still the chief labour source, but they usually ride in special motorized carriers, thereby increasing the speed and precision of their work. (Image courtesy of Pioneer Hi-Bred International, Inc.)

but, to this day, there is no completely satisfactory explanation for the phenomenon of heterosis in maize or in any other species[14]. Fortunately, a lack of understanding has never hindered the use of the phenomenon.

But in the 1920s, these problems were all in the future. The 'hybrid maize' enthusiasts were occupied primarily with finding inbreds that made outstanding hybrids. As with many interest groups, the 'hybrid maize breeders' came to know each other and developed an informal exchange of information and materials. They needed each other's inbreds, for no one had enough of them to make a series of good double-cross hybrids.

In the 1920s (and for some decades thereafter), the primary source of ideas, theories and germ plasm was the public-sector maize breeders at the agricultural colleges and in the USDA. They published their findings in the scientific literature and, importantly, furnished breeding materials, such as inbred lines, to all that asked. The public sector through the extension services (departments through which farmers' and scientists exchange information) of its agricultural colleges, also effectively educated the farming community (and the interested non-farming public) about the advantages of hybrid maize.

Without the contributions from the public sector, the commercial maize breeders probably could not have succeeded in the early years, for individually they simply did not have enough inbred lines or enough knowledge about how best to make and test hybrids[15].



Hybrid maize. Within ten years of Jones' proclamation, the first breeders were producing successful hybrids. Beginning in the early 1930s, interest in, and demand for, hybrid maize rose steadily among farmers in the United States[16] (FIG. 2a). Maize breeders have continually turned out higher-yielding hybrids, year after year[17–19] (FIG. 2b), and farmers have adopted them after cautious trials on their own farms. In 1997, United States maize yields averaged 8 tons hectare^{-1}, compared with 1 ton hectare^{-1} in 1930 (REF. 20).

Hybrids were not entirely responsible for advances in maize yields, however. Starting around the 1950s, the increasingly widespread use of synthetic nitrogen fertilizers, chemical weed killers, and more efficient planting and harvesting machinery also contributed to higher yields[17–19,21].

Surprisingly, improvements in heterosis have not contributed to higher yields. Experiments have shown that heterosis (calculated as the difference in yield between a single cross hybrid and the mean of its two inbred parents) is unchanged over the years. The yields of the inbred lines have risen at almost the same rate as hybrid yields[22]. It seems that yield gains have come primarily from genetic improvements in tolerance to stresses of all kinds (such as tolerance to disease and insects, dense planting, drought or low soil fertility). The newer hybrids are tougher than their predecessors and shrug off droughts (for example) that would have damaged the older hybrids and devastated their open-pollinated parents.

Figure 2 | **Maize hybrids: area planted and yield potentials. a** | Per cent of maize area planted to hybrids, from 1930 to 1960, in Iowa (red) and in the United States (green). During the 1930s, hybrids almost completely replaced open-pollinated varieties in most of the Corn Belt and, by 1960, virtually all maize plantings in the United States were hybrid. Yield gains paralleled increases in area planted to hybrids. Iowa maize yields advanced on average from 2 tons hectare^{-1} in 1930 to 5 tons hectare^{-1} in 1960; United States maize yields advanced from 1 ton hectare^{-1} in 1930 to 4 tons hectare^{-1} in 1960. (Adapted from REF. 20.) **b** | Grain yields (in tons hectare^{-1}) of 36 popular hybrids introduced in central Iowa from 1934 to 1991, according to tests conducted in central Iowa in 1991–1994. New maize hybrids yield more than their predecessors, and are also continually being improved for other traits, such as disease resistance and tolerance to drought. Researchers have concluded that, on average, improvements in hybrids have been responsible for about 50–70% of the on-farm yield gains since their introduction, and changes in agronomic practices (such as more fertilizer and better weed control) have been responsible for the remainder. (Adapted from REF. 18.)

