"Cattle Genomics Research at UC Davis"

Alison Van Eenennaam

Animal Genomics and Biotechnology

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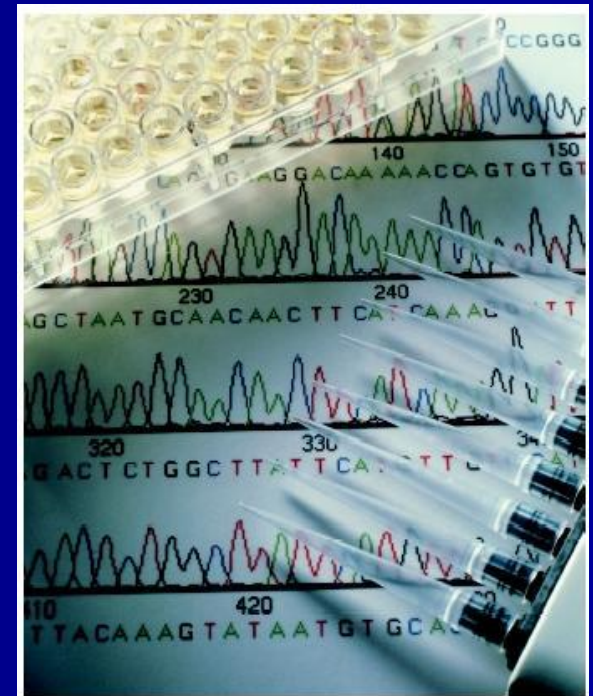
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Animal breeders have used the resemblance between relatives to select parents of the next generation and make genetic change

Breeding Objective

"*A breeding objective need not be economic. For example, in many companion animal species it is tempting to believe that the breeding objective must be the maintenance of a ridiculous appearance and congenital abnormalities*!"
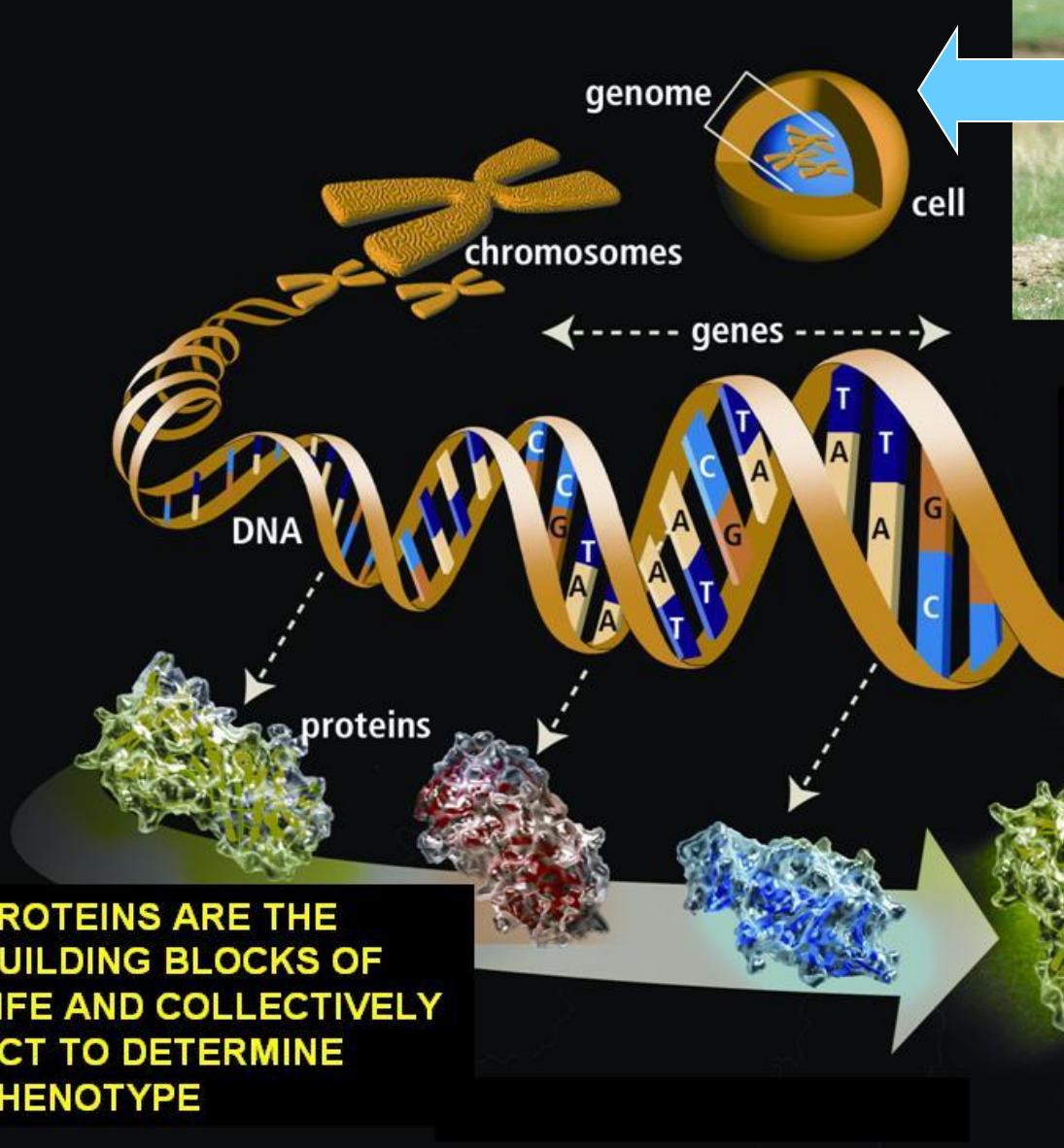
(John Gibson, UNE)

Rate of change is accelerated when breeders can accurately identify those individuals that have the best genetics at a young age

ΔG =   *intensity of selection X*

accuracy of selection X

(√genetic variance in population   /

generation interval)

