



# W142: The Genetic Basis of Host Susceptibility to Bovine Respiratory Disease

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US Bovine Respiratory Disease

Coordinated Agricultural Project

<http://www.brdcomplex.org>



The “Integrated Program for Reducing Bovine Respiratory Disease Complex (BRDC) in Beef and Dairy Cattle” Coordinated Agricultural Project is supported by Agriculture and Food Research Initiative Competitive Grant no. 2011-68004-30367 from the USDA National Institute of Food and Agriculture.



# Overview



- What is Bovine Respiratory Disease (BRD)
- What is the BRD CAP
- Advantage of selecting for disease traits
- Challenges of selecting for disease traits
- Research overview of BRD CAP
- Development of phenotyped and HD SNP genotyped BRD case:control datasets



# What is Bovine Respiratory Disease?

- Leading cause of death in both dairy and beef cattle
- Economic losses to industry—estimated > US\$700 million/year
- Responsible for 22.5% of mortalities in unweaned dairy heifers, 46.5% in weaned dairy heifers, and 28% of non-predator losses in cattle and calves
- Disease associated with many pathogens, both viral and bacterial
- Exacerbated in times of stress





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# Background and Rationale

*"Year in and year out, diseases of the respiratory system are a major cause of illness and death in cattle from 6 weeks to two years of age. Sadly, this is as true today as it was 30 years ago despite development of new and improved vaccines, new broad spectrum antibiotics, and increased fundamental knowledge as to the cause of disease"*

- Bovine Respiratory Disease (BRD) has been extensively studied since the 1800s, and yet it remains prevalent
- More effective vaccines have not decreased the morbidity or mortality of BRD
- Mortality has increased as vaccine efficiency has increased
- 1.4% of all US feedlot cattle perish before reaching harvest weight
- **Need to develop new approaches to tackle BRD**

Montgomery, D. 2009. Bovine Respiratory Disease & Diagnostic Veterinary Medicine. Proceedings, The Range Beef Cow Symposium XXI. December 1, 2 and 3 2009, Casper, WY. Pages 1-6.



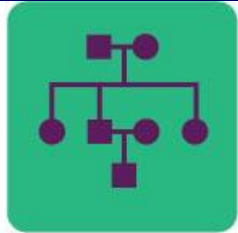


# BRD Coordinated Agricultural Project (BRD CAP)

*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*



Agriculture and Food Research Initiative Competitive Grant no. 2011-68004-30367



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# Potential benefits of genomics are greatest for economically-important traits that:

- Are difficult or expensive to measure
- Cannot be measured until late in life or after the animal is dead
- Are not currently selected for because they are not routinely measured
- Have low heritability

Yep, looks like all of 'em were susceptible





# Issues in the development of genetic approaches to select against susceptibility to BRD

## ■ Disease resistance heritabilities tend to be low, especially under field conditions

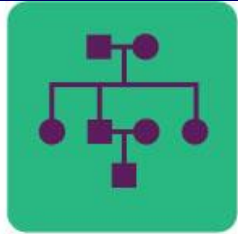
- suboptimal diagnosis (e.g. not all sick animals are identified and healthy animals may be incorrectly diagnosed as ill),
- some susceptible animals will appear resistant to a disease when in fact they have not been exposed to the disease agent.

Bishop, S. C., and J. A. Woolliams. 2010. On the genetic interpretation of disease data. Plos One 5: e8940.

## ■ In feedlot calves, heritability estimates were low and ranged from 0.04 to 0.08 (Snowder et al., 2006). When the observed heritability estimate was transformed to an underlying continuous scale, the estimate increased to 0.18

Snowder, G. D., L. D. Van Vleck, L. V. Cundiff, and G. L. Bennett. 2006. Bovine respiratory disease in feedlot cattle: environmental, genetic, and economic factors. J Anim Sci 84: 1999-2008.





