The welfare,economic, and genetic impacts of recessive genetic factors (RGFs)

Alison Van Eenennaam

Animal Biotechnology & Genomics
Cooperative Extension Specialist
Department of Animal Science
University of California
Davis, CA, USA
Ph: 530 752-7942
alvaneenennaam@ucdavis.edu

http://animalscience.ucdavis.edu/animalbiotech/

Overview

- Overview of recessive genetic factors (RGFs)
- Animal welfare implications of RGFs
- Economic implications of RGFs
    - Then and now
- Genetic implications of RGFs
    - Breed association responses
- Extension implications

There are a large number of genetic abnormalities in cattle occurring in a variety of breeds.

Images from an article by David S. Buchanan, NDSU

http://www.ag.ndsu.edu/williamscountyextension/livestock/genetic-defects-in-cattle

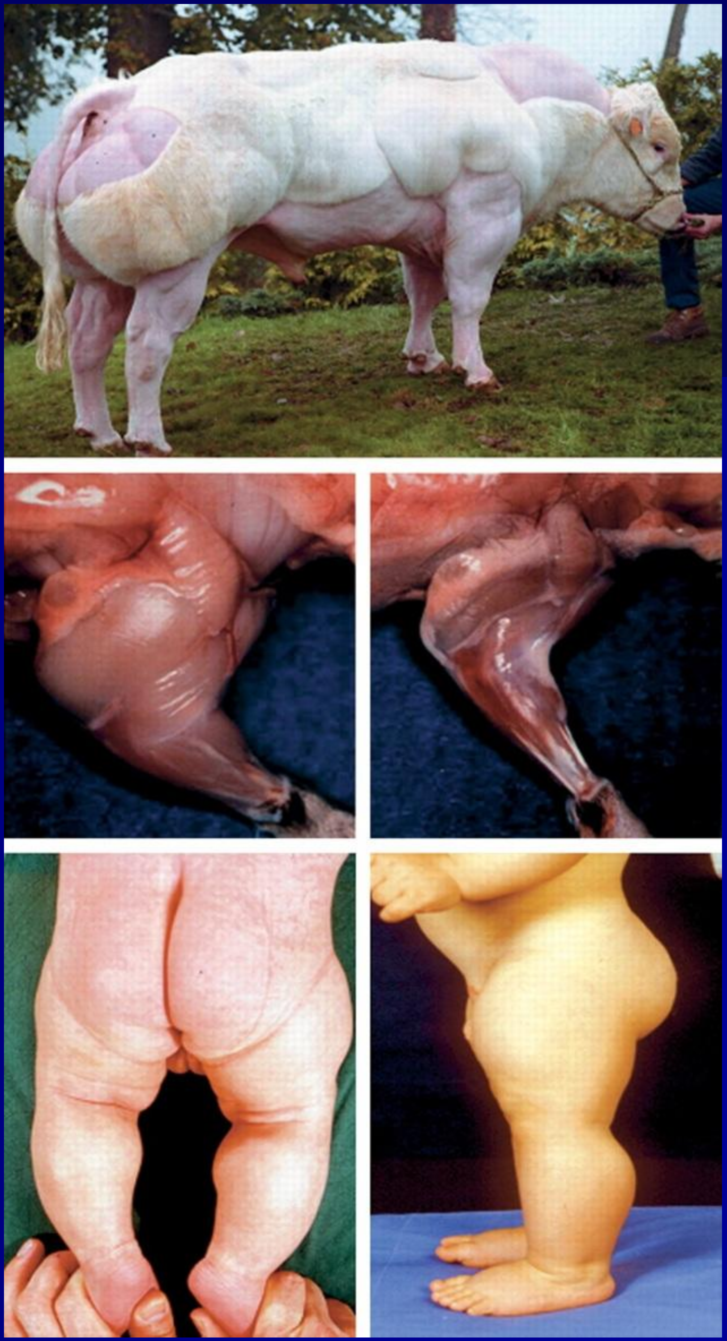
How Academic versus General audiences respond to various aspects of communication

Communication aspect	Academic
Main information channel	Audio and visual
Structure	Information is fine
Mode of response	Cerebral
Need humour?	Not necessarily
Like sincerity?	Suspicious of it
Sex appeal?	Potential disaster
Prearoused?	Yes
Effective elements	Information
Effective organs	Head
Preferred voice	Robotic

Olson, R. 2009. **Don't be such a scientist. Talking substance in an age of style**. Island Press.