The genome age

genome

cell

chromosomes

genes

DNA

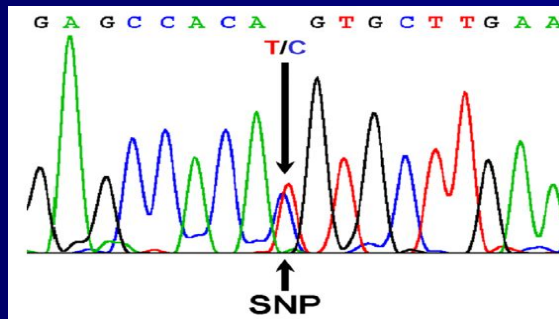**GENES CONTAIN INSTRUCTIONS FOR MAKING PROTEINS**

proteins

PROTEINS ARE THE BUILDING BLOCKS OF LIFE AND COLLECTIVELY ACT TO DETERMINE PHENOTYPE
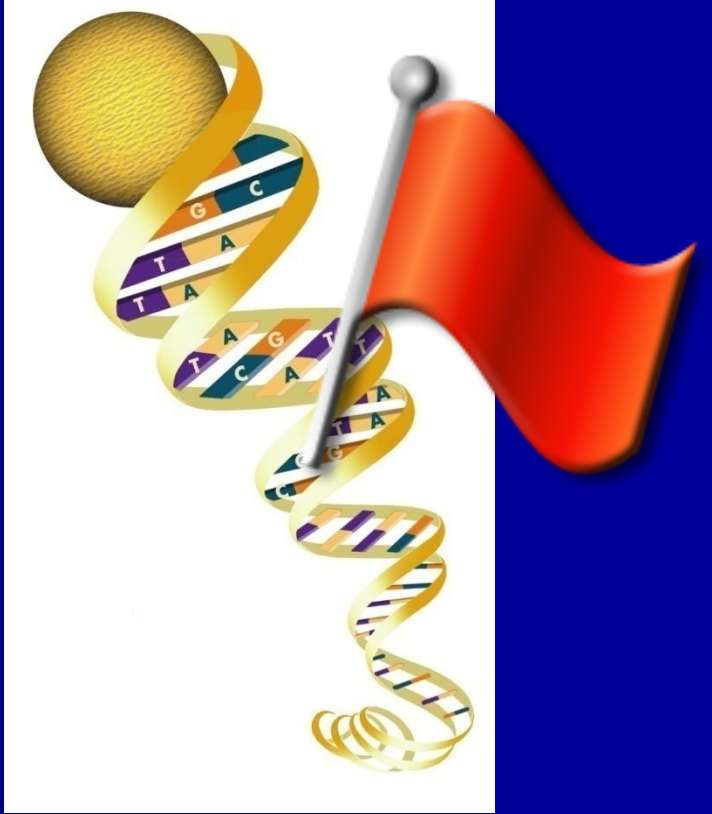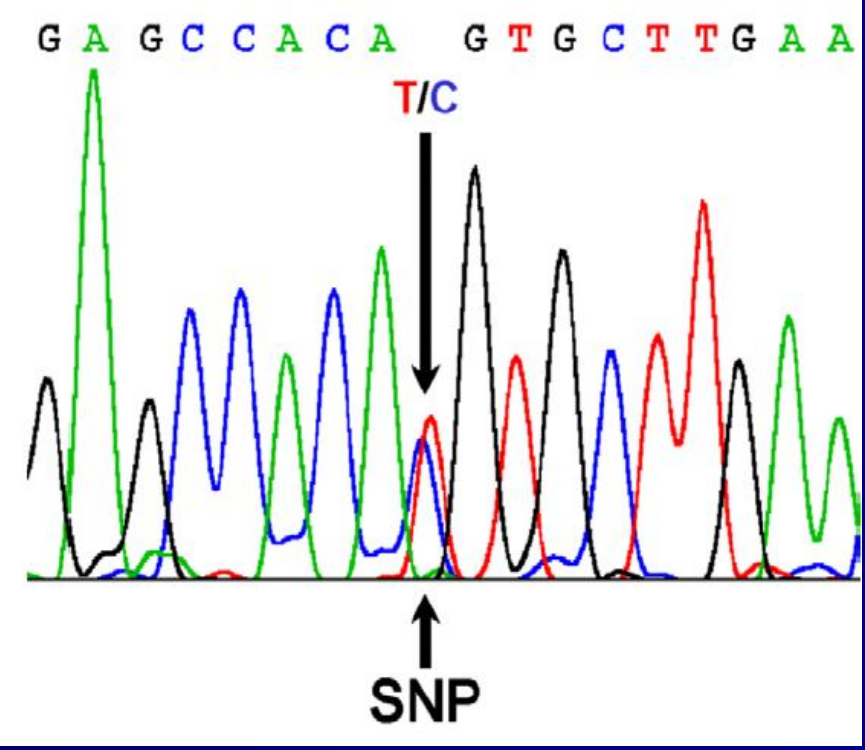
What is a Genetic Marker ?

A DNA sequence variation that has been associated with a given trait in one or more populations

We want to use DNA markers (SNPs) in addition to pedigree and performance information to help select the best animals

High-throughput genotyping technology enabled a new approach

- The sequencing of the bovine genome allowed for the development of a 50,000 marker chip!