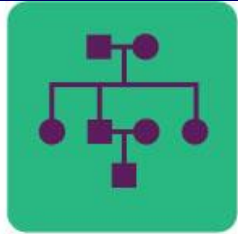
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# Need for large discovery populations

- The ready availability of dense single nucleotide polymorphism arrays (i.e. SNP chips) has given rise to hitherto unforeseen opportunities to dissect between-host variation and identify possible genes contributing to this variation using genome wide association studies
- To have the requisite power to meaningfully quantify genetic variation or perform a genome scan using a dense SNP chip it is necessary to have datasets comprising observations **on several thousands of individuals.**

Bishop, S. C., and J. A. Woolliams. 2010. On the genetic interpretation of disease data. Plos One 5: e8940.



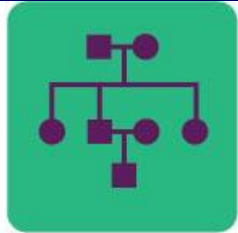


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# Need for careful “case” definition

- For studies of infectious diseases this usually necessitates utilizing field data because challenge experiments of a sufficient scale will not be possible.
- However, such field data is very ‘noisy’
  - diagnosis of infection or disease may be imprecise; it can be difficult to determine when infection of an individual occurred
  - it is often unclear whether or not apparently healthy individuals have been exposed to the infection
- These factors add environmental noise to the epidemiological data.

Bishop, S. C., and J. A. Woolliams. 2010. On the genetic interpretation of disease data. Plos One 5: e8940.



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# No one said we are targeting the low hanging fruit



## *Low Hanging Fruit*





# However, BRD resistance is a very valuable target

- The presence of genetic variation in resistance to disease, coupled with the increased consumer pressure against the use of drugs, is making genetic solutions to animal health problems increasingly attractive.

Newman, S. and Ponzoni, R.W. 1994. Experience with economic weights. Proc. 5<sup>th</sup> World Congress on Genetics Applied to Livestock Production. 18:217-223.

- Considerable weighting (6X growth traits) was given to decreasing the feedlot incidence of BRD in a terminal beef sire selection index simulation.

Van Eenennaam, A. L. and M. D. MacNeil. 2011. What weighting should be given bovine respiratory disease (BRD) resistance in selection decisions? Pages 61-68 in Proceedings of the Beef Improvement Federation 43<sup>rd</sup> Annual Research Symposium and Annual Meeting.



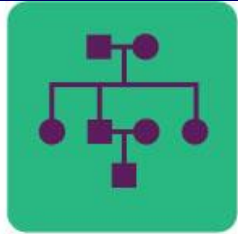


# Other animal industries have successfully targeted selection for disease resistance

- In dairy cattle, selection programs have been developed to take advantage of genetic variability in mastitis resistance, despite the fact that the heritability of clinical mastitis is low and mastitis resistance has an adverse correlation with production traits
- Chicken breeders have long used breeding to improve resistance to avian lymphoid leucosis complex and Marek's disease
- Swine PRRS virus (Jack Dekker's talk this morning)

Stear, M. J., S. C. Bishop, B. A. Mallard, and H. Raadsma. 2001. The sustainability, feasibility and desirability of breeding livestock for disease resistance. *Res Vet Sci* 71: 1-7





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# BRD CAP: BRD field datasets

Case:control field datasets are being developed for bovine respiratory GWAS

- 6000 animals – case:control design
  - 2000 dairy calves diagnosed on a collaborating dairy calf rearing ranch (CA)
  - 2000 feedlot cattle diagnosed on a collaborating feedlot (TX)
  - 1000 dairy (NM) and 1000 beef (NV) case:control animals will be used to validate loci associated with BRD in the discovery populations
- All will be genotyped on 800K high density SNP chip
- Pathogens are being characterized using bacteriology and virology
  - Genotype x pathogen interactions



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# Year 1: CA Dairy Calf Ranch: 70,000 head capacity



**Jessica Davis, DVM**

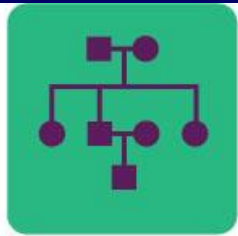
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**Sharif Aly, DVM**

**Pat Blanchard, DVM**

California Animal Health and  
Food Safety Laboratory System















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# 