




Genetically Modified Foods, Inflammation, and Autoimmune disease

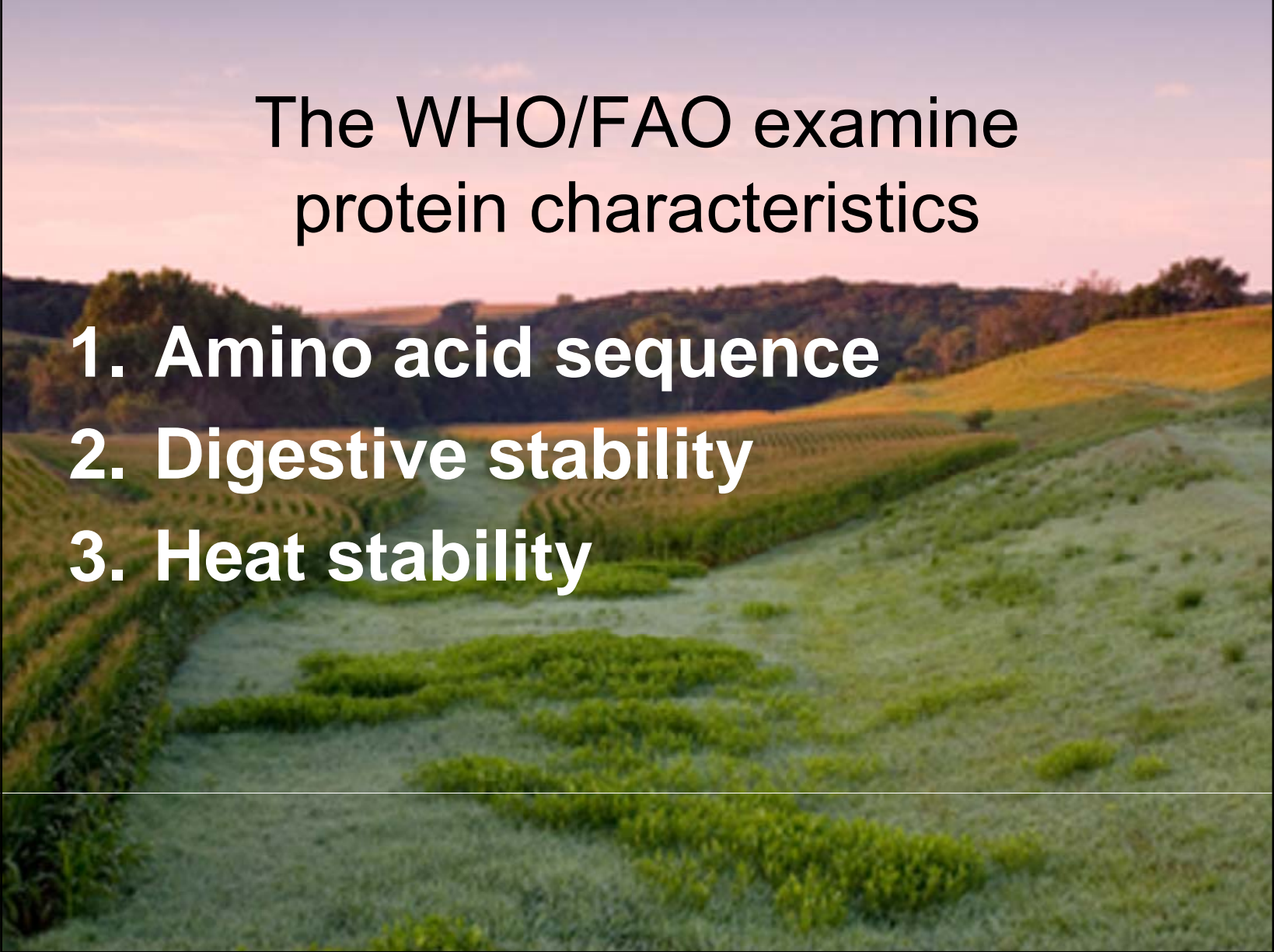
A survey of immune reactions in
GMO animal feeding studies

By Jeffrey M. Smith and Amy L. Dean, D. O.



First possible cause of problems: The Transgene Product

- **Bt**
- **Roundup Ready**
- **Viral transgenes**



The WHO/FAO examine protein characteristics

- 1. Amino acid sequence**
- 2. Digestive stability**
- 3. Heat stability**

Criteria 1: Compare 6 amino acids with epitopes of known allergens (where IgE antibodies attach)

- **Roundup Ready canola: Identical to shrimp allergen**
- **Roundup Ready soybeans: Identical to dust mite allergen**
- **Papaya: Matches allergen sequence**
- **Corn: Bt (Cry1Ab) shares 9–12 amino acids with vitellogenin, an egg yolk allergen**
- **“The similarity...might be sufficient to warrant additional evaluation.”**

(Gendel)

2: Digestive Stability

- The Bt protein Cry1Ab (Mon 810 and Syngenta's Bt-11 corn) resists breakdown in simulated digestion
- 10% survived for 1-2 hours
- Fragments typical of food allergen size (15 kilodaltons).

(Noteborn)

3: Heat Stability

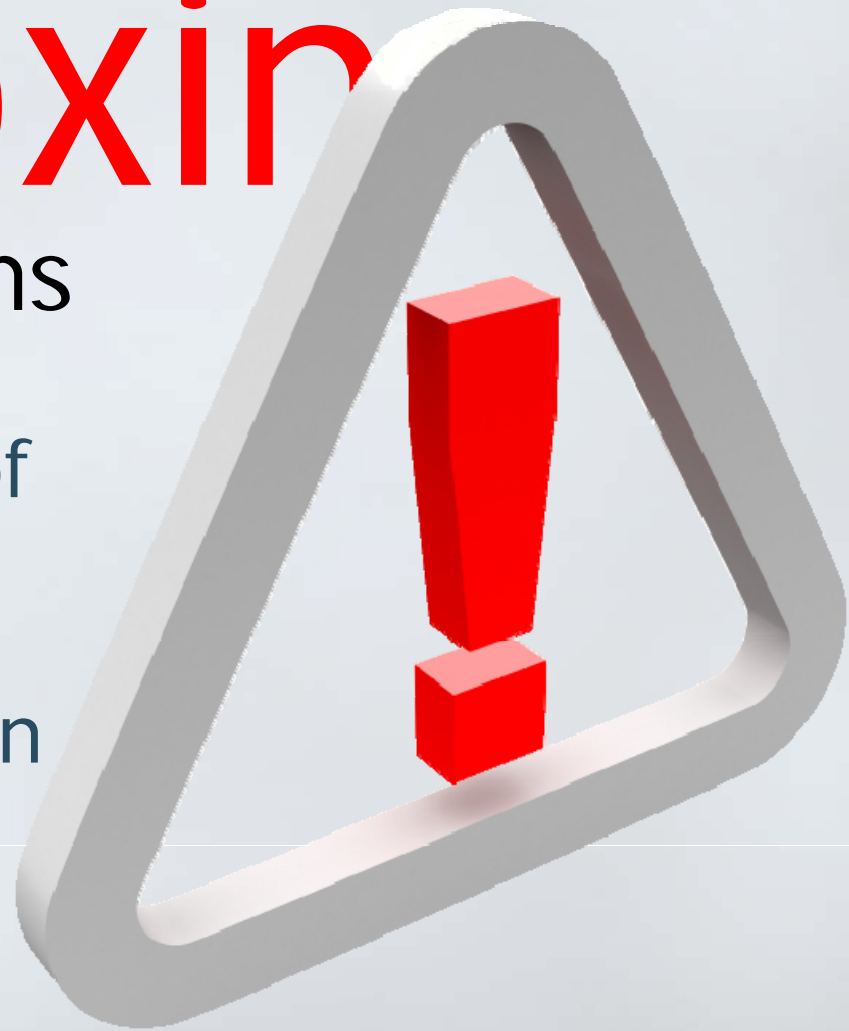
- Cry1Ab has “relatively significant thermostability...comparable to that of...Cry9C protein” found in StarLink corn.”

