APPENDIX

Title: AN ANALYSIS OF ILLOCUTIONARY ACTS IN DISCOVER MAGAZINE

Source: DISCOVER MAGAZINE April 2013 Edition

Chimeras in the lab may lead to improved stem cell therapy.

The world’s first chimeric monkeys were created in a laboratory last year, and they offer surprising new insights into embryonic stem cell therapy. One reason for often poor treatment outcomes may be that we’re using embryos that are, strangely just too old.

Researchers have long been able to create chimeras—offspring with more than two parents—in rodents like mice by combining embryos so tiny they consist of only eight cells in all. At this early stage of their development, embryos are made of pluripotent stem cells, each of which can give rise to many, though not all, tissue types. Previous attempts to do the same in monkeys, however, have failed—a disappointment because monkeys are more similar than mice to humans, and thus likely a better harbinger of how stem cell treatments will fare in people.

“Stem cells function far differently in mice than in monkeys,” says biologist Shoakhtev Maliga, a senior scientist in the Division of Reproductive and Developmental Sciences at Oregon National Primate Research Center and lead author of the monkey study. “If we’re going to bring stem cells to the human clinic, we need to know exactly how those stem cells will work. In mice, you can inject pluripotent stem cells from a black mouse into the embryos of an albino mouse (in the womb of a mother mouse) and they will get along well, and you’ll end up with a black-and-white-spotted mouse chimera. In the monkey, when we tried injecting 30 or 30 laboratory-cultured pluripotent stem
The Chimeric Advantage

The ability to create chimeras from stem cells not only in mice but in other animals, including primates, could prove to be a major advance in biomedical science. In a 2009 study, University of Georgia at Athens cloning expert Steve Sice created 29 chimeric piglets by injecting pluripotent stem cells into pig embryos before implanting them into a surrogate womb. Although it wasnt the first time chimeric pigs were created, it was the first time they came about using cloned pluripotent cells. And because pigs are genetically closer to humans than mice are, success in creating chimeric pigs from stem cells offered renewed hope that the technology could lead to better pharmaceutical testing or stem cell therapies.

But the most significant part of these finds, says bioethicist Jason Robert of Arizona State University, is that research on rodents (or pigs) may not be directly applicable to humans. Even rhesus macaques, he says, are not the ideal nonhuman primate to study, since they are not as closely related to us as chimpanzees. We need to ask if we learn more if we studied other animals—more expensive animals that are closer to humans. If our ultimate goal is to take human cells and transplant them into human subjects, we want to know ahead of time that they will behave and integrate well.

"If we're going to bring stem cells to the human clinic, we need to know exactly how those stem cells will work." Mitalipov couldnt agree more. "Stem cell therapies hold great promise," he says, from possible treatments for brain disease to heart disease and age-related disorders. "No drug could restore functional tissue the way that stem cells could." But given the difficulty of achieving monkey chimeras from pluripotent cells, Mitalipov thinks we might need to derive an entirely new stem cell class for regenerative medicine in humans: the all-powerful totipotent cells.

Meanwhile, the monkeys will be weaned and raised to adulthood. "We will see if these three monkeys can have normal offspring. We will want to see if these chimeras persist through the generations," Mitalipov says. 3 JILL REMARK
Annual Checkups Are a Waste of Time

CONVENTIONAL WISDOM: Annual checkups are an important part of a healthy lifestyle.

CONTRARY VIEW: Purely routine checkups might do more harm than good.

A ounce of prevention is worth a pound of cure, they say. Getting annual physical exams to check under the hood and make sure everything is working properly seems like a sensible approach that can help us live longer, healthier lives. After all, detecting serious illnesses at their earliest and most treatable stage can save lives.

But it turns out this widely held notion doesn’t stand up to scientific scrutiny. New Danish research has found no evidence that routine checkups increase longevity or reduced the risks of dying from diseases like cancer or heart disease. While the findings are counterintuitive, “the study adds to growing evidence that periodic exams in otherwise healthy adults are a waste of money and may even lead to overdiagnosis and unnecessary treatments,” says medical researcher Lars Kragballe of the Nordic Cochrane Centre in Copenhagen.

To investigate this idea, Kragballe’s team pooled data from 14 previous studies involving nearly 180,000 people, comparing participants who were offered regular checkups with those who saw their doctors only when they had a complaint. In looking at both groups, researchers found no difference in the number of overall deaths, or even deaths due to cancer or heart disease. The checkups apparently made no difference.

A handful of studies also suggested that general health checks had no impact on reducing hospital admissions, disability, time off from work, or the anxieties of worried but healthy people. In fact, patients who got annual physi- cals were more likely to be misdiagnosed with high blood pressure or high cholesterol, making them more likely to be prescribed unnecessary drugs to treat these ailments. A few trials even indicated that large numbers of people learned they had harmless, but nevertheless alarming, medical abnormalities.

Experts suspect the reason for this unexpected result is that people who genuinely need to see a doctor regularly—the elderly, sufferers of chronic medical conditions, and people with a family history of diseases like diabetes or cancer—already do. Calling for yearly physicals for otherwise healthy people tends to draw in the “worried well,” who don’t seem to derive any added benefit from the extra attention. More is not always better,” says Dominic MacAuley, a physician and editor at the British Medical Journal who wrote an editorial accompanying the study. “Calling for systematic, assembly-line health checks consumes precious medical resources—in doctors’ time and unnecessary treatments and tests—that could be better used elsewhere.”

