Dolly, BST, and transgenic animals: Cloning around with animals and genes

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Introduction

- Growing use and demand for agricultural animal biotechnology
- Biomedical purposes
  - Genetic selection
  - Gene therapy
  - e.g., for humans & companion animals
  - Disease management

Areas of ethical concern about animal biotechnology

- Safety/risk
  - What are the long/short-term effects?
  - Environmental impact
- Distributive justice
  - Who benefits?
- Animal welfare
  - Is the animal harmed?

rBST (bovine somatotropin)

rBST

- rBST
  - Naturally occurring protein
  - Produced and secreted from anterior pituitary
  - Regulates growth, stimulates milk production, improves productive efficiency
- Banned in European Union nations
- Synthesized using recombinant DNA techniques
  - bovine somatotropin (rbst)

Kunkel, 2000

rBST (Bovine Somatotropin) Applications

- Approved by the FDA in 1993
- Currently used by over 30% US dairy farmers
- Marketed as Posilac® by Monsanto
- Primary objectives:
  - Improve milk production in cows
    - up to 10-15 %
  - Increase production efficiency (yield/unit feed)

Ethical questions arising from use of rBST

- Health risks to humans?
  - Is rBST milk safe for human consumption?
  - Is there increased risk for developing allergies?
  - Should rBST milk be labeled?
- Animal welfare
  - Are cows injected with bST harmed?
    - Reports of increased mastitis, decreased conception rates, inflammation from repeated injections, arthritis, lameness

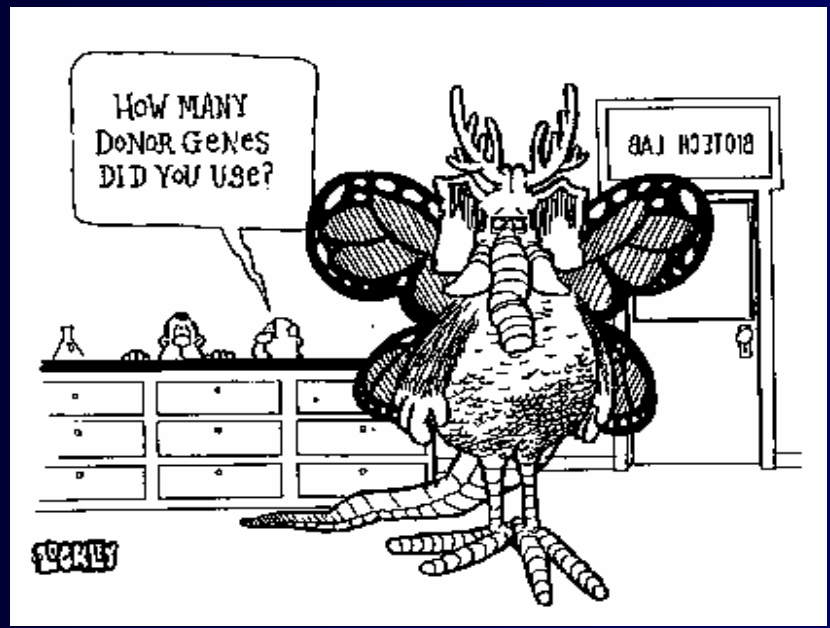
Ethical questions arising from use of growth promotants

- Distributive justice
  - Idea that small dairies would be even more disadvantaged than large commercial dairies
  - Potential for biotech to contribute to demise of small farms
    - Loss of choices in products offered

Transgenic animals

Transgenic animals

- Transgenic animals carry and express genetic information not normally found in that species (Singleton, 1999)
- “Frankenfoods”; “Pharm animals”; “Manimals”



Transgenic animals

- First transgenic mouse produced in 1981
  - Human growth hormone inserted into a mouse (Singleton, 1999)
  - Used to produce monoclonal antibodies and anti-inflammatory agents $\Rightarrow$ useful for disease and infection treatment

Transgenic mouse compared to normal littermate. The transgenic mouse has had human growth hormone gene inserted into its genome.

Uses of Transgenic Animals

- Applications
  - Basic science: tools for fundamental research in agriculture, biology and medicine
  - Model development and progression of human disease e.g., CF
  - Facilitate xenotransplantation (animal-human organ transfer)

Singleton, 1999

Uses of Transgenic Animals

- Commercial use of farm animals to express highly desirable products
  - sheep modified to produce biologically active tissue plasminogen activator (TPA--therapeutic agent for human clotting disorders)
  - Factor VIII and Factor IX used to treat clotting disorders (hemophilia)
  - lactoferrin in milk; lactoferrin is an antibacterial protein used to treat immunosuppressed patients; (could be incorporated into infant formula)

