Recent Research & Developments in Transgenic Animals

A Tool for Improved Food Quality and Animal Well-being

Subgroup on Research, Development and Extension of Agricultural Biotechnology

The 9th APEC Workshop on Technical Cooperation, Capacity Building, Risk Management and Emerging Issues in Agricultural Biotechnology
Santiago, Chile
November, 2005

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What has been done ?

Transgenic Livestock goals

1. Create new animal products 
2. Improving animal well-being and food safety 
3. Improving production efficiency & nutritional quality
4. Xenotransplantation  

2

Characteristics of Transgenic Animals

Transgene in every cell in the body - usually

- 50% of transgenic's offspring are transgenic - usually
- 50-60% of transgenics carry functional transgene
- Amount of transgene product produced is highly variable
- Making transgenic livestock is: - inefficient,
  - slow,
  - requires a range of scientific expertise

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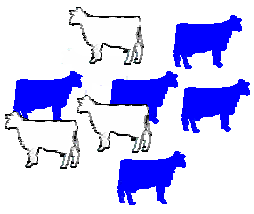

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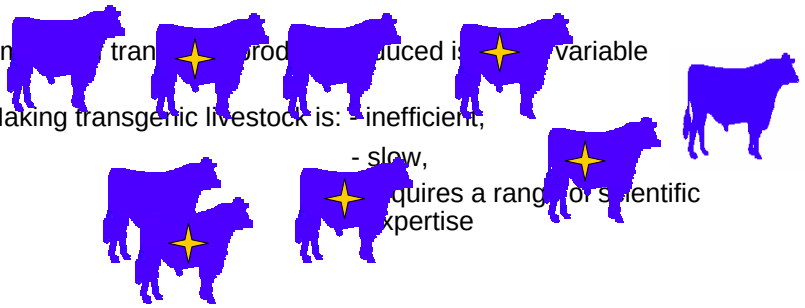

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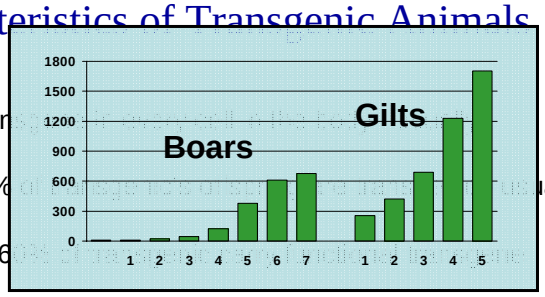
Characteristics of Transgenic Animals



- Tran[illegible]
- 50%[illegible]ually
- 50-6[illegible]

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6

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Health risk – transgene dependent

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How do we make transgenic livestock?

- Pronuclear microinjection
- Somatic Cell Nuclear Transfer (Cloning)
- Sperm-mediated gene transfer
- Virus-mediated gene transfer
- Restriction Enzyme Mediate Integration
- Electroporation

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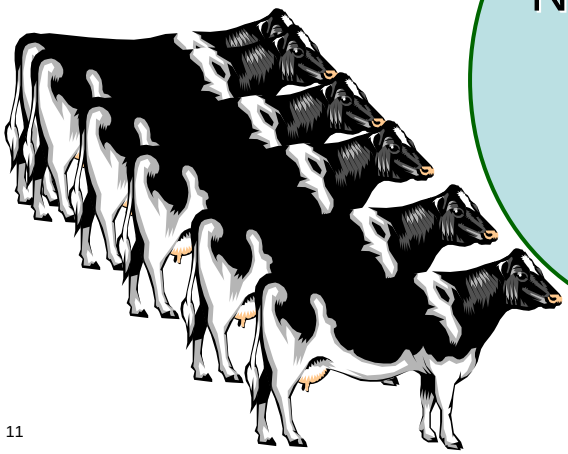
Why use Cloning to make Transgenic Cattle ?

Why Clone ?