But this shouldn’t be used as an excuse to skip dreaded physician’s visits, cautions Michael LeFevre, a family physician at the University of Missouri medical school and co-chair of the U.S. Preventive Services Task Force, a group of independent experts that evaluates the benefits of preventive measures. “Many adults don’t need an annual checkup, but they do need to see their doctors frequently enough to get the preventive services—mammograms, screenings for sexually transmitted diseases—that we know work,” LeFevre says.

Linda Marsa is a DISCOVER contributing editor and author of five New York Times bestsellers: "How a Hair Dryer Could Harm Our Health."
HOW I REDISCOVERED THE ENDURING IMPORTANCE OF NEIGHBORHOODS

In 2011, Robert Sampson, a professor of social sciences at Harvard, received the Stockholm Prize in Criminology, the field’s equivalent of a Nobel. Last year he published his magnum opus, *Great American City: Chicago and the Enduring Neighborhood Effect* (University of Chicago Press, 2012), based on his research as scientific director of the Project on Human Development in Chicago Neighborhoods. Sampson helped pioneer the concept of collective efficacy, a measure of neighbors’ willingness to act for each other’s benefit. He sees it as having as strong an effect on children’s well-being as do families, poverty, and schools.

I grew up in the 1960s in Utica, a declining industrial city in upstate New York. Cops patrolled the halls of my high school. A lot of my friends ended up in serious trouble. By the time I left, Utica had lost about 40 percent of its population. I’ve been a city-spill wave since. When I go into different neighborhoods in any city, I think of them as having identities, personalities. While at SUNY Buffalo, I saw how starkly neighborhoods could change over a short distance, from the college section to a dangerous area, say, or a working-class neighborhood.

My work is about the fundamental importance of place. Many scholars today say that technology and globalization have rendered us placeless, but the counterexamples have it wrong—cities are back. Whether it’s Chicago, New York, or Boston, the news is quite good. People are coming back, crime has declined, economies are improving, and cities are once again becoming desirable places to live and work. Even in Utica, Bosnian immigrants are moving in, and there’s a sense that the city has stabilized.

Immigration is actually one of the factors behind the national decline in crime rates. My work in Chicago, which followed 6,200 kids (though not all were immigrants) for eight years, has shown that first-generation kids tend to have much lower violence rates, 50 percent less, than the third generation. And concentrated immigrant enclaves are generally protective of public safety and well-being.

The theory of “broken windows,” that signs of disorder in a neighborhood lead to an increase in crime, was interesting but incomplete. My observations in Chicago suggested that it’s not so much broken windows that matter, but broken neighborhoods. It’s all about the context and perceptions in individual neighborhoods—the sense of collective efficacy.

If you lose a kid who appears to be lost on a street, will an anonymous stranger ask, “Can I help you? Are you lost?” If a stamped, addressed envelope is found on the street—something we actually tested—will someone pick it up and put it in a mailbox? A neighborhood that does these things works, because its people are willing to help one another. That’s what we mean by collective efficacy.

I’m not talking about being bosom buddies with your neighbor. What’s important is a working trust, a sense of civility. That’s why the “stop and frisk” program carried out by New York City police is counterproductive. Surveys have shown that these actions increase alienation and cynicism. Neighborhoods with high levels of legal and moral cynicism are where violence persists. High incarceration rates can also have unintended effects at the neighborhood level. In Chicago, we found that the number of incarcerated residents is more than 40 times higher in some block communities compared with those in white communities.

When incarceration rates in a neighborhood get so high, it becomes an expectation for its members to wind up incarcerated. It becomes normative, and that contributes to a self-reinforcing cycle of disadvantage.

But rather than think negatively about just tamping down violence, I have a vision of urban life that is fundamentally positive. If you provide conditions of safety and perceived trust and civility in social and public spaces, people will want to live there. They’ll invest and develop a sense of ownership. Fundamentally, collective efficacy is about a community’s— and then its inhabitants’—well-being.

AS TOLD TO DOR HERLEY

Universitas Sumatera Utara
What is Fanning His Temper?

A brilliant attorney’s nasty behavior could cost him his career, unless I can get to the bottom of it.

Bill, a managing partner of a prominent local law firm, frequently used me as a psychiatric consultant for the firm’s personnel issues. So I wasn’t surprised to get a call from him about his partner, Steve. We had spoken about Steve several times in just the past year. This time, Bill sounded desperate. “He’s finally done it,” Bill said. “I just have two questions for you. First, what the hell is wrong with him? And second, can it be fixed? If not, I’ll have to leave the firm.”

Brilliant, demanding, and aggressive, Steve had been terrifying associates and support staff for as long as anyone could remember. He was kept on because he brought in lots of work and because he was a valuable mentor.

This time, the problem was something Steve had done outside the office. Running late for court, he had run a red light. When he saw flashing blue lights in his rearview mirror, he just drove faster, stopping only when another police car pulled in front of him. Officers approached his car, one with his weapon drawn. Steve, who handled a good deal of litigation for the city, immediately began yelling at them.

“Don’t you know who I am?” he demanded to know. “I’m the guy the mayor turns to for legal advice when you clowns get yourselves into trouble.”

What the f— are you stopping me for? I’m due in court.” One of the officers tersely explained the illegality of running the red light, reckless driving, speeding, and failing to stop. Steve took the ticket and drove off, cursing and vowing to get the officer fired.

Word of the encounter quickly spread. Confounded by Bill, Steve admitted that he had mouthed off to the police officers, but claimed that he had every right to do so. Bill told Steve he needed to take two weeks off and get a psychiatric evaluation, or lose his job. That’s when Bill called me.