(Noteborn)

Bt-toxin

Industry claims
Bt:

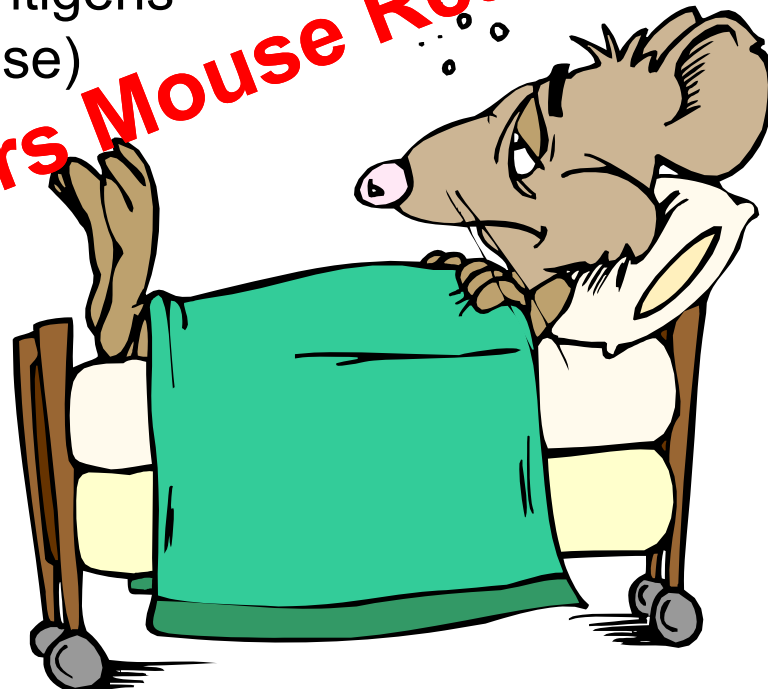
- Has a history of safe use
- Is destroyed during digestion
- Is not active in mammals



Bt-toxin:

- Is highly immune stimulating (immunogenic) – both mucosal and systemic responses
- As potent as cholera toxin
- Induces IgG, IgA, IgM responses
- (Dose dependent response observed)
- Is an adjuvant for other antigens (induces immune response)

Bt (Cry1Ac) Triggers Mouse Reactions



(Vazquez-Padron)

Bt-toxin:

- Produced enhanced immune response to Hepatitis B surface antigen, Bovine serum albumin for IgG, IgM, and IgA antibodies. (Proposed vaccine adjuvant.)
- Is as potent an immune stimulator as cholera toxin
- Cry1Ac is similar in structure to Cry1Ab used in most Bt corn

(Vazquez, Scand. J. Immunol)

Bt in Mice, con't



Bt Spray Affects Humans



Bt sprayed over Vancouver and Washington:

- 500 health complaints; 6 went to emergency room for allergies or asthma.

Farm workers:

- Eye, nose, throat, respiratory irritation, skin irritation, itching, swelling, allergic rhinitis, fever, altered consciousness, and seizures.

Farm workers exposed to Bt pesticides

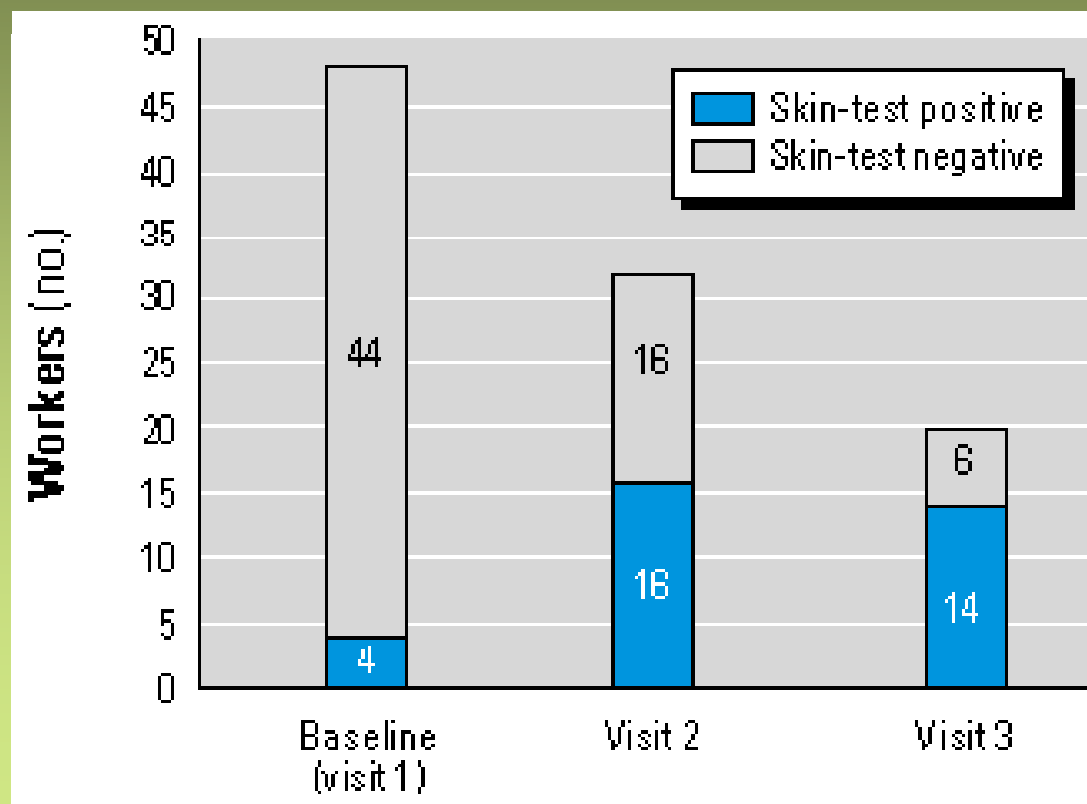


Skin prick tests with Btk antigens in high, medium and low exposure groups.

(Screens patients with suspected IgE mediated allergies—mediated by B cells)

(Bernstein)

“The number of positive skin-prick tests ... increased 1 month after exposure and persisted for 4 months after repetitive exposure.”



