Biotech on the Horizon

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http://ucbrep.info
GREENPEACE
Magazine
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IT Came from the Grocery Store

The HORROR of Genetic Engineering
Do you know what's in the food you're buying?
I won't eat anything that's genetically modified...

It could be unhealthy...
PUBLIC CONCERNS ABOUT BIOTECHNOLOGY

- Ethics of genetic modification (interfering with nature)
- Safety of food and of introducing genetically engineered organisms into the environment
- The alleged radical novelty, unpredictability, or irreversibility of biotechnology
- Possible negative impacts on employment or small farms
- Trust or lack of trust of government regulatory agencies
- Enhancement of corporate power and ownership of intellectual property
- Negative Globalization - Possible exploitation of developing countries
- Possible mistreatment of animals
True or False: “Ordinary Tomatoes Do Not Contain Genes, while Genetically Modified Ones Do”

- Canada: 52% False, 33% True, 15% Don't Know
- United States: 45% False, 45% True, 10% Don't Know
- Austria: 34% False, 22% True, 44% Don't Know
- France: 32% False, 39% True, 29% Don't Know
- Germany: 36% False, 20% True, 44% Don't Know
- Italy: 35% False, 44% True, 21% Don't Know
- Netherlands: 51% False, 27% True, 22% Don't Know
- Sweden: 46% False, 24% True, 30% Don't Know
- Switzerland: 48% False, 21% True, 31% Don't Know
- United Kingdom: 40% False, 38% True, 22% Don't Know

1996 - 1998

Slide from Tom Hoban, NC State
True or False: “By Eating a Genetically Modified Fruit, a Person’s Genes Could also Be Changed”

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1996 - 1998

Percent Response

False (Correct)  Don’t Know  True
"Genetically Modified Animals are Always Bigger than Ordinary Ones"

<table>
<thead>
<tr>
<th>Country</th>
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<td>Ireland</td>
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EuroBarometer, Macer, Einsiedel, Hoban & Miller surveys
The Cow Pock or the Wonderful Effects of the New Inoculation!
James Gillray (1757-1815) Photographic reproduction of an etching appearing in Vide--The Publications of ye Anti-Vaccine Society, June 12, 1802, National Library of Medicine
Biotech Crops – 200 m Acres grown by 8.25 million farmers in 17 countries in 2004 = 20% growth - 90% resource-poor LDC farmers

US 45% corn, 85% soybean acreage and 76% of cotton

Substantial net economic benefits at the farm level amounting to a cumulative total of $27 billion.

The technology has reduced pesticide spraying by 172 million kg

Reduced the environmental footprint of pesticide use by 14%.

Significantly reduced the release of greenhouse gas emissions - GM crops accounted for a reduction in 9.4 billion kg of carbon dioxide emissions in 2004 which is equivalent to removing five million cars from the roads. (Brookes and Barfoot 2005)

China, BT cotton eliminated use of 156 M Lbs pesticides (Rozelle, 2004)

80% reduction in pesticides - 100s lives saved

Up to 90% reduction in mycotoxin fungi that produce fumonisins
Regulation of Biotech Crops

FDA, USDA, EPA

- Commercialization takes 7 to 10 years and nine stages of review

- Biotech crops and foods are more thoroughly tested than conventional varieties (which are “assumed” to be safe)
  - One early type of biotech soybean alone was subjected to 1,800 separate analyses

- Toxicity studies (as necessary) (5 items)

- Nutritional content (7+ items) Substantial equivalence with parent variety

- Allergenicity potential

- Environmental aspects (5 items)

Public debate is often driven by emotion not reason.


- Declaration signed by over 4,000 scientists 25 Nobel Laureates

The World Health Organization (WHO) June 2005 Report

- “Modern food biotechnology, human health and development: an evidence-based study.” The report concludes, “GMOs offers potential of increased agricultural productivity, improved nutritional values that can contribute directly to enhancing human health and development.