In my role as a psychiatric consultant on workplace behavioral health matters, I’m often asked to evaluate people whose behavior is about to cost them their jobs. The person being evaluated is always a key source of information, but evaluations of fitness for duty and disability also require more objective reports. So I asked Steve’s law partners what they thought was going on. They reported that Steve had always been tough on people, but there had been a turn for the worse in the past few years. He was more irritable, more abrupt, and no longer seemed to enjoy his work. Clients had asked if Steve was having health problems, especially given his recent behavior.

“Don’t you know who I am?” he demanded to know. “I’m the guy the mayor turns to for legal advice when you clowns get yourselves into trouble.”

“I’m due in court.” One of the officers tersely explained the illegality of running the red light, reckless driving, speeding, and failing to stop. Steve took the ticket and drove off, cursing and vowing to get the officer fired.

“Don’t you know who I am?” he demanded to know. “I’m the guy the mayor turns to for legal advice when you clowns get yourselves into trouble.”

“I’m due in court.” One of the officers tersely explained the illegality of running the red light, reckless driving, speeding, and failing to stop. Steve took the ticket and drove off, cursing and vowing to get the officer fired.

Steve grudgingly acknowledged that things had gotten worse over the past three years. Assertive and demanding by nature, in the past he had felt in control of his world. Now he was always on edge and prone to emotional outbursts. He was exhausted and had lost his motivation. He no longer enjoyed doing things he used to enjoy, a symptom known as anhedonia—Greek for “lack of pleasure.” He was more forgetful and not as accurate or productive as he once was.

“I’m due in court.” One of the officers tersely explained the illegality of running the red light, reckless driving, speeding, and failing to stop. Steve took the ticket and drove off, cursing and vowing to get the officer fired.

Steve grudgingly acknowledged that things had gotten worse over the past three years. Assertive and demanding by nature, in the past he had felt in control of his world. Now he was always on edge and prone to emotional outbursts. He was exhausted and had lost his motivation. He no longer enjoyed doing things he used to enjoy, a symptom known as anhedonia—Greek for “lack of pleasure.” He was more forgetful and not as accurate or productive as he once was.
as he had been, but he wondered if this was just a function of turning 55.

What Flipped the Switch?
It seemed clear that Steve’s sudden and aggressive behavior reflected more than just an unpleasant disposition. A number of physical illnesses can cause such dete-
rminations in behavior. Leading contender,
a lone and in combination, include endocrine disorders like thyroid disease and diabetes, cardiac disease, infectious diseases, neurological conditions, and cancer. But Steve’s primary care physician had given him a clean bill of health, other than moderate hypertension and a 20-pound weight gain over the past several years.

Next on my list was substance abuse, which is notorious for contributing to problematic behaviors. But Steve denied using illegal drugs, misusing prescription medications, or drinking excessively. His physical exam and lab work were consistent with this, as were his partners’ reports. With the obvious physical illnesses and substance abuse ruled out, it was time to consider psychiatric disorders. It was possible that Steve had a personality disorder—a longstanding, maladaptive pattern of experiencing and interacting with the rest of the world. Steve’s interactions with me, the reports from his partners, and his history were all consistent with a personality disorder; or at least a worrisome exacerbation of some very negative personality traits. But Steve’s personality had been the same since he was in college. While his aggressiveness didn’t necessarily make him a pleasant guy, it had served him well professionally. He also had friends and a wife of many years. So the evidence for a full-blown personality disorder was not strong. I needed to focus on what could have caused an exacerbation of his pre-existing traits.

While several psychiatric problems, including depression, might explain Steve’s worsening behavior, his irritability, sad mood, decreased energy, and difficulty sleeping weren’t severe enough to make a conclusive diagnosis.

Too Little Air
It was with the exploration of Steve’s sleep problem that things got interesting. Sleep deprivation can have many physical and mental effects, including impaired cognitive and physical performance, increased errors, decreased immune response, and changes in mood. Disturbed sleep can be both a symptom and a cause of conditions such as depression, bipolar disorder, and changes in personality similar to Steve’s. In some studies, brain scans of severely sleep-deprived individuals are similar to those of psychopaths, people with an extreme form of antisocial personality disorder.

So I asked Steve about his sleeping. He fell asleep just fine, he said, but was restless during the night and woke up feeling unrested, usually with a headache.

"Do you snore?" I asked.
"Let's put it this way," Steve said. "I've had people pound on the walls of hotel rooms at night complaining that I was keeping them awake."

"Does your wife ever notice that you stop breathing while you are sleeping?"
"She flips out when that happens and pokes me to make sure I'm still alive."

Steve was describing classic symptoms of sleep apnea, a condition in which a person either stops breathing entirely or has impaired airflow during sleep, depriving the brain, and the rest of the body, of oxygen. Sleep apnea can cause hypertension, vascular problems, and cognitive and behavioral changes.

In the most common form of sleep apnea, obstructive sleep apnea, the upper airway becomes blocked as muscles relax during sleep, air being forced over the obstruction causes snoring. A variety of factors can cause the condition, including having a short, thick neck; gaining weight; and using substances that cause excessive sleepiness, like medications or alcohol. Not everyone with obstructive sleep apnea looks like Steve, but his physique fit the classic profile. Sleep apnea moved up on my list of possible diagnoses.

Steve’s primary care physician agreed to send Steve for a polysomnogram, an overnight study in a sleep laboratory in which the patient’s airflow, oxygen levels, muscle movements, heart rhythm, and brain waves are monitored. Steve expressed skepticism that he would be able to sleep in a strange place connected to all those machines. But he fell asleep easily and woke up only when the technician entered the room when his oxygen saturation level had repeatedly dropped to 85 percent.

