



Join the I-SIS mailing list; ente your email address

 html asci

I-SIS is a not-for-profit organisation, depending on [donations](#), membership fee [subscriptions](#), or [merchandise](#) sales continue its worl Find out more abt membership [her](#)

Cartoons by Cinc McLeod [more](#)

Witness Statement

January 27, 2001 Prof. Joe Cummins Professor Emeritus
of Genetics University of Western Ontario
jcummins@uwo.ca

"Three issues in the safety of genetically modified crops"

It is a privilege and an honor to participate in this important review of the safety of genetically modified crops. I thank the commission for considering the matters that I have submitted below.

The issues that I will comment on include first: Genetically Modified (GM) Baculovirus vectors used in crop insect control and mammalian gene therapy. The second issue : Bacillus thuringiensis (Bt) toxins reportedly toxic to mammals. The third issue: The impact of bacterial genes in GM crops on the immune system (the CpG effect).

I will comment on each issue below and separately provide copies of key references in pdf format.

GM Baculovirus vectors: Baculovirus are virus that infect insects, they are very stable and may remain dormant in the environment for years before infecting insects. The virus can be purified and produced in quantity to be used in insect control. Since the virus multiplies and persists, its use in pest control seems promising. The virus alone has a relatively low killing power and slow action. When a gene for a potent toxin such as scorpion toxin or a gene affecting a juvenile hormone is added to the virus, it kills faster and fewer insects survive infection. Numerous field tests of modified virus sprayed on crops have been undertaken, often accompanied by loud expressions of concern from the public. Soon after GM virus were developed for insect control, it was found that baculovirus were capable of infecting human liver cells and produced relatively little toxicity to the infected cells. For that reason baculovirus vectors were developed to treat liver disease. Interestingly, the fact that baculovirus can infect human liver cells seems to have been ignored by those developing the virus for commercial pest control. The following discussion will deal with the use of baculovirus vectors and their safety. I understand that there has been a great deal of pressure to hasten approval of the GM baculovirus for pest control.

Ecological considerations for the impact of recombinant baculovirus insecticides have been studied extensively (Richards et al 1998). The study focussed on baculovirus containing scorpion toxin because that construction has been most widely studied. Impact on non-target insects is extrapolated from insects of related phylogeny, a practice difficult to defend. The recombinant baculovirus was very persistent and capable of reshaping an ecosystem. Modification of baculovirus host range specificity has been achieved by inserting or deleting genes (Theim 1997).

Baculovirus is a circular DNA duplex, it replicates in the insect cell nucleus and replication is prone to the generation of defective genomes by deletion (Wu et al 1999). The mode of virus replication seems to make the recombinant virus highly unpredictable and prone to generating potentially undesirable variants. This important finding has not yet been taken into account in risk analysis of recombinant baculovirus insecticides and gene therapy vectors.

Views and goods advertized are not necessarily endorsed by Science in Society or the Inst. of Science in Society.

[Bt Margin](#)

Increase your investment potential and diversify with margin lending.
[BT.com.au](#)

[Jehovah Witness](#)

Your guide to the movement. Visit [Beliefnet.com](#) and learn more
[www.Beliefnet.com](#)

[T-cell Epitope profiles](#)

Epibase® unveils the epitopes and related immunogenicity of proteins.
[www.algonomics.com](#)

[Cancer Treatment](#)

The Gerson Hospital provides for proven cancer immuno-treatment
[www.gersonhospital.com](#)

[Trend Micro Online Store](#)

Award-winning virus protection plus firewall, anti-spyware & much more!

Shop.TrendMicro.com/au/

[Hot Stock Alert](#)

Ethanol, Biofuels, Alt Energy Gulf Ethanol Corp (OTC:GFET)

www.GulfEthanolCorp.com

[Stop AIDS And HIV](#)

Effective AIDS/HIV product. New, powerful Immune System Tea.

health-reports.com

[NZ Spam & Virus Filter](#)

No software or hardware required. Take control of your inbox today

www.ctscanmail.com

The scorpion toxins used with recombinant baculovirus have been selected to avoid human neurotoxicity, and as much as possible toxicity to non-target animals. However, the allergenicity of toxins and their behavior, as for example, in triggering autoimmunity in human liver infection, has not yet been studied. In insect control the depressant toxin was more effective than the excitatory toxin in recombinant baculovirus (Gershburg et al 1998).

