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Taking Science Seriously in the GM Debate

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Science in crisis

If there is one thing that distinguishes the Third World from the industrialised countries, it is that they take science a lot more seriously than we do in the GM debate.

I was researcher and university lecturer of genetics throughout the mid-1970s to the early 1980s when new discoveries on the fluid genome made headlines every week. Researchers back then were building a new paradigm, dispelling once and for all the notion that a gene is constant and independent of context. The thought that a gene could be patented as an

invention probably never crossed their mind. And if it did, they would have dismissed it as a joke. Craig Venter of Celera may have only just discovered that genetic determinism cannot deliver the goods after he's sequenced the human genome. But many of us knew that genetic determinism had died with the revelations of the fluid genome, if not before [1]. And now, almost two decades later, science is in crisis in more ways than one.

The paradigm change that should have occurred, did not. On the contrary, the scientific establishment remained strongly wedded to genetic determinism, which has misguided genetic engineering, making even the most unethical applications appear compelling, such as 'therapeutic' human cloning, for one [2]. Bioethics became a contradiction in terms as rampant commercialisation of science took hold.

Since the 1980s, preoccupation with patenting and start-up companies has compromised the quality of molecular genetics research, stifling basic science and innovation, and failing to serve the public good. Worse still, many scientists are consciously or unconsciously ignoring scientific evidence of the hazards. I got involved in the genetic engineering debate in 1994, to try to inform our policymakers and the public, and to start debate and discussion from within the scientific community.

For the past seven years, I have had to follow developments in genetic engineering science much more carefully and extensively than many of the practitioners, only to find that all my fears concerning the problems and dangers of genetic engineering are being confirmed. I shall highlight some of these before going to discuss what needs to be done.

Genetic engineering superviruses

The top news in the Jan. 13 issue of the *New Scientist* [3] was on a deadly virus created accidentally by researchers in Canberra Australia, who were trying to genetic engineer a contraceptive vaccine for mice [4]. They spliced a gene for the protein interleukin-4 (IL-4) into a relatively harmless mousepox virus in the hope that IL-4 would boost the immune system. When they injected the recombinant virus into mice belonging to a strain genetically resistant to mouse-pox virus, all the mice died. IL-4 suppressed both natural killer cells and cytotoxic lymphocytes responses to viral infection. The recombinant virus also killed 50% of the genetically resistant mice that were immunized against mouse-pox virus.

That is not all. The IL-4 gene, spliced into the vaccinia virus, was found to delay clearance of the virus from experimental animals, and to undermine the animals' anti-viral defence [5, 6]. Vaccinia and mouse-pox both belong to the family that contains the human smallpox virus, raising the spectre of biological warfare. But the far greater danger lies in the unintentional creation of deadly pathogens in the course of apparently innocent genetic engineering experiments. Some scientists are already creating viruses deliberately in their laboratories, just to show it could be done, or in the course of cloning existing viruses [7]. And dangerous recombinant viruses and bacteria may also be inadvertently created in making vaccines against AIDS, as Yugoslav virologist Veljkovic has been warning since 1990 [8].

The *New Scientist* editorial [9] accompanying the report remarked that five years ago, when

biomedical researchers were asked if genetic engineering could create "a virus or bacteria more virulent than nature's worst", they replied it would be "difficult if not impossible".

Some of us have been warning of 'accidents' such as this for at least the past six years. The basic tools of genetic engineering are bacteria, viruses and other genetic parasites that cause diseases and spread drug and antibiotic resistance. All that fall into the hands of genetic engineers are exploited. Genes from dangerous agents, including antibiotic resistance genes, are profusely mixed and matched, or recombined. As every geneticist should know, recombination of genetic material is one of the main routes to creating new strains of bacteria and viruses, some of which may be pathogens. (The other route is mutation.) Moreover, the predominant orientation of genetic engineering in the past two decades has been to design artificial GM constructs and vectors that cross species barriers and invade genomes, both of which will enhance horizontal gene transfer and further increase the chance for recombination.

We published a detailed review on the possible links between genetic engineering and the recent resurgence of drug and antibiotic resistant infectious diseases in 1998 [10]. We were by no means the first. Those who pioneered genetic engineering declared a moratorium in Asilomar in the mid- 1970s precisely because they were concerned about this dire possibility. Unfortunately, overwhelming pressures for commercial exploitation cut the moratorium short. The scientists set up guidelines, based largely on assumptions that have all fallen by the wayside as the result of new scientific findings. The two most important findings are the persistence of nucleic acids in all environments including the gut of animals, and the ease with which nucleic acids can get into all cells, especially those of human beings, as shown in so-called gene therapy research [11].

Instead of tightening the guidelines, our regulators have relaxed them. Transgenic wastes are being recycled as food, feed, fertilizer and landfills under the current EC Directive on Contained Use [12], and I would not be surprised if this applies also in the US. There is a lesson to be learned from the 650 or more adverse reactions associated with gene therapy trials, including several deaths. The same kinds of constructs are made, whether it is to genetic engineer human beings or plants and animals, and the same crude first generation technology is used.