- Can simultaneously test 50,000 markers

With high density (50K) SNP chips it is possible to:

- Divide genome into 50,000 chromosome segments based on marker intervals

- Marker density must be sufficiently high to ensure that all of the genes affecting a traits are "linked" (close to) a marker

- Idea is to capture all genetic variance with evenly spread markers and assign an "EPD" value to each segment

What is needed for "genomic" selection?
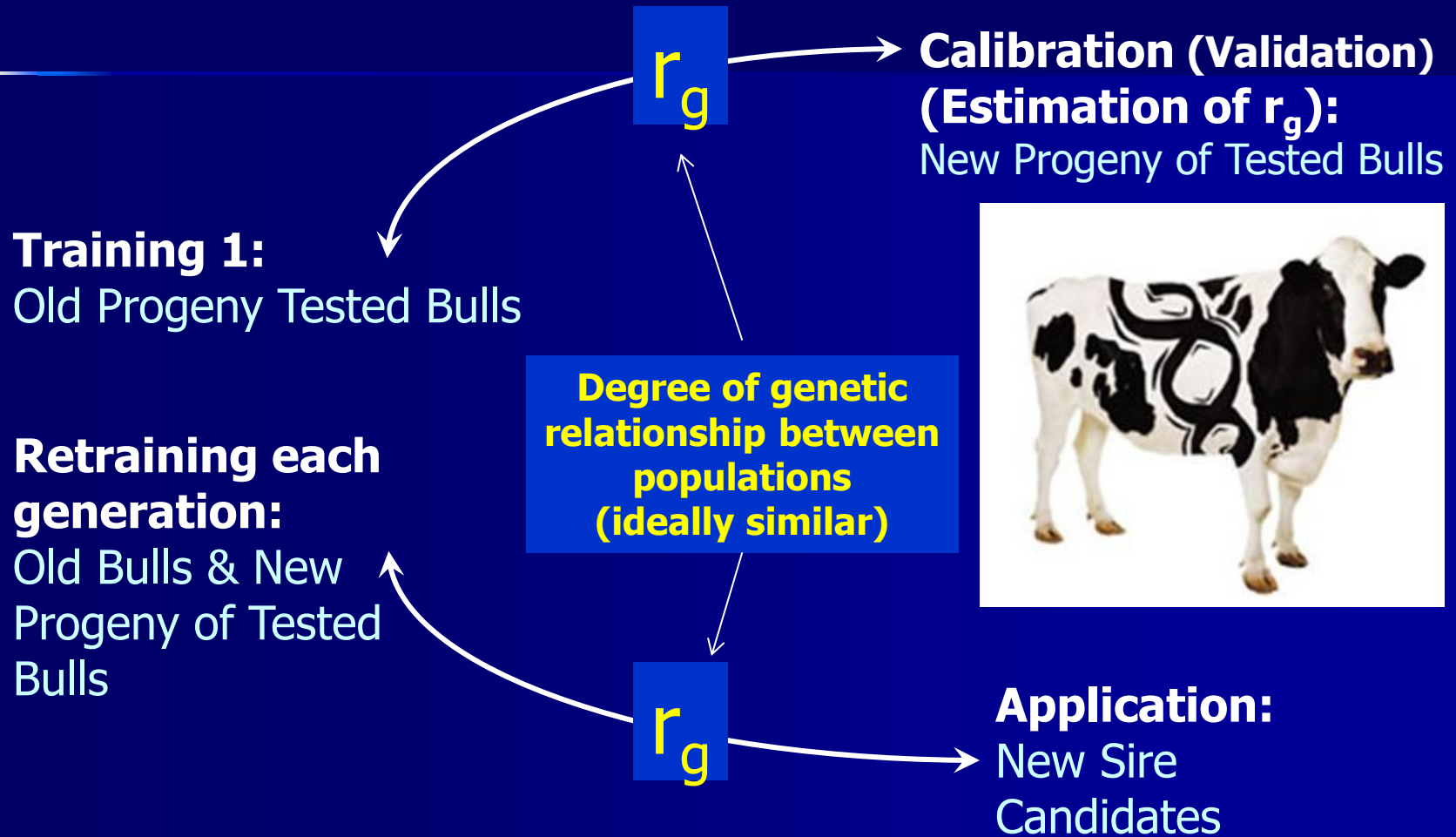
THEORY

- Population
- Phenotypes
- Genotypes

Training = estimate the value of every chromosome fragment contributing variation in a population with phenotypic observations

Prediction = the results of training can then be used to predict the merit of new animals, not contained in the training data set
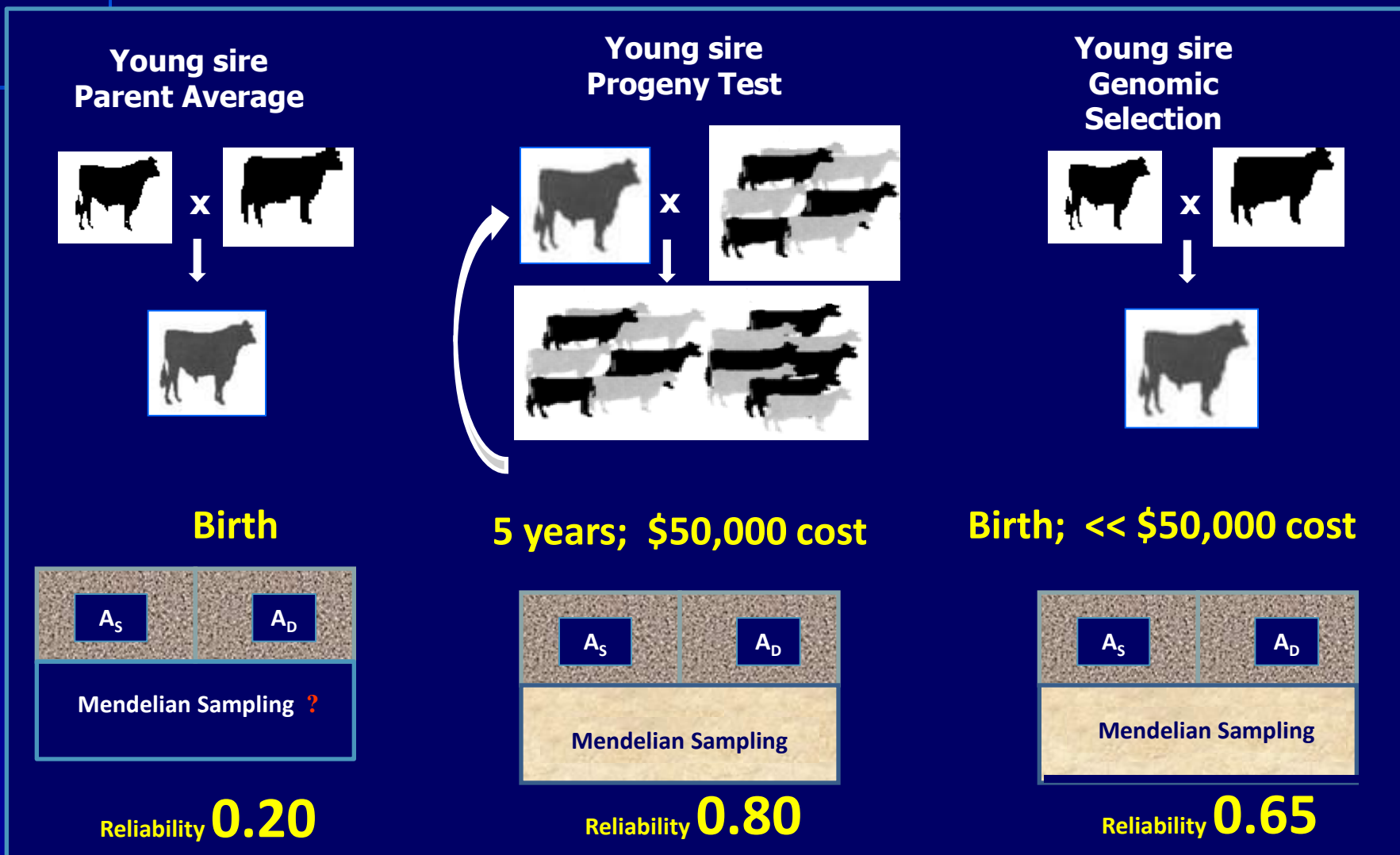
Implementation of Genomic Selection

