Cloning Technology: Myths and Facts

Emerging Issues in Global Meat Trade

Cloning and Country of Origin Labeling (COOL)

September (18th and 19th) 2008
Cloning: Science and Mythology

What I’m going to talk about

- Some basic definitions & cell biology
- How we make clones
- Demythification
What is a Gene?

- Basic unit of heredity
- Made of DNA molecules (deoxyribose nucleic acid)
- Arranged on chromosomes
- Chromosomes come in pairs (maternal + paternal)
- Chromosomes reside in cell’s nucleus
Background definitions

A eukaryotic cell

- plasma cell membrane
- endoplasmic reticulum
- nucleus
- golgi
- ribosome
- mitochondria
- lysosome
- chromosomes
Background definitions

Chromosome unwound

Anatomy of a gene

Coding region
(Structural sequence)

Off / On Switch
(Regulatory element)
(Promoter sequence)

Termination
Background definitions

What is a Cloned Animal?

A copy of an animal produced asexually

Maternal (identical) twins – a natural example

Just another selective breeding tool

Two kinds of man made clones

- Embryonic clones

- Somatic cell clones
Fact or Fiction # 1

Man made cloning is new technology

Fiction

✓ Embryo “twinning” has been done since the 80’s

✓ Vegetative propagation (plant cloning) has been done for over 200 years – grapes, potatoes, bananas
How are animals cloned?

Embryonic cloning

2-cell stage embryo

Morula stage embryo (8 - 32 cells)
How are clones made?
Clones, circa 1980

Seven calves from a single embryo
Background definitions

More facts

Sheep and cattle have been cloned since 1980

Clones produced in the 80s were ….

So why is there such a fuss about clones now?
Well Hello, Dolly...

Dolly was cloned from a SOMATIC cell

Significance

• Can “reproduce” a known entity
Well Hello, Dolly...

Dolly was cloned from an **ADULT cell**

**Significance**

- Can “reproduce” a known entity
Cloning doesn’t make biological sense

Textbooks said

- Embryonic cell’s potential limitless
- Differentiated cell’s potential finite
- Differentiated cells utilize only a subset of genome
- De-differentiation not possible
Cloning doesn’t make biological sense

Textbooks need revision

- Embryonic cell’s potential limitless
- Differentiated cell’s potential finite
- Differentiated cells utilize only a subset of genome
- De-differentiation not possible
How are somatic cell clones made?

- Build a transgene (optional)
- Harvest oocytes (unfertilized eggs)
- Fabricate cloned embryos
- Transfer clones to surrogate mothers
- WAIT!
Somatic-Cell Cloning (Somatic Cell Nuclear Transfer)

1. Remove chromosomes from egg
2. Add cell with desired genetic information
3. Embryo culture
4. Transfer to surrogate mom
Are cloned embryos normal?

Differentially expressed genes (out of 5,174) in normal & ART embryos

Normal (In vivo) vs. In Vitro Fertilized (198)

Normal vs. Clone (50)

Clone vs. In Vitro Fertilized (133)

Smith, et al. PNAS, 2005
How efficient is Nuclear Transfer?

- Enucleation – 85%
- Couplet formation – 20 to 60%
- In vitro development – 40% (blastocyst/couplet)
- In vivo development – 15% (calves born/embryo)

- Overall efficiency 6% (calves / somatic cells)

How efficient is Nuclear Transfer?

In Context

- NT (academic) ≈ 90% embryonic / fetal loss
- NT (commercial) = ?
- Normal livestock repro. ≈ 20 – 30% fetal loss
- Women ≥ 50% embryonic / fetal loss
Fact or Fiction # 2

Clones are genetically identical

Fact and Fiction

✓ Split embryos are identical

✓ Nuclear transfer embryos are not identical
Background definitions

A eukaryotic cell
Background definitions

Enucleated

- nucleus
- plasma cell membrane
- endoplasmic reticulum
- golgi
- ribosome
- mitochondria
- lysosome
- chromosomes
Background definitions

Enucleated – but still some genes left

Mitochondria
(37 genes)
Fact or Fiction # 3

Clones **don’t** look and act the same as the clonee

Fact – even for split embryos

- Looks – spots, bands, coat patterns are mostly developmentally determined

- Behavior – a quantitative traits

  \[ \text{Phenotype} = \text{Genetics} \times \text{Environment} \]
Fact or Fiction # 4

Clones are born old – same age as clonee
Fact or Fiction # 4

Clones are born old – same age as donor

Fiction
Fact or Fiction # 5

Offspring of Clones are Clones of Clones

Fiction

 ✓ Offspring are produced by sexual reproduction
 ✓ Genome a mix of maternal & paternal genes
 ✓ Offspring not necessarily the same sex
 ✓ Offspring are no more alike than offspring

Family resemblance
Fact or Fiction # 5

Clones are safe to eat?

Fact – but question is probably irrelevant
Fact or Fiction # 5

Clones are safe to eat?

Fact

Meat and Milk from Clones of Cattle, Swine, and Goats, and the Offspring of All Clones, are as Safe to Eat as Food from Conventionally Bred Animals
Fact or Fiction # 5

Clones are safe to eat

Question is probably irrelevant

Doesn’t make economic sense

A clone costs – (Tens ? of) thousands

Carcass value – < $1,000 / steer, dressed
Take home lessons

✓ Clones are genetically identical copies – almost
✓ Cloning is less efficient than normal reproduction
✓ Phenotype = Genetics by Environment interaction
✓ Offspring of clones are not clones
✓ Clones & offspring are as safe to eat as any animal
✓ Clones are too expensive to eat
✓ Greatest long term impact: Biology to be learned
Just the beginning