“Cost-benefit considerations of livestock genomics: who pays, who benefits”

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Biotechnology is used a lot in animal agriculture – need to be very specific about which one you are talking about as they are associated with different cost and benefits.

**PRODUCTION**
- Bovine somatotropin
- Beta-agonists
- Implants
- Ionophores
- Genetically engineered feed (i.e. GM corn, soy)
- Antibiotics
- Cages/feedlots
- Vaccines
- Castration/dehorning

**GENETIC**
- Cloning
- Genetic engineering
- Gene editing of target genes e.g. myostatin, prion protein
- Genomic selection
- Embryo transfer
- Artificial insemination
- Estrus synchronization
- Crossbreeding
- Selective breeding programs

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Our charge

"There are many economic issues associated with developments in livestock genomics. Some of the issues that will be discussed by this panel – what issues are ripe for research in the economic area?

The aim of this workshop is to assist Alberta researchers identify the most pressing GE3LS issues that would be suitable for economic research.
The majority of Americans oppose scientific research into genetic modifications of animals - irrespective of self-assessed knowledge level.

<table>
<thead>
<tr>
<th>Knowledge of Transgenic Animals</th>
<th>Favor</th>
<th>Oppose</th>
<th>Don't Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nothing 32%</td>
<td>20</td>
<td>55</td>
<td>25</td>
</tr>
<tr>
<td>A little 32%</td>
<td>22</td>
<td>61</td>
<td>17</td>
</tr>
<tr>
<td>Some 28%</td>
<td>39</td>
<td>54</td>
<td>7</td>
</tr>
<tr>
<td>A lot 6%</td>
<td>38</td>
<td>55</td>
<td>7</td>
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“The public opposes research into genetic modifications of animals”

- The majority (55%) of Americans believe that the “genetic modification” of animals is morally objectionable.


- It should be noted that in this same study, consumer acceptance of traditional animal crossbreeding techniques was only 31 %, with 50% of respondents finding such practices morally wrong!

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There is little organized activist opposition to conventional animal breeding which has DRAMATICALLY modified domestic livestock.
Animal breeders have been genetically modifying animals for faster growth and improved feed conversion for many years using selective breeding.

1957 vs. 2001 chickens


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US Public Attitudes Towards Specific “Modern Animal Biotechnologies”
(International Food Information Council Survey of US, 2005)

And in some cases using the process of recombinant DNA (rDNA) and in some cases using the process of recombinant DNA (rDNA).

GROWTH ENHANCEMENT IN TRANSGENIC ATLANTIC SALMON BY THE USE OF AN “ALL FISH” CHIMERIC GROWTH HORMONE GENE CONSTRUCT

Shao Jun Du, Zhiyuan Gong, Garth L. Fletcher\(^1\), Margaret A. Shears\(^1\), Madonna J. King\(^1\), David R. Idler\(^1\) and Choy L. Hew\(^*\)

Research Institute, The Hospital for Sick Children and Departments of Clinical Biochemistry and Biochemistry, University of Toronto, Toronto, Canada M5G 1L5. \(^1\)Ocean Sciences Centre, Memorial University of Newfoundland, St. John’s, Newfoundland, Canada A1C 5S7. *Corresponding author.

We have developed an “all fish” growth hormone (GH) chimeric gene construct by using an antifreeze protein gene (AFP) promoter from ocean pout linked to a chinook salmon GH cDNA clone. After microinjection into fertilized, nonactivated Atlantic salmon eggs via the micropyle, transgenic Atlantic salmon were generated. The presence of the transgene was transgenic Atlantic salmon by using an “all fish” transgene consisting of a promoter derived from an ocean pout antifreeze protein (opAFP) gene\(^9\), and the GH cDNA clone from chinook salmon\(^10\).

University of Toronto/Memorial University of Newfoundland, Canada


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Fish reach adult size in 16 to 18 months instead of 30 months.

Founder female in 1989

Growth Curves (Growout)

AquAdvantage Salmon

Standard Salmon
<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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</thead>
<tbody>
<tr>
<td>September 1995</td>
<td>AquaBounty submits Investigational New Animal Drug (INAD) application with FDA for fast-growing salmon with intent to commercialize</td>
</tr>
<tr>
<td>September 2010</td>
<td>Public Veterinary Medicine Advisory Committee (VMAC) meeting to consider data on safety and efficacy of AquAdvantage salmon Held in Washington DC</td>
</tr>
</tbody>
</table>
The public VMAC meeting held in Washington, DC was intended to increase transparency, clarity, and public confidence in the GE animal regulatory process.