- From a health perspective, indirect benefits reduction in ag chemical usage, enhanced farm income, crop sustainability and food security, particularly in developing countries.
SECRETLY, HUMAN RESEARCH CONTINUED...
Animal Biotechnology - Applications

- Recombinant vaccines and therapeutics, e.g. rabies, rinderpest in vaccinia delivery vectors
- Diagnostics
- Marker assisted selection
- Improved nutrition - supplements, enzymes - Phytase, Carbohydrases
- Transgenics
  - Agriculture Applications
    - disease resistance
    - improved productivity
      - improved growth rate
    - improved metabolism
    - improved milk quality
    - improved meat quality (increased protein)
    - reduced fat
- Advantage:
  More efficient production of animal-derived foods.
  Fewer resources produce same amount of food: less waste.
- Medical Applications
  - produce valuable proteins in milk, blood or urine
  - Xenotransplantation
  - Disease and developmental models
Mice
Rats
Pigs
Cattle
Goats
Sheep
Fish
Chickens
Rabbits
Fish attractive candidates
• produce eggs in large quantities outside the body.
• aquaculture one of the fastest growing food-sectors
• Since 1984, aquaculture has expanded 10% pa, 3% for livestock meat
• 1.6 percent rate of growth for capture fisheries (FAO 2000).
Better Quality Farm Animals

• Serguei Golovan with Wayne the low-phosphate pig.
• Better food us – adoption to available diets
• Healthier milk/meat composition
Transgenic Goats for

Anti-microbial properties
Changes in processing properties:
- decreased clotting time
- increased curd strength

Anti-microbial activity against pathogens and cold spoilage bacteria

Changing milk fat
Decrease saturated Fatty acids
In ruminants increase anti-carcinogenic, anti-inflammatory CLA
Triglycerides (TG) found in the milk of the echidna, a primitive monotreme, differ from those found in the milk of any other mammal in that they have a fatty acid distribution similar to that found in vegetable oils. Alison Van Eenennaam is cloning and characterizing the substrate specificity of the echidna TG biosynthetic enzymes with a view to making “vegetarian” milk!
<table>
<thead>
<tr>
<th>Protein</th>
<th>Use</th>
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<td>a -1 - antitrypsin</td>
<td>anti-inflammatory</td>
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<td>Anti-thrombin III</td>
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<td></td>
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<td>C1 inhibitor</td>
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<tr>
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<td>burns, bone fracture, incon</td>
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<td>Factor IX &amp; VIII</td>
<td>hemophilia</td>
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**Animals made using nuclear transfer.
Nexia's lead products are biomaterials and pharmaceuticals. Recombinant proteins in the milk of transgenic BELE goats. Nexia will further process the milk to purify recombinant products. BioSteel filaments 80 steel -where strength and flexibility are required, such as medical devices or body armor.

Protexia is a recombinant version of butyrycholinesterase, (BChE) found naturally in small quantities in animal and human blood. BChE is bioscavenger, binds nerve agents before they reach the brain and other sensitive sites. Mitigates xenotoxin but the quantity found naturally in human blood is quickly overrun by a nerve-agent challenge.
Bring in the Clones?

- High-merit farm animals
- Preserve endangered species banked tissue
- Duplicate valuable “pharm” animals
- Create homogeneous populations of cells, tissues and even organs for therapeutic transfer for organ failure patients.
- Unique tool to study gene function, genome activation, cancer, aging and development
Cloning by Nuclear Transfer at UCDavis

Donor cells are grown in tissue culture.

Donor cell nucleus is transferred to recipient egg.

Cloned embryo is transferred to surrogate mother.

Pregnancy is monitored by ultrasound.

Tissue biopsy is taken from donor cow, Daisy.

The two cloned calves, Dot and Ditto, on display at the State Fair, were born May 2003.

Here's Rosie
Xenotransplantation

- 60,000 people annually need an organ transplant, only half actually receive a transplant.
- Approximately 3,000 people die each year waiting for a transplant.
- Roslin knockout pigs, for gal-a-1,3-gal sugar residues, prevent hyperacute rejection of xenogenic tissues.
- Imutran has successfully produced transgenic pigs that express the human shield protein, decay accelerating factor (DAF).
- Cellular therapies such as transplantable cells that produce insulin for treatment of diabetes.
Marathon Mouse

- 23 August 2004: Marathon Mouse: Ron Evans et al. genetically engineered an animal that has more muscle, less fat and more physical endurance than their littermates.
- Increasing the activity of a single gene - PPAR-delta.
- Mice ran 1,800 meters stayed on the treadmill an hour longer than controls, which stayed running 90 minutes and travel 900 meters.
- They also seem protected against weight gain that follows a high fat, high calorie diet
**Microinjection v. Somatic Cell Nuclear Transfer**

- **Pronuclear Injection**
  - Random insertion (unpredictable outcome)
  - Low efficiency (costs of recipients is very high)