r_g → **Calibration (Validation) (Estimation of r_g):** New Progeny of Tested Bulls

Training 1: Old Progeny Tested Bulls

Retraining each generation: Old Bulls & New Progeny of Tested Bulls

Degree of genetic relationship between populations (ideally similar)

r_g → **Application:** New Sire Candidates

Slide modified from Marc Thallman, US MARC

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Animal Genomics and Biotechnology Education

Breeding value prediction in Dairy Sires

Graphic kindly provided by Gonzalo Rincon

| Young sire Parent Average	Young sire Progeny Test	Young sire Genomic Selection
Birth	**5 years; $50,000 cost**	**Birth; << $50,000 cost**
Reliability **0.20**	Reliability **0.80**	Reliability **0.65**

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Dairy industry suited to WGS
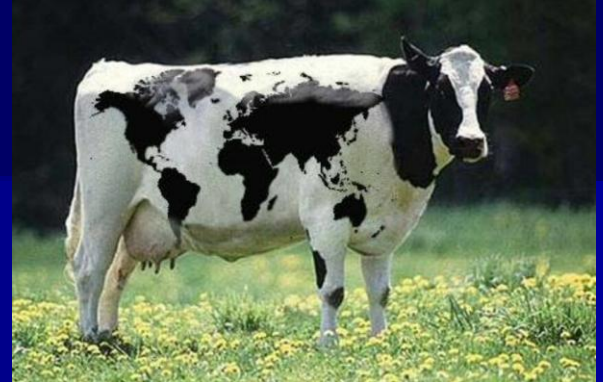
- High use of AI

- Mostly one breed

- Clear selection goal (total net merit)

- Large number of high accuracy A.I. sires for training

- Extensive, uniform collection of data on traits

- Central evaluation (AIPL) receiving <u>genotypes</u>

- Obvious way to increase rate of genetic gain

- AI companies funding the genotyping because they get a clear cost savings in terms of young sire program

Animal Genomics and Biotechnology Education
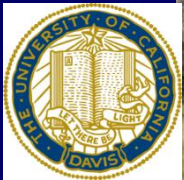
The Beef Cattle Industry

- Little use of AI
- Relatively few high accuracy sires for training
- Multiple competing selection goals – cow/calf, feedlot, processor – little data sharing between sectors
- Few/no records on many economically-relevant traits
- Many breeds, some small with limited resources
- Crossbreeding is important
- No centralized "national" cattle evaluation
- Not clear who should pay for testing

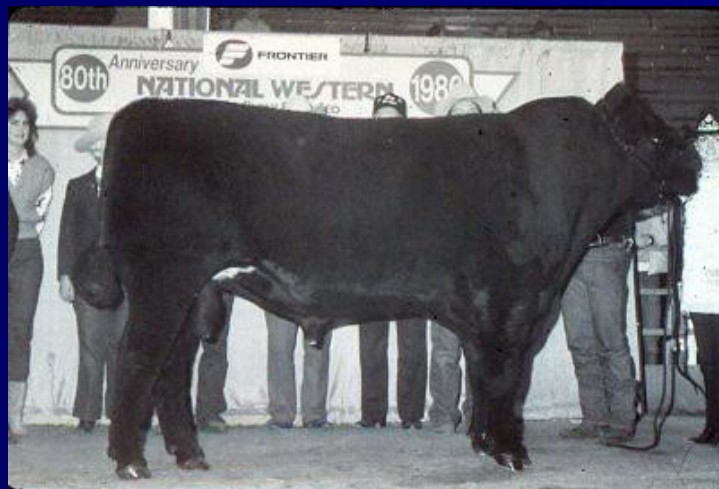# Historically not all beef cattle breeding objectives have been economic