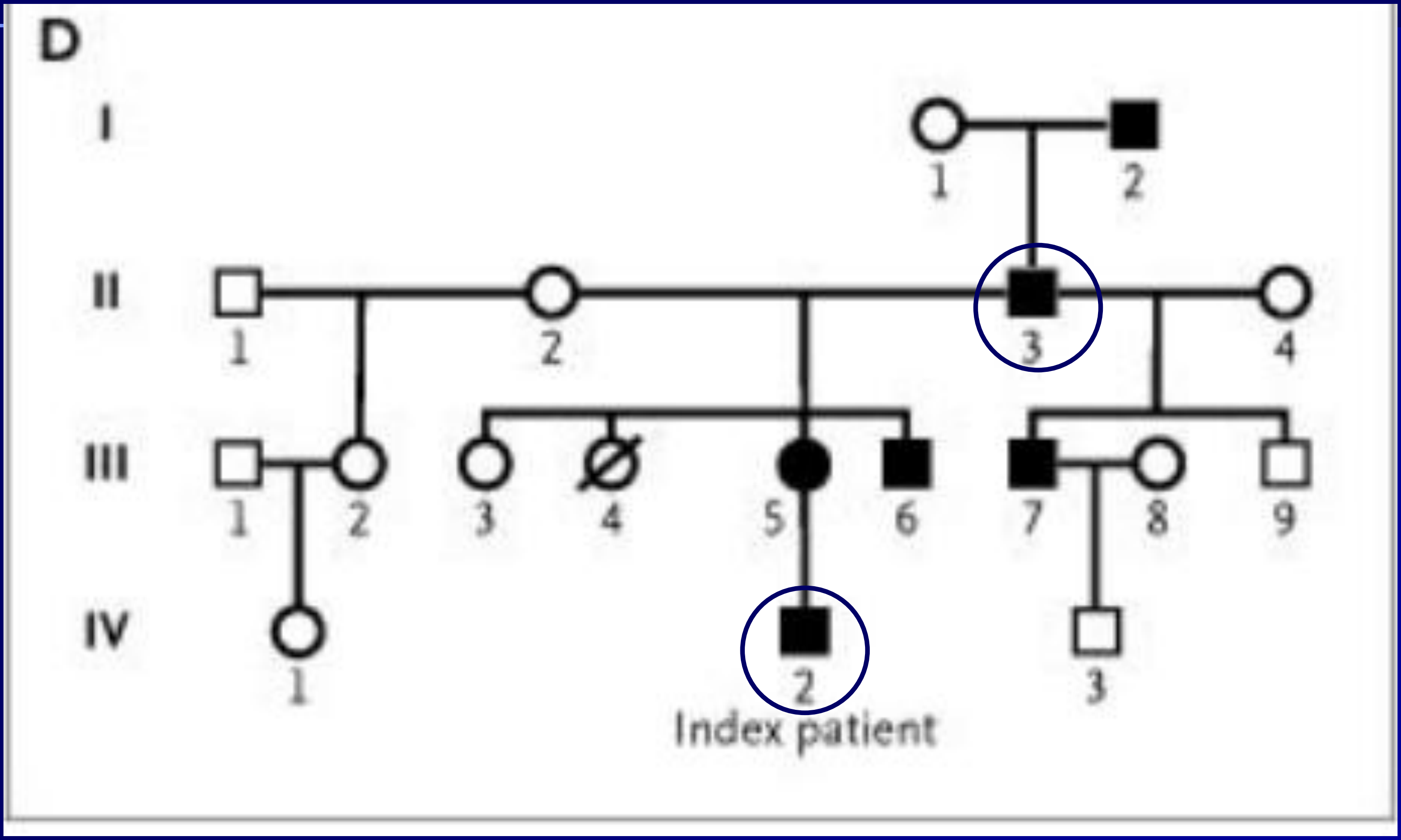
Myostatin:
mutations in cattle, mice and humans

Phenotypic comparisons of: "double muscled" bull homozygous for loss-of-function allele at the myostatin (MSTN) locus, mouse, and human.



Womack J E Genome Res. 2005;15:1699-1705

A healthy woman who was a former professional athlete gave birth to a son after a normal pregnancy. No family members aside from the mother were available to provide samples for genetic analysis. The identity of the father was not revealed.



Myostatin Mutation Associated with Gross Muscle Hypertrophy in a Child. 2004. N Engl J Med 350:2682

Prediction of deleterious human alleles

- An average human carries approximately 2,000 deleterious amino acid variants
- Only a small fraction of deleterious amino acid-altering SNPs segregating in human population lead to total loss of function of the affected protein, and the rest must have relatively mild effects.
- Even currently very rare brother–sister marriages which produce offspring have a reasonable fecundity since they constituted >30% of all marriages in some societies
- According to official census returns from Roman Egypt (first to third centuries CE) preserved on papyrus, 23.5% of all documented marriages in the Arsinoites district in the Fayum (n = 102) were between brothers and sisters.
- Calculated they had a mean coefficient of inbreeding of F = 0.15-0.20)

Sunyaev et al. 2001. Prediction of deleterious human alleles. 2001. Hum. Mol. Genet. 10 : 591.