The technician had Steve put on a breathing mask connected to a machine that generates air pressure, helping to keep the airway open. This therapy, called continuous positive airway pressure, or CPAP, ensures that the brain gets enough oxygen. With CPAP in place, Steve’s oxygen saturation was fine. The sleep specialist recommended that Steve continue the treatment at home, and also that he lose some weight and avoid alcohol at bedtime.

Two weeks later, Steve told me he had started feeling better almost immediately. He awoke feeling rested, his headaches were gone, and he felt more on top of things. His wife had even commented that he was calmer and less irritable.

I recommended that Steve return to work. I warned Bill that treatment for sleep apnea would not necessarily reverse Steve’s habit of treating others poorly, but it would give him more control over his behavior. I was hopeful that with clear expectations set on his behavior, the firm would see a new and improved Steve.

My hopes proved to be justified. Six months later, Steve’s mind was clearer, his work had improved, and he was back to mentoring the younger attorneys and serving his clients.
NOT LONG AFTER MIDNIGHT ON JULY 9, 2011, six men descended on a fenced-in field at biovativ, a research facility in the northern German town of Gross Lusewitz. It was a clear, warm Saturday night, and the 115-acre farm was lit by a half moon.

Moving quickly, the men surrounded the night watchman. Shining their flashlights in his face and threatening him with pepper spray and clubs, they frisked him, took his flashlight and keys, and smashed his cell phone. Then they headed directly for their target, a potato patch the size of a tennis court. Within minutes, the potatoes—part of a research project run by the nearby University of Rostock to see if rabbit vaccines and plastic polymers could be grown in plants—had been ripped out of the ground or trampled.

Two nights later, at a farm 100 miles to the south, the scene repeated itself almost exactly. This time, a dozen masked men overpowered two guards at the Oplingen Plant Science Garden, hopped a waist-high wire fence and trashed a plot of genetically modified potatoes, along with part of a nearby stand of transgenic wheat. As police cars sped toward the farm, the raiders melted into the night. "It's years of lab work and greenhouse work destroyed," says Uwe Schrader, one of the farm's two managers. "There won't be any results.

Both the farm in Gross Lusewitz and the Oplingen fields are paid by multinational seed and chemical companies like Monsanto, BASF, and Syngenta to conduct field trials with genetically modified crops. But instead of targeting corporate greed, these raids signaled something else. The wrecked potato trials, proof-of-concept experiments funded with public money and years away from any commercial application, were sponsored by university biology departments. "They targeted these particular trials to weaken research in Germany," says Kerstin Schmidt, CEO of biovativ.

The irony is thick because techniques used to insert genes from one organism into another were developed in European university labs more than 30 years ago, and the first stabs at commercial cultivation of so-called "transgenic" crops occurred in Europe's fields. Yet genetically modified organisms (GMOs) are now restricted from cultivation in Austria, Hungary, France, Luxembourg, Germany, and Greece. Of the
IT'S YEARS OF LAB WORK AND GREENHOUSE WORK DESTROYED. THERE WON'T BE ANY RESULTS.” – UWE SCHRADE

395 million acres of so-called “biotech” crops planted globally in 2011, 282,911 were in Europe, according to the International Service for the Acquisition of Agri-biotech Applications, a pro-GMO nonprofit. That’s 0.07 percent of the world’s total. American farmers, on the other hand, planted 170 million acres of transgenic crops last year; 90 percent of the soy grown in the U.S. is genetically modified. Brazil and Argentina grew tens of millions of acres of genetically modified cotton, soy, and corn. India is climbing onto the GMO bandwagon as well.

For the labs that started it all, the impact has been devastating, "Scientists develop a fruit and have something that works and they’re excited about, and they simply can’t afford to get the testing through,” says Terri Raney, a senior economist at the Food and Agriculture Organization in Rome.

THE PUBLIC FACE OF PROTEST

For a hard-core group of protesters combating genetically modified crops through whatever means necessary, that’s excellent news. Blue-eyed and burly, beekeeper Michael Grodm is the face of Germany’s best-known anti-GMO campaign, a loosely organized network of activists called “Gendreck Weg,” or “Gene Trash Gone.” Since 2005, Gendreck Weg has organized well-publicized “field liberations” aimed at destroying open-air tests of genetically altered crops.

Drawing on the time-tested tactics of the civil rights movement, Grodm made sure “liberations” were announced months in advance; demonstrators arrived in photogenic convoys of tractors, wearing hazmat suits or beekeeper’s hoods. After ripping up plots of genetically altered corn, wheat, or potatoes, they sometimes planted organic varieties, calling it a “corn exchange program.”

“We had to go out into the fields and do it in a very public way, so the population wouldn't see us as criminals,” Grodm says. “Hundreds of police show up, and it's interesting for the press too.”

Activists made a point of styling around afterward, hoping to be apprehended. Since his first arrest, in 2008, Grodm has spent more than a month in jail for everything from trespassing and contempt of court to refusing to pay token fines. He’s also been served with restraining orders from U.S. agribusiness giant Monsanto, something he was happy to violate. “If they send me to jail again, I’ll go in smiling, and come out smiling,” he says.

I met Grodm at Tomnord Castle, a dilapidated stone fortress on top of a hill near Erfurt, where he lives communally with about 60 other people. A dirt road winds up from a valley full of nearly pruned farm fields to the castle’s dry moat. After a lunch of lentil soup, brown rice, and home-pressed apple juice in the castle’s communal dining room, I follow the beekeeper-turned-activist to a small gatehouse where he lives with his partner and their son.