Photo taken in 1949 at Red Bluff Bull Sale, CA.
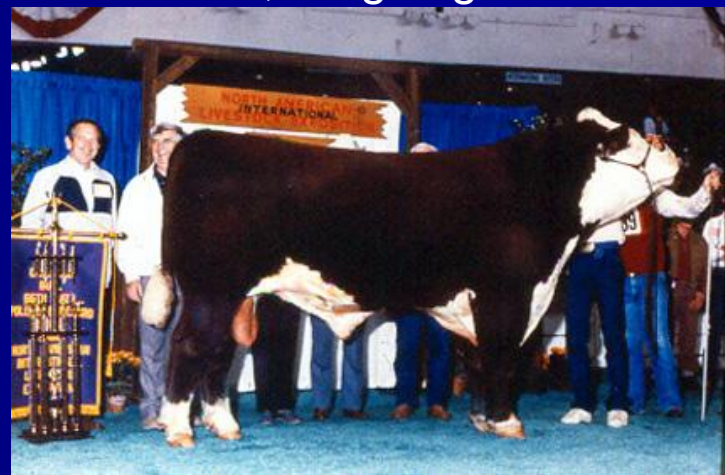Kindly provided by Cathy Maas from Crowe Hereford Ranch, Millville, CA.

1953. Grand Champion Angus Female, International, 1953

1950. Grand Champion Steer, International, weighing 1025 lbs

1986. "Coblepond New Yorker" weighed 2529 lbs and measured 65 inches tall at 35 mos. (Frame 10) when he was Denver Champion.

1988 Grand Champion Bull, National Polled Hereford Show (frame 10).

Images from Harlan Ritchie's historical review of type
https://www.msu.edu/~ritchieh/historical/cattletype.html

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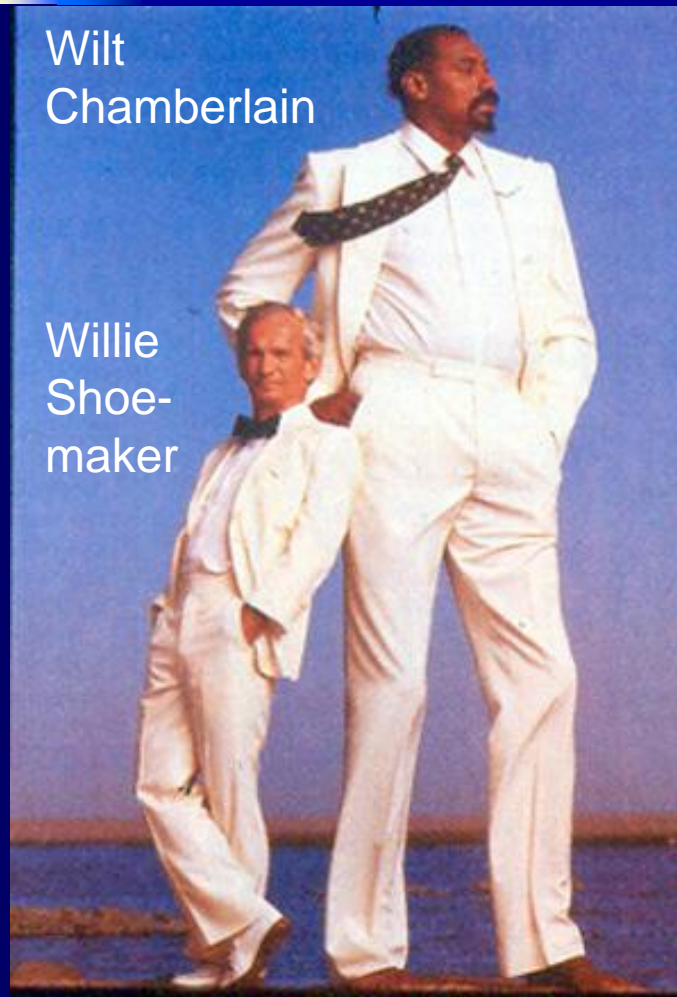
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We can make genetic changes in our cattle (and our dogs) - the question is are we making profitable change?

Wilt Chamberlain

Willie Shoe-maker

Killed same day at IBP in Iowa:
The small female weighed 835 lbs and was extremely fat. The large male weighed 1900 lbs and was very lean.

Images from Harlan Ritchie's historical review of type
https://www.msu.edu/~ritchieh/historical/cattletype.html

Alison Van Eenennaam UC Davis

Animal Genomics and Biotechnology Education

"Integrating DNA information into beef cattle production systems."

Alison Van Eenennaam, Animal Science, UC Davis (PD)
Dan Drake, UCCE Siskiyou County, CA
Kristina Weber, PhD student, Animal Science, UC Davis

Siskiyou County Producer Collaborators:
Jack Cowley, Cowley Rancher, CA
Dale, Greg, & Richard Kuck, Kuck Ranch, CA
Matt Parker, Mole-Richardson Ranch, CA
Processor Collaborators:
Harris Ranch Beef Company, Coalinga, CA
Los Banos Abattoir, Los Banos, CA
Software Collaborators:
- Jim Lowe, MidWest Microsystems, NE

Other Contributors/Collaborators
Dr. Jerry Taylor, University of Missouri, MO
Dr. Mike Goddard, University of Melbourne, Australia
Dr. Darrh Bullock,, University of Kentucky, KY
Dr. Leslie "Bees" Butler, UC Davis, CA
Dr. Dorian Garrick, Professor, Iowa State University, IA
Dr. John Pollak, US Meat Animal Research Center, NE

USDA United States Department of Agriculture — National Institute of Food and Agriculture

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Animal Genomics and Biotechnology Education

Objectives:
"Integrating DNA information into beef cattle production systems"

- The overall objective of this project is to develop a genotyped, phenotyped population to enable the evaluation and/or assessment of different DNA-enabled approaches for predicting the genetic merit of herd sires on commercial beef ranches.

- The research objective is to compare the current means of genetic prediction of herd sires (i.e. breed-based expected progeny differences) with DNA-assisted genetic predictions, and "commercial ranch" genetic evaluations based on the performance of their offspring under field conditions.