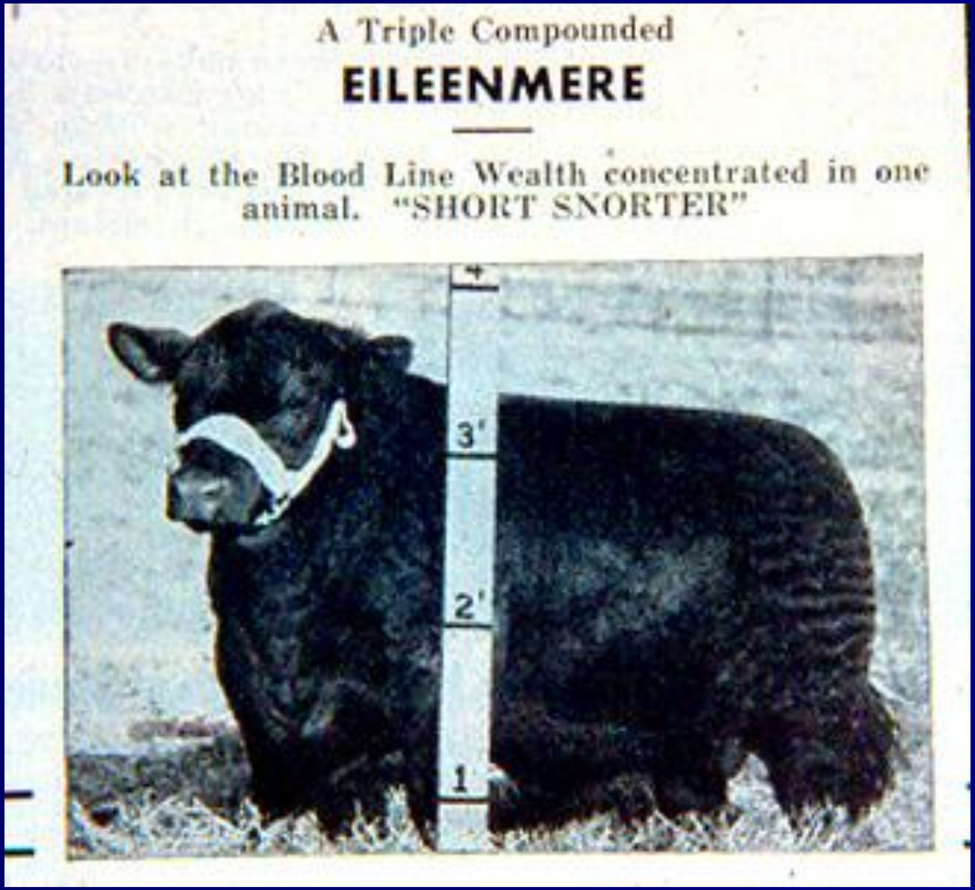
Animal welfare implications of recessive genetic factors

Genetic Defects in Dogs

- Every one of the 50 most popular pedigree-dog breeds has at least one aspect of its physical conformation that predisposes it to a disorder.
- "*The association of some of these conditions with official breed standards…make conformational extremes an area which needs to be addressed to safeguard the welfare of pedigreed dogs in the future*."

Asher et al. (2009) Inherited defects in pedigree dogs. Part 1. Disorders related to breed standards. The Veterinary Journal. 182: 402-411.

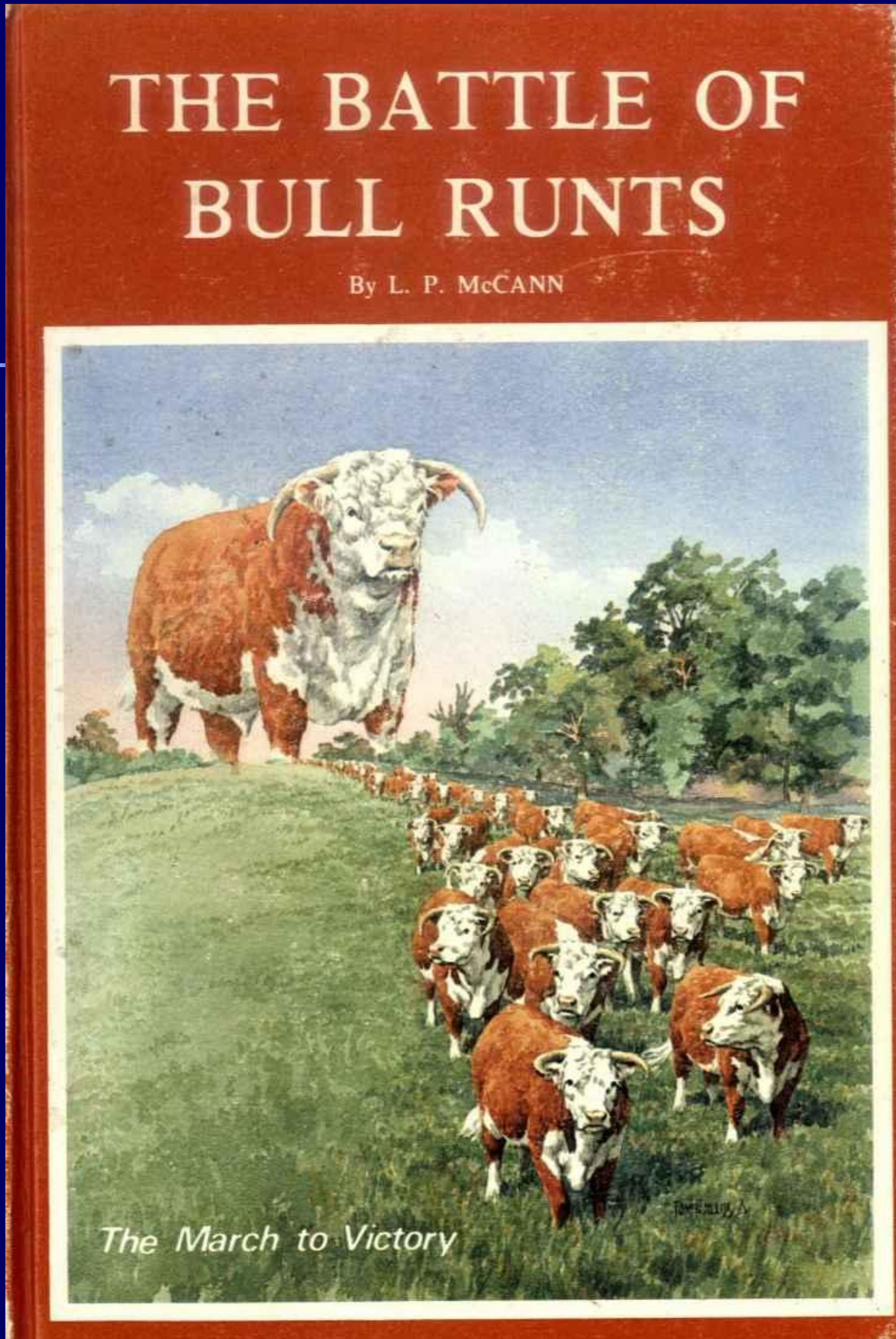
Economic implications of recessive genetic factors



An early '50's advertisement that superimposed a measuring stick in the picture of this bull who was nick-named "Short Snorter."