Serum antibody test (*Bt* extracts)



- Significantly higher IgG and IgE response in high exposure workers. Unexposed controls had no response.
- Some workers had IgG antibodies prior to first spray from exposure in years prior
- Specific IgE antibody levels in workers before first spray, increased after 1 month and remained elevated 4 months later



Symptoms

- Some workers reported respiratory, eye, and skin symptoms
- Those with significant reactions may have found work elsewhere (Healthy Worker Effect)

Implications

- “This is the first report of immune responses occurring in farm workers exposed to Bt-containing pesticides”
- “Exposure to Btk spray may lead to allergic sensitization”
- Shows allergic potential for environmental bacteria – a phenomena seen in relatively few bacteria
- Shows that, contrary to assertions, humans are reactive to Bt-toxin

Expert advisors to the EPA:

Mouse and farm worker studies:

“Suggest that **Bt proteins could act as antigenic and allergenic sources. ... Only surveillance and clinical assessment of exposed individuals will confirm the allergenicity of Bt products.”**

(EPA Scientific Advisory Panel 2001)

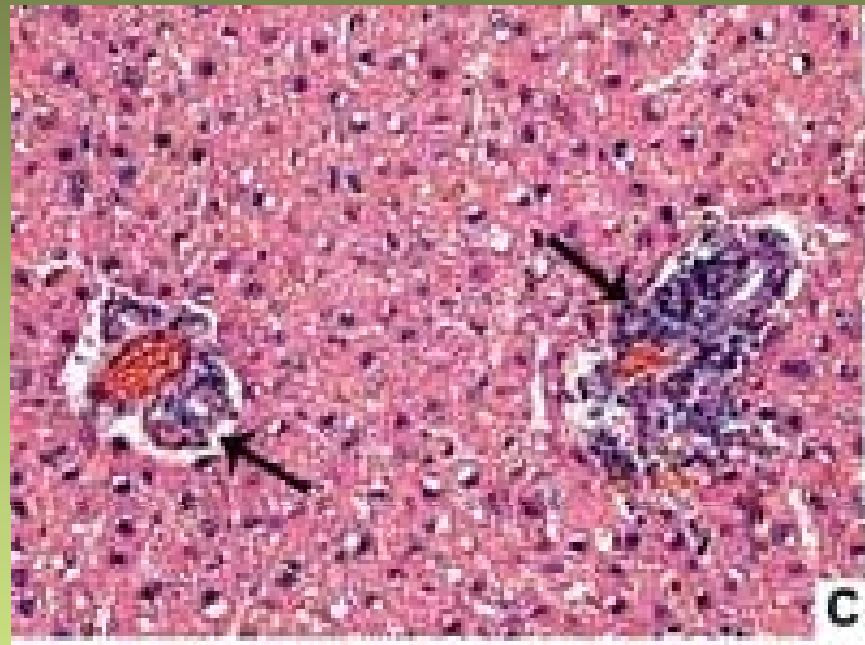
Bt in crops

- Thousands of times more concentrated than the spray
- Designed to be more toxic
- Has properties of a known allergen



Bt Corn in Rats (3 generations)

- Mononuclear cells (macrophages) infiltrate into the liver— inflammatory response



(Kilic and Akay)

Weaning and old mice fed Bt corn

(Mon 810)

Weaning mice:

- Changes in T cells, B cells and T cell subsets – $CD4^+$ and $CD8^+$, $\gamma\delta$ (gamma delta) T cells, $\alpha\beta$ (alpha beta) T cells

Old mice:

- Changes in B cells, T cells, $\gamma\delta$ T cells



(Finamore)

Age Factors

Old mice fed 90 days showed similar pattern to weaning mice fed 30 days

“The immune system during weaning and aging can less efficiently or inappropriately respond to external stimuli than during adult age”



(Finamore)

B Cells—a small lymphocyte (antibodies fight antigens)

Weaning mice, 30 days	B cells were lower in intraepithelial lymphocytes (IELs) and blood, Higher in spleen
Weaning mice, 90 days	B cell higher in IELs and blood
Old mice, 90 days	B cells lower in IELs and blood

Cytokines

(Immune signaling molecules)

“These cytokines (IL-6, IL-13, IL12p70, MIP-1b) are involved in allergic and inflammatory responses”

(Finamore)

Increased only in weaning mice

	Associations
IL-6	Rheumatoid arthritis, inflammatory bowel disease, osteoporosis, multiple sclerosis, various types of cancer (multiple myeloma and prostate cancer)
IL-13	Allergy, allergic rhinitis, ALS (Lou Gehrig's disease)
MIP-1b	Autoimmune disease and colitis. Elevated in lung fluid of patients with mustard gas pulmonary fibrosis

Increased in weaning & old mice

	Associations
IL-12p70	Inflammatory bowel disease, multiple sclerosis

Increased only in weaning mice

	Association
$\gamma\delta$ (gamma delta) T cells	<p>Regulates immune system – modulate inflammatory response re: infection and autoimmune disease.</p> <p>In humans: elevated in asthma, in the IELs of children with untreated food allergies, in the duodenum (small intestine) of children with juvenile arthritis or connective tissue diseases with gastrointestinal symptoms.</p>

CD4+ (helper T cells)

Weaning mice, 30 days	Higher in IELs, spleen, and blood
Weaning mice, 90 days	No difference
Old mice, 90 days	Lower in IELs, higher in blood

CD8+ T cells

Weaning, 30 days	Elevated in spleen, lower in blood
Weaning, 90 days	No change
Old mice, 90 days	Lower in blood

$\alpha\beta$ Alpha beta T cells

Weaning mice
30 days

Lower in IELs,
lower in blood

IgG & IgE

“Preliminary results indicate an increase of total IgG and IgE in both weaning and old mice fed MON810 maize as compared to its parental control maize”

(Finamore)



Implications

“Problems may arise when the immune system develops and functions inappropriately, resulting in inefficacy to develop tolerance toward harmless food proteins with consequent immunologic disorders”

i.e. broad spectrum food allergies

90 day Bt corn study (Mon 863)

Measure	Function	Potential indicator
Increased Basophil Counts	Creates histamine	May indicate allergic reaction
Increased Lymphocyte Counts	Immune reactions to fight infections, etc.	Lymphocytes increase in the presence of infections, cancer, various toxins, and disease states
Increased White Blood Cell Counts	Same as above	Can result from bacterial infections, inflammation, leukemia, trauma, and stress

(Burns)

Mice fed GM corn

NK603 (RR) x MON 810 (Bt)

- Higher spleen weights (F2 males only)
- Dense fibrillar component (DFC) values of spleen lymphocytes elevated (males only) – indicating increased activity
- **439 genes dysregulated – including interleukin signalling pathway genes**

(Velimirov)



Rats fed Bt rice

28 day	IgG1 and IgA (trend) response
90 day	IgG2 response, Significant decrease in white blood cells

Antibody responses found in control groups that were exposed to GM food dust.



(Kroghsbo)

Bt cotton!

Laborers in India
reported allergic
reactions to Bt
cotton





**Itching all over the body,
eruptions, wounds,
discoloration**



The Sunday India, 10/26/08

- **Hospital records:** "Victims of itching have increased massively this year . . . related to BT cotton farming."
- **Pharmacy manager:** "Almost every cotton worker from this village suffers from itching."