PN M



NT uses 1/3 as many animals

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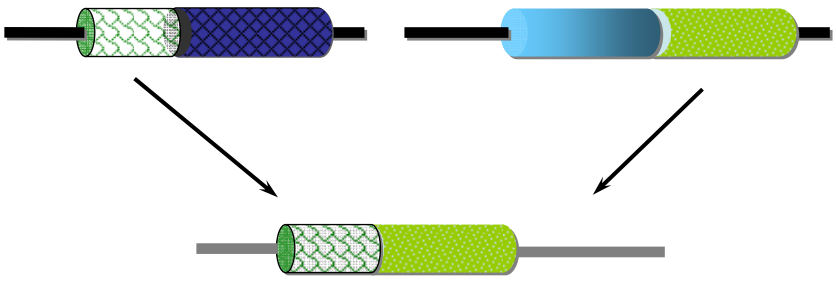
Fusion Gene (designer genes)

Gene A
(milk protein gene)

Gene B
(blood clotting factor gene, liver)



Fusion Gene A-B
(clotting factor produced in milk)

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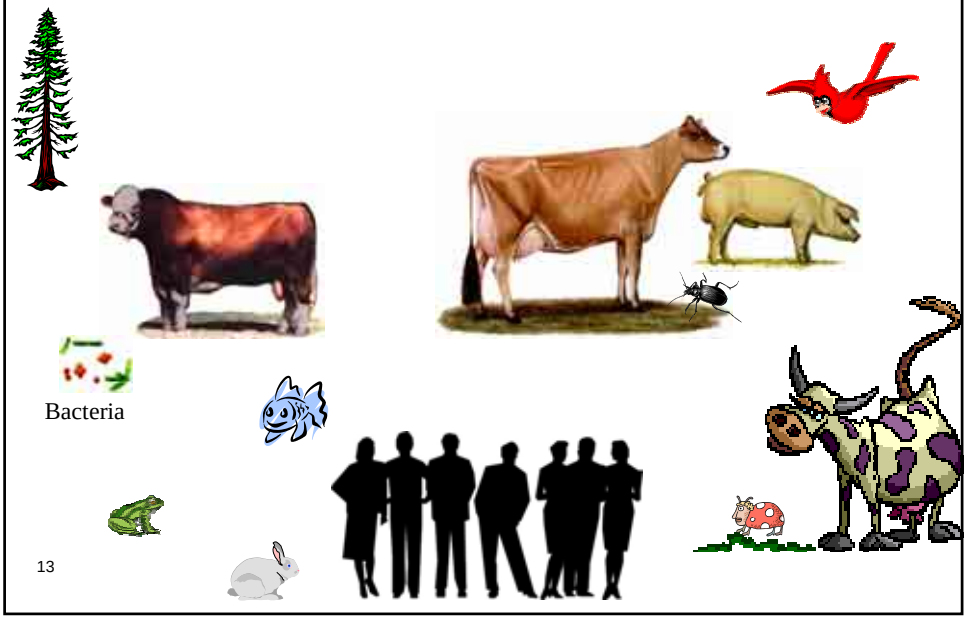
Where do the genes come from ?



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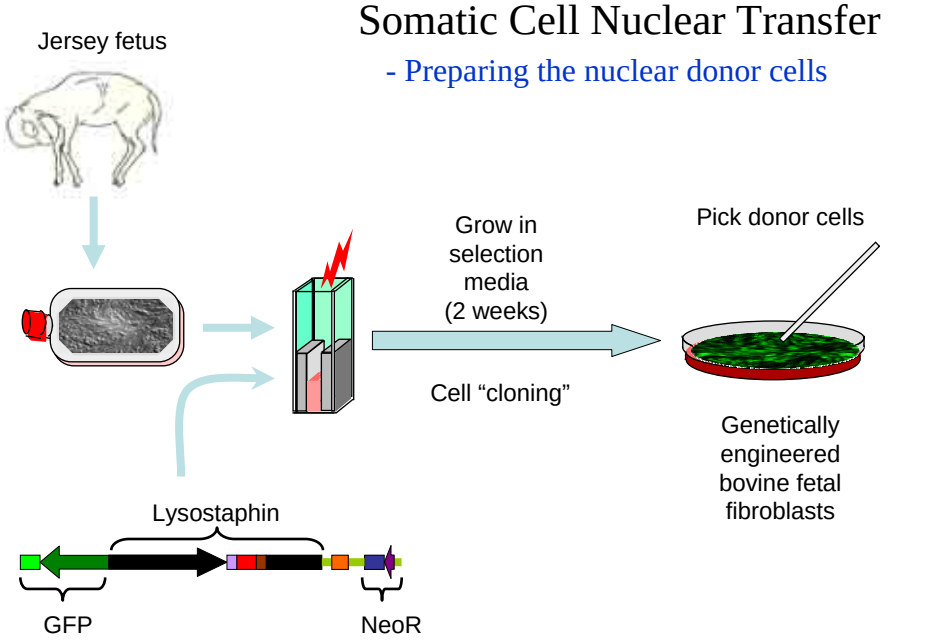
Somatic Cell Nuclear Transfer