Based upon his height and age, he was less than a frame score 1.

Image from https://www.msu.edu/~ritchieh/historical/shortsnorter.jpg



A 1956 survey of Hereford breeders in the USA identified 50,000 dwarf-producing animals in 47 states.

Through detailed pedigree analysis and test crosses, the American Hereford Association, in concert with breeders and scientists, virtually eliminated the problem from the breed. Because carrier status was difficult to prove and required expensive progeny testing, some entire breeding lines were eliminated.

Arthrogryposis multiplex; aka Curly Calf

- From a scientific standpoint, AM is the complete deletion of a segment of DNA that encompasses two different genes
- One of these genes is expressed at a crucial time in the development of nerve and muscle tissue. The mutation results in no protein being produced from this gene and therefore it is unable to carry out its normal function so homozygotes show phenotype

From September 8 – November 3, 2008 identified genetic problem, developed test, and released carrier status of 736 bulls!

- In the 11 months following the release of the test, the AAA posted the results of tests for AM on about 96,247 cattle.
- **This amounts to $2.4 million in testing costs**
- Of these, 20% (19,529) were carriers of AM. **That leaves 23,638 bulls and more than 53,000 heifers which tested as free of AM.**
- **At $4K/bull and $2K/heifer ~ $200 million of suspect animals shown to be free of RGF allele**

Based on calculations in Buchanan, D.S. 2009. Genetic Defects in Cattle. http://www.ag.ndsu.edu/williamscountyextension/livestock/genetic-defects-in-cattle

Neuropathic Hydrocephalus (NH)

Photo Credit: David Steffan – University of Nebraska

Congenital Contractural Arachnodactyly (CA) "Fawn Calf Syndrome"

Photo Credit: Anderson and Garrick , NALF

Estimates of US and Australia genetic testing costs (Angus)

	US	AUSTRALIA
AMF	113,526	12,021
NHF	77,067	9,936
CAF	28,837	2,532
TOTAL NUMBER	294,054	34,991
COST (@ $25/test)	7,351,350	874,775

Numbers kindly shared by Bryce Schumann, American Angus Association; and Carel Teseling, Angus Australia

Genetic implications of recessive genetic factors

"*Carrier animals….their overall breeding value worth may outweigh the economic value of carrier status*"

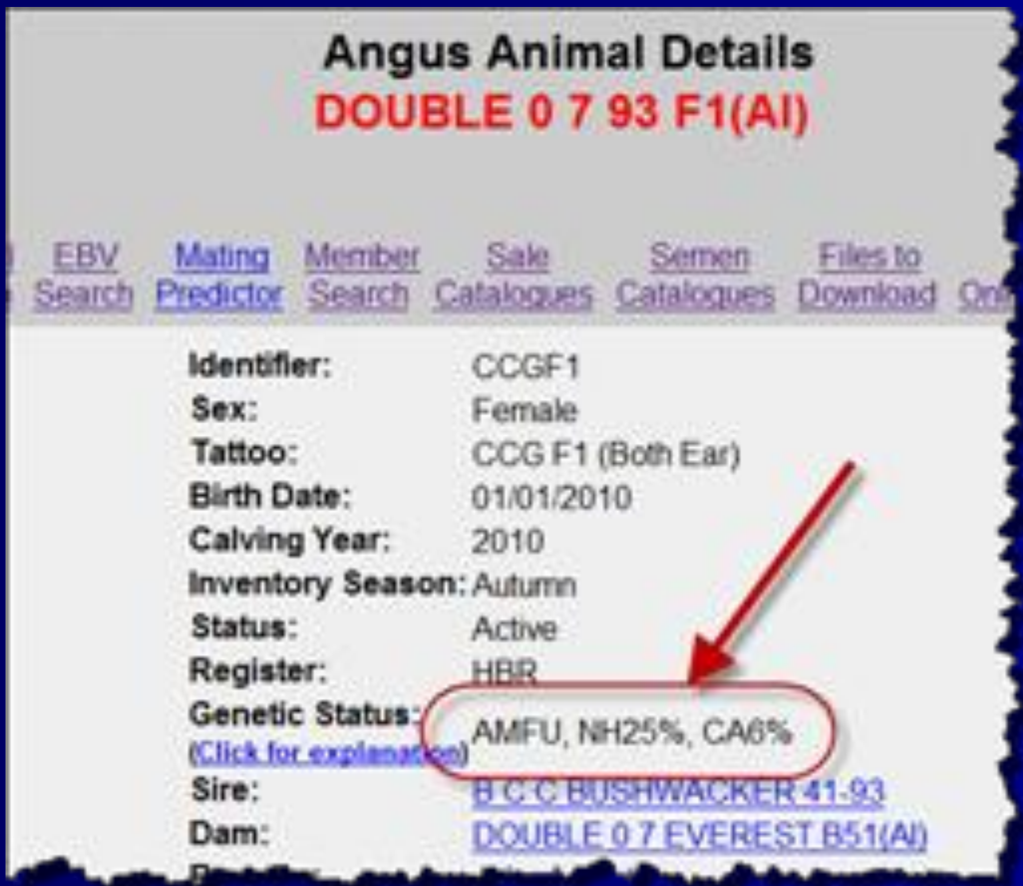
Chalier C. et al. (2008) Highly effective SNP-based association mapping and management of recessive defects in livestock. Nature Genetics 40:449-454

Should the market decide or should this choice be directed by industry (e.g. disallowing registration of known carriers)?