The instability of transgenic lines

The instability of transgenic lines has been well known since 1994, particularly in connection with gene silencing. This not only affects agronomic performance, but also safety. We have drawn attention to the *structural* instability of GM constructs in general, which may enhance horizontal gene transfer and recombination, especially because the cauliflower mosaic virus (CaMV) 35S promoter, present in practically all GM crops already commercialized or undergoing field trials, actually has a recombination hotspot. We raised our concerns in a series of scientific papers [13-16].

In the course of debating with plant molecular geneticists in UK's top research institute, the John Innes Centre (JIC), we discovered that the CaMV 35S promoter is active, not only in all plants, bacteria, algae and yeast, but also in animal and human cells [17, 18]. None of our

critics was aware that the promoter is active in human cells, including a molecular geneticist on the UK Agriculture & Environmental Biotechnology Commission set up to oversee our farmscale field trials [19].

This year, researchers in JIC admitted in their annual report that GM crops are unstable and prone to recombination. But when we pointed this out [20], they issued a strong denial, and accused us of ignoring one of their papers where they claim to have demonstrated that transgenic rice lines are stable. I have since reviewed that paper in detail [21] and concluded, "A generous interpretation of the data presented would suggest that 7 out of 40 (18%) transgenic rice lines may be stable to the R3 generation." In other words, at least 82% of the lines are unstable. That paper is not at all exceptional in making claims in the abstract, and often in the title, which are not supported by the evidence presented [22]. No reply has yet come from the JIC since. My colleague, Prof. Joe Cummins has summarised more up-to-date literature showing that all GM crops may be unstable [23].

Roundup Ready soya has consistently performed less well than non GM soya over the years, and this year's seeds are experiencing problems in germination, according to a report from the University of Missouri [24].

Terminator crops at large

Last December, I was asked to act as expert witness in defence of citizens who have taken civil action against GM crops which they strongly believe to be a threat to health and biodiversity. Among the crops were GM oilseed rape varieties used to produce F1 hybrids belonging to AgrEvo UK (now Aventis). At the time, I was also preparing a joint submission, with two other scientists, to the consultation document, "Guidance on Best Practice in the Design of GM Crops" put out by the UK Government's Advisory Committee for Release to the Environment (ACRE). One of the main 'enabling technologies' for 'best practice' suggested in the document is precisely Agrevo's seed/pollen sterility system, for it prevents GM gene flow.

It soon dawned on us that the GM oilseed rape lines undergoing field trials in the UK are engineered with 'terminator technology' - so named by critics because it renders harvested seeds sterile - for no other reason than to enforce corporate patents on GM seeds. Not only that, according to AgrEvo's application, similar crops produced by the company Plant Genetic Systems (PGS), a subsidiary of AgrEvo, have been undergoing field-trials in Europe since the beginning of 1990.

In the US, similar male sterile lines engineered with the 'terminator-gene', barnase have been tested at least as early as 1992. There have been 115 field trials, the vast majority done without risk assessment, as the first environmental assessment came up with 'FONSI' -- Finding of No Significant Impact. Crops modified for male sterility include rapeseed, corn, tobacco, cotton. Brassica oleracea, potato, poplar, chicory, petunia and lettuce. The USDA commercial release data include 4 crops with barnase: a corn and a canola by AgrEvo, a chicory by Bejo, and another corn by Plant Genetic Systems.

Separately, the other genetic component in terminator crops, site-specific recombinase, has

also been engineered into corn and papaya, and there have been 14 field trials between 1994 and 1998, with no environmental impact assessment at all.

There are more than 150 US patents listing barnase or site-specific recombination or both, the oldest, on site-specific recombinase, going back to 1987.

The first terminator patents that came to public attention were those jointly owned by US Department of Agriculture and Delta and Pine Land Company, which Monsanto had intended to acquire. The novelty in those patents is the proposal to combine the terminator-gene system with the site-specific recombinase system, giving the company complete control over the hybrids as well as proprietary chemicals that control gene expression.

As a result of universal condemnation and rejection, Monsanto had announced it will not commercialise terminator crops, to everyone's relief. Research and development, however, have continued unabated. Everyone has assumed such crops only exist in theory, when they have been out there for more than 10 years.

It is no coincidence that simultaneous consultation went on in the United States on the USDA-Delta and Pine terminator patents. The USDA has since committed itself to commercial development of the technology, and, like the UK ACRE, also argued in its favour because it could prevent GM gene flow. But it cannot [24], because male sterile lines will be pollinated by non GM crops, and there is no way to prevent horizontal gene transfer.

On the contrary, the increased complication of the constructs may enhance horizontal gene transfer and recombination. The genes and gene products themselves are also known to be harmful. The terminator-gene barnase kills cells by breaking down RNA, an intermediate in the expression of all genes. The recombinase, in theory, breaks and rejoins DNA at specific sites, but is far from accurate and can scramble genomes. A male transgenic mouse engineered with only one copy of Cre recombinase was 100% sterile, because the recombinase enzyme managed to scramble the genomes of both daughter spermatids when they are still connected by a cytoplasmic bridge [25]. The mouse genome does not even have the *lox* sites recognised by the Cre recombinase.