- An additional objective is to determine the costs and benefits associated with the application of DNA-based technologies on commercial beef operations

aka "California Commercial Ranch Project"

Commercial Angus bulls

2400 cows/year

Progeny

×

Data collection:
AAA EPD & pedigree

↓

Sample collection:
For genotyping

↓

MBV

Ranch and harvest data Collection

↓

Genotyping

↓

Paternity Determination

Assessment of DNA-enabled approaches for predicting the genetic merit of herd sires on commercial beef ranches

Kristina Weber
Animal Biology
Ph.D. student
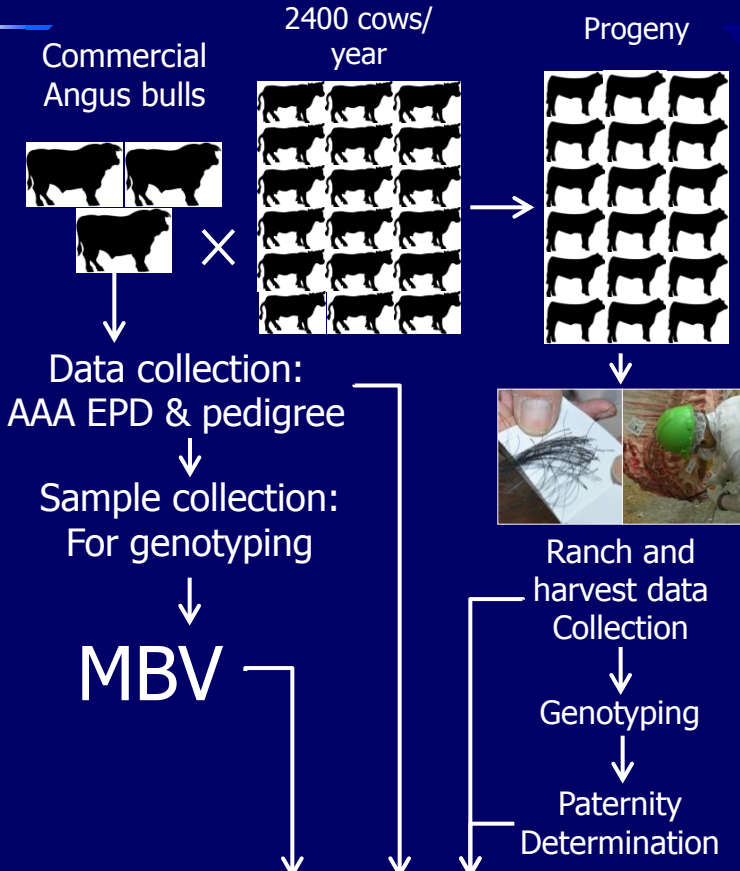
Four collaborating ranches:
- Cowley (900 cows)
- Kuck (500 cows)
- Mole-Richardson (700 cows)
- UC Davis (300 cows)

Approximately 120 Angus herd bulls, and 2,400 cows per year on project

Sample and phenotype collection

Calving Date	Ranches	WW	Feedlot In-Weight	Carcass
Pre-project	2	~550 head	~460 head	~620 head
Spring 2009	2	Fall 2009: ~600 head	Fall 2009/ Winter 2010: ~500 head	Spring/Summer 2010: ~450 head
Fall 2009	4	Winter/Spring 2010: ~1500 head	Late Summer/ Fall 2010: ~900 head	Winter 2011: ~850 head
Spring 2010	2	Fall 2010	Fall 2010/ Winter 2011	Spring/Summer 2011
Fall 2010	4	Winter/Spring 2011	Late Summer/ Fall 2011	Winter 2012
Spring 2011	2	Fall 2011	Fall 2011/ Winter 2012	Spring/Summer 2012
Fall 2011	4	Winter/Spring 2012	Late Summer/ Fall 2012	Winter 2013
Total records	4	**7000 records >20 collection trips**	**4500 records Sent electronically**	**4500 records >35 collection trips**

"Identification of gene targets for improved efficiency and sustainability of beef production using exome capture, RNA-seq and high density SNP genotyping technologies. "

Objectives: Using next generation sequencing technologies to find gene targets associated with residual feed intake (RFI) and correlated or component traits such as dry matter intake (DMI), methane production, mitochondrial respiration, composition of gain, and carcass traits in beef steers.

Through the identification of genes that regulate beef production efficiency at several physiological levels, gene targets for more efficient and sustainable beef production may be identified.

Kristina Weber
Animal Biology
Ph.D. student

Alison Van Eenennaam UC Davis

Animal Genomics and Biotechnology Education

"Genomic Interrogation of the Putative Etiological Agent of Epizootic Bovine Abortion (EBA)"

EBA is leading cause of beef cattle abortion in CA
45,000-90,000 calves lost annually
Vector *Ornithodoros coriaceus* (Pajaroello tick)

approx. 1 cm
Ornithodoros coriaceus adult
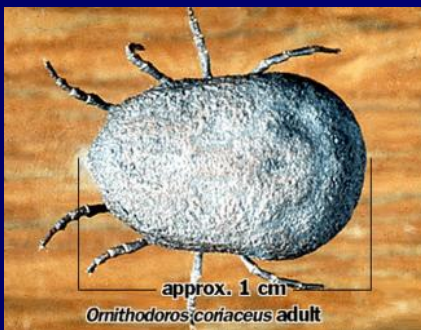
Bryan Welly,
Animal Biology
MS student

UC Davis Collaborators:
Dr. Jeff Stott
Myra Blanchard
Dr. Juan Medrano

- Assemble a reference genome for the novel deltaproteobacterium which is the etiologic agent of epizootic bovine abortion (EBA)

- Identify highly transcribed bacterial genes as possible candidates for a recombinant vaccine

UCDAVIS
UNIVERSITY OF CALIFORNIA

Alison Van Eenennaam UC Davis

Animal Genomics and Biotechnology Education

"Identification and management of alleles impairing heifer fertility while optimizing genetic gain in Angus cattle"

