

Mae-Wan Ho



European Parliament Briefing 20 October 2004 Brussels

GM Crops Global Stats. 2003

	mHa	%
World	67.7	100.0
USA	42.8	63.2
Argentina	13.9	20.5
Canada	4.4	6.5
China	2.8	4.1
S. Africa	0.4	0.6

Soya Maize Cotton OSR	mHa 41.4 15.5 7.2 3.6	% 61.2 22.9 10.6 5.3
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	mHa	%
Herb. tol.	49.7	73.4
Insect. res	. 12.2	18.0
Both	5.8	8.6

GM Crops

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GM crops occupy just 1.3% of the world's 5019.6 mHa agricultural land

Nearly 84% are confined to the USA and Argentina

Sources: www.fao.org; www.isaaa.org

he World from GM

Biotech Investment Busy Going Nowhere

Claire Robinson exposes the financial woes of the biotech industry

Biotechnology is the answer to problems ranging from hunger in Africa and Asia to obesity in the West. This was the upbeat message from the industry's promotional showcase, the BIO 2004 conference, which took place in San Francisco in June. In launching the conference, BIO (the Biotechnology Industry Organisation) trumpeted, "the biotechnology industry is performing



in its falling bottom line. As the New Zealand Herald said, "Investment in genetically modified food is drying up in the world's biggest GM market, the United States, because consumers in the rest of the world are not willing to buy its products."

Roger Wyse of Burrill and Company, the biggest investment firm focused on life sciences, said the consumer backlash against GMOs had forced a lull in projects aimed at modifying food. "We are probably looking at three, four or five years before the GMO issue subsides sufficiently that we will feel comfortable investing in it," he said.

Lack of investment has led to massive losses. Back to Ewing: "Last year, this industry lost \$5.4 billion, and has lost a staggering \$57.7 billion since BIO last held its annual conference in San Francisco in 1994, according to an Ernst and Young study. Only a few companies have been consistently profitable in the 30 years since biotech was born - a few, such as Amgen and Genentech, fantastically so. Remove up of its products, selling stocks has become a biotech industry lifeline. In 2003, US biotech firms raised almost \$4 billion by selling new stock to investors, according to Burrill & Co. The same year, US biotechs as a group posted almost that much in losses. Only 12 of the 50 largest biotechs turned a profit in 2003.

Meltdown continues

In the UK, the biotech meltdown continues apace. Earlier this year, it emerged that two biotech firms linked to science minister and donor to the Labour Party, Lord Sainsbury, are facing serious financial difficulties. Diatech Ltd, which holds several patents for techniques designed for use in GM foods, has gone into liquidation, while biotechnology investment firm Innotech is making huge losses.

At the end of June, the British GM science lobby despaired at news that Anglo-Swiss biotech giant Syngenta was withdrawing from the UK and transferring to North Carolina in the US. Syngenta was

Living with the Fluid Genome By Mae-Wan Ho

Author of International best-seller, Genetic Engineering Dream or Nightmare?

Inside Science Living with Fluid Geno

Mae

Inside Science

Living with the Fluid Genome

Mae-Wan Ho

Readership General public, suitable for all post-16 educational levels and as university course-book

s university course-book

The biotech empire is showing all the signs of collapsing because it's got the science wrong.

Read this riveting inside-story of the fluid genome from a scientist who has been warning that genetic engineering is both dangerous and futile for over a decade.

Find out why the whole biotech enterprise, from GM crops to gene drugs and human

Central Dogma of Molecular Biology



The Fluid Genome



Ecological environment

The Central Dogma

$$\mathsf{DNA} \longrightarrow \longrightarrow \longrightarrow$$

Natural Genetic Engineering

*Precisely regulated by the organism as a whole

Artificial Genetic Engineering *Crude and Uncontrollable



CHARACTERISATION OF COMMERCIAL GMO INSERTS: A SOURCE OF USEFUL MATERIAL TO STUDY GENOME FLUIDITY.



<u>Cécile Collonnier</u>¹, Georges Berthier¹, Francine Boyer¹, Marie-Noëlle Duplan¹, Sophie Fernandez¹, Naïma Kebdani¹, André Kobilinsky², Marcel Romaniuk¹, Yves Bertheau¹

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(2) Laboratoire de Biométrie et Intelligence Artificielle UR341, Domaine de Vilvert, Jouy-en-Josas Cedex 78 352, France

Introduction

Labelling of food and feed containing more than a defined threshold of ingredients derived from authorized GMOs is mandatory in countries such as Europe, Japan, Australia and New Zealand. Reliable GMO identification and quantification methods are needed to comply with these regulations. Mostly based on PCR amplification (end point and quantitative real time PCR), GMO detection tests can be specific of recurrent regulatory sequences and genes (screening), construct-specific, or event-specific. Development of such tests requires the sequencing and the detailed characterisation of the GMO inserts and their edge-fragments. By contributing to the localization of the preferential integration sites, and by revealing unexpected rearrangements, duplications of genetic elements and/or inserts, these analyses show that commercial GMOs are a source of valuable material to study genome fluidity, especially DNA placement, recombination and repair mechanisms.