Pew Initiative, 2001

Other benefits of transgenic technology in farm animals

- Alter milk composition
  - Reduced beta- lactoglobulin ⇒ reduce allergies
  - Reduced lactose ⇒ aid lactose intolerance
  - Increased antimicrobial proteins
    - Could prolong shelf-life of milk
    - Could reduce gastrointestinal problems

Pew Initiative, 2001

Other benefits of transgenic technology in farm animals

- Production of new materials
  - E.g., transgenic goats have been bred to produce milk with proteins from spider genes
  - Result: create very strong material similar to spider silk, which can't be commercially produced

Pew Initiative, 2001

Transgenics in aquaculture

- Some species researchers are working with
  - catfish, carp, tilapia, striped bass, clams, oysters, shrimp, and abalone
- Traits under investigation in transgenic fish
    - Faster growth rates (3-11 times faster) & more efficient feed utilization
    - Increased tolerance to cold water
    - Improved disease resistance

Animal cloning

"The Dolly era"

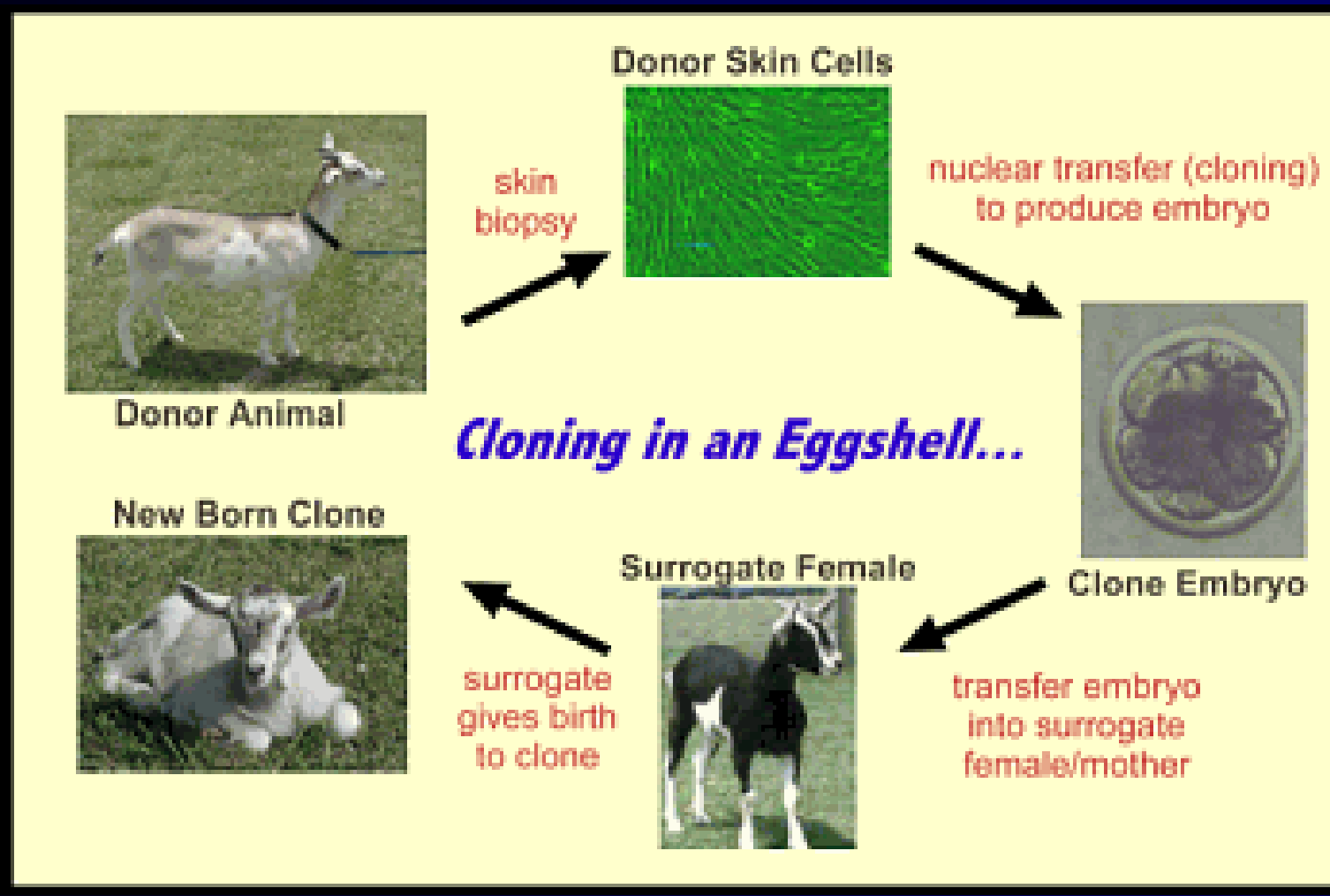
Cloning: a very brief history

- **1997: Dolly--first successful cloning of adult animal**
- **1997: Rhesus monkeys cloned**
- **1998: Cloned calves reported**
- **2001: Cloned pigs reported**
- **2001: Cloned gaur--first endangered species**
- **2001: First reported human embryo cloning**
- **2002: First cloned pet (cat)**

?