As his towheaded, red-cheeked toddler sleeps soundly on the couch next to him, Grodm tells me biotechnology research is nothing more than a stealthy effort to wipe out Europe’s organic farmers—and beekeepers like him. "I don't think it's a sincere effort to do science," he says. "Their strategy is to contaminate things here to open the door for GMO agriculture. If I were a scientist that really wanted to study this, what would I do? I'd go to America, where everything's already contaminated.”

Grodm accuses labs like biowatch of deliberate sloppiness, saying they intentionally mislabel test plots and allow seeds and pollen from experimental plants to contaminate nearby fields. The beekeeper says he’s afraid that once genetically altered plants are set loose in the European environment, there
will be no way to call them back. "There's no good gene technology. It's like atomic energy—once you open the door, you can't close it," he says. "We can't get rid of it once it's out in the world."

I ask Grodzik if Gendreau's job had anything to do with the recent nighttime assaults in Gross Luessevitz and Oplingen. He smiles and leans back on the couch. "That's not our thing, but you can't really control it," he shrugs. "I can only tip my hat to the people who did this and congratulate them. They probably prevented a much greater form of violence by keeping these plants from contaminating humanity's seed stocks."

WHO NEEDS ANOTHER GREEN REVOLUTION?

Even though decades of research haven't turned up any conclusive evidence that genetically modified plants pose a health risk, barely a quarter of Europeans are willing to see them become part of the food supply. Many see no need: The continent's population is expected to peak in just 25 years, and dwindle after that.

But Europe is an exception. The world is fast approaching a breaking point. Already at 7 billion, the global population is expected to increase by 2 billion to 3 billion in the next 40 years before leveling off. With much of the world's prime farmland already under the plow, there's not much wiggle room to feed those extra mouths. The Food and Agriculture Organization of the United Nations estimates that by 2050 the world will need to produce 70 percent more food, including an additional billion tons of cereals, to keep up with population growth.

We have been here before. In the years after World War II, basic principles of public health and sanitation dramatically extended life expectancy around the world. One consequence was an equally dramatic shortfall in food supplies.

One man had a lot to do with changing that. Beginning in 1944, Iowa-born biologist Norman Borlaug spent nearly 30 years in Mexican fields, crossing different kinds of wheat strains by hand. Using conventional breeding techniques, Borlaug's crucial breakthrough was creating sturdy-stalked dwarf wheat with high-yielding varieties, resulting in a plant that was both extremely productive—when given ample fertilizer—and strong enough to hold up under the weight of large clusters of grain.

Borlaug's modifications increased the productivity of Mexican wheat farmers sixfold over traditional varieties. Agronomists went on to breed "semi-dwarf" rice plants using the same principles, fundamentally altering a crop that half the world relies on for daily sustenance. The world went from food shortage to food surplus; meanwhile, its population more than doubled.

Admirers called these breakthroughs the Green Revolution. But not everyone was pleased. The new crop strains were dependent on mechanization, controlled irrigation, and artificial, petroleum-based fertilizers for their astonishing productivity, making it hard for small farmers to compete and dramatically increasing the use of pesticides. In many cases, the hybrid seeds had to be repurchased from seed companies each year, helping to turn a handful of American and European seed breeders into corporate giants.

The excesses of the Green Revolution were decried by activists from the start. "In perceiving nature's limits as constraints on productivity that had to be removed," Indian physicist Vandana Shiva wrote in 1991, "American experts spread ecologically destructive and unsustainable agricultural practices worldwide."

Others have argued that the Green Revolution saved hundreds of millions of people in several nations from starvation as their numbers outstripped food production. In 1970, when Borlaug was awarded the Nobel Peace Prize, he suggested that the search for more

ANTI-GMO GRASS-ROOTS EFFORT GAINS GROUND IN U.S.

Anti-GMO food activists in the U.S. don't stage late-night guerrilla raids, vandalizing farms snatched in harvest gear. Instead, they're more likely to patrol the corridors of power in sport jackets, lobbying lawmakers for oversight or suing biotech companies in court.

But even without these tactics, American activists, including a host of scientists, have been raising skepticism about GMO foods. "The science just hasn't been done," says Charles Benbrook, an agricultural policy expert at Washington State University and a leading voice of dissent.

Today, about 10 percent of the corn, soy, and cotton grown in the U.S. are genetically modified to be either resistant to pests or tolerant of herbicides, including the popular weed killer Roundup, so that farmers can spray throughout the growing season without harming crops. While the harvest from most of these crops is used to feed cows, pigs, and chickens, some genetically engineered corn and soybeans have made their way into the human food chain and are used to make tortillas, corn syrup, and even gelatin for coloring. Today, about 75 percent of processed foods contain genetically engineered ingredients, a use change that Gary Hirshberg, chairman of the activist coalition Just Label It, calls an "unprecedented agricultural experiment being conducted at America's dinner tables."

As a result, thousands of products containing foreign or altered genes have been eaten by millions of people. But since these products weren't labeled or tested by impartial scientists, there is no way to trace back potentially adverse health consequences, activists say. A handful of scientists even speculate that genetically modified crops and the pesticides used to cultivate them may be partly responsible for the increased incidence of illnesses such as asthma, allergies, ADHD, and gastrointestinal disorders. A few animal studies have raised rodent flags, including some showing intestinal damage; structural changes in the kidneys, pancreas, and spleen; infertility; low birth weights in mice; and cancers in rats. But proving a causal
 productive crops was never-ending. "We may be at high tide now, but ebb tide could soon set in if we become complacent and relax our efforts," he said.