American Angus Association registration policy regarding RGFs

DATE	AM	NH	CA
Recognized as genetic defect by American Angus Assoc.	November 15, 2008	June 12, 2009	July 14, 2010
Commercial test becomes available	January 1, 2009	June 15, 2009	October 4, 2010
Number of carriers recorded (current as of April 2011)	35,151	33,148	6,325
HEIFERS: Must test & all can register if born before or on	December 31, 2011	June 14, 2012	October 4 , 2013
HEIFERS: Only non-carriers can be registered if born on or after	January 1, 2012	June 15, 2012	October 5, 2013
BULLS: Must test & all can register if born before or on	December 31, 2009	June 14, 2010	October 4, 2011
BULLS: Only non-carriers can be registered if born on or after	January 1, 2010	June 15, 2010	October 5, 2011

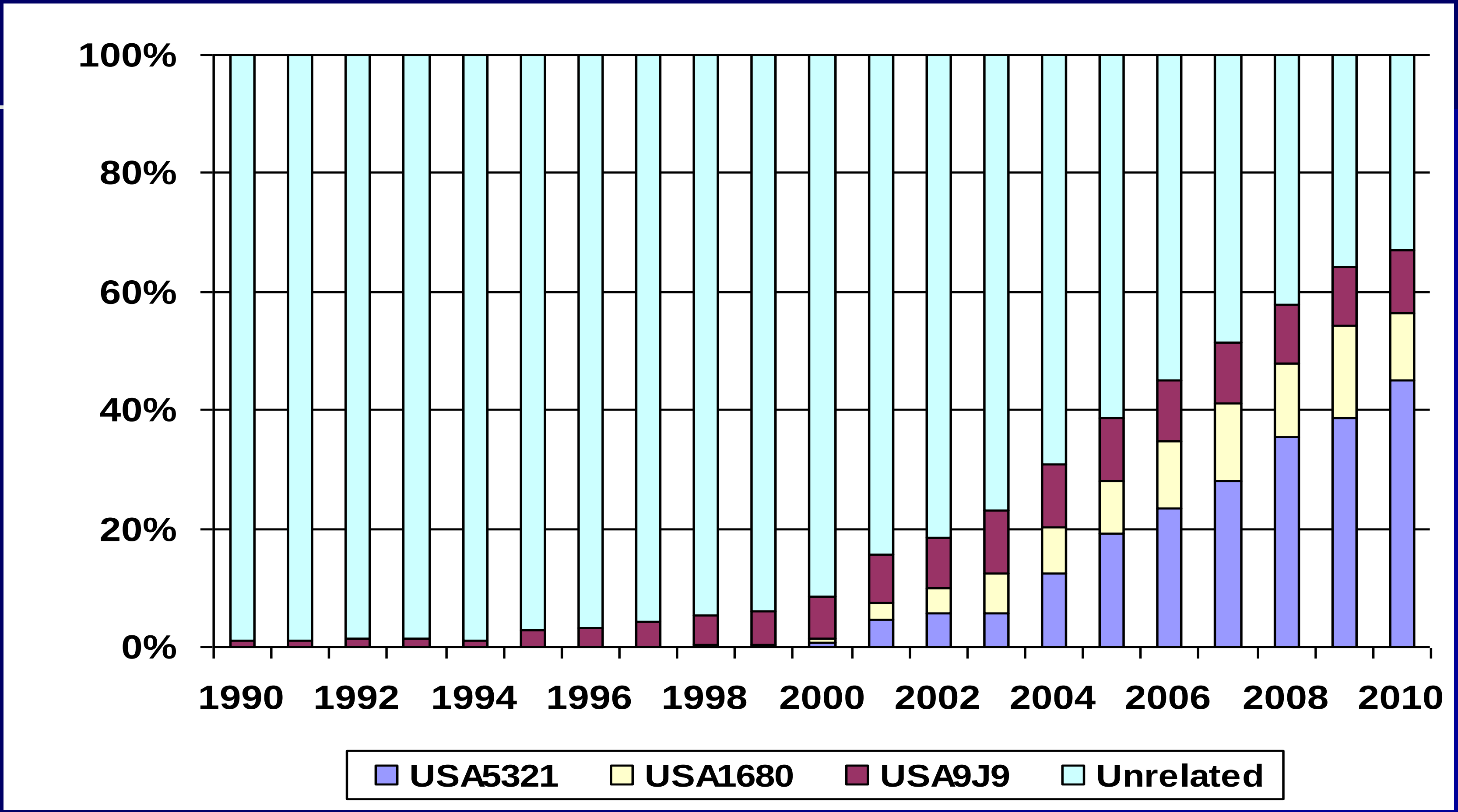
Angus Australia provides probability data on animal in database