Cloning methods (overview of nuclear transfer)

- Nuclei extracted from cultured cells (embryo, fetus or adult)
- Nuclei inserted into egg cells which have their original nucleus removed (nuclear transfer)
- Egg cells with the transplanted nuclei then implanted into a foster mother for development


Donor Skin Cells
skin biopsy
nuclear transfer (cloning) to produce embryo
Donor Animal
Cloning in an Eggshell...
New Born Clone
Surrogate Female
Clone Embryo
surrogate gives birth to clone
transfer embryo into surrogate female/mother

Cloning Applications

- Produce superior livestock
- Facilitate “pharm” animal production
  - **Human therapeutic proteins**
- Facilitate xenotransplantation
  - **Safer source of organ and tissue transplants**
- Provide defense against bio-terrorism
  - Hematech and the Dynport Vaccine Corporation developing cloned cows to produce antibodies to botulinum toxin in milk

Other Cloning Applications

- Model human cloning techniques
- Save/recover endangered species
- “Resurrect” treasured pets
  - (e.g. Genetic Savings and Clone) **http://www.savingsandclone.com**

Transgenics and cloning

- The reality:
  - Very expensive technology
  - Technologies still need to be refined
    - large numbers of repetitions required to produce viable offspring in animals
  - Applications currently very limited--predominantly used for biomedical purposes

Ethical issues associated with transgenics and cloning

- Technology isn't perfected yet
  - Very low success rate
  - High mortality rates

Ethical issues associated with transgenics and cloning

- **Safety/risk of consumption**
  - According to the U.S. Food and Drug Administration
    - Cloned animals probably safe to raise and eat
    - Transgenic ones may not be safe to consume

Ethical issues associated with transgenics and cloning

- Animal welfare
  - ⇑ birth weights, longer gestation, difficult births in clones
  - Poor survival rate of fetuses using some techniques
  - Anatomical, physiological, behavioral abnormalities

Ethical issues related to transgenics and cloning

- Suffering of transgenic animals
  - Case of Beltsville pigs (human GH introduced)
    - High mortality, arthritis, gastric ulcers, degenerative joint disease, infection, lethargy
- Cloned animals
  - Shortened life spans, health problems
- What happens to animals born without transgene?

Additional concerns regarding transgenics and cloning

- Implications for application of technologies to humans
- Moral concerns: “are we playing God?”
- Impact on ecosystems and genetic diversity
  - What if GE organisms escape reproduce?
  - what might be the impact of limited gene pools on livestock faced with new (deadly) pathogens?
  - Potential for GE animals to move into areas previously unused for agriculture $\Rightarrow$ disrupt fragile ecosystems
    - habitat preservation issues for wild animals

Additional concerns regarding transgenics and cloning

- Time factor
  - mistakes can occur more rapidly with GE than conventional methods of animal selection (e.g. selective breeding)
  - loss of incremental steps $\Rightarrow$ lose ability to evaluate results at each step
    - e.g. traditional breeding allows time for evaluation, correction, reversal
- Ownership and legislation

Additional concerns regarding transgenics and cloning

- Lack of controls to prevent GE animals from entering the food chain (e.g., cows that produce drugs in their milk)
  - One reported instance of meat from GE animals used in a food product

NAS, 2002

Animal biotechnology and law

- “Any food system practice that does not allow individuals who do not want to consume meat or milk from clones to act upon their values at a reasonable cost is ethically unacceptable and ought to be illegal.” (Thompson, 1997)

Responsibility to the public: education

- Need for public education to facilitate understanding & discussion of biotech
- Need for informed consent
- Foisting of technology is wrong, not technology itself (Thompson, 1997)

Conflicts of Interest

(Hodges, 2000)

- “Politicians do not like probabilities
- “Scientists do not like ethics”
- “Consumers and users do not like risk”
- “Business does not like waiting”

References & additional reading

- Fraser, V. 2001. What's the moral of the GM food story? . Ag & Env. Ethics. 14 (2) 147-159.
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- Smith, T. Biotechnology and Global Justice. 1999. J. Ag & Env. Ethics. 11 (3): 219-242.
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- Genetic engineering and animal welfare: preparing for the 21st century. (Eds. J. Gonder, E. Prentice & L. Russow). 1999. Scientists Center for Animal Welfare: Greenbelt, MD.

Questions

- Should farm animals be bioengineered for food production systems?
- Is it ethically responsible to clone animals given the potential harms? (Another way to look at this question: Do the benefits of animal cloning and transgenics outweigh the harms?)
- Should some types of scientific investigations (e.g., cloning) be banned?
- Are scientists responsible for how their research is used?