*Upper
respiratory*

Eyes

Skin

Overall

*Bt
Spray*

sneezing
runny nose
asthma

watery
red

itching burning
inflammation
red, swelling

fever

some in
hospital

*Bt
cotton*

sneezing
runny nose

watery
red

itching burning
eruptions
red, swelling

fever

some in
hospital

Bt itself as allergen

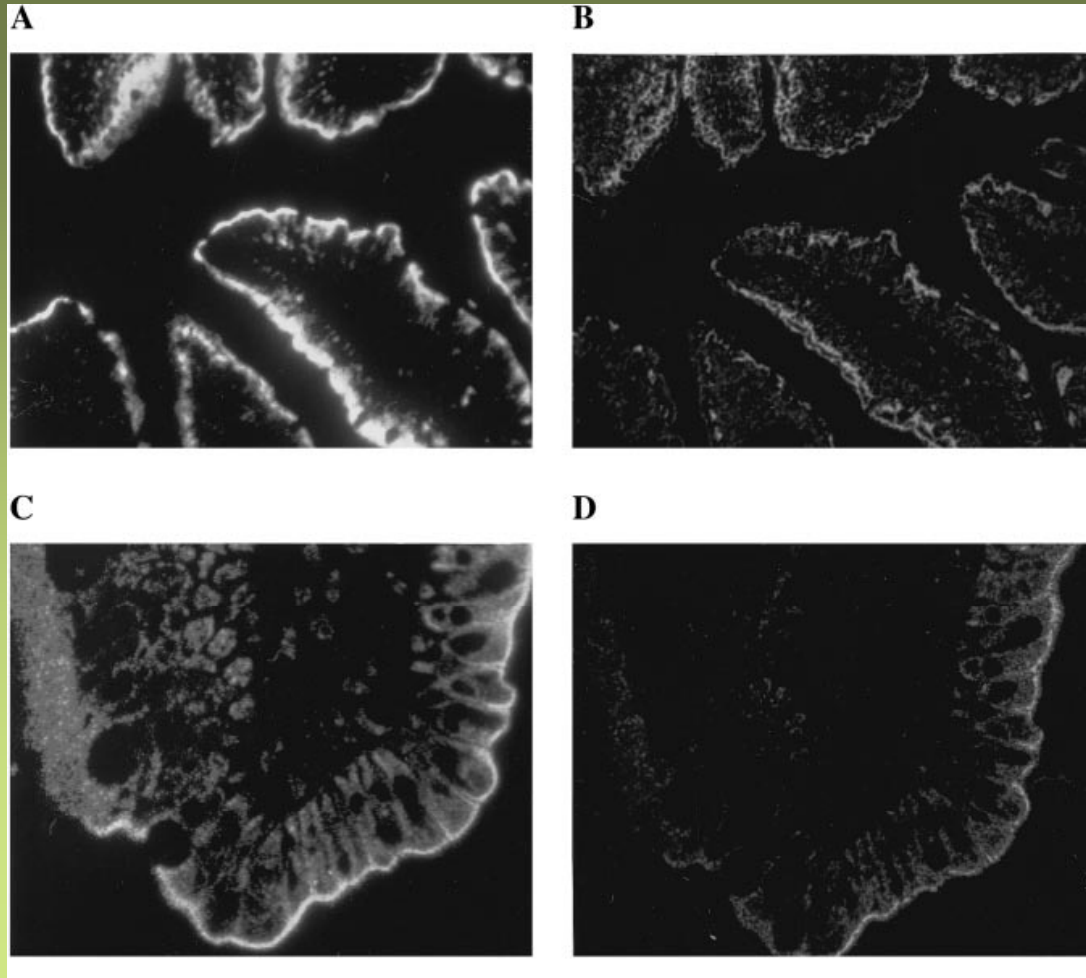
Cry proteins may be processed and presented to immune system by antigen presenting cells (APCs), indicating that Bt is an antigen.

(Vazquez – Biochem and BioPhysical Research Communications)

Alternative Bt causation

Bt
protein
binds to
Jejunum

(Vazquez-Padron, 2000)

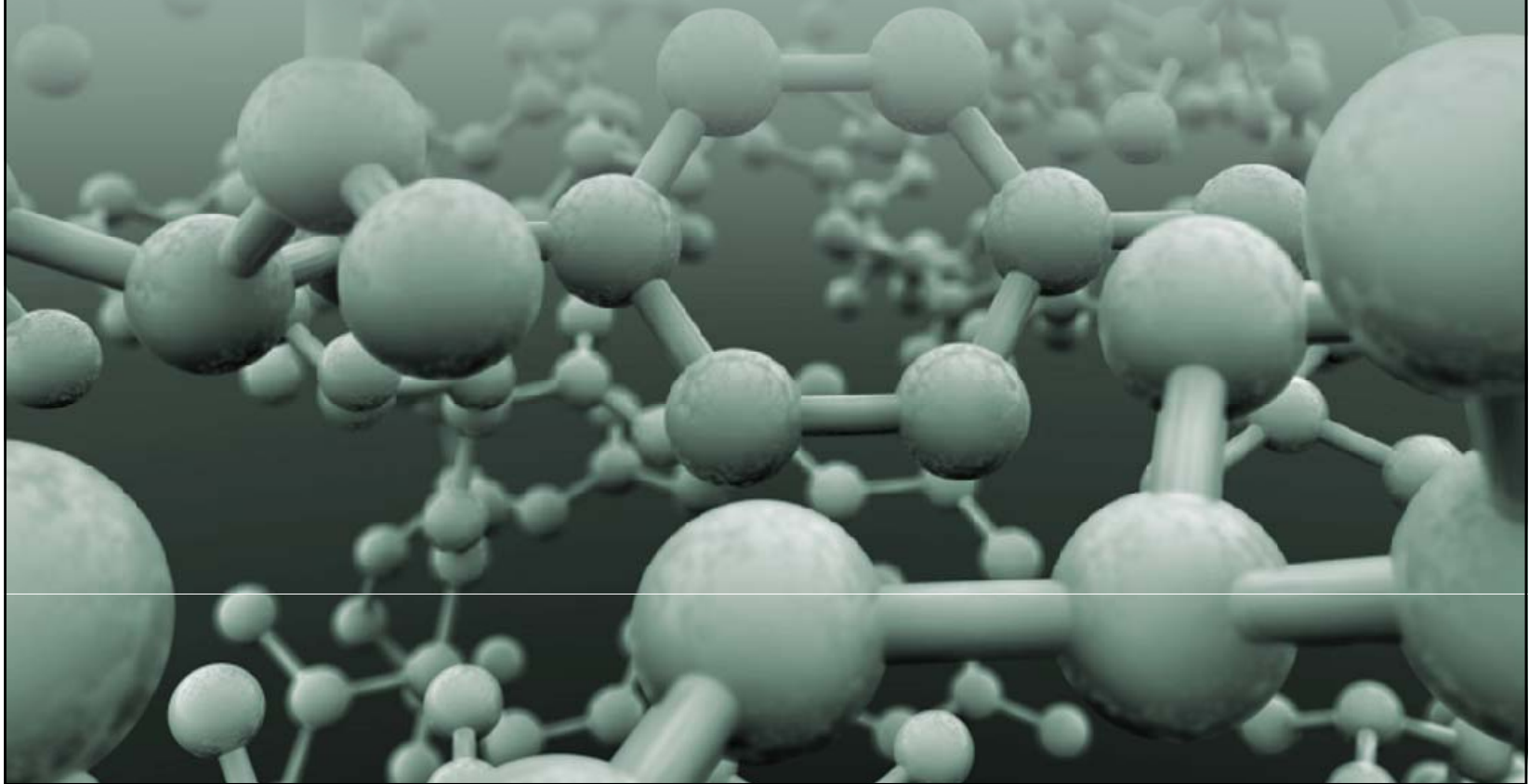


Alternative Bt causation

Leaky gut

Second reason for problems

The protein may be different than intended





The transgene sequence may:

