Breeding programmes for GM farm animals

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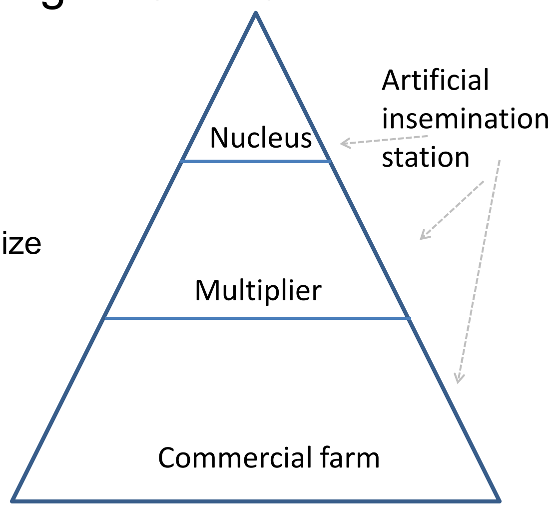
Breeding - Definition

- Breeding goal
- Inbreeding
- Effective population size
- Heritability
- Breeding value
- Genetic gain



Breeding programs in livestock breeding

- Design of breeding programs depend on species
- Mostly one male mated to multiple females (exceptions in fish)
- Definition of breeding goal (traits to improve)
- Choice of selection traits (traits to record)
- Data recording – which animals (own performance, offspring or other relatives)
- Use of breeding values for selection decision
- Selection of best animals for next generation

Convential breeding

- Modest rates of response to selection for individual traits (0.5–3.0% per year)
- Permanent, cumulative changes

⇒ Large increase in production efficiency over time

Restriction for GM farm animals

- Legislation
- Consumer acceptance
- Technique
- Efficiency
- Which traits
- Implementation in breeding program

Transgenic strategies vs Selective breeding

Transgenic strategies

+ Fast success (e.g. medicine production)
+ New technologies (higher success)
+ Fast introduction of 'new' alleles and genes

Conventional breeding

+ Tested over many years
+ Huge improvement (over time)
+ New marker based methods (more specific breeding)

Clark and Whitelaw (2003) Nature reviews genetics 4: 825ff;
Wheeler (2003) J. Anim. Sci. 81(Suppl. 3): 32–37

Transgenic strategies vs Selective breeding

Transgenic strategies
- Most traits governed by many genes
- Introgressing transgenes difficult
- High financial commitment
- Negative side effects (e.g. pleiotropic)
- Risks (e.g. virus resistance: persistent asymptomatic infection)

Conventional breeding
- Time consuming
- Co-selection of undesirable traits
- Favourable alleles must be present in parents

Clark and Whitelaw (2003) Nature reviews genetics 4: 825ff;
Wheeler (2003) J. Anim. Sci. 81(Suppl. 3): 32–37

Breeding programs in livestock breeding

- Breeding goals depend on purpose (food, company, performance, conservation)
- Economic relevance
- Population size important – relatedness between parents

⇒ Development of breeding program for novel population (e.g. GM animals) will need to take relationships into account

Example transgenic breeding program

Male founder

Founders birth	9 month
Founders offsprings birth	32 month
Birth of homozygotes	55(+) month
Homozygotes reproduce	78 month

Adapted from: Seidel, 1993 *J. Anim Sci* 71:26-33

Additional technologies

- Use of other reproductive techniques might speed up the last steps and reduce the generation interval
- Use of other biotechnologies (artifical insemination, in vitro fertilisation, embryo splitting, sperm sorting...)
- Information on the genome → sequencing

Applications of biotechnology

A genetically engineered salmon (top) grows twice as fast as its wild counterpart (bottom).

BIOTECHNOLOGY

Transgenic salmon nears approval

Slow US regulatory process highlights hurdles of getting engineered food animals to dinner tables.

"…horse cloning is now a reproducible technique that offers the opportunity to preserve valuable genetics and notably to generate copies of castrated champions" (Galli et al., 2008)

A leap into the unknown: Cloned eventing horse Tamarillo is groomed for success

The Independent 23 June 2014

Example: Mastitis

- Most common disease in dairy cows (costs estimated to be 192 mio SEK only in Sweden)
- Huge effect on animal welfare
- Economic loss for farmer (milk cannot be used, animals need to be treated, some culled)
- Use of antibiotics in animal production
- Decreased production efficiency = less sustainable

Mastitis reduced from 30 to 15 cows/year in a 100 cows herd
$\Rightarrow$ Costs reduced by € 8095 (5% of the economic net return/herd)

C Nielsen (2009) Doctoral Thesis SLU;
A Eriksson (2013) Master Thesis SLU

GM dairy cows producing lysozyme

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Research

Generation of mastitis resistance in cows by targeting human lysozyme gene to β-casein locus using zinc-finger nucleases

Xu Liu[1,2], Yongsheng Wang[1,2], Yuchen Tian[1,2], Yuan Yu[1,2], Mingqing Gao[1,2], Guangdong Hu[1,2], Feng Su[1,2], Shaohui Pan[1,2], Yan Luo[1,2], Zekun Guo[1,2], Fusheng Quan[1,2] and Yong Zhang[1,2]

[1]College of Veterinary Medicine, and [2]Key Laboratory of Animal Biotechnology, Ministry of Agriculture, Northwest A&F University, Yangling, Shaanxi 712100, People's Republic of China

Liu et al, 2014. *Proc. R. Soc. B 281, 20133368*

To be considered

- **Vulnerability** of monoculture to disease (keeping alleles in population) Fahrenkrug (2010) J. Anim. Sci. 88: 2530-9
- Control undesirable **correlated responses** in other traits Fahrenkrug (2010) J. Anim. Sci. 88: 2530-9
- Potential opportunities for animal production more challenging; greater demands on cost, efficiency, consumer acceptance and relative value of the product Laible (2009) Comp. Immun. Microbiol. Infect. Dis. 32: 123–137

To be considered

- Current studies often not resulted in effect hoped for, or unwanted **side-effects**
  Laible (2009) Comp. Immun. Microbiol. Infect. Dis. 32: 123–137
- How many transgenic animals in the testing phase? – different pleiotropic effects possible
  Maga (2005) Trends in Biotechn. 23: 11
- Research results often **controversial**, and effects shown (also on animal welfare) differ between studies
  Maga and Murray (2010) J. Anim. Sci. 88: 1588–1591

Will is be feasible to design a breeding program for GM animals for food production?

- Do we need a different strategy to allow for faster improvement?
- Do we want to change a trait identified in few animals or introduce a 'new' trait?
- What are the costs and estimated gains from a breeding program using GM animals?
- What technical issues do we need to consider?
- How much inbreeding can we afford ?
- How about other traits (health, production, reproduction)?