Recombinant baculovirus containing *Bacillus thuringiensis* toxin have not proven successful in controlling insect pests (Martens et al 1995). However, recombinant baculovirus modifying juvenile hormone proved effective in insect control (Bonning et al 1999). Recombinant baculovirus containing an antisense fragment to the c-myc oncogene proved effective in target insect control (Lee et al 1997). The behavior of the myc oncogene recombinant vector bears careful study regarding non-target animals and its impact during human liver infection.

Baculovirus vectors efficiently transfer genes into human liver cells (Hofmann et al 1995; Boyce and Bucher 1996). The vectors transferred into human liver tissues most effectively in perfused liver tissue because serum components hampered virus transfer (Sandig et al 1996). Human conditions associated with defects in complement should allow liver transfer of recombinant baculovirus. Inhibitors of complement facilitate baculovirus gene transfer (Hofmann and Strauss 1998). Hybrid baculovirus-adenovirus vectors have been used to deliver genes to human cells (Palombo et al 1998). Baculovirus vectors have been used to deliver hepatitis B to human liver efficiently to allow study of hepatitis B drug therapy (Delaney et al 1999). Baculovirus vectors proved very effective in delivering genes to human brain cells (Sarkis et al 2000). Crops treated with baculovirus may be promoted as "brain food".

In conclusion baculovirus vectors are being used to control insect pests because they are effective and persist for a long time in the environment. Baculovirus vectors are also being used in gene therapy of human liver. These areas of research seem to exist as two solitudes and the risks of one are not evaluated in the context of the other. The most disconcerting finding is the one showing that replication of the baculovirus is inherently unpredictable. However, there may be some who believe that we should all have unlabelled liver gene therapy with our salad.

References

1. Bonning, B, Possee, R and Hammock, B "Insecticidal efficacy of a recombinant baculovirus expressing JHE-KK, a modified juvenile hormone esterase" 1999 *J Invertebr Pathol* 73,234-6
2. Boyce, F and Bucher, N Baculovirus-mediated gene transfer into mammalian cells" 1996 *Proc. Natl Acad Sci USA* 93,2348-52
3. Delaney, W, Miller, T, and Isom, H "Use of the hepatitis B virus recombinant baculovirus-Hep G2 system to study the effects of beta 2',3' dideoxy 3'thiacycydine on replication of hepatitis B virus and accumulation of covalently closed circular DNA" 1999 *Antimicrob Agents Chemother* 43,2017-26
4. Gershburg, E, Stockholm, D, Froy, O, Rashi, S, Gurevitz, M and Chejanovsky, N "Baculovirus mediated expression of a scorpion depressant toxin improves the insecticidal efficacy achieved with excitatory toxins" 1998 *FEBS Lett* 422,132-6
5. Hofmann, C, Sandig, V, Jennings, G, Rudolph, Schlag, P and Strauss, M "Efficient gene transfer into human hepatocytes by baculovirus vectors" 1995 *Proc. Natl Acad Sci USA* 92,10099-103
6. Hofmann, C and Strauss, M "Baculovirus mediated gene therapy in the presence of human serum or blood facilitated by inhibition of the complement system" 1998 *Gene Ther* 5,531-6
7. Lee, S, Qu, X, Chen, W, Poloumieko, A, MacAfee, N, Morin, B, Lucarotti, C and Krause, M "Insecticidal activity of a recombinant baculovirus containing an



antisense c-myc fragment" 1997 J Gen Virol 78,273-81

8. Martens, J, Knoester, M, Weijts, F, Groffen, S, Hu, Z, Bosch, D and Vlack, J
"Characterization of baculovirus insecticides expressing tailored *Bacillus thuringiensis* Cry1A9b) crystal proteins" 1995 J Invertebr Pathol 66,249-57

9. Palombro, F, Mociotti, A, Recchia, A, Cortese, R, Ciliberto, G and LaMonica, N
"Site specific integration in mammalian cells mediated by a new hybrid baculovirus-adeno-associated virus vector" 1998 J Virol 72,5025-34

10. Richards, A, Matthews, M and Christain, P "Ecological considerations for the environmental impact evaluation of recombinant baculovirus insecticides" 1998 Ann Rev. Entomol 43,493-517

11. Sandig, V, Hofmann, C, Steinert, S, Jennings, G, Schlagg, P and Strauss, M
"Gene transfer into hepatocytes and human liver tissue by baculovirus vectors" 1996 Human Gene Ther 20,1937-45

12. Sarkis, C., Seugera, C, Petres, S, Buchet, D, Riet, J, Edelman, L and Mallet, J.
"Efficient transduction of neural cells in vitro and in vivo by a baculovirus derived vector" 2000 Proc Natl Acad USA 97,14638-43