Mutate or
truncate

Rearrange

Be read
differently

Produce
multiple
proteins

Changes in GM Protein

- **GM Soy**
 - 4 new RNA variants may create new proteins
- **Mon 810**
 - Truncated transgene
 - Protein is a combination of transgene and native DNA coding
- **Mon 863**
 - Point mutation

The protein may:



- Be folded differently
- Have different molecules attached

**Altered
protein in
GM peas
may have
made them
deadly**

*Agricultural
Food Chemistry,
2005*



GM peas with aAI



GM fed mice:

**Delayed type hypersensitivity
(DTH)
(used to determine preexistent
cell mediated immunity –
mediated by T cells)**

**IgG1 significantly higher in
mice fed TG peas**

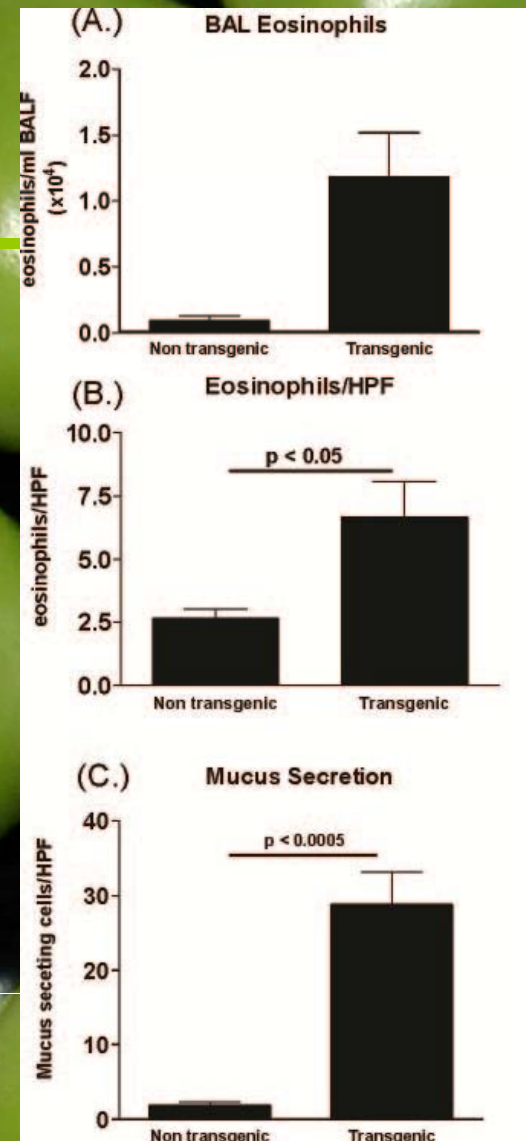
**Sensitized to egg white protein
alone—strong Th₂ type
response**

(Prescott)

Th2 type immune response

Characterized by:

- Pulmonary eosinophilia
- Mucus hypersecretion
- Airway hyper reactivity



Th2 cytokines

Pathway:

Th2 cells secrete interleukins IL-4, IL-6, IL-10 – which turn on IgE production by B cells, increase mast cells, and increase eosinophils

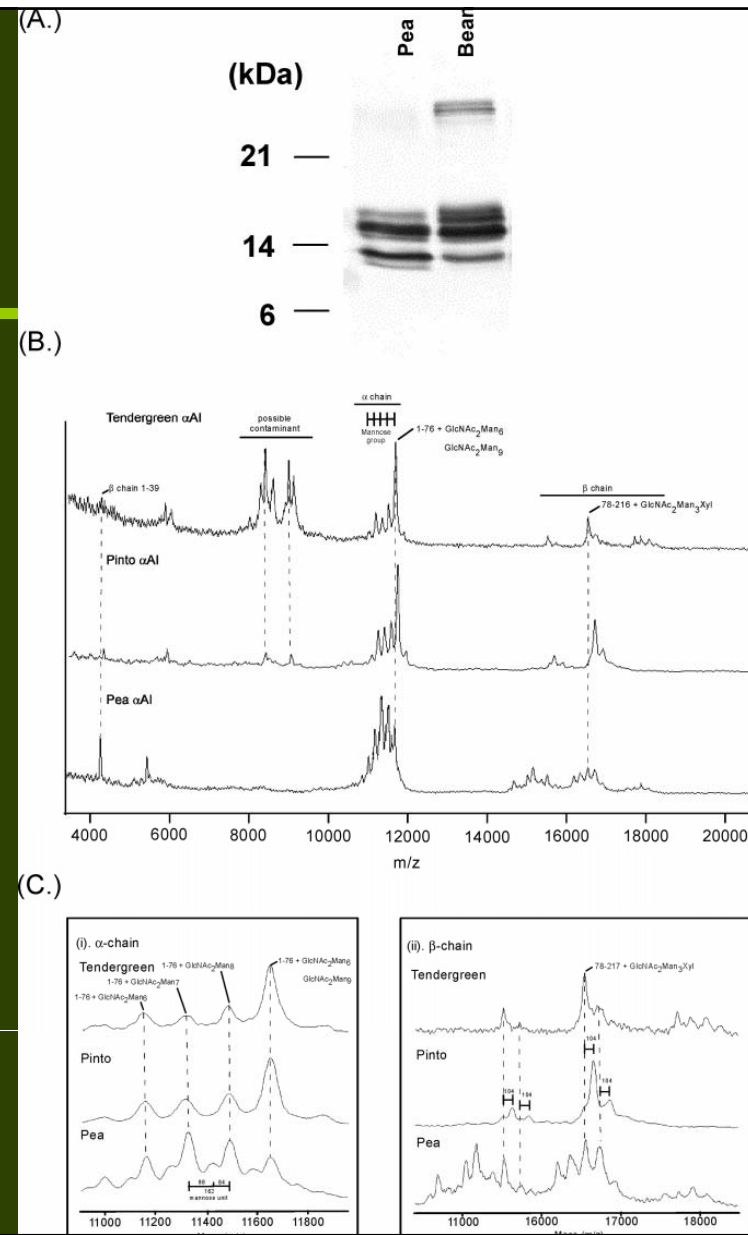
- Th2 diseases
 - Allergy
 - Asthma
 - Lupus
- Chemical Sensitivity
- Inflammatory Bowel Disease