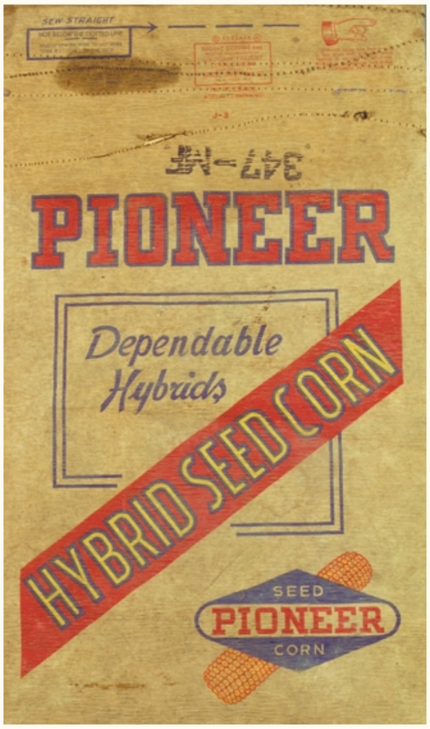


Figure 3 | **The introduction of hybrid maize seeds.** The 'seed corn companies' effectively and energetically introduced hybrid maize to cautious farmers. They recruited well-known and respected farmers as part-time salesmen, working on commission. They gave small amounts of free seed of new hybrids to farmers and encouraged the prospective customers to compare them with their present varieties on their own farms and using their own farming methods. The salesman and/or his supervisor often would help the farmer harvest the comparison. In the process, the sales people learned about the farmers' needs and desires in maize hybrids, which they passed on to the breeders. So, the relationship between farmers and seed companies from the beginning was almost on a neighbour to neighbour basis. The relationship remains much the same today, with modifications because of the changing nature of farming and farmers (much larger scale, more advanced technologically and more business-like).
Image courtesy of Pioneer Hi-Bred International, Inc.

An important change in hybrid seed production and performance was, in a sense, a byproduct of the increases in inbred yield. By the 1960s, the newest inbreds were so high-yielding that it became practical to use them as seed parents, and so to produce single cross hybrids for sale. The best single crosses always yielded more than the best double crosses but, as noted earlier, commercial production of single cross hybrids was not feasible in the first decades of hybrid maize breeding because of the low yield potential of inbreds from that era.

Public and private breeders. In the early years of the hybrid era, people were undecided about how to deliver hybrids to the farmer. Farmers had the option to produce them on their own farm using single cross parent seed purchased from the agricultural colleges, or to purchase 'ready to plant' hybrid seed from farmer cooperatives or from commercial seed companies (FIG. 3). All methods were tried, but in the end the seed companies turned out to be the farmers' choice.

Once the advantages of hybrids (and the fact that farmers would buy them) were shown, seed companies sprang up across the country, especially in the Corn Belt states[15] (FIG. 4). Starting with four pioneering companies, the numbers grew exponentially in the 1930s. By 1995, 305 independent companies were involved with the production and sale of hybrid maize seed. As with most industries, a small number of large companies dominated the business, accounting for perhaps 70% of the sales. Despite their small market share, the small companies have an important role in the industry. They provide an alternative to farmers who do not want to buy from the larger companies.

The exchange of information and breeding materials among private- and public-sector breeders changed as the seed industry matured. Almost from the beginning, seed companies kept the pedigrees of their hybrids secret and they soon stopped trading their inbred lines. By about the mid-1930s, all exchange of inbreds and other advanced breeding materials was one-way, from the public to the private sector.

The roles of the public- and private-sector breeders also changed. The large companies with strong breeding programmes had increasingly less need for inbreds developed by the public sector, although the smaller companies still depended on them. Over time, 'foundation seed companies' were formed expressly to breed inbred lines for lease to the small seed companies, thereby filling the role of the public-sector breeders. The public-sector breeders in turn shifted their primary emphasis from the development of inbreds and hybrids to studying the theoretical basis for producing improved inbreds and hybrids, as well as other needed aspects of maize-breeding research.

The relationship between public and private sector breeders still remains close; they have mutually supportive roles in the nation's maize breeding programme.

Consequences of hybrid maize

Acceptance. In the opening paragraphs of this article I asked why the maize hybrids were accepted without public outcry in the 1930s, even though farmers had to give up their status as independent seed savers, and even though hybrids as such were looked on as strange new creations of science. Having traced the development of hybrid maize, these and related questions can be addressed.

Farmers gave up their status as independent seed savers because they found by experience that they would profit more by doing so. They were already giving up their status as independent power suppliers on their farms, for example, as they moved from horse power to tractor power and from hand harvest to mechanical maize pickers.

Although farmers viewed hybrids as new and strange creations of science, they saw no adverse effects on either their crops or their livestock. It is true that, in the early days, some farmers feared that the abnormally high yields from hybrids would drain the soil of needed fertilizer elements. And there were complaints about some of the first hybrids, to the effect that the kernels were too flinty and hard for cows to chew. Seed companies bred new hybrids to satisfy the second complaint, and the first concern turned out to be without foundation if normal soil fertility practices were used.

The farmers' primary fear was not that science might create unmanageable 'monsters' (today's widespread point of view), but that scientists claimed more power to help agriculture than they really possessed.