GeneProb used to estimate the probability of every animal in the database being a carrier based on all ancestor and descendant DNA test results

Figure courtesy of Carel Teseling, Angus Australia

Percentage of USA9J9 descendants Angus Australia database by birth year



Future Direction 1995 GAR Precision 1990 9J9 1979

Allen, J. M. and C. F. Teseling. 2011**. Information empowers – Arthrogryposis multiplex in Angus Australia.** Proc. Assoc. Advmt. Anim. Breed. Genet. 19: *in press*

The percentage of possible AM, NH, and CA carriers born in Angus Australia, 2004-2010

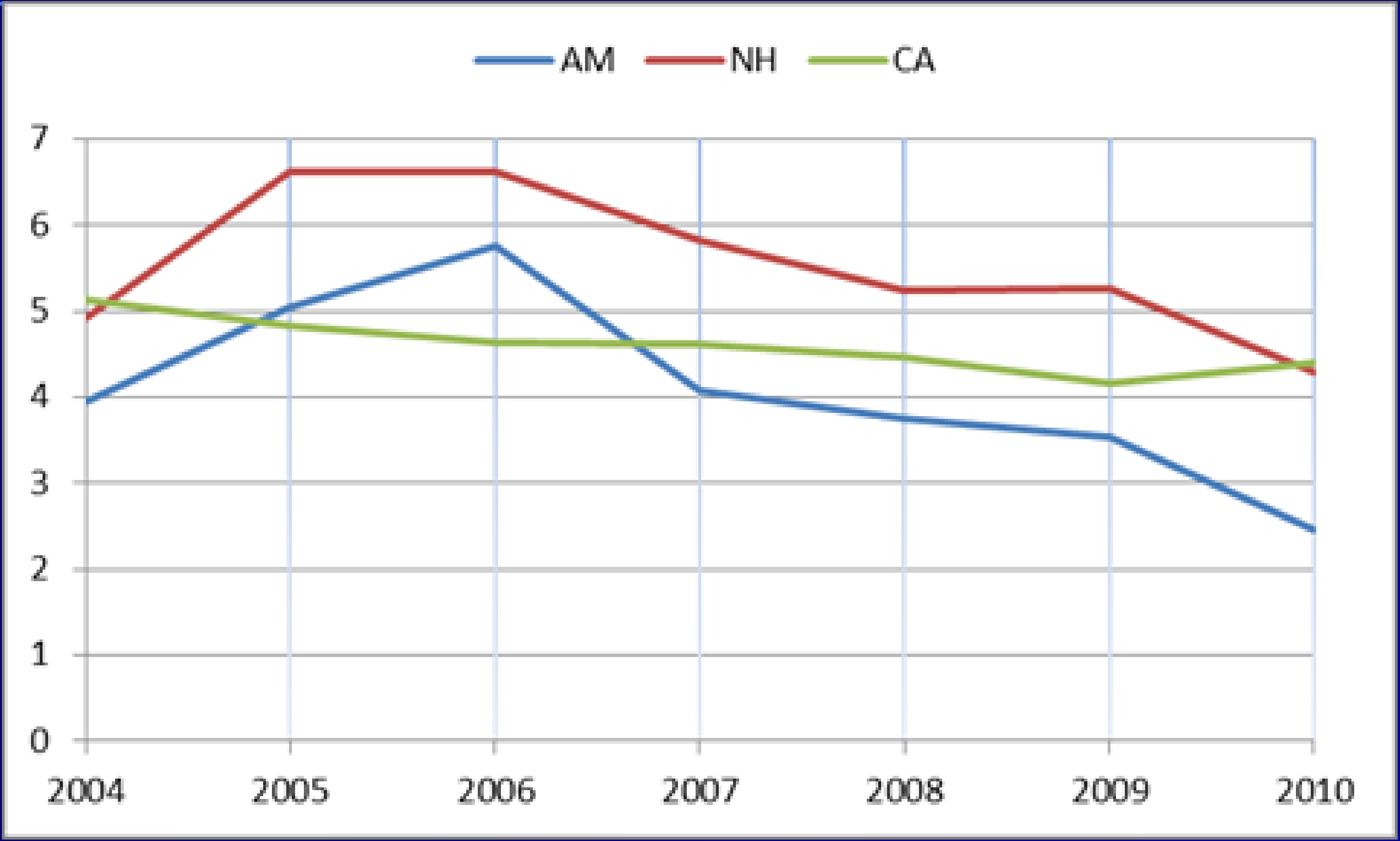
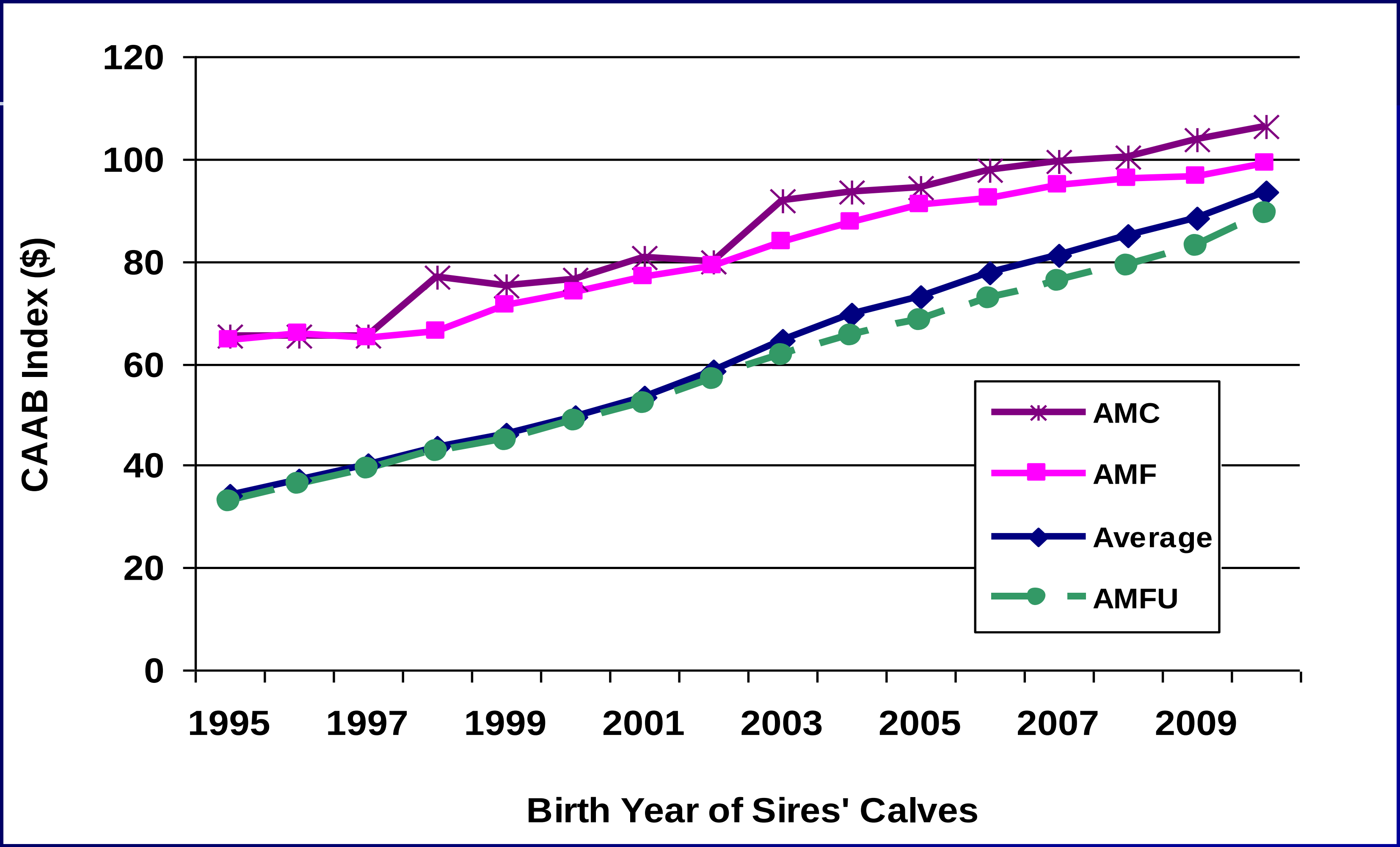