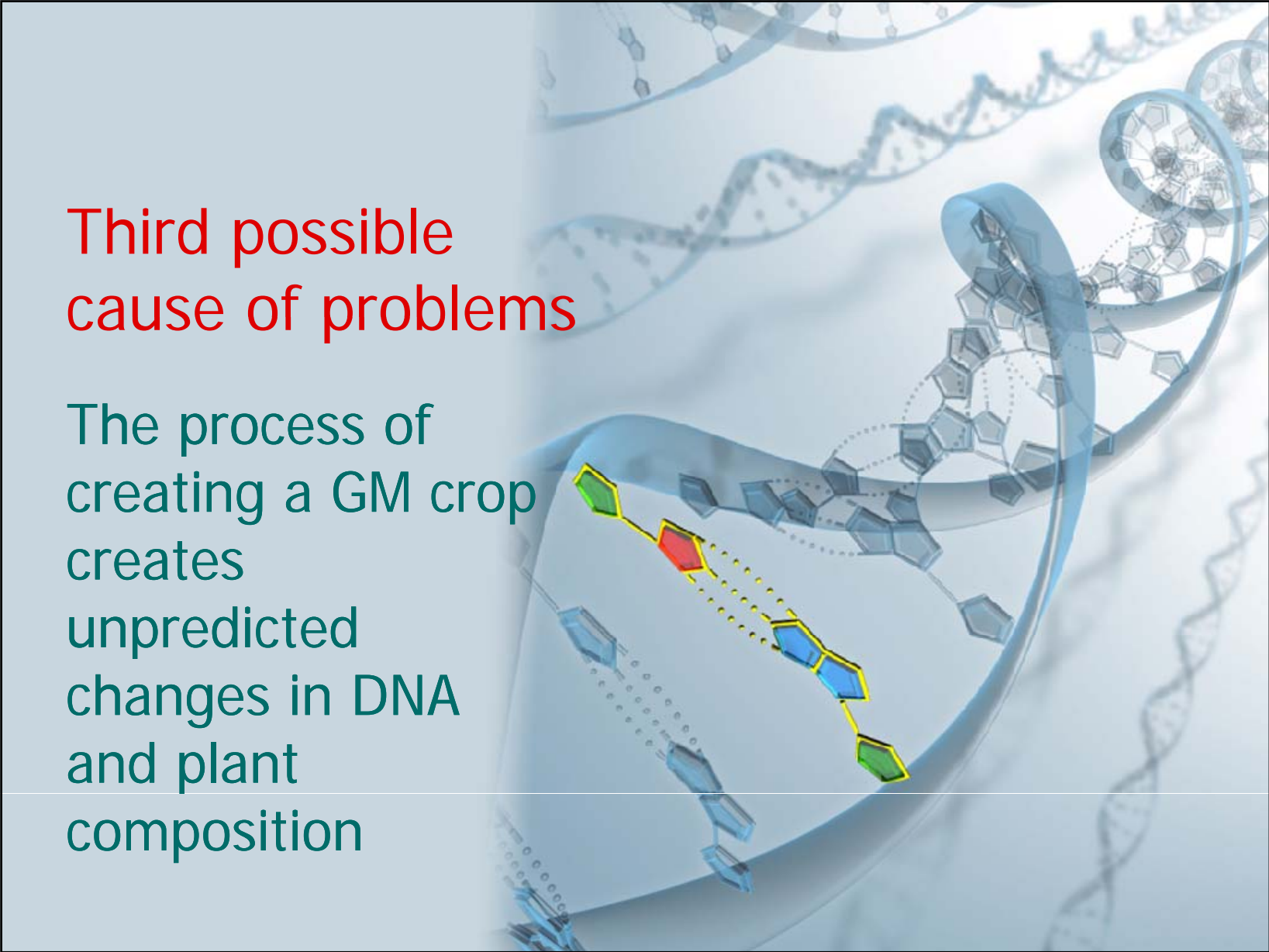


The Cause? Post translational modification

- Mass spec and Immunoblot of pea- α AI:
- Changes in the protein structure - potential for being a new antigen

(Prescott)



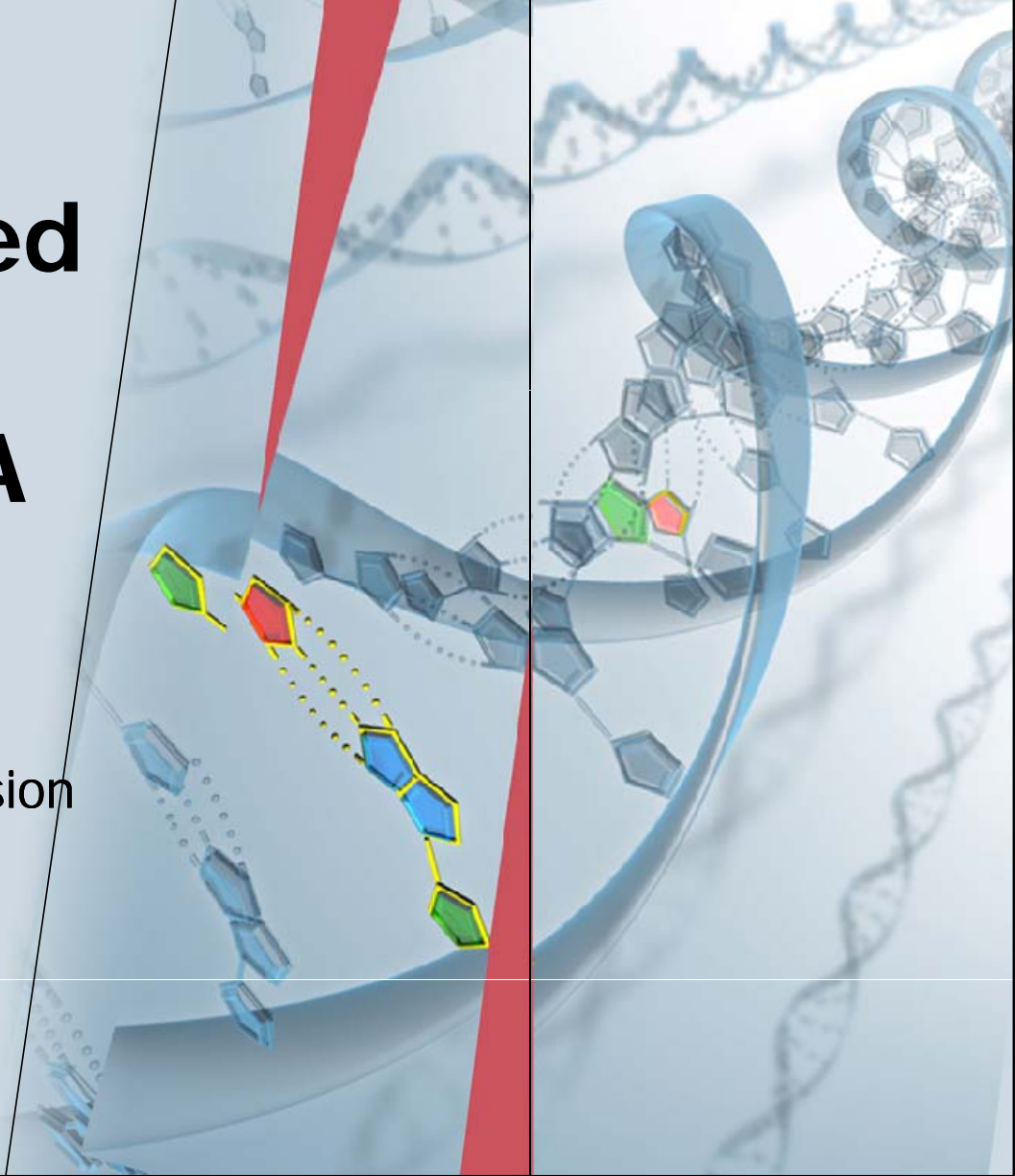


Third possible cause of problems

The process of
creating a GM crop
creates
unpredicted
changes in DNA
and plant
composition

Unexpected changes in the DNA

- Mutations (2-4% of DNA)
- Deletions
- Altered gene expression (up to 5%)



Changes in Mon 810 corn



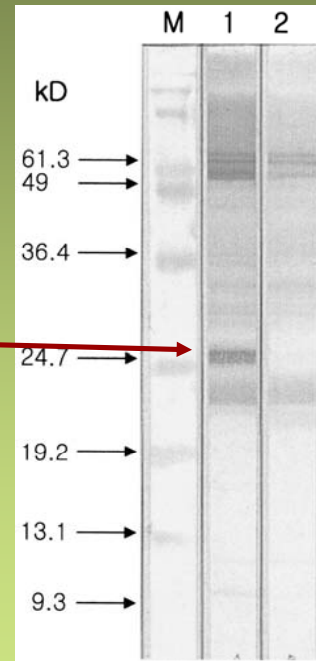
“Interestingly, a newly expressed spot (SSP 6711) corresponding to 50 kDa gamma zein, a well-known allergenic protein, has been detected. Moreover, as a major concern, a number of seed storage proteins (such as globulins and vicilin-like embryo storage proteins) exhibited truncated forms having molecular masses significantly lower than the native ones.”