- Preparing the nuclear donor cells



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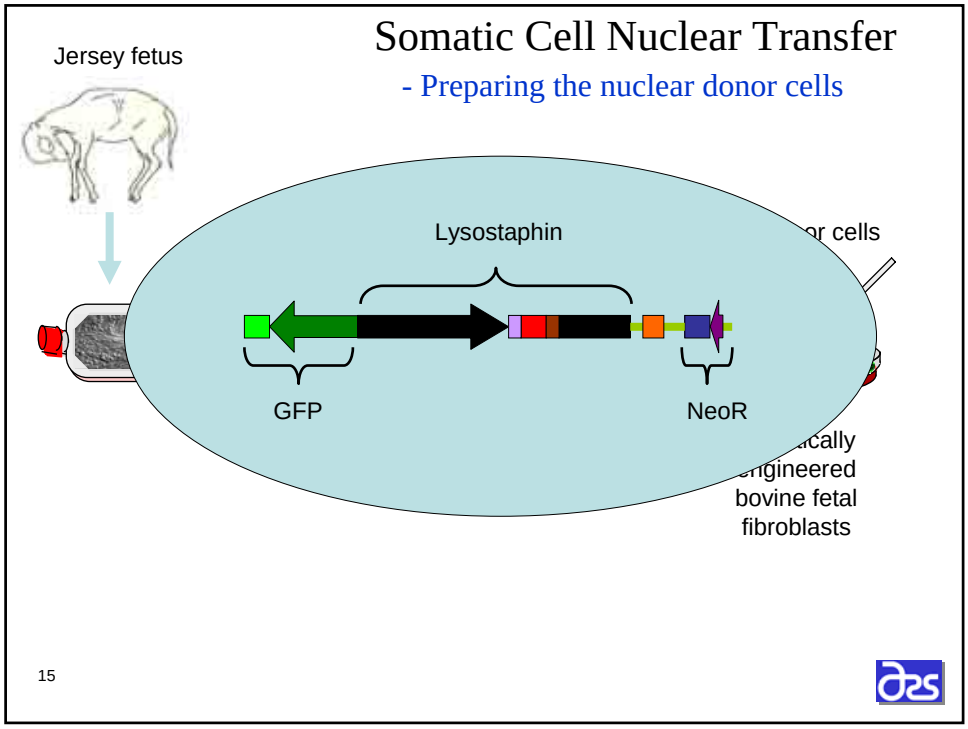
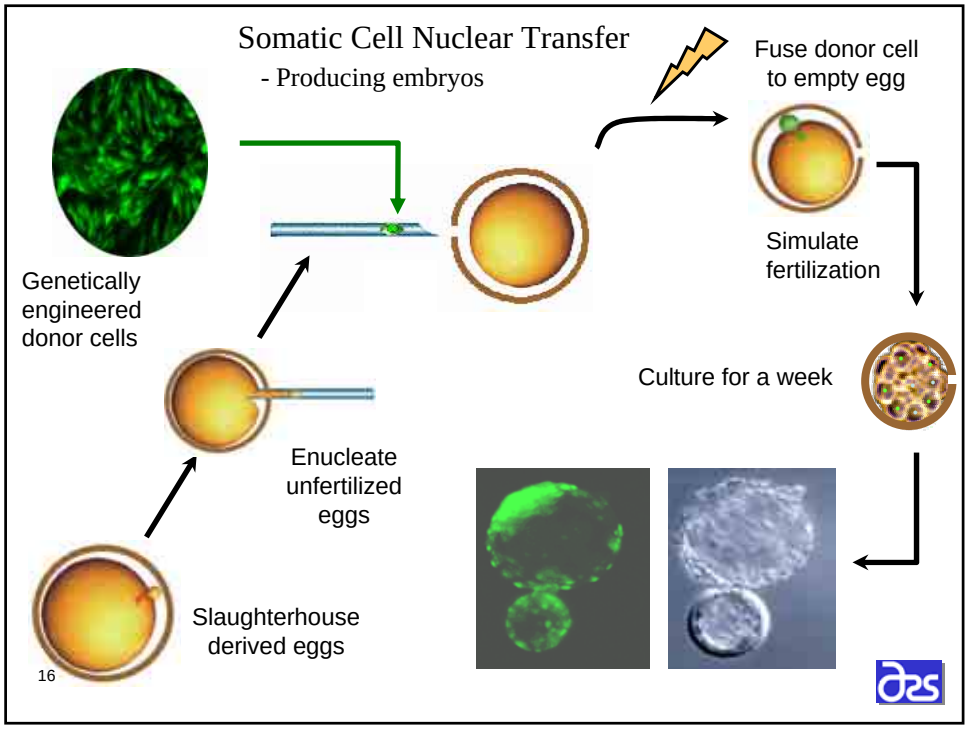