"There is little benefit to society if attempts to increase public participation in the regulatory process are used as an opportunity to vilify technology."


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## Timeline of AquAdvantage regulatory process

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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</thead>
<tbody>
<tr>
<td>1989</td>
<td>• Founder AquAdvantage fish produced in Canada</td>
</tr>
<tr>
<td>1995</td>
<td>• FDA review of AquAdvantage salmon begins (INAD)</td>
</tr>
<tr>
<td>2001</td>
<td>• First regulatory study submitted by Aqua Bounty Technologies to U.S. FDA for a New Animal Drug Applications (NADA)</td>
</tr>
</tbody>
</table>
| 2009 | • FDA guidance on how GE animals will be regulated  
• FDA approval of first GE animal pharmaceutical  
• Final AquAdvantage regulatory study submitted to FDA |
| 2010 | • FDA VMAC meeting on AquAdvantage salmon (9/20/10) |
| 2011 | • Political efforts to defund FDA, ban fish, delay approval |
| 2012 | • FDA released “FONSI” finding of environmental assessment |
| 2014 | • **AquaBounty Total R&D investment > $60 million to develop and bring the AquAdvantage salmon through the regulatory approval process *thus far*** (D. Frank, CFO, AquaBounty, pers. comm.)  
• Still waiting for regulatory decision on AquAdvantage salmon  
• Development of GE animal technology moving to other countries with more predictable policy environments |

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What the implications of having to spend $60+ million to bring a fast-growing GE fish to market, when conventional fish (and other animal) breeders routinely develop all manner of fast-growing animals that are associated with the same set of risks?

$60,000,000!!

1957 vs. 2001 chickens

<table>
<thead>
<tr>
<th></th>
<th>1957</th>
<th>2001</th>
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<tbody>
<tr>
<td>43</td>
<td>57</td>
<td>71</td>
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<tr>
<td>85 d.</td>
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</table>

NOT REGULATED

REGULATED

$0
It is often stated that AquAdvantage is precedent setting – but many people already think they eat genetically modified animals – and they do – it is just that modifications were not done with rDNA.
Genetic engineering is a form of animal biotechnology that allows for the transfer of beneficial traits from one animal to another in a precise way that allows for improved nutritional content or less environmental impact. (IFIC, 2012)

**Genomics** is a way of evaluating the genetic makeup of farm animals to help make breeding decisions that will result in producing better offspring for improved meat, milk, and egg quality. (IFIC, 2012)

**What is your overall impression of animal genomics?**

![Bar chart showing attitudes towards genetic engineering and genomics](http://www.foodinsight.org/Resources/Detail.aspx?topic=2012ConsumerPerceptionsofTechnologySurvey)
Genomic Selection (GS)

Factors that improve accuracy of GS:
- Large number of animals in training population
- Number of SNP markers being genotyped
- Small effective population size
- High heritability of the trait to be improved
- Small number of large-effect QTL influencing trait
- High level of genetic relationship between training and selection candidates

Genotypic and phenotypic information from selected animals used to recalibrate marker effects to maintain prediction equation accuracy

Predict genetic merit of selection candidate within breed based on genotype

Selection candidate population
Genotypes used to predict genetic merit

Large training population
- Phenotyped
- Genotyped

Estimate marker effects for phenotyped traits
Predict genetic merit of selection candidate within breed based on genotype

Not predictive in other breeds/strains/lines

Genomic Selection (GS)

GS may offer selection criteria for traits that are not currently considered in breeding objectives due to an absence of objective, quantifiable measures upon which to base selection decisions.

The GS approach is clearly attractive for difficult to measure traits such as reproductive success and longevity in varied environments, efficiency of nutrient utilization, animal temperament, stress susceptibility, innate resistance or susceptibility to disease, adaptability, and reduced GHG emissions.

In theory, GS offers the opportunity to provide DNA-based selection criteria for multiple hard-to-measure traits simultaneously.

Genomic Selection (GS)

- Considerable investment in both genotyping and phenotyping will be required to develop the large phenotyped and genotyped reference populations that will be required to realize the full potential of GS.

- For disease surveillance, it might be possible to integrate GS approaches using the phenotypes that are collected as part of routine government-funded disease surveillance (e.g. collection of case-control samples).