Why do DNA rearrangements occur ? - In plants, exogenous DNA transfer elicites a wound response which activates nucleases and DNA repair enzymes. The transferred DNA is thus, either degraded or used as a substrate for DNA repair, resulting in its potential rearrangement and incorporation in the genomic DNA (Takano et al. (1997) Plant J 11: 353-361.) Furthermore, specific transforming plasmid structure and construct properties can enhance recombination events all along the transformation process. Indeed, some genetic elements can act as **hotspots** and undergo recombination at high frequency. It is, for example, the case for the 3^o end of the CaMV 35S promotor - an imperfect palindrome of 19 by when it is in conjunction with specific flanking sequences derived from transforming plasmid structure and constraints and so occur in the **borders** of the T plasmid of *Agrobacterium tumfacciens*, especially in the right border which contains an imperfect palindromic sequence of 11 bp. The 3^o end of the nos terminator is also theoretically highly prone to recombination (Kohli et al. (1999) Plant J. 17(6): 591-601). Hot spots may lead to tandem transgene repeats with interspecer by aland MA sequences in a single genetic locus. Presence of several inserts may also result from multimerisation in the plasmid before transformation or from multiple insertions. - In addition to cellular mechanisms controlling the transgene integration, subsequent selection procedures of the GM material may introduce further genomics (Hermander et al. (2003) Transgenic Res. 12: 170-189).



What are the DNA rearrangements observed in GMOS ? The results presented here in the different frames show that various kind of rearrangements occur in GMOs: deletion (Mon810, GA21, B1176), recombination (T25, GT8 40-3-2, B1176), tandem or inverted repeats (T25, GA21, GT8 40-3-2, B1176), moreover, in addition to insert recombinations, rearranged fragments of the insert can also be scattered in the genome (Mon810).

When do they occur ? Rearrangements of transforming DNA have been reported both in direct and indirect transformation. Recombination may occur between plasmid molecules **before or during** the transformation, or between plasmid and genomic DNA **during or after** the transformation.



How do they occur? In higher plants, most rearrangements involve illegitimate recombination during DNA double-strand break repair (DSBR) (Sargent et al. (1997) Mol. Cell Biol. 17: 267-277). Plasmid junctions are predominantly formed by microhomology dependent illegitimate recombination mainly based on single-strand annealing of complementary tails, followed by repair synthesis over the remaining gaps (Kohli et al., 1999). Several other mechanisms can also be involved in DNA rearrangement, such as non homologous end joining (rare), or polymerase slipping and template switching sometimes leading to deletion (Cf cruciform P35S - green frame).



Where does the insert go ? Transferred DNA preferential insertion sites include mobile elements such as retrotransposons (T25, Mon810, GA21), but also repeated sequences (Bt11 maize insert (Syngenta) is located in a tandem repeated sequence motif (Zimmermann et al. (2000) Lebensm-Wiss u-Technol 33: 210-216 i Røming et al. (2003) Eur. Food Res. Technol. 216: 347-354). Many retrotransposons containing long terminal repeated sequences in these regions could then give rise to altered spatial and temporal expression patterns of genes in close proximity. Moreover, defective retrotransposons can transpose by the use of trans-acting factors, which could potentially affect the genetic stability of the recombinant DNA insert (Jank and Halsberger (2000) Tiblech 18: 326-327).

Conclusion

Studying GMOs structure is necessary to develop reliable quantification and detection tests complying with the different regulations, but it also leads to ask **fundamental questions about genome fluidity**. Many of the mechanisms involved in recombinant DNA integration are similar to those underlying **genome evolution**. Therefore, characterised **GMO** inserts are a very **good model to study the molecular systems involved in DNA rearrangements** in general. Furthermore, GMO progenies can be used to compare the evolution of an exogenous DNA insert to those of mobile or non mobile genetic elements already present in the plant genome. Lastly, characterising different GMO cultivars produced with the same initial construct should provide information on the effect of the genomic background on the DNA insert stability. The European Commission is acknowledged for financial support through the Fifth (EC) Framework Programs: projects QPCRGMOFOOD (2000-2003) nº QLK-CT-1990-1030) and GMOCHIPS (2001-2004) nº G6RD-CT-2000-00419.