Figure 4 | **Maize quality control in the early years.** The fledgling seed companies devised a 'sorting belt', allowing inspectors to examine every ear before shelling. They wanted to be sure the seed ears were free of damage from disease or insects, and of the right type. Women replaced men in many of the seed production operations during the Second World War, when young men were in the armed services.
Image courtesy of Pioneer Hi-Bred International, Inc.

There was no concern whatsoever about the adverse effects of hybrid maize on human health or ecosystems. In the 1930s (the decade of 'The Great Depression'), the overriding public concern was to have ample and affordable supplies of food, clothing and shelter.

An important difference between then and now is that hybrids of the 1930s were made by genetic manipulations that used 'natural methods' of gene transfer (pollen to stigma), whereas today's transgenic crop varieties require 'unnatural' laboratory manipulations. (Gene transfer across very wide taxonomic distances does occur in nature but not through gene guns or tissue culture, and the products are not multiplied and distributed so widely and rapidly as transgenic farm crops.). Although the operations and products of hybrid maize breeding were thought of as 'unnatural' (or at the least, highly unusual) in the 1930s, they are no longer considered as such; they are thought of as an application of a natural phenomenon.

Perhaps the most important difference is that, in the 1930s, there were no social/environmental organizations conducting powerful campaigns to educate the non-farming public sector about the possible dangers (to health, the environment or society) of growing or eating crop varieties created with 'unnatural' techniques (for example, REFS 1,23,24). In the 1930s, to convince farmers of the utility and safety of these new creations — hybrids — was sufficient to ensure their acceptance by all. Today, one primarily must convince the non-farming public of the safety of the new creations of genetic engineering. The farmers' opinion also counts, but only secondarily.

A final difference is that, contrary to the 1930s, today's scientific establishment has not taken the lead to introduce and explain transgenic crop varieties to the public and often is divided in its opinions on this subject, as well as on the general topic of biotechnology in plant breeding. The scientists are not alone in this regard; the entire question of biotechnology and its applications is complicated and controversial for reasons that go well beyond science. As one commentator has stated[25], "the larger biotechnology debate … is riddled with ideological, ethical, and other normative evaluations… [As] history keeps teaching us, ideology and world view will not easily be influenced by the results of scientific research".

One can speculate that use of hybrid maize might have been hindered or even blocked, if today's socio-economic, food and environmental concerns and today's healthy economy had prevailed in the United States in the 1930s, concurrent with the 1930s state of knowledge about genetic manipulation. But perhaps it is not realistic to expect that today's environmental and food quality concerns could exist without support from today's advanced biological knowledge.

Effects. Despite the enthusiastic acceptance of hybrid maize by American farmers (and indirectly by the non-farming public) it will be beneficial to look briefly at the effects (favourable or otherwise) of hybrid maize, biologically, economically and sociologically, during the past 70 years.

Genetic diversity of maize on the farm has been reduced, primarily because hybrids are more genetically uniform than open-pollinated varieties. Genetic diversity provides protection against unexpected kinds of weather, disease and insect pests.

However, genetic diversity on the farm is only one kind of diversity[26]. Breeders work from a large pool of genetic diversity in the highly diverse 'breeding pools' from which they extract inbred lines. They also can 'cross in' breeding materials from anywhere in the world, giving them opportunity to add an almost uncountable number of new traits as they are needed. Hybrids therefore increasingly have more built-in genetic diversity and their genetic components change every year, as new hybrids replace outdated older ones. It seems fair to say that, in a given season, individual farmers work with less diversity but, over the years, they have access to more diversity than in pre-hybrid days.

Today's hybrids are more tolerant to stress than were the open-pollinated varieties of the 1920s and earlier[27,28]. However, the hybrids' increased robustness has encouraged farmers to apply heavier amounts of fertilizer (especially nitrogen), because the hybrids can take advantage of the increased nutrient supplies without suffering from the stress of more rapid growth and higher productivity. So indirectly, hybrids (along with all modern cereal varieties) have contributed to ground water pollution.

Mechanization of maize growing (in particular of harvesting machinery) has been encouraged by use of hybrids because they do not lodge (fall over) as much as open-pollinated varieties. These hybrids are more amenable to machine harvest, and so have aided the trend towards larger farms and fewer farmers.

The heightened yields of hybrids have benefited farmers economically, in particular the most efficient ones. They, in turn, have enlarged their operations (helped also by the adaptation of maize hybrids to mechanization) and so farm numbers have decreased. Maize production on the whole is more efficient, but some farmers in particular have suffered.