THE NEXT BIG THING

By the 1980s, scientists had declared gene modification the next big thing. The breakthrough heralding the new age came from Belgium, where Ghent University biologist Marc van Montagu and Jeff Schell were studying a bacterium called Agrobacterium tumefaciens. Shaped like a tiny pill, the bacterium lives in the soil and causes infected plants to grow what amount to plant tumors, often as large as golf balls. Researchers showed that A. tumefaciens was altering the genetic code of infected plant cells by lending them genes, causing them to grow out of control. No one wants to give plants tumors. But if two entirely different organisms—a bacteria and a plant—could swap genes, then the potential for altering crops directly by gene transfer was vast.

Today, van Montagu runs a small institute out of a paper-strewn office at Ghent University dedicated to producing genetically modified crops for the developing world. A wood statue of Gandhi sits on his desk. High on a bookshelf is a bust of his great-grandfather, a founder of Belgium's Socialist party. As a student in the early 1950s, van Montagu followed in his footsteps, leading Belgium's student socialist movement and taking trips to communist Poland, Czechoslovakia, and Russia. With a lilting Flemish accent, thick glasses and a bucktoothed smile, the 79-year-old has the energy of a much younger man, eagerly reminiscing about his lab's heyday in the 1970s.

Years of research confirmed the team's early hunch. Inside each bacterium were structures called plasmids, free-floating strands of genetic code. The A. tumefaciens plasmids broke into the plant cell and penetrated its DNA, inserting up to 25,000 base pairs of its own. The plasmid of plasmid DNA altered the cell's behavior, hijacking it and causing uncontrolled growth.

Understanding how the crown gall bacteria altered plant cells without destroying them was a critical breakthrough, one that opened an entirely new set of possibilities. It meant that researchers could take out the plasmid DNA that caused crown galls and replace it with carefully selected bits of genetic code from other organisms. Using the bacteria’s backbone—plasmids as delivery vehicles, new genes confering valuable traits could be slipped into a plant’s DNA. With enough tinkering, it was theoretically possible to add the massive size and speedy growth of the African manioc plant to what, say, drought-tolerant rice.

To test the discovery, van Montagu drew on a popular organic pesticide derived from another bacteria, Bacillus thuringiensis or Bt, which is still sprayed on organic farms today. Bt produces a protein that is deadly to a very narrow category of pests, including the corn boron worm. Van Montagu first isolated the DNA responsible for producing the bug-killer protein, then spliced it into the genome of A. tumefaciens. He used this genetically altered version as a Trojan horse to implant the protein into tobacco plants, which could then manufacture their own pesticides.

In the three decades since van Montagu’s breakthrough, transgenic crops have been adopted faster than any technology in the history of agriculture. Between 1996 and 2011, the number of connection, especially in humans, is tricky. "These studies raise questions that demand answers, but the government has chosen thus far not to do that," Benbrook says.

In fact, the FDA has ruled that because DNA is in every living organism, crops engineered with added genes are "substantially the same" as other foods and are no different from crops genetically modified through conventional breeding techniques. But that point of view rings hollow to some scientists.

"There is no credible evidence that GMO food are safe to eat and no significant safety testing is required by FDA," coauthors biologist David Schubert of the Salk Institute of Biological Studies in La Jolla, California.

Yet a litmus test of sorts may be here soon. Later this year, sweet corn, which is fortified with natural insecticides built into its DNA, will debut on supermarket shelves in the U.S. "The corn is the first GMO food crop made for human consumption that people will consume in large quantities, so we'll see what effect they have," Benbrook says.

What we do know is that constantly spraying genetically modified crops with Roundup has increased our dependence on this toxic weed killer and spawned a new generation of herbicide-resistant superweeds, Benbrook points out. These renegade weeds are increasingly plaguing farmers and have driven a 7 percent increase in herbicide use since 1996.

The nascent anti-GMO movement is pushing back. In September 2011, Iowa’s Republican Governor Terry Branstad signed into law a bill that requires all food products containing genetically modified organisms to be labeled as such. But critics accused Branstad of bowing to the right-wing bloc and setting the state back. The law was repealed in February 2012.

Chemical plants like Monsanto, DuPont, Dow and Syngenta have spent billions on their own lobbying efforts, and the outcome is too close to call.

The future of genetically modified foods will depend on how they are labeled, whether they are viewed with mistrust or accepted as mainstream, and whether consumers can be reassured of their safety.
acres planted with genetically modified crops worldwide went from 4 million to 395 million, a 9.000 percent increase in the space of 15 years.

GMO-FREE ZONE
Yet Europe remains an island of determined opposition. At an experimental greenhouse visited, not far from van Montagu's Ghent University office, growing experimental transgenic rice requires biohazard protocols that seem more appropriate to culturing Ebola. Seedlings are individually bar coded and transported in locked black trunks emblazoned with a biohazard sign. Irrigation water is sterilized using ultraviolet light and trucked to purification stations. Harvested plants are steamed for two hours at over 200 degrees Fahrenheit to make sure there's no chance of a seedling surviving.

That's the way organic farmers want to keep it. Back in Germany, I visit Volker Rottstock, a sturdy, white-haired farmer who greets me at the door of his house wearing a navy T-shirt and blue work pants: His dog, a black and white Munsterlander, is by his side. Rottstock's 400 acres outside Berlin are devoted to potatoes, grain, and grass for his herd of 100 cattle. A sign in German on the barnyard gate reads, "We Work Without Genetic Technology."

On the cracked concrete floor of his barn, the year's inseeded crop is spread out in a layer a few inches thick. "When I can, I dry seeds without electricity. I use the sun, the wind," he says, leading me past an ancient East German Trabant car and into an Ivy-covered brick farmhouse sporting new solar panels on the roof.