Somatic Cell Nuclear Transfer
- Preparing the nuclear donor cells
Jersey fetus
Lysostaphin
GFP
NeoR
bovine fetal
fibroblasts
15


Somatic Cell Nuclear Transfer
- Producing embryos
Fuse donor cell
to empty egg
Simulate
fertilization
Genetically
engineered
donor cells
Culture for a week
Enucleate
unfertilized
eggs
Slaughterhouse
derived eggs
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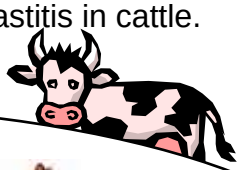
The Mastitis Project

Goal: Reduce incidence and susceptibility to mastitis in cattle.



Facts about mastitis

- Staphy[illegible]

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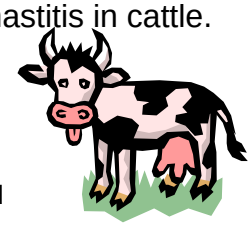

Facts about mastitis

- A third of dairy cows in the U.S. become infected
- Mastitis costs US producers ≈ $2 Billion / year
  - Treatment costs
  - Reduced milk yield, shelf-life, cheese yield
  - Animal well-being diminished, premature culling
- Vaccines and antibiotics are minimally effective

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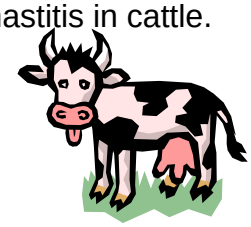

Facts about mastitis

- **<u>Disease is on every dairy farm</u>**
- *Staphylococcus aureus* accounts for about a third of cases

Staph. aureus

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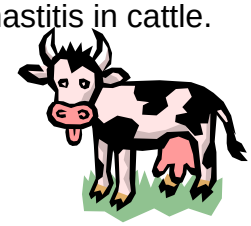

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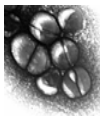

Staph. aureus

- Antibiotics don't work very well
- Highly contagious
- Culling is usually the only solution

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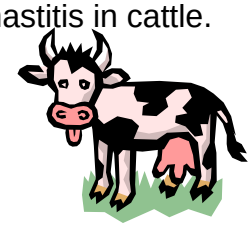

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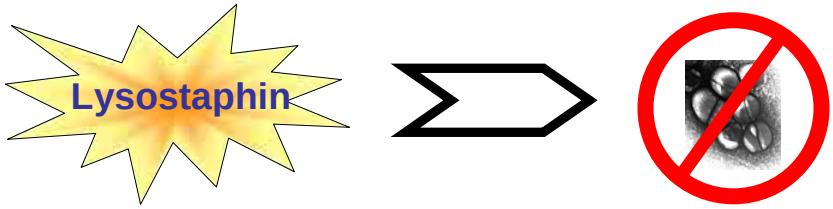