13. Thiem, S "Prospects for altering host range for baculovirus bioinsecticides" 1997 Curr Opin Biotechnol 8,317-22

14. Wu, Y and Lui, G and Carstens, E "Replication, integration, and packaging of plasmid DNA cotransformation with baculovirus viral DNA" 1999 J Virol 73,5473-80

Bacillus thuringiensis toxins reportedly toxic to mammals: *Bacillus thuringiensis* (Bt) is used both as an insecticidal spray and as a source of toxin genes for incorporation into GM crops. The spray is used extensively in organic agriculture and in that capacity it is safe so long as the food products are washed to remove the bacterium and its spores. The GM crops have toxin in each and every cell and cannot be cleaned to remove the toxin. Bt is also used as an aerial spray to control moths damaging forest resources but in that capacity the spray is used in urban centers and parks and schoolyards have been sprayed while children were playing. Teschke et al (2001) found that Bt spray drifted for over a kilometer from the target area of the spray well beyond the area predicted.

Aerial spraying with *Bacillus thuringiensis* (Bt) has been allowed in urban settings even though there is evidence that the spray causes gastric problems and illness within the people directly contacting the spray. New evidence shows that those exposed to the spray may develop a distinct allergic response. Bernstein et al. (1999) found that field workers exposed to Bt spray experienced allergic skin sensitization and induction of IgE and IgG antibodies to the spray. There was a significant increase in positive skin tests 1 and 4 months after exposure to Bt spray and there was evidence that number of positive responses increased with increasing exposure of the workers. Vazquez-Padron et al (1999) found that the Bt toxin Cry 1 Ac was a potent immunogen in mice when administered by intraperitoneal injection or intragastric administration. The exposure caused greater antibody production than did cholera toxin. People prone to allergy should avoid the districts slated for spraying and pray for rain to wash away the residues.

Bt has been implicated in human illness and distress in the past but current evidence suggests that people with weak immune systems (older people, very young people, people treated for cancer or people with AIDS) may face toxic shock and death from breathing the spray. Hernandez et al (1999) took a Bt strain they had isolated from severe human necrosis and found to induce necrosis in the skin of immunosuppressed mice and intranasally infected immunocompetent mice. The mice died within 8 hours in a clinical toxic-shock syndrome. It has also been found that Bt may have *Bacillus cereus* like toxins (Azam et al 2000).

Recently there has been considerable international concern about the contamination of the human food chain with StarLink corn containing *Bacillus thuringiensis* (Bt) toxin Cry 9. Bt Cry 9 toxin had evident

allergenicity in test animals and had been approved for use in animal feed alone but was found to have contaminated corn and corn products destined for human consumption. Bt toxins are the products of a number of genes and genes that differ between Bt varieties.

The EPA review of the Bt toxin Cry 9 is found at:

http://www.epa.gov/oppbopd1/biopesticides/cry9c/cry9c-peer_review.htm

"The results of intraperitoneal injection of corn powder extracts into BN rats indicate that both the control and transgenic corn powders are able to induce IgE or reaginic [**regain is the allergist's term for IgE antibody**] antibody responses by the PCA assay [**PCA is the passive cutaneous anaphylaxis assay**]. The use of corn powder immunogen decreases the rate of the immune response to the Cry9C protein compared to the bacterial preparation. However, the lowest responding dose for Cry9C was similar for the two preparations (between 0.1 and 0.4 µg Cry9C). The control challenge test with the heterologous antigen of control corn powder or transgenic corn powder in the day 42 sera samples indicated that there was significant reactivity from the corn portion of the extracts themselves in the PCA assay. It is unclear, given this background reactivity, how conclusions can be made about the reactivity of the Cry9C protein alone. The PCA results from oral sensitization with ovalbumin II, control corn extract, bacterial Cry9C and transgenic corn (apparently supplemented with bacterial Cry9C) indicated that an IgE or reagin antibody response was elicited in naïve Sprague-Dawley rats.

Ovalbumin sensitized serum produced a low frequency of responders and a weak dose response between the 5.0 and 50.0 mg/kg dose levels on days 28 through 42. The control corn also produced a positive oral sensitization response but this was only examined at the 50 mg/kg dose. Oral dosing with bacterial Cry9C have a positive PCA response as did the Cry9C amended transgenic corn extract. The frequency of response to bacterial Cry9C began to diminish in day 42 sera. The Cry9C amended transgenic corn had a higher frequency of responders and the frequency remained high on day 42 PCA response. Western blot analysis indicated that Cry9C protein bands could be recognized in the rat sera from both exposure routes."