David Patterson, University of Missouri, MO
Jerry Taylor, University of Missouri, MO
Michael Smith, University of Missouri, MO
Scott Brown, University of Missouri, MO
Alison Van Eenennaam, UC Davis, CA
Mike MacNeil, DeltaG consulting, MT
Brian Kinghorn, Armidale, Australia

Dave Patterson, PD
University of MO

USDA
United States Department of Agriculture
National Institute of Food and Agriculture

Alison Van Eenennaam UC Davis

Animal Genomics and Biotechnology Education

"Identification and management of alleles impairing heifer fertility while optimizing genetic gain in Angus cattle"

- **The overall objective of this project is to improve reproductive rates in cattle by identifying genes which cause embryonic or early developmental mortality.**
- Identify and characterize the impact of genes associated with reproductive failure in cattle;
- Develop a fertility EPD (Expected Progeny Difference) based on genotype information for these specific genes that will provide estimates of the genetic value of an animal;
- Develop economic selection indexes for beef producers that will support selection and breeding decisions, inclusive of fertility;
- Develop economic estimates that are based on improvements in reproductive rates for the beef industry;
- Develop decision support software for beef producers that will improve breeding schemes using selection indexes and new mating selection strategies based on sire and dam genotypes;

The long-term goal of this project is to improve reproductive rates of US beef cattle based on improvements in selection to improve overall profitability to the herd enterprise.

Genotype-Driven Screens for Embryonic Lethals

- Sequence bulls and identify SNPs that are predicted to have a disruptive effect on protein structure (also called causative DNA sequence variants **DSV**)

- Develop chip of DSVs and sequence large number of healthy individuals to identify embryonic lethals

- True embryonic lethals should never be observed in the homozygous state among healthy animals and the resulting departure from Hardy-Weinberg equilibrium should be statistically significant

- Carrier status of the sire and dam should have a negative effect on fertility traits

Missing homozygotes....

Harmful recessive effects on fertility detected by absence of homozygous haplotypes.

VanRaden PM, Olson KM, Null DJ, Hutchison JL.

Animal Improvement Programs Laboratory, Agricultural Research Service, USDA, Beltsville, MD 20705-2350, USA. paul.vanraden@ars.usda.gov

Abstract

Five new recessive defects were discovered in Holsteins, Jerseys, and Brown Swiss by examining haplotypes that had a high population frequency but were never homozygous. The method required genotypes only from apparently normal individuals and not from affected embryos. Genotypes from the BovineSNP50 BeadChip (Illumina, San Diego, CA) were examined for 58,453 Holsteins, 5,288 Jerseys, and 1,991 Brown Swiss with genotypes in the North American database. Haplotypes with a length of ≤ 75 markers were obtained. Eleven candidate haplotypes were identified, with the earliest carrier born before 1980; 7 to 90 homozygous haplotypes were expected, but none were observed in the genomic data. Expected numbers were calculated using either the actual mating pattern or assuming random mating. Probability of observing no homozygotes ranged from 0.0002 for 7 to 10^{-4} ^{5} for 90 expected homozygotes. Phenotypic effects were confirmed for 5 of the 11 candidate haplotypes using 14,911,387 Holstein, 830,391 Jersey, and 68,443 Brown Swiss records for conception rate. Estimated effect for

If allele frequency of SNP is 50% A: 50%T then expect 25% AA; 50% AT, 25% TT

If see 33% AA and 66% AT then have a case of missing homozygotes (i.e. TT is likely lethal)

Haplotypes Affecting Fertility and their Impact on Dairy Cattle Breeding Programs

Dr. Kent A. Weigel, University of Wisconsin

- The exact genes and their underlying biological roles in fertilization and embryo development are unknown, but it is assumed that the outcome of inheriting the same haplotype from both parents is failed conception or early embryonic loss.

- **The reactive approach of attempting to eradicate every animal with an undesirable haplotype is not recommended in light of their economic impact, and is not practical given the likelihood that many more undesirable haplotypes will be found.**

- Producers should neither avoid using bulls with these haplotypes nor cull cows, heifers, and calves that are carriers, because this will lead to significant economic losses in other important traits.

- Computerized mating programs offer a simple, inexpensive solution for avoiding affected matings, so producers should use these programs and follow through on the mating recommendations.

"Integrated program for reducing bovine respiratory disease complex in beef and dairy cattle"
(aka BRD CAP)

"Long-term goal is to reduce the incidence of BRD in beef and dairy cattle by capitalizing on recent advances in genomics to enable novel genetic approaches to select for cattle that are less susceptible to disease"

Jim Womack, PD
Texas A&M

USDA

United States Department of Agriculture

National Institute of Food and Agriculture

Alison Van Eenennaam UC Davis

Animal Genomics and Biotechnology Education

BRD CAP COLLABORATORS

www.brdcomplex.org

Bovine Respiratory Disease Complex Coordinated Agriculture Project

TEXAS A&M UNIVERSITY

- **Jim Womack, PD**
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- Scott Dindot
- Noah Cohen
- Chris Seabury
- Lawrence Falconer
- Lauren Skow
- Gary Snowder

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- **Milt Thomas**
- Mark Enns

United States Department Of Agriculture — Agricultural Research Service

- Mike MacNeil
- Curt Van Tassell

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- Shannon Neibergs

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- Tim Ross

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- Shiela McGuirk (WI)
- Adroaldo Zanella (Norway)
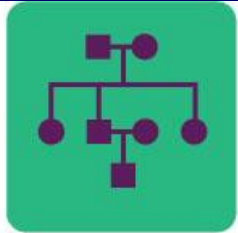
Year 1: CA Dairy Calf Ranch: 70,000 head capacity

Bovine Respiratory Disease Complex Coordinated Agriculture Project

Jessica Davis, DVM
Intern at Veterinary Medicine Teaching and Research Center, University of California, Davis; Tulare
Terry Lehenbauer, DVM
Sharif Aly, DVM
Pat Blanchard, DVM
California Animal Health and Food Safety Laboratory System