(Zolla)

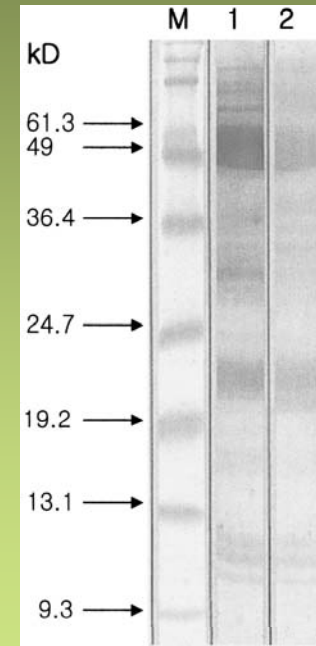
GM vs wild soybeans (difficult to compare)

Unique protein band
at ~25 kDa, binding
with IgE.

Potential new
allergen



GM soy



Wild soy

(Yum)

Follow-up needed

- Either “the 25-kDa band may be a protein unique to the GMO soybean, an intermediate product in response to the gene recombination process,” or
- “Soybean materials . . . may evolve differently under different harvesting environments.”

GM vs wild soybeans (difficult to compare)

- 8 of 13 children skin tested positive to soy, also responded to GM soy.
- 7 of 8 children who tested positive for GM soy also responded to wild soy.

(Yum)





GM soy has increased soy allergen

Trypsin inhibitor
(soy allergen)
up to 7 times higher
in cooked GM soy
(Not denatured from
cooking!)



Rats fed GM potato (GNA lectin)

- **Lining of the small intestine showed elevated lymphocyte counts**
- **Thymus and spleen showed changes**
- **White blood cells responded more slowly**

(Ewen and Pusztai)



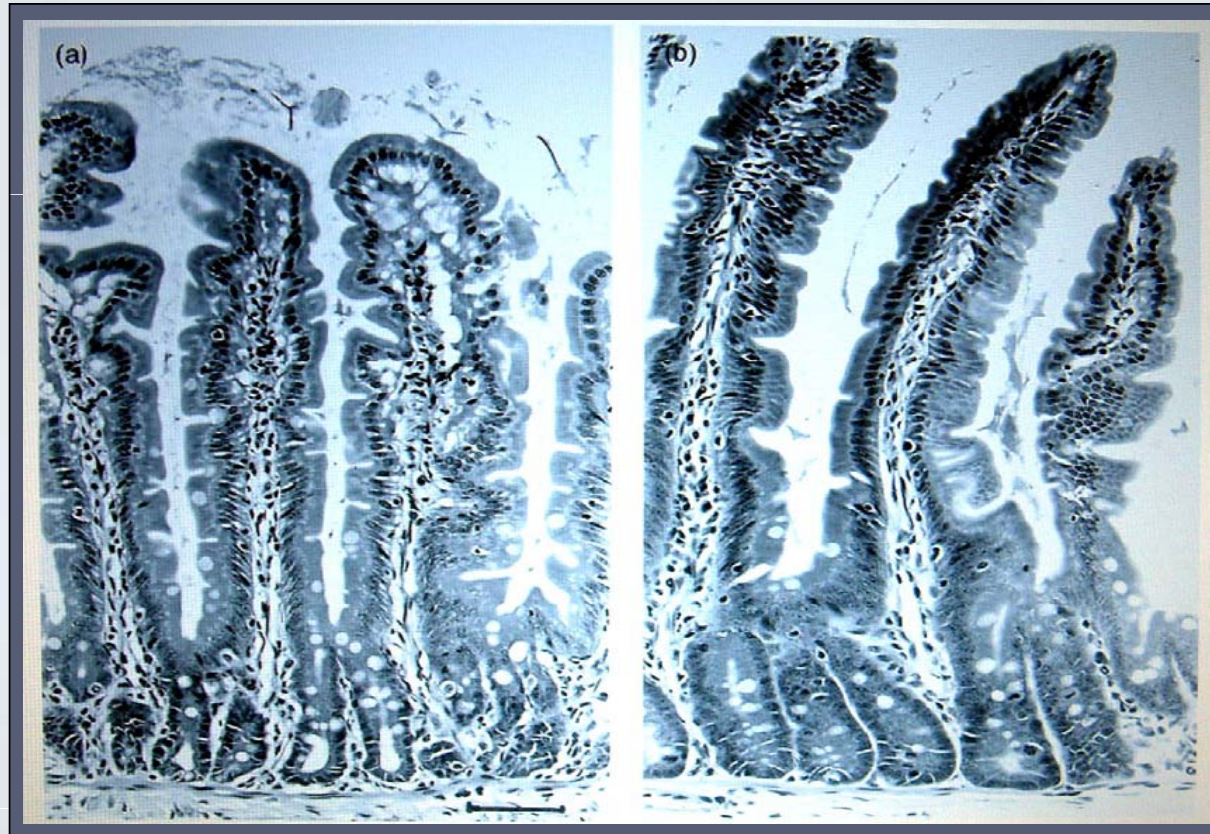
GM potatoes damaged rats (10 or 110 days)

Rats developed

- **Potentially pre-cancerous cell growth in the digestive tract**
- **Smaller brains, livers and testicles**
- **Partial atrophy of the liver**

(Lancet, 1999)