In 2006, word got around that one of Rottstock's neighbors was thinking about planting a dozen acres of transgenic corn. It felt like a direct threat. If transgenic pollen drifted into his organic-certified fields, Rottstock would be unable to sell his potatoes and wheat at the premium that organic food commands. He helped rally locals to pressure his neighbor into calling off the crop and gathered signatures from some 200 acres farmers who have pledged to avoid transgenic crops as well.

Gene Trash Gone leader Grenell agrees there's no room for compromise: Europe must be kept biotech-free, he insists, or he and other small organic producers like Rottstock will be wiped out. "These companies keep calling for coexistence, but I call it XO-existence," the beekeeper says. "They just want to knock us out—it's the biological equivalent of locking a wolf and a sheep in a pen together to see which one survives."

The sheep has managed to prevail. In January 2012, Europe's anti-biotech movement won a significant battle, though not the war. In the wake of the activists' attacks, German chemical giant BASF raised a white flag, announcing it would move most of its field trials out of Europe and halt efforts to develop crops intended for the European market alone.

POLITICAL PLANT SCIENCE
As transgenic crops have spread around the world without the apocalyptic environmental consequences activists initially foretold, objections to the technology have shifted away from scientists. When I asked European parliamentarian Martin Hauling, an outspoken anti-GM activist who owns an organic farm and dairy in central Germany, whether science would ever be able to prove to him transgenic crops were safe, he said I was thinking about planting a dozen acres of transgenic corn. It felt like a direct threat. If transgenic pollen drifted into his organic-certified fields, Rottstock would be unable to sell his potatoes and wheat at the premium that organic food commands. He helped rally locals to pressure his neighbor into calling off the crop and gathered signatures from some 200 acres farmers who have pledged to avoid transgenic crops as well.

Gene Trash Gone leader Grenell agrees there's no room for compromise: Europe must be kept biotech-free, he insists, or he and other small organic producers like Rottstock will be wiped out. "These companies keep calling for coexistence, but I call it XO-existence," the beekeeper says. "They just want to knock us out—it's the biological equivalent of locking a wolf and a sheep in a pen together to see which one survives."

The sheep has managed to prevail. In January 2012, Europe's anti-biotech movement won a significant battle, though not the war. In the wake of the activists' attacks, German chemical giant BASF raised a white flag, announcing it would move most of its field trials out of Europe and halt efforts to develop crops intended for the European market alone.

POLITICAL PLANT SCIENCE
As transgenic crops have spread around the world without the apocalyptic environmental consequences activists initially foretold, objections to the technology have shifted away from scientists. When I asked European parliamentarian Martin Hauling, an outspoken anti-GM activist who owns an organic farm and dairy in central Germany, whether science would ever be able to prove to him transgenic crops were safe, he said I was

RISK & RESPONSE
With debate over genetically modified foods so fierce, it's difficult for objective science to remain above the fray. Here, four recent studies illustrate the conflicting viewpoints, which leave basic questions of safety and effectiveness under contention. **Gillian Cohnson**

<table>
<thead>
<tr>
<th>STUDY</th>
<th>RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRO-GMO: A review of 24 studies of GM crops, mostly corn and soy, found that they &quot;do not suggest any health hazards&quot; in rats, mice, or other animals. The studies monitored growth, blood chemistry, tissue health, and a number of other characteristics affecting mortality; they found only minor differences between GM and non-GM groups, with no toxic effects.</td>
<td>Each gene-crop-environment combination must be analyzed on its own merits and risks,&quot; says Doug Gurian-Sherman of the Union of Concerned Scientists, so it's impossible to generalize these results to future GM crops.</td>
</tr>
<tr>
<td>ANTI-GMO: A two-year study found that rats fed GM Roundup-tolerant corn had higher rates of tumors, hormonal abnormalities, and other issues, including kidney and liver problems.</td>
<td>A review by the European Food Safety Authority concluded that the study was &quot;of insufficient scientific quality for safety assessments,&quot; citing small study groups, inadequate controls, and other methodological concerns.</td>
</tr>
</tbody>
</table>
| PRO-GMO: Monitoring of fields across the Midwest showed that corn altered to produce the natural insecticide manufactured by Bt bacteria suppresses corn borers, a major pest, over a wide area. As a result, nearby conventional corn is also protected. | The region-wide suppression of corn borers is a benefit, but a small one in terms of productivity," says Gurian-Sherman. "My 2009 report found about a 3 to 4 percent yield benefit from Bt insect resistance. That is OK, but is much less than from breeding and improved agronomy."
| ANTI-GMO: Reliance on herbicide-resistant crops has contributed to a global proliferation of resistant weeds, which researchers predict will lead to increased herbicide use and an environmentally costly arms race against the leafy pests. | The issue of herbicide-resistant weeds is not essentially a problem related to genetic modification. It is more a problem of a type of agriculture lacking proper management. Definitely using a short crop rotation with always the same herbicide precocises the development of tolerant or even resistant weeds. "—Hans-Jörg Jäcksen, Leibniz Universität Hannover |
GROWING CONCERNS: GMO CROPS WORLDWIDE

In 2011, genetically modified crops were cultivated commercially in 29 countries. The United States led the way with 170.5 million acres of commercial genetically modified crops grown, while Brazil, Argentina, India, and Canada each grew more than 27.4 million acres.

But ecologists, in particular, express misgivings about transgenic crops because from their perspective, molecular biologists have a narrow view of how plants work outside the lab. By ignoring the potential that transgenic crops have to crossbreed with wild relatives, they risk imposing a monoculture on the diverse biological world. By encouraging farmers to continue planting just a handful of crop strains, critics say widespread use of a few varieties of GMO crops might limit genetic diversity, and thus the ability to survive in altered form when pests or other hazards unexpectedly arise.