Figure courtesy of Carel Teseling, Angus Australia

Average Long Fed CAAB Index for sires by birth year



Allen, J. M. and C. F. Teseling. 2011**. Information empowers – Arthrogryposis multiplex in Angus Australia.** Proc. Assoc. Advmt. Anim. Breed. Genet. 19: *in press*

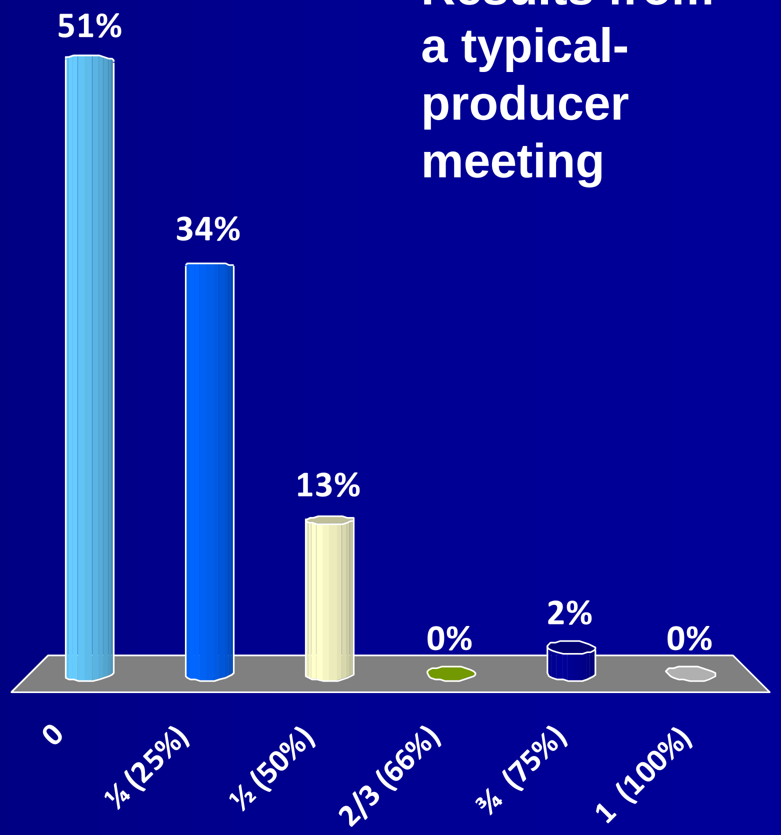
Early extension education about dwarfism explaining carriers and inheritance

Image from Special CollectionsUniversity Libraries, Virginia Tech:
http://spec.lib.vt.edu/imagebase/agextension/boxseven/screen/AGR3618.jpg

If you breed a curly calf carrier cow (AMC) to an curly calf free bull (AMF), what is the chance that the offspring will be stillborn as a result of being curly calf?