The quote above from the EPA provides clear evidence Cry 9 in corn is allergenic in mammals. The fact that corn powder alone is allergenic has been known by those milling corn. The Cry 9 allergin was recognized in the corn powder. Consequently, Cry 9 GM corn is significantly enhanced in its ability to cause allergy in mammals. Tests such as the passive cutaneous anaphylaxis (PCA) and laboratory examinations such as Western blots which isolate and identify particular antibodies (the test is similar to the DNA fingerprint used in crime detection) provide strong evidence that Cry9 is an allergin. The repeated claim that GM corn modified with BtCry9 is "suspected" of causing allergy seems a peculiar use of language by those claiming to be superior scientists.

These results show that an allergic (IgE) response was associated with Cry9 in corn powder. Cry 9 containing corn was fed to millions of farm animals, and probably as many humans eating corn products contaminated with corn designated only for farm animal use. Thus, any evidence indicating IgE response to Cry 9 corn should be taken very seriously and not be allowed to be buried by bureaucrats.

Another study (Fares and El-Sayed 1999) shows that Bt Cry 1 toxin which is used extensively in corn and cotton products (oil and seed meal) used in human and animal food damages the mammalian ileum. Damage to the ileum can produce chronic illness such as fecal incontinence and/or flu like upsets of the digestive system.

Ileum: Final and longest segment of the small intestine. It is specifically responsible for the absorption of vitamin B12 and the reabsorption of conjugated bile salts. The ileum is about 4 m (13 feet) in length and extends from the jejunum (the middle section of the small intestine) to the ileocecal valve, which empties into the colon (large intestine). The ileum is suspended from the abdominal wall by the mesentery. The smooth muscle of the ileum's walls is thinner than the walls of other parts of the intestines, and its peristaltic contractions are slower. The ileum's lining is also less permeable than that of the upper small intestine. Small

collections of lymphatic tissue (Peyer's patches) are embedded in the ileal wall, and specific receptors for bile salts and vitamin B12 are contained exclusively in its lining; about 90 percent of the conjugated bile salts in the intestinal contents is absorbed by the ileum.

In conclusion, Bt in bacterial spores is probably safe for food because the toxin can be washed off. GM Bt toxins, however, cannot be washed off. Bt toxins have been found to be allergenic or to create damage to the digestive system of mammals. Bt spray to control forest moths is unsound when large urban centers are sprayed and drift is poorly controlled and accounted for.

References

1. Bernstein, I, Bernstein, J, Miller, M, Tiewzieva, S, Bernstein, D, Lummus, Z, Selgrade, M, Doerfler, D and Seligi, V "Immune responses in farm workers after exposure to Bacillus thuringiensis pesticides" 1999 Environ Health Perspect 107, 575-82
2. Fares, N and El-Sayed, A "Fine Structural Changes in the Ileum of Mice Fed on -Endotoxin-Treated Potatoes and Transgenic Potatoes" 1999 : Natural Toxins Volume 6, 219-233
3. Hernandez, E, Ramiisse, F, Cruel, T, leVagueresse, R and Cavallo, J "Bacillus thuringiensis serotype H34 isolated from human and insecticidal strains 3a3b and H14 can lead to death of immunocompetent mice after pulmonary infection" 1999 FEMS Immunol Med Microbiol 24, 43-7
4. Tayabali, A and Seligi, V. "Human Cell Exposure Assays of Bacillus thuringiensis Commercial Insecticides: Production of Bacillus cereus-Like Cytolytic Effects from Outgrowth of Spores" 2000 Environmental Health Perspectives 108, 919-30
5. Teschke, K, Chow, Y, Bartlett, K, Ross, A and van Netten, C "Spatial and Temporal Distribution of Airborne Bacillus thuringiensis var. kurstaki during an Aerial Spray Program for Gypsy Moth Eradication" 2001 Environ Health Perspect 109: 47-54
6. Vazquez-Padron, R, Moreno-Fierros, L, Neri-Bazan, L, de la Riva, G, and Lopez-Revilla, R "Intragastric and intraperitoneal administration of Cry 1Ac protoxin from Bacillus thuringiensis induces systemic and mucosal antibody response in mice" Life Sci 64, 1897-99