Photo credit: Jessica Davis

Bovine Respiratory Disease Complex Coordinated Agriculture Project

Standardization of BRD Diagnosis

- 1000 case and 1000 control 30-60 day old calves
- Use Dr. Sheila McGuirk's calf respiratory scoring chart
  - Temperature, eyes, ears, nose, +/- cough
  - Additional clinical signs: tachypnea, dyspnea, position of head, appetite
  - Give score and either enroll or not (5 or greater to enroll as case)
- Sample collection
  - Blood for DNA extraction and high density SNP genotyping
  - Nasal swab and deep pharyngeal swab to identify viruses (PCR: IBR, BVD, BRSV, and Corona) and bacteria (*Manheimia haemolytica, Pasteurella multocida*, and *Histophilus somni*, and Mycoplasma spp.) present in the nasopharyngeal and pharyngeal recesses

SCHOOL OF VETERINARY MEDICINE
University of Wisconsin-Madison

Calf Health Scoring Criteria			
0	1	2	3
Rectal temperature			
100-100.9	101-101.9	102-102.9	≥103
Cough			
None	Induce single cough	Induced repeated coughs or occasional spontaneous cough	Repeated spontaneous coughs
Nasal discharge			
Normal serous discharge	Small amount of unilateral cloudy discharge	Bilateral, cloudy or excessive mucus discharge	Copious bilateral mucopurulent discharge
Eye scores			
Normal	Small amount of ocular discharge	Moderate amount of bilateral discharge	Heavy ocular discharge
Ear scores			
Normal	Ear flick or head shake	Slight unilateral droop	Head tilt or bilateral droop

Blood collection

Deep pharyngeal swab collection

Nasal swab

Sampling location of deep pharyngeal swab
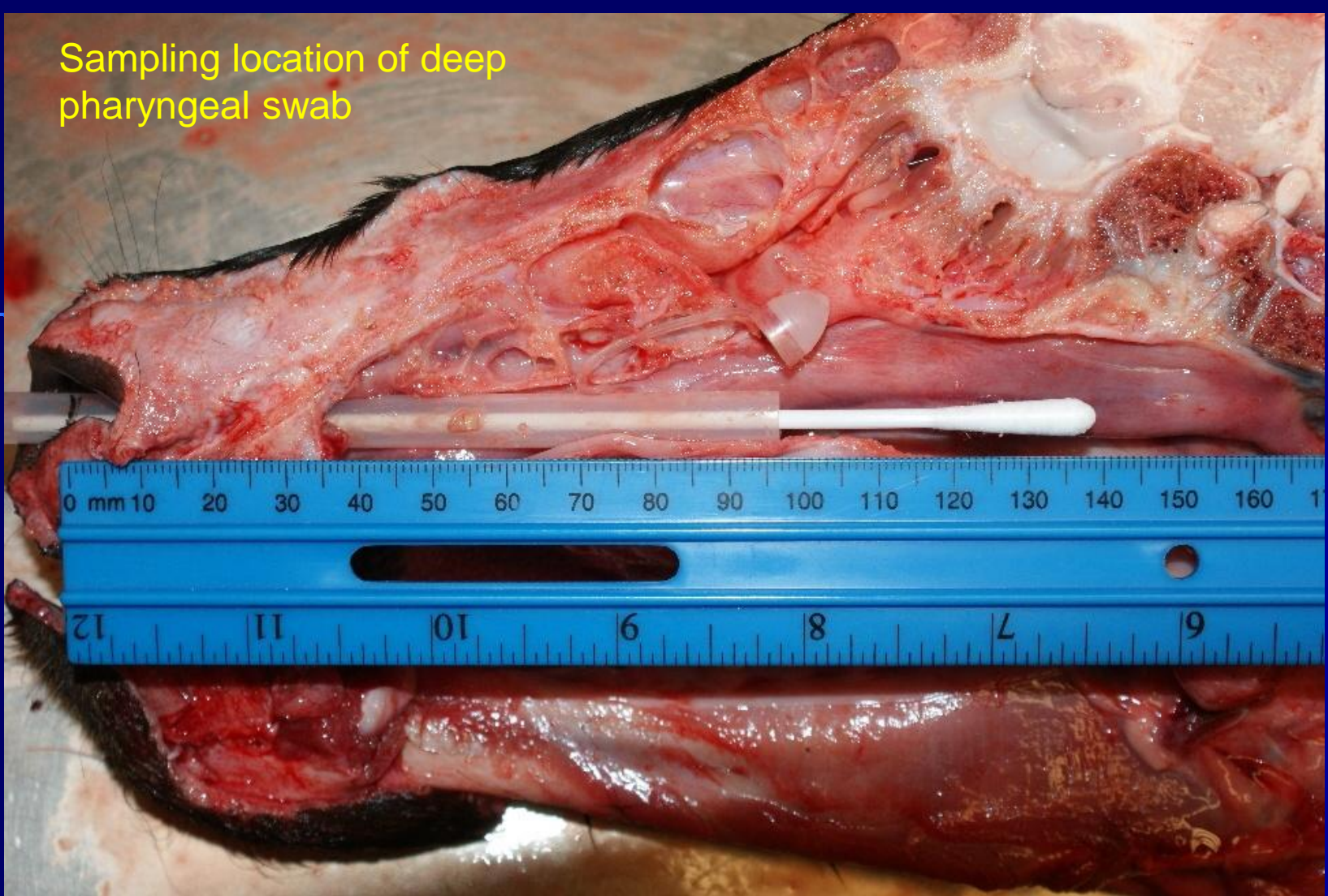
To culture organisms associated with BRD, pharyngeal swabs offer a less invasive, less stressful and more rapid alternative to broncheoalveolor lavage.

Photo credit: Jessica Davis

animalscience.ucdavis.edu/animalbiotech

Contact information

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