- **Nuclear Transfer with Transgenic Cells**
  - Random insertion or homologous recombination
  - Speed and efficiency
    - ultimately more efficient production of transgenics
    - Potential to make very precise genetic changes (gene targeting) insert into cloned offspring
    - requires fewer animals
    - new health products come on line more quickly
    - speed xeno-transplantation - change surface antigens of donor organ to make less antigenic

- **First generation clones (Fo) may have epigenetic abnormalities.**
Potential Problems

- Cloning may reduce genetic variability
- Cloning is currently an expensive process. Lots of money and biological expertise. Technique has 2-3% success rate.
- There is a risk of disease transfer between donor animals and the recipient.
- Life expectancy? Because clones are derived from an existing adult cell, it has “older” genes. Degeneration
- Inadvertent selection of undesirable characteristics
- Genetic Problems? Genetic imprinting? Epigenetic effects
  Cytoplasmic inheritance X inactivation, shortened telomeres
  Large Offspring Syndrome
- So far, most clones have appeared to be perfectly normal.
- Jaenisch found abnormal regulation of genes in cloned mice
  Mann found disruptions in total transcript abundance and allele-specificity of expression for 5 imprinted genes. Only 4% recapitulated a blastocyst mode expression for all 5 genes
- Epigenetic errors early in clone development reprogramming is inefficient, some epigenetic information lost.
Biomedical: xeno mobilization of new infectious agents.

Food/feed:
- New proteins, and food safety concerns posed by biological activity, allergenicity, or toxicity evaluated on case-by-case
- Cloned animals: degree genomic reprogramming results in altered gene expression that raises food safety concerns.
- Substantial Equivalence
- No current evidence that food products derived from adult somatic cell clones or their progeny present a safety concern.

Environment
- Escape and become established in the natural environment.
- Current reg framework not adequate – esp. arthropods.

Animal Welfare
- Concerns regarding the potential to cause pain, physical and physiological distress, behavioral abnormality, and health problems, also potential to alleviate or reduce those problems.

Technical capacity of the agencies to address potential hazards
Transgenic/ cloned animals under development regulated by one or more FDA Centers. As part of the INAD submission, Researchers must document their plans regarding the disposition of all investigational animals. Important in the case of food animal species

- Milk/Meat from Clones voluntarily withheld from food supply
- Procedures for biopharm animals (producing drugs or biologics) the Center for Veterinary Medicine (CVM) serves as a consulting group to the other FDA Centers food and feed safety evaluation.
- Gene-based modifications of animals for production or therapeutic claims fall under CVM regulation as new animal drugs.
- Investigational applications are filed where adequate safety data exists
- Sponsor may request disposition of animals for food or for processing into animal feed components.
- To date, no transgenic animals have been approved for use as human food. A very limited number have been approved for rendering into animal feed components.
CLONED ANIMAL PRODUCTS

- Milk and meat products from cloned cattle, pigs and goats are safe for consumers to eat – FDA 2003
- By 2006 grocery stores are most likely to sell meat and milk from the offspring of cloned animals. Parents will not be slaughtered for food because of their high price tag except where improved meat is the endpoint.
- A cloned calf can sell for as much as $82,000. An average calf sells for less than $1,000.
- ViaGen Inc., owned by Exeter Life Sciences, and Cyagra, is eagerly awaiting the FDA's decision on commercialization. Smithfield Foods Inc., the top U.S. pork producer, technology development contract with ViaGen.
- Cloned cattle between six and 18 months of age are "virtually indistinguishable" from their conventional parents, and can give birth to healthy offspring.
- Concerns about cloned animals immediately after birth. Many of the young animals are susceptible to under-developed respiratory and cardiovascular systems.
- The agency said the risk was small. "Given that live neonatal clones are unlikely to enter the food supply, they pose an extremely limited risk for consumption as food"
Consumer Perception 2005
International Food Information Council (IFIC)

• Less than 0.5% of those who are avoiding something said they had avoided foods produced through biotechnology.
• 62% expect food biotechnology to provide benefits for them and their families over the next five years,
  – better health/nutrition
  – improved food quality/taste/variety.
• Respondents would purchase if
  – Benefits in quality and taste (50%),
  – Healthy oil (41%)
  – Health and nutrition (31%),
  – Reductions in chemicals and pesticides (64%),
• Over 55% support FDA Labeling policy for biotech foods
  – 76% could think of no information “not currently included on food labels” that they would like to see
  – On an open-ended basis, only one percent name biotechnology as a labeling issue.
BIOETHICS PANEL ON CLONING
“Although humans make sounds with their mouths and occasionally look at each other, there is no solid evidence that they actually communicate among themselves”