The impact of bacterial DNA on the immune system (the CpG effect): Essentially all of the GM crops marketed or being field tested presently contain bacterial sequences as a part of the plasmids used for delivering genes and many of the primary crop protection genes are of bacterial origin. Such genes include Bt and most herbicide tolerance genes. DNA vaccines have generated a huge literature and clinical applications showing the activity and cellular incorporation of DNA administered by oral, inhalation, injection, vaginal or dermal application (Molling 1997, Donnoley et al 1997 and Gurunathan et al 2000). Ingestion of bacteria does not appear to be an effective means of delivering DNA because the bacterial cell walls effectively contain the nucleic acid (for example, in yogurt the milk products are digested but the bacteria of the culture are passed intact). Lysis genes have been found necessary and effective in triggering release of DNA for mucosal vaccine delivery (Jani and Mekalanos 2000). In contrast, the crops eaten by animals release oligonucleotides and DNA peptide complexes during digestion and such molecules circulate to a significant degree.

The bacterial genes used in constructing GM crops have a property that impacts on the immune system over and above the ability to produce antibodies. Eukaryote DNA has relatively low frequencies of the dinucleotide motif CpG and that motif is methylated and plays a role in gene regulation while bacteria and their viruses have a high frequency of the CpG motif that is usually unmethylated. Apparently the CpG motif in DNA molecules and oligonucleotides provides a signal that the immune system recognizes and initiates a primary sequence of reactions leading to activation of the immune system leading to inflammation (Manders and Thomas 2000 and Gurunathan et al 2000). Oligonucleotides rich in the CpG motif are used to enhance immunization. Inflammation is an essential

part of the immune response but it adversely affects existing conditions such as autoimmune disease. Furthermore, it has been found that CpG oligonucleotides rescue B cell lymphoma cells from anti-IgM mediated growth inhibition (Han et al 1999). The oligonucleotide acts as a promoter of lymphoma.

Finally, Gorecki and Simons (1999) pointed out a danger to the fetus in DNA vaccination of the mother. That danger was the creation of tolerance in the fetus leading to individuals more susceptible to infection and/or they may become carriers. The introduction of genes with bacterial CpG motif to the fetus is likely to have untoward consequences.

In conclusion, the bacterial genes used in GM crops have been found to have significant impacts on the individuals ingesting GM crops. The impacts include inflammation and lymphoma promotion. The consequence of GM food genes being incorporated into the chromosomes of somatic cells of those consuming GM food and their unborn has been ignored by those charged with evaluating the hazards of GM crops.

References

1. Donnelly, J, Ulmer, U, Shiver, J and Lui, M. "DNA Vaccines" 1997 Annu Rev Immunol 15, 617-48
2. Gorecki, D and Simons, J "The dangers of DNA vaccination" 1999 Nature Medicine 5, 126
3. Guunathan, S, Klinman, D and Seder, R. "DNA Vaccines" 2000 Annu Rev. Immunol 18, 927-74
4. Hsu, S, Chung, S, Robertson, D, Ralph, L, Chelvarajan, R and Bondada, S 1999 "CpG oligodeoxynucleotides rescue BKS-2 immature B cell lymphoma from anti-Ig-M-mediated growth inhibition by up-regulating of egr-1" International Immunology 6, 871-9
5. Jain, V and Mekalanos, J "Use of lambda phage S and R gene products in an inducible lysis system from Vibrio cholerae and Salmonella enterica servovar Typhimurium-Based vaccine delivery systems" 2000 Infection and Immunity 68, 986-9
6. Manders, P and Thomas, R "Immunology of DNA vaccines: CpG motifs and antigen presentation" Inflamm Res 49, 199-205
7. Molling, K "Naked DNA for vaccine or therapy" 1997 J Mol Med 75, 242-6
8. Schubert, R, Renz, D, Schmitz, B and Doerfler, W "Foreign (M13) DNA ingested by mice reaches peripheral leucocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA" 1997 Proc. Natl Acad Sci USA 94, 961-6

Best Deal at Amazon



Total Micro (310-1093-TM) AC Adapter for Dell Latitude C540.
Free Shipping, In Stock, Free Shipping:
orders over \$25... at Amazon

Description Best Deals Search

AC Adapter, Manufacturer: Total Micro, PN: 3101093tm

The Institute of Science in Society, PO Box 51885, London NW2 9DH
telephone: [44 20 8452 2729] [44 20 7272 5636]

[Contact the Institute of Science in Society](#)

MATERIAL ON THIS SITE MAY NOT BE REPRODUCED IN ANY FORM WITHOUT EXPLICIT PERMISSION, PLEASE CONTACT enquiries@i-sis.org.uk