Two Latest Incidents in GM Safety

Monsanto's GM maize Mon863 containing a Bt biopesticide Cry3Bb1against the corn root worm was given a positive assessment by the European Food Safety Authority despite "very disturbing" health impacts including kidney malformations and increase in white blood cells in male rats and high blood sugar and reduced immature red blood cells in female rats.

Villagers in the south of the Philippines living near GM maize plots suffered from serious illnesses when the GM maize came into flower in last year, and again this year. Prof. Terje Traavik of the Norwegian Institute of Gene Ecology in Tromsø examined the blood of 39 villagers and found antibodies to Cry1Ab produced by the GM maize as biopesticide against the cornborer.





Fig. 16.1. Comparison of the stomach mucosa of rats fed with raw GM potato diet (b) shows marked thickening due to hypertrophy of mucosal cells in comparison with that of rats given the parental line (a) (bar = 100μ m).





Fig. 16.2. Histology of the jejunum and ileum of rats fed raw GM or parent potato diets. Jejunal crypt length and cells exhibit marked enlargement after feeding rats GM potato diets for 10 days (b) in comparison with those of rats given parental line potato diets (a). The villus length is similar in both, but intraepithelial lymphocyte cell counts appear to be increased on the GM potato diet. In the ileum, both crypts and villi of rats on GM potato diets are elongated (d) in comparison with parent potato-fed rats (c) (bar = 100 μ m).



Fig. 16.3. The mucosa of the caecum demonstrates little change. Differences between GM-fed (b) and parent line potato-fed rats (a) are slight, while the colonic mucosa is moderately thickened in GM-fed rats (d) compared with that of rats given the parental line (c) (bar = $50 \mu m$).

Spot the Common Factor *

Sick	rats	Monsanto	Bt maize Cry3Bb1
Sick	humans	Philippines	Bt maize Cry1Ab
Dead	cows	Hesse Germany	Bt maize Cry1Ac?
Sick	rats	Pusztai et al	GNA-potato
Sick	mice	Fares & El-Sayed	Bt potato Cry1Ab
Sick	rats	US FDA	Antisense Tomato
Dead	Chickens	Aventis	Glufosinate-tolerant maize

* The GM process, GM construct or both



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Science in Society

" By far and away the most

Rethinking Health



One of the most significant discoveries over the past 50 years is that genes and genomes are dynamic and fluid.

Rethinking Health



Most geneticists are still focussing on gene sequences to find out which gene variants go with which diseases. But that's a serious mistake, and for more reasons than one.

Dr. Mae-Wan Ho reports.

genes downstream. The metabolic intermediate donating the methyl group to CpG is S-adenosylmethionine; and its availability will be influenced by dietary intake of methyl-donors and other co-factors necessary for its synthesis. That may be one way early nutrition can affect adult susceptibility to disease.

Patterns of DNA methylation are in part determined by transposable elements mobile genetic units - scattered throughout the human genome, making up more than 35% of the genome. Most transposons are silenced by methylation, but a subset of them is metastable (not quite stable), and can change in methylation, thereby affect-

Diet Trumping Genes

The Fluid Genome



Ecological environment

The Central Dogma

$$\mathsf{DNA} \longrightarrow \longrightarrow \longrightarrow$$



The Rainbow and The Worm

The Physics of Organism

Mae-Wan He

The Physics of Organisms

by Mae-Wan Ho Institute of Science in Society

Readership: General

Contents

- What is It to Be Alive?
- Do Organisms Contravene the Second Law?
- Can the Second Law Cope with Organized Complexity?
- Energy Flow and Living Cycles
- How to Catch a Falling Electron
- Towards a Thermodynamics of Organized Complexity
- The Seventy-Three Octaves of Nature's Music
- The Coherent Excitation of the Body Electric
- How Coherent is the Organism?
- Life is All the Colours of the Rainbow in a Worm
- The Liquid Crystalline Organism
- Crystal Consciousness
- Quantum Entanglement and Coherence
- The Ignorance of the External Observer

A serious, in-depth enquiry into Schrödinger's question, "What is Life?" and at the same time, a celebration of life itself



Mae-Wan Ho

2 nd Edition



nergy, Productivit

Generations of ecologists have puzzled over the causes of biodiversity and its relationship with

productivity.

Dr. Mae-Wan Ho investigates.

& **Biodiversity**

The secret of his is not to be found in the molecular nuts and bolts in living organisms, instead it may be in how organisms use energy, giving concrete meanings to renewable living energy and sustainability

A contraction of the law

"Why are there so many kinds of animals?"