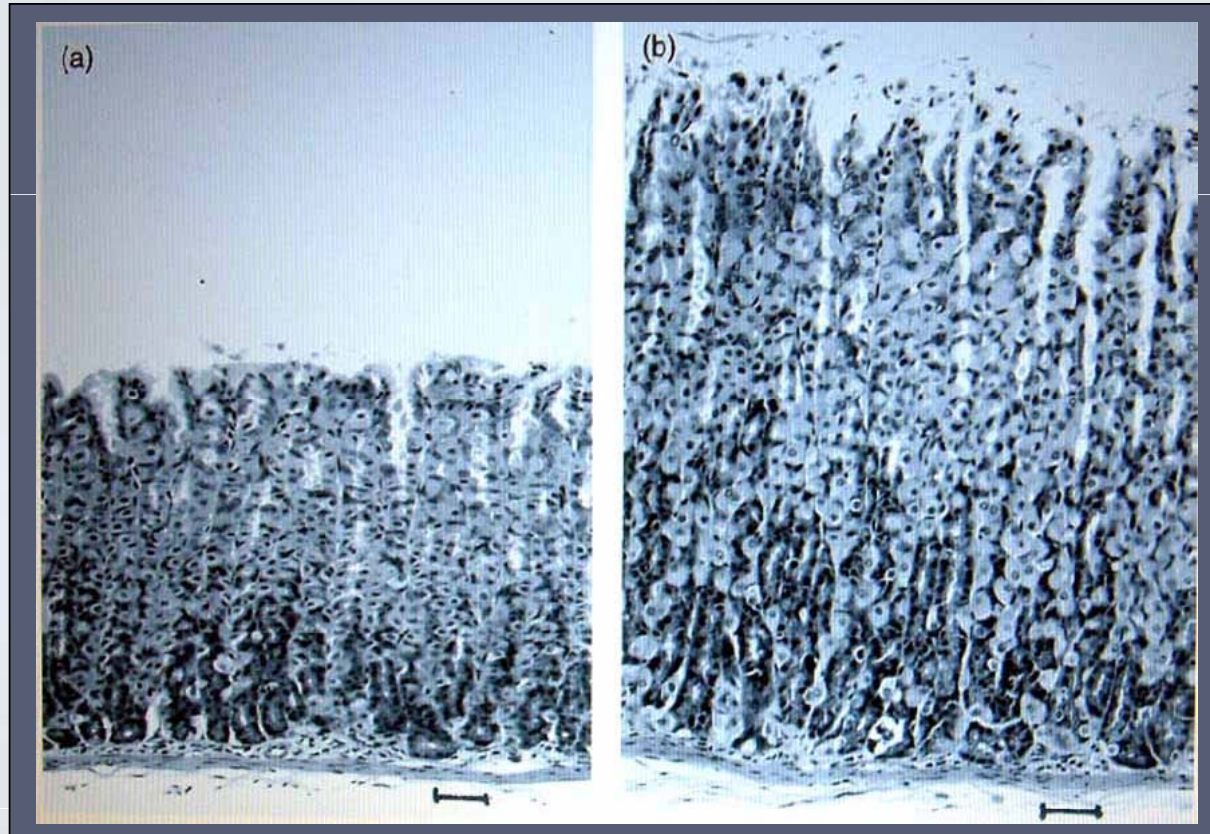
Intestinal Wall



Non-GM

GM

Stomach lining



Non-GM

GM



L-tryptophan produced by GM bacteria

Killed about 100 and caused
5,000-10,000 to fall sick



Eosinophilia Myalgia Syndrome (EMS)

Enormous rise in eosinophils

Fourth possible problem



More herbicide residues
in herbicide tolerant crops

More Roundup (glyphosate) residues



Symptoms of exposure:

- Eye irritation, rashes, itchy skin, nausea, sore throat, asthma, difficulty breathing, headache, lethargy, nose bleeds, dizziness
- Damage cell cycle, human placental cells
- Increased risk of non- Hodgkin's lymphoma, miscarriages, ADD, Parkinson's

More Liberty (Glufosinate) residues



“Mock neurotransmitter,” structurally similar to glutamic acid

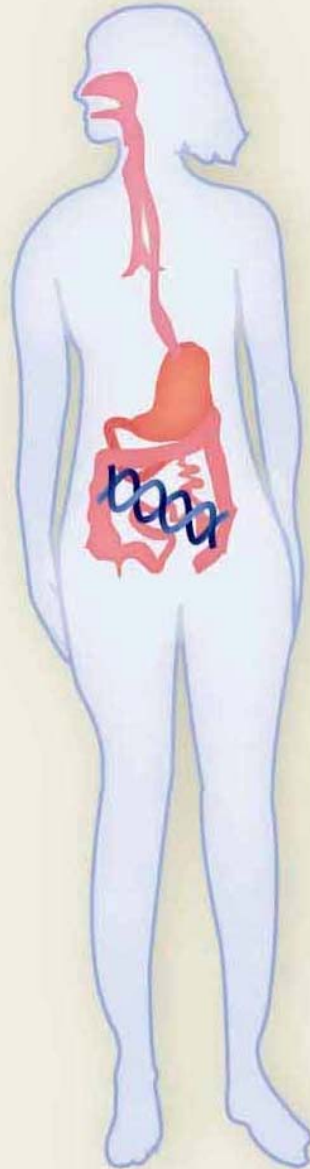
- Stimulates central nervous system, kills brain cells
- Fetal or infant exposure: can affect behavior, retard growth, increased death rates, interfere with forebrain development, and cause cleft lips
- Adult exposure: unconsciousness, respiratory distress, convulsions, a kidney disorder

Both Roundup and Liberty



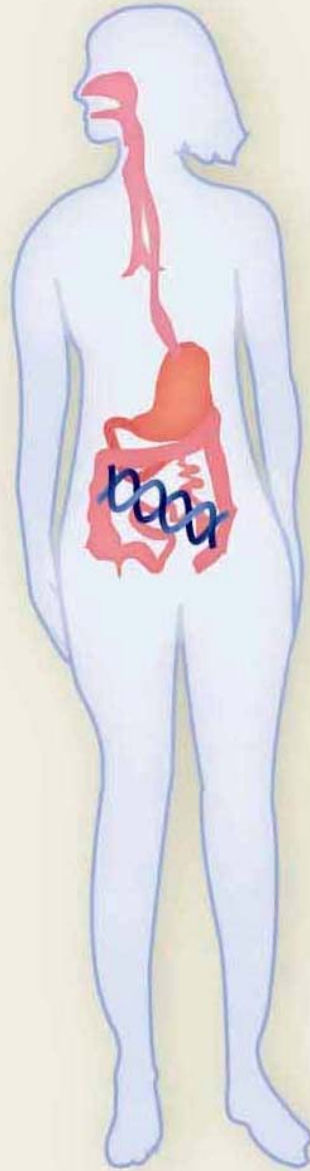
Have antibacterial properties
and may affect gut bacteria

Fifth
possible
problem



Gene
transfer to
gut bacteria
or
into our
DNA

The Only
Human
Feeding
Study on
GM Crops



Roundup
Ready
genes
transferred
to intestinal
bacteria

- Promoter
- Antibiotic resistant marker
- Roundup Ready gene
- Liberty Link Gene
- Viral gene
- Bt gene



What can transfer?



*Sixth possible cause:
Altered digestive capacity*

- Digestive enzymes reduced
 - Altered gut bacteria



Six causes

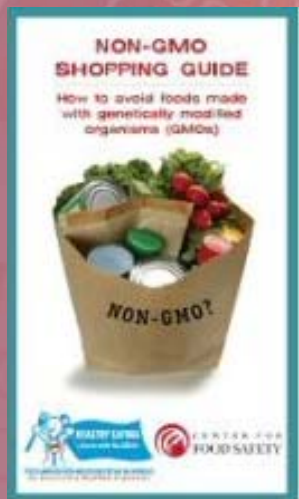
- 1. Transgene product (Bt)**
- 2. Protein changes (peas)**
- 3. GM process (new antigens)**
- 4. Herbicide residues**
- 5. Transferred genes**
- 6. Reduced digestive capacity**

Campaign for Healthier Eating in America



www.ResponsibleTechnology.org

Distribution of patient education materials





jeffrey@*Seeds of Deception*.com

www.**ResponsibleTechnology**.org

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