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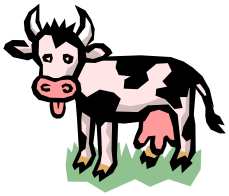
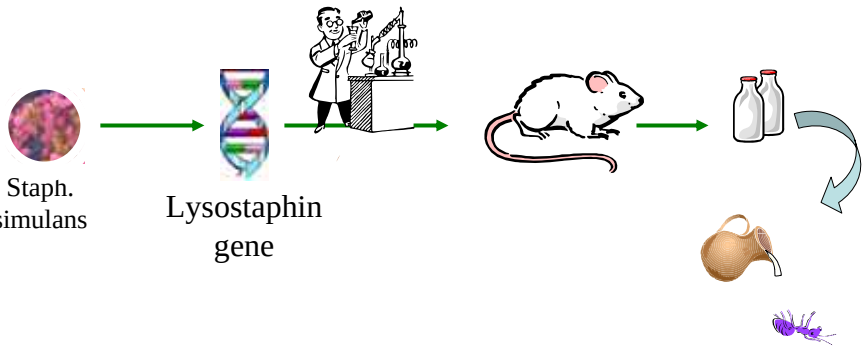
Resistance to Mastitis



- ✓ Lysostaphin gene isolated from S. simulans
- ✓ Attached to mammary gland promoter
- ✓ Introduced into mice
- ✓ Milked mice



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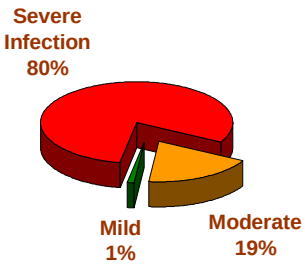
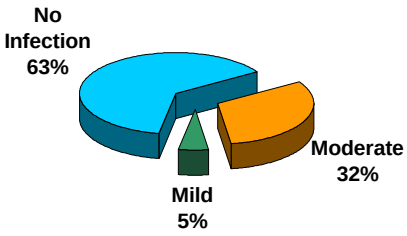
Lysostaphin protects GM mice against mastitis

Results of infection study



Normal mice



Genetically Modified mice

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First genetically modified cows carrying a disease resistance gene

Annie

GEM

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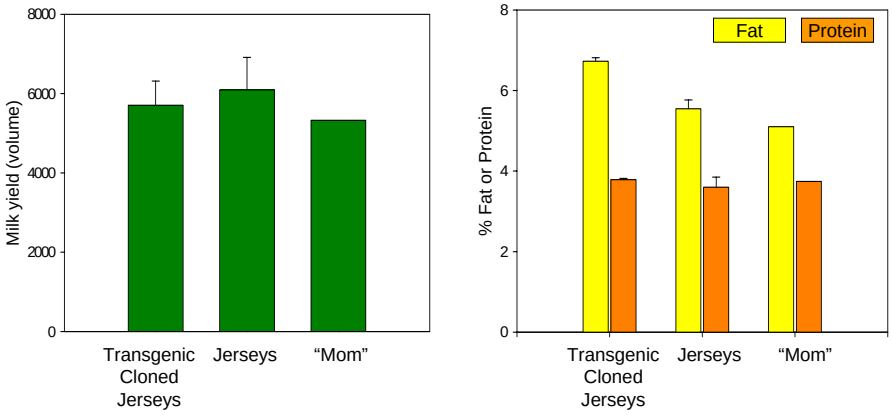
Estimated adult performance of Transgenic clones and their "Mother"



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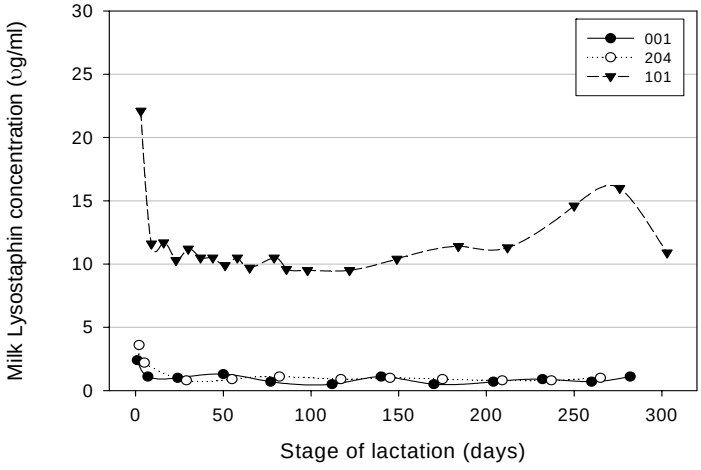
Lysostaphin in milk (1st lactations) of transgenic cloned Jerseys