Future prospects

Hybrid maize now has spread over all commercial maize growing regions of the industrialized countries such as North America and Europe, and also the industrial agriculture sections of developing countries such as Argentina, China and Brazil.

The story of the development of hybrid maize in Europe may be instructive. As the European economy improved after the Second World War, meat became more popular and this increased the demand for feed grains, including maize. American maize hybrids were not adapted to the European climate, except in the south. European breeders developed inbreds from early European flint varieties. The flint inbreds, hybridized to United States inbreds, gave high yielding hybrids with adaptation to the cool growing season of northern Europe. Hybrid maize is now an important crop in all continental European countries south of the Baltic, wherever commercial grain farming is important.

Biotechnology (including genetic transformation) is in the future of hybrid maize breeding everywhere in the world, but when it will achieve widespread use is uncertain. The expense of applying biotechnology is high and it will be difficult for seed companies to make a profit without raising seed prices on transgenic hybrids. But farmers will buy such higher priced hybrids only if they believe they will more than recoup their extra investment in seed. Additionally, a powerful campaign against GMOs (genetically modified organisms) intends to block use of transgenics in both animal and crop agriculture (especially aiming at agribusiness). The outcome of this campaign will notably affect, possibly in a negative fashion, the direction and utility of the quintessential commercial seed breeding activity, hybrid maize.

But the fundamental knowledge that accrues from research in molecular biology of plants is scientifically so empowering that I cannot imagine a future in which biotechnology will not be beneficially applied to maize breeding (or any other biological manipulation). It will be applied, however, with more delay and more difficulty than imagined two decades ago by its proponents.

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Links

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SCIENCE AND SOCIETY

Human embryonic stem cell research: ethical and legal issues

John A. Robertson

The use of human embryonic stem cells to replace damaged cells and tissues promises future hope for the treatment of many diseases. However, many countries now face complex ethical and legal questions as a result of the research needed to develop these cell-replacement therapies. The challenge that must be met is how to permit research on human embryonic tissue to occur while maintaining respect for human life generally.

Embryonic stem (ES) cell research offers the hope of cell-replacement therapy for diseases such as Parkinson disease, diabetes and cardiac myopathy, but formidable scientific and clinical challenges must be overcome before such therapies could become available[1,2]. For example, scientists need to learn how to direct pluripotent ES cells to differentiate into the required cell or tissue type[3]. Clinicians must then determine the transplanted cells' immune compatibility with the host, and where, and in what amounts, to replace cells in diseased organs to achieve a therapeutic effect. These scientific efforts are also complicated by ethical concerns about obtaining human ES cells from aborted fetuses or from the destruction of early human embryos. The resulting controversy has delayed or stopped human ES cell research in some countries, and could affect the extent to which human ES-cell derived therapies are developed and used. This article will survey the main ethical and legal issues that arise from human ES cell research, and how public policy should accommodate them.

Legality of human embryo research

Legal treatment of the use of human fetal tissue or the destruction of human embryos to obtain ES cells for research varies widely throughout the world. The United States, the United Kingdom and many other countries permit the use of human fetal tissue for research when a woman's decision to donate fetal tissue is clearly separate from the decision to abort. Although most American states permit ES cell research that requires the destruction of human embryos, federal law prohibits the direct funding of embryo destruction to obtain such cells[4,5]. However, federal law permits the funding of research on human embryonic tissue that has been derived with private funds, provided that guidelines for how these cells should be derived have been followed[6]. Although the United Kingdom at present only permits human embryos to be used to study infertility, contraception and birth defects, an expert group at the Department of Health has recommended that embryo research involving cell-based treatments be added to the list of acceptable purposes[7]. Germany and France prohibit destructive embryo research, whereas other European Union members are split on the question[8,9]. Australia also has a mixture of positions, with the state of Victoria specifically banning "destructive embryo research" that produces ES cells for research[10], whereas the states of New South Wales and Queensland permit it according to the guidelines of the Australian Medical Research Council[11].

A legal ban on destroying human embryos to produce ES cells, however, does not mean that research on ES cells legally derived in another jurisdiction is also prohibited. The United States Congress' ban on federal funding of human embryo research restricts only federal support for the derivation of human ES cells. The ban does not affect research on human ES cells that have been derived by using private funds, provided that National Institutes of Health (NIH) regulations for how those cells were derived have been observed[6]. Similarly, human ES cell research is now occurring in Victoria, despite its ban on embryo destruction, with cells derived in Singapore where their destructive derivation is legal.

Some countries or states, including Michigan in the United States[12] and Victoria in Australia, now ban human cloning without drawing a distinction between cloning