On top of that, critics say GMO crops have not been proven universally safe, and they must be evaluated one by one. Doug Gurian-Sherman, senior scientist at the Union of Concerned Scientists in Washington, D.C., and a former regulator for the Environmental Protection Agency, likens traditional breeding to rearranging the deck chairs on a familiar ship. "In most cases we're working with varieties where the genes and their products have been consumed for millennia," he says, although even then, dangerous traits can emerge.

Genetic engineering, on the other hand, can introduce genes that have never been in the food supply, with unknown consequences. "Genetic engineering is fundamentally different. It's disingenuous to say this is a new and more precise way to do breeding," Gurian-Sherman says. "I don't think it's as inherently risky as some people say, but I do think the risks are higher."

THE TRAIT MILL GRINDS ON

Sitting in the university conference room, looking pale and a little sad under the fluorescent lights, van Montagu seems dispirited when I ask him how things could have gone so wrong for the
technology he helped pioneer. "For a scientist, science looks obvious," he says. "I guess you can say we were naïve."

Naïve, and unlucky. Wellesley College agricultural policy specialist Robert Paarlberg says transgenic plants may have been the victims of bad timing. In spring 1996, Britain was in the middle of the mad cow crisis. Food safety officials in Britain had assumed consumers that bovine spongiform encephalopathy, or mad cow disease, could not be transmitted to humans by eating beef from sick cows. They were wrong. Hundreds of thousands of cows were slaughtered and incinerated, and dozens of people were infected with a deadly brain-wasting disease. "Europe was traumatized," Government regulators told consumers they had nothing to fear, and they did," Paarlberg says.

That same spring, Monsanto began selling farmers genetically modified seeds. European consumers baulked. Environmental groups labeled the new crops "Frankenfoods," tying the technology to corporate behemoths like Monsanto and emphasizing the risks of biotech.

While the first transgenic plants sparked fear and controversy, suspicion seemed to stop at the fields' edge. The same basic methods are used to coax bacteria and algae to synthesize plastics and biofuels. The pharmaceutical industry uses genetically modified bacteria and animals to produce insulin, vaccines, and a wide variety of drugs. Such applications, Paarlberg argues, are widely accepted because they provide clear benefit to consumers in the form of green fuel or reliable medicine.

"We have no problem with genomics," says Karuna Chandrasekaran, a campaigner for the London-based Friends of the Earth. "Our problem is with their application in GMOs."

Perhaps that is because genetically modified crops, which boost productivity and lower cost of chemicals and fuel, benefit multinational corporations and farmers, but not consumers themselves. And to scientists like Jacobson and van Montagu, that is most frustrating of all. While the European Union has spent some $400 million in the past 25 years on biotech crop research, the vast majority has gone toward risk-assessment studies and not improving the crops themselves. Between legal expenses and the high-security field trials needed to comply with European safety laws—not to mention the risk that field trials will be destroyed—bringing a product to market can cost upward of $15 million, making developing GMOs so expensive only profit-driven agricultural businesses can afford it.

If they're going to fulfill their promise, next-generation transgenics will have to do more than just protect plants from pests or weeds: the race is on to create super crops that will be more fruitful while resisting droughts or floods. Others might be engineered to include nutrients like beta carotene, iron, and vitamin A. Instead of one gene to fight off insects or disease, crops will be engineered with "stacks" of resistance genes to prevent pests from evolving resistance to a single approach.

All that will require far more knowledge about how genetic modification changes a plant. In the effort to get there, Europe could still be a hub. On a frosty March day, I pull up to a sprawling, nondescript greenhouse in Ghent. Pietr Puzio, an amiable Polish biologist, asks me to leave my camera in the car. He hands me a lab coat, safety glasses, and disposable paper booties and usher me into what may be the world's most sophisticated greenhouse.

As we step inside, I'm hit by a blast of tropical heat. Plastic conveyer belts running along waist-high steel platforms wind through the 32,000-square-foot facility. A small boombox plays Bob Marley's "Could You Be Loved" as workers in blue coveralls transplant fragile rice seedlings to transparent plastic pots filled with a proprietary soil mixture. Despite the chill outside, I soon find myself sweating as I follow Puzio down rows of grass-green plants. Inside, it's at least 82 degrees Fahrenheit, ideal for genetically modified rice.

The biotech facility belongs to a subsidiary of BASF Plant Science, and despite the European locust, the chemical giant has not pulled out. Around the clock, 365 days a year, about 8,000 plants at a time make their way through the greenhouse, each individually tracked with radio-frequency ID chips tucked into their transparent containers. The plants periodically snake through dressing-size cabinets, where a suite of imaging equipment captures the plants' growth from seven angles. "Every week they're photographed from every corner and every side, like models on the catwalk," Puzio says with pride.

Each year, the facility can analyze the changes wrought by tweaking up to 1,000 genes, each one expressed and evaluated in over 100 different model plants. Cerevally named the TraitsMill, it is the centerpiece of BASF's effort to breed the next generation of genetically modified crops. The information gathered from these rice plants will be used to create drought-resistant corn and crops that will grow in depleted soil, perhaps on marginal land in the United States or Asia. If the rice does the right way, BASF will make a lot of money.

But outside, a cold wind is blowing. Whatever comes out of this lab will likely never drink a Belgian rain, or spread its leaves under the German sun. And someday soon, the researchers here—along with their colleagues across the continent—will switch off the lights and move on to greener pastures.

Andrew Curry is a journalist and freelance foreign correspondent based in Berlin, Germany.