Terminator insects give wings to genome invaders

The US Department of Agriculture has approved field release of GM pink bollworms this summer, made with a mobile genetic element, *piggyBac*, already known to jump many species. The element was first discovered in cell cultures of the cabbage looper, where it caused high mutations of the baculovirus infecting the cells, by jumping into the viral genome. In experiments in silkworms, researchers already found evidence that the inserts were unstable, and had a tendency to move again from one generation to the next [26].

"These artificial transposons are already aggressive genome invaders, and putting them into insects is to give them wings, as well as sharp mouthparts for efficient delivery to all plants and animals... The predictable result is rampant horizontal gene transfer and recombination across species barriers. The unpredictable unknown is what kinds of new deadly viruses

might be generated, and how many new cases of insertion mutagenesis and carcinogenesis they may bring..." [27].

"Food biotech is dead"

I have presented only a small fraction of the scientific findings indicating problems and dangers specific to genetic engineering, which both the practitioners and regulators are ignoring or dismissing. These and other concerns have persuaded more than 410 scientists from 55 countries around the world to sign an Open Letter to all Governments demanding a moratorium on environmental releases of GMOs because they are unsafe, and a ban on patenting life-forms and living processes because those patents are unethical. They also demand support for non-corporate, sustainable, organic agricultural methods that can truly bring food security and health for all (www.i-sis.org.uk).

Since we launched the Open Letter two years ago, the terms of the GM debate have shifted. It is no longer a moratorium that is needed. GMOs, as currently made, are unsafe and unsustainable, as well as immoral. We must abandon GM crops and all other attempts to genetic engineer plants, animals and human beings with a technology that is widely acknowledged to be unreliable, uncontrollable and unpredictable.

Even the corporations are coming around to the view that "Food biotech is dead" [28]. One by one, Aventis, Monsanto and Syngenta have announced they will concentrate on genomics and marker assisted conventional breeding. Though meanwhile, they are still forcing the world, especially the Third World to accept GM crops.

But the whole world is in revolt. The governments of Thailand and Sri Lanka, among others, have banned GM crops and GM imports. In Indonesia, armed guards had to be sent to protect Monsanto's shipment of cotton seeds, which have already been shown not to perform as well as the indigenous non GM variety [29]. In the Philippines, mass demonstrations are taking place against GMOs and the International Rice Research Institute (IRRI) by MASIPAG (Farmer Scientist Partnership for Development) and other ngos. They condemn IRRI for restructuring sound traditional practices over the past 40 years to make farmers dependent on chemical inputs produced by corporations, the same corporations that are now forcing GMOs on farmers with the help of IRRI [30]. People are demanding farmer's rights over the genetic resources in the collection and genebanks of IRRI and they renounce any form of IPR. Those sentiments are widely shared, not just all over the Third World, but in Europe and the United States.

The organic revolution

Europe is fed up with the intensive corporate agriculture that has brought BSE and the food and mouth epidemic now threatening to get out of control, and is going organic in earnest. The annual growth rate in organic agriculture in Europe from 1989 to 1999 averaged 25%, which, extrapolated forward, would lead to 10% of Western European agriculture being organic by 2005, and 30% by 2010 [31]. The same is happening in the rest of the world. As scientists, we must take all evidence seriously.

Organic and sustainable agricultural practices and technologies are succeeding, documented in study after study, despite the appalling lack of research funding compared to the hundreds millions that have gone into biotech. At least 3% of the arable land, some 28.9m hectares in Africa, Asia and Latin America are already farmed sustainably, with impressive gains in crop yield as well as social, economic and health benefits [**32**]. Organic farming is also working well in the United States and Europe, with yields matching and even surpassing agrochemical agriculture. Organic farms are good for wild-life, supporting many more species of plants, songbirds butterflies spiders, earthworms **[33]**. We need organic farming for the world to feed itself and for the planet to regenerate and thrive.

Sustainable agriculture is also important for alleviating, if not reversing global warming. A new report shows that sustainable agriculture can contribute significantly, not only to reducing consumption of fossil fuel, but increasing sequestration of carbon in the soil **[34]**.

Sustainable agriculture is predicated on a holistic, ecological perspective anathema to reductionist mechanistic science. Mechanistic science has been thoroughly discredited in the course of the 20th century. Mechanical physics went first of all with relativity and quantum physics. Biology was the last to go with the new genetics.

The new genetics is radically ecological, organic and holistic. That is why genetic engineering, at least in its current form, can never succeed. It is based on misconceptions that organisms are machines, and on a denial of the complexity and flexibility of the organic whole.

The challenge for western scientists is to develop a holistic science to help revitalise all kinds of non-corporate sustainable agriculture and holistic medicine that can truly bring food security and health to the world.

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