The was the question asked by detriguested watorget Europh Hustmann in USB the pertensity of Donesh Chan of Species a question has rehained as enginate baday as fillies then

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SCIENCE IN SOCIETY 21, SPRING 2004

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Loss of Biodiversity in Food Plants from Monocultures of the Green Revolution

Species consumed by people	7 000
Species in 90% world food crops	103
Species providing 60% calories	
& 56% protein	3
(ric	e, wheat, maize)

(Lori Ann Thrupp, World Resources Institute, Washington DC, 1998)



Diversity and Productivity in a Long-Term Grassland Experiment

David Tilman,¹* Peter B. Reich,² Johannes Knops,³ David Wedin,⁴ Troy Mielke,¹ Clarence Lehman¹

Plant diversity and niche complementarity had progressively stronger effects on ecosystem functioning during a 7-year experiment, with 16-species plots attaining 2.7 times greater biomass than monocultures. Diversity effects were neither transients nor explained solely by a few productive or unviable species. Rather, many higher-diversity plots outperformed the best monoculture. These results help resolve debate over biodiversity and ecosystem functioning, show effects at higher than expected diversity levels, and demonstrate, for these ecosystems, that even the best-chosen monocultures cannot achieve greater productivity or carbon stores than higher-diversity sites.





One Duck Ten Thousand Treasures



HARVEST With only a few sheep and a shovelful of dung, local farmers are reclaiming their land from the Sahara. Fred Pearce reports

IT MUST be true. We've been told it so many times. The over-tarmed and overgrazed softs of Africa, especially on the fringes of the Sahara, are losing their fertility and eroding away. As the population grows, poor farmers are mining the last goodness from their sold. Their aninals graze the grasslands away to nothing and the desert sands move in. Environmentalists say it, development economists say it; politicians say it; soil scienture say it.

"An area the size of Somalia has become desert over the past 50 years. The same fate now hiratens more than one-third of the African continent," says the UN Field and Agriculture organization, adding that "the main cause is mismanagement of the fand." Its sister body the IN Environment Programme claims that 900 million Africans face starvation as their soils crumle away. UNLP masternainded a UN Desertification Convention in 1996 in an effort to reverse in frend.

But out in the shimmering heat of and Africa, where tens of millions of farmers scratch a ving from the soil, new meanch suggests that this apocalyptic vision is little more than a irage. Farmers are finding ways to intensify their farming methods without destroying their guidations continue in he fed. In places the desert sands are even retreating. Indeed, for most are at most times, the whole notion of descritification increasingly looks like a myth. Consider the dusty desert margins of northern Nigeria around the ancient caravan city of

no, for example. Here, population density has soared to levels similar to Belgium, and some per cent of the land is now cultivated. Rainfall is declining, the availability of chemical ferser has fallen by 80 per cent, and only the richest farmers can afford high-yielding grain attes or impation. The poor make do with small scraps of sandy soils. Surely these fields should turning to desert dust as yields plummer, hunger spreads and refugees head for the cities? at that's not what I haw when agricultural scientist BB Singh, who heads the Kano office of International institute of Tropical Agricultural scientist BB Singh, who heads the Kano office of International institute of cooker spread sure busy with fruit and vegetable stalls behind them the fields were already green with bushes laden with the first cowpear. iden the burning sun, we visited Ado, a farmer who tends a 2-hectare plot on the outsidir's and the burning sun, we visited Ado, a farmer who tends a 2-hectare plot on the outsidir's and the burning sun, we visited Ado, a farmer who tends a 2-hectare plot on the outsidir's and the burning sun, we visited Ado, a farmer who tends a 2-hectare plot on the outsidir's and the burning sun, we visited Ado.

adume village, 50 kilometres northwest of Kano. Allo was exultant. The previous year, he harvested just two bags of cowpeas from his plot. This year, he got seven bags for the same t. He took me behind the high mind walls of his compound to an inner sanctum where vasons for his success were bleating. He used to let his sheep roam free. Now he had half rem of the animals lethered in his backyard, munching away at straw left over from his cand creating a large pile of memory design.





* Adopt Sustainable Agriculture

* Ban

GM crops

Independent Science Panel

ISP	Independent Science Panel www.indsp.org	
	The Independent Science Panel (ISP) is a panel of scientists from many disciplines, committed to the Public Good. Read our statement <u>here</u>	the Promotion of Science for
Home About ISP GM ISP Launch Online Store Contact	Some members of the Independent Science Panel at the launch conference, 10 May 2003, in London. In the launch conference, 10 May 2003, in London.	The Case for a GM-free Sustainable World136 page report compiled by the Independent Science Panel Read the summary Download the reportAdd your signature to show your endorsement of this report here
	 The Independent Science Panel was launched with a one-day conference entitled 'GM Crops: Do We Need Them? Are They Safe?' (read more about the conference) A Report was simultaneously released 'The Case for a GM-free Sustainable World' (read more about the report) 	Did You Miss the Launch? Or perhaps you didn't catch all the lectures; don'tworry there are audio, video and printed presentations from the ISP launch conference available in the <u>ISP online store</u> .



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