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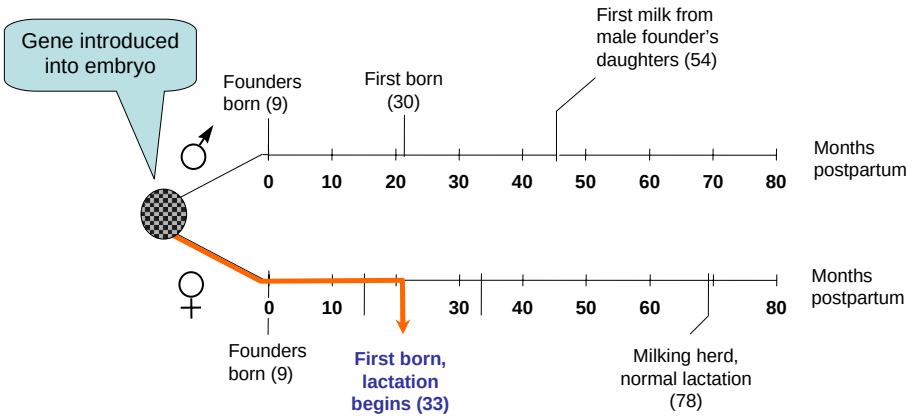
Time it takes to get results



2 ½ years to first product production
4 ½ years to significant production

27

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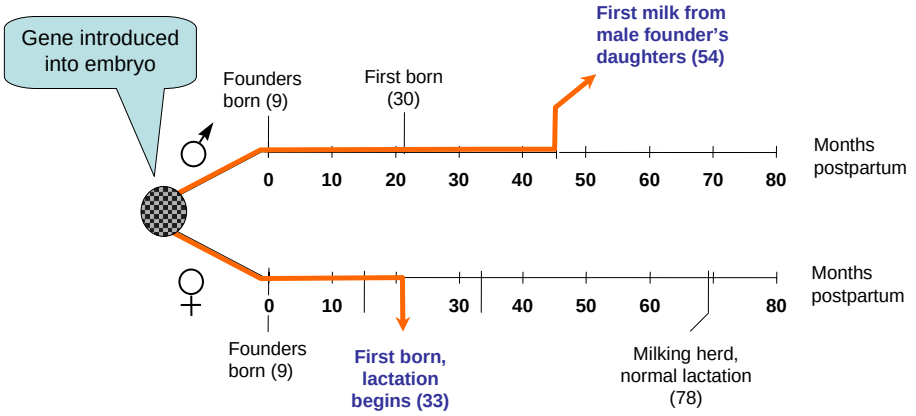

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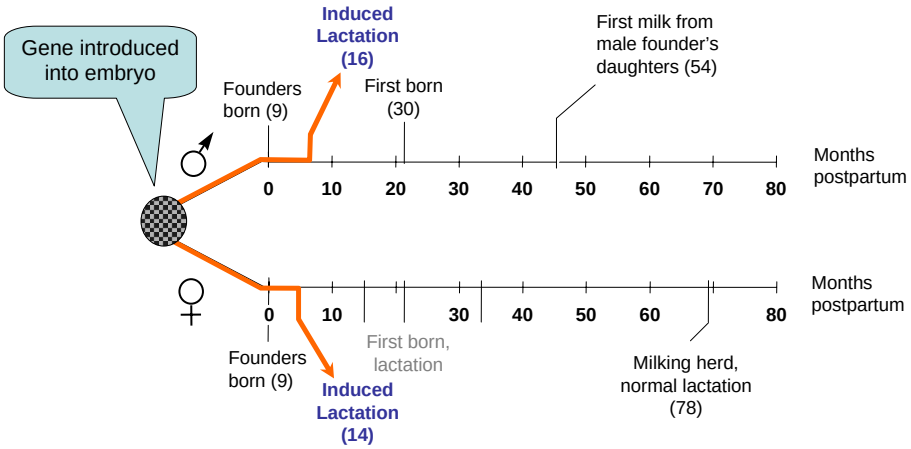