- These approaches may ultimately reveal a sub-set of markers of sufficiently large effect that they can be cost-effectively combined into a reduced SNP DNA.

- This strengthens the case for government and industry investment in GS initiatives.
Figure 8

Broiler industry structure and global estimate of bird numbers (modified from Reference 100) alongside estimates of timeline and genetic expressions derived from a single pedigree female broiler chicken (Dr. Rachel Hawkin, Cobb-Vantress, personal communication).

Seedstock Sector

Nucleus and multipliers herds

Commercial Cow-Calf Producers (as of 1/1/2012)
- 30 million head beef cows
- 734,000 operations (Avg. 40 cows)
- > 80% run less than 50 cows

Stockers/backgrounders (as of 1/1/2012)
- 11.69 million head

Feedlots (2011)
Those 1920 operations (3%) with 1,000+ head capacity market over 88% of fed cattle in US

Processors (2010)
- 28.4 million head killed
- 7 operations killing more than 6 million head
- Top three processed 75% of 2010 kill

Genomic Selection (GS)

- In the absence of vertical integration, breeding goals will be developed based on the individual producer’s financial interests. The producer is the one investing in breeding stock and in a competitive market their decision will be based on the ways they perceive their animals contribute to farm profit.

- If there is market failure (e.g. there is no price incentive associated with the inclusion of improved animal welfare in breeding objectives), then alternative approaches will need to be implemented to incentivize their inclusion such as subsidized breeding, regulations, fines for poor welfare or increased prices for products labelled according to specific welfare grades.

Genomic Selection (GS)

- Although on the surface GS may arouse less public opposition because it utilizes naturally occurring genetic variation, some associated applications to reduce generation interval that are enabled by GS may be seen as contrary to animal welfare.

- These include the use of germ line approaches to shorten the generation interval, such as the harvest of oocytes from calves that are still in utero, or an approach where breeding is essentially done in the laboratory using GS to predict the Estimated Breeding Value (EPD) of cells derived from *in vitro* meiosis events.

- The rate of genetic change in the dairy industry has increased several FOLD since the implementation of GS.

LIVESTOCK GENOMICS TOPICS RIPE FOR ECONOMIC RESEARCH

- Cost:benefit analysis (including opportunity costs forgone) of regulations – how should benefits be included in evaluations?
- Economic implications of asynchronous approvals and trade disruption effects in the absence of international harmonization
- Economics of the protest industry – public costs and benefits
- Economic implications of regulating gene editing technologies
- Who pays for genetic improvement of traits that are a public good but subject to market failure?
- What are the implications of genomic selection to optimum breeding program design?
- Will genomic technologies hasten the vertical integration of animal breeding/industries in beef?
Consumers’ awareness of animal biotechnology is consistent, with just over half reporting some awareness.

Q28. First of all, how much have you read or heard about applying the science of biotechnology to animals? Would you say you have heard...?
Impressions of Animal Biotech

Almost half of Americans are favorable towards animal biotechnology

2012

Favorable

10%

23%

Not favorable

13%

13%

Neutral 25% n=381

Don’t know enough to form an opinion 16%

(Among those who were “not favorable”): Why are you not favorable toward using biotechnology with animals that produce food products:

I don’t have enough information 55%

I don’t understand the benefits of using biotechnology with animals 42%

I don’t eat milk or dairy products 5%

Other 16%

Q29. What is your overall impression of using animal biotechnology with animals that produce food products such as meat, milk, and eggs? Would you say you are...?

Q29A. Why are you not favorable toward using biotechnology with animals that produce food products? Check all that apply.
Half of Americans are favorable towards animal genomics.

2012

- Not Favorable: 15%
- Neutral: 35%
- Favorable: 50%

Q33A. Genomics is a way of evaluating the genetic makeup of farm animals to help make breeding decisions that will result in producing better offspring for improved meat, milk, and egg quality. What is your overall impression of animal genomics?
Impressions of Genetic Engineering

Almost half of Americans are favorable towards genetic engineering

2012

<table>
<thead>
<tr>
<th>Favorable</th>
<th>15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not favorable</td>
<td>29%</td>
</tr>
<tr>
<td>Not at all favorable</td>
<td>8%</td>
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</tbody>
</table>

Q34A. Genetic engineering. Genetic engineering is a form of animal biotechnology that allows for the transfer of beneficial traits from one animal to another in a precise way that allows for improved nutritional content or less environmental impact. What is your overall impression of genetic engineering in animals?