1. 0
2. ¼ (25%)
3. ½ (50%)
4. 2/3 (66%)
5. ¾ (75%)
6. 1 (100%)

Results from a typical-producer meeting



Ideally cattle would be genotyped once early in life and genotypes shared among production sectors to derive the maximum value from the fixed DNA collection and extraction costs

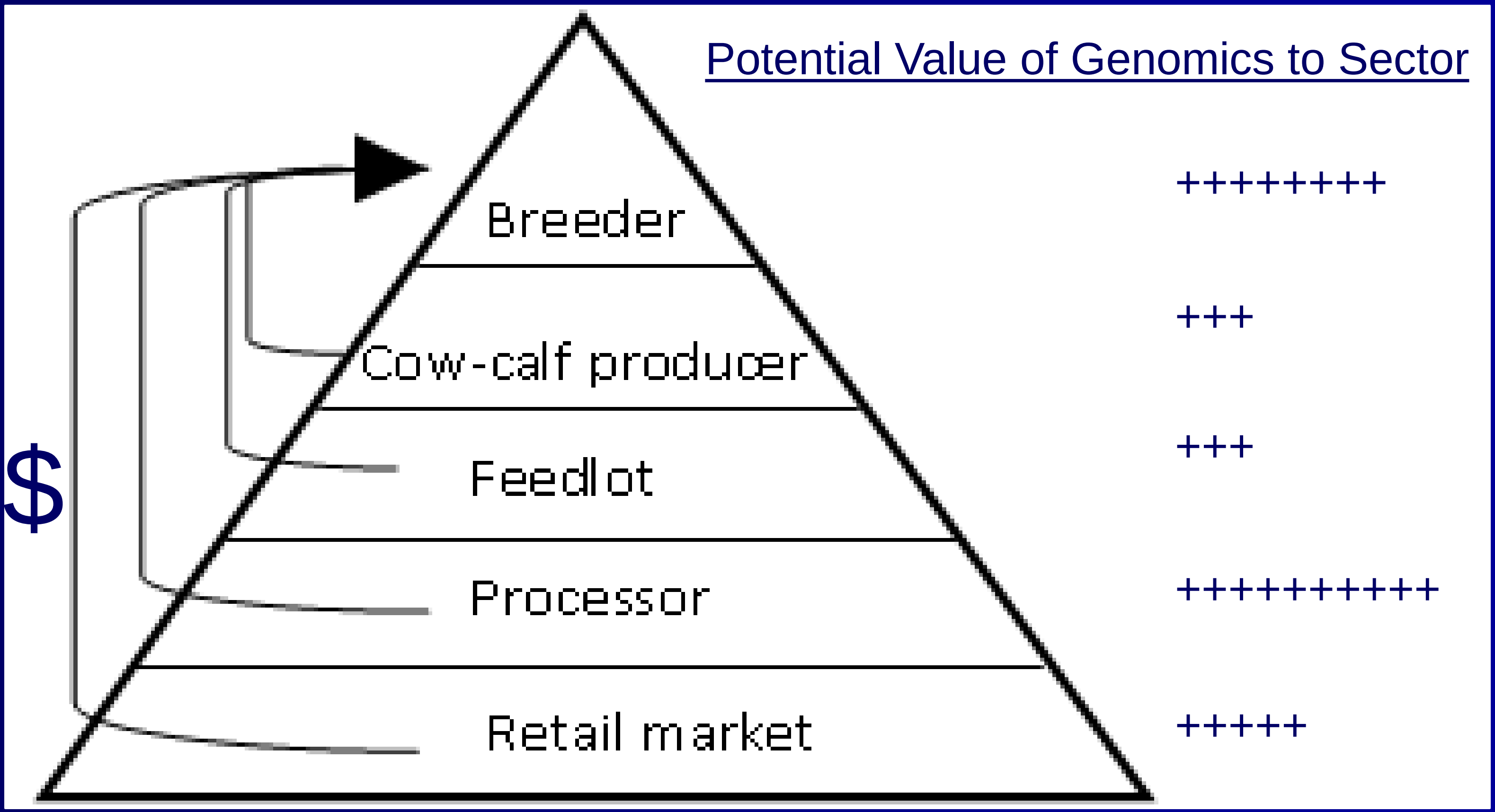


Figure from McEwan, J. C. 2007 Current status and future of genomic selection. Proceedings of the New Zealand Society of Animal Production 67: 147-152.

Some questions that remain

- If all animals carry recessive genetic factors/defects – how should "defects" be managed
- Can 50K or 800K data be also used to identify carrier status to spread the costs of DNA extraction. If so does it infringe on diagnostic test patents/IP
- Can we use genomics to better manage RGFs
- Are appropriate decision support tools available for producers

Thanks to Bryce Schumann, American Angus Association; David Buchanan, North Dakota State University; and Carel Teseling, Angus Australia for helpful discussions and/or providing data for the preparation of this presentation.

USDA United States Department of Agriculture

National Institute of Food and Agriculture

National Research Initiative Grant no. 2009-55205-05057
From the USDA National Institute of Food and Agriculture