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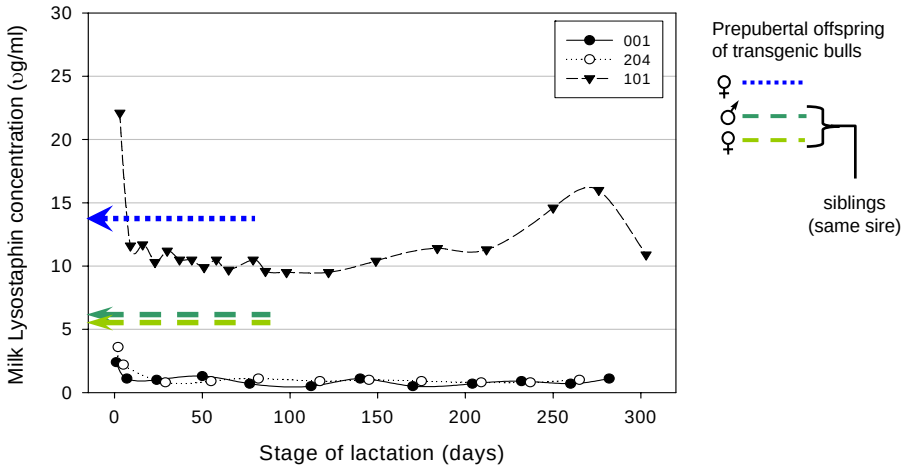
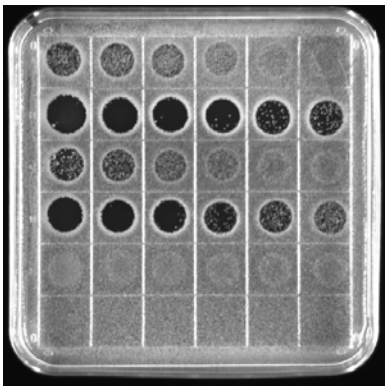
Lysostaphin in milk (1st and Induced lactations) of transgenic cloned Jerseys



Lysis of *S. aureus* by Milk from Transgenic Cows

Dilution of Milk 0 2 4 8 16 32



Tg 001

Tg 101

Tg 204

rLysostaphin

Non-tg 102

No sample

rLys conc. 1 0.5 .25 .13 .06 .03 μg/ml

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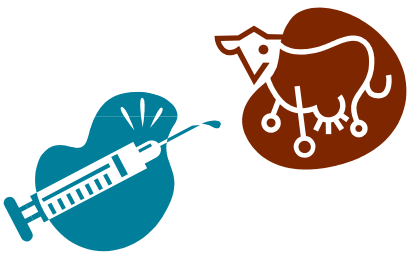
Lawn ≈ 10^5 c.f.u.

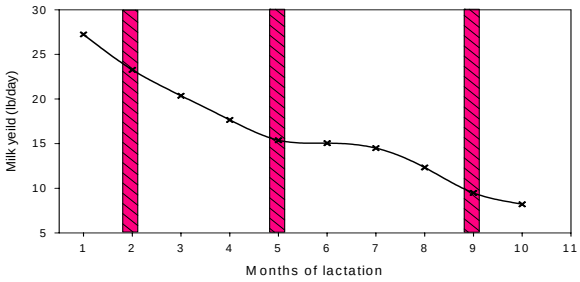
S. aureus Challenge



Saline in 1 gland

S. Aureus in other 3

Lactation curve – timing of infections



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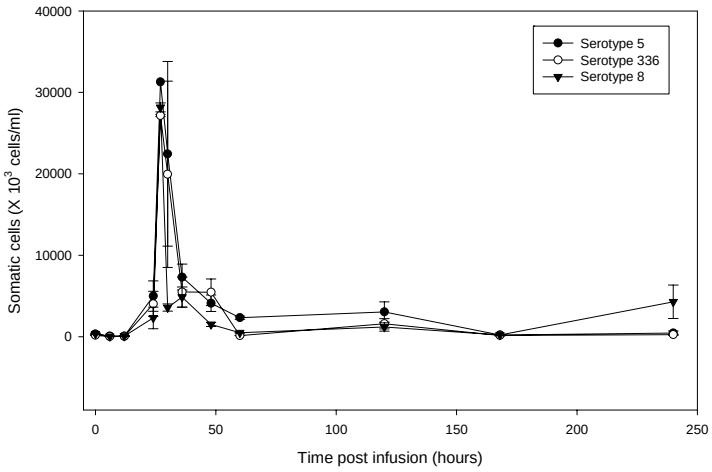
S. aureus strain did not influence somatic cell count

10 Non-transgenic controls



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Milk collected 6 hours after Staph. aureus challenge*

Non-transgenic

Saline

Non-transgenic 2234

Transgenic

Saline

Transgenic clone 101

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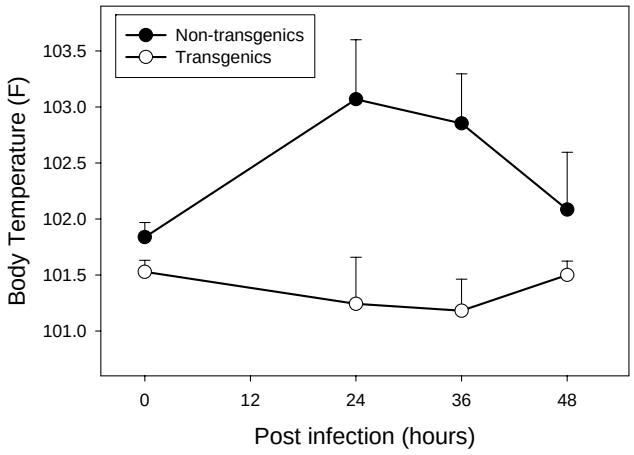
S. aureus infusions

3 Transgenic, 10 Non-transgenic controls



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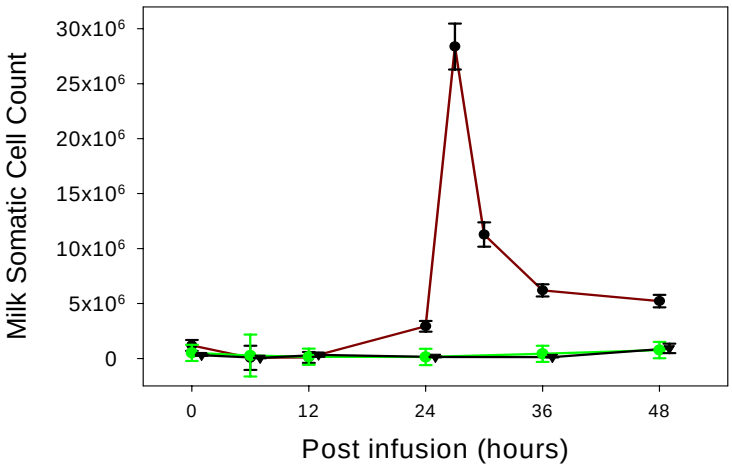
S. aureus infusions

3 Transgenic, 10 Non-transgenic controls



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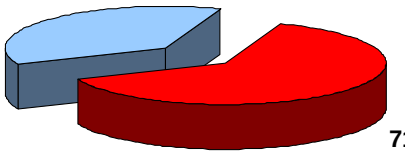
Infection rate

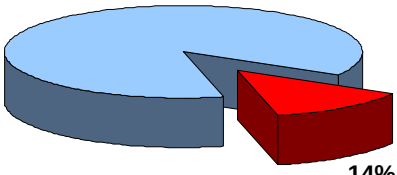
Non-transgenic controls



71% Infected

48 glands tested

Transgenic Clones



14% Infected

21 glands tested

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Future plans

- Immediate: Is the lysostaphin milk OK ?
- Identify additional anti-mastitis peptides
- Can we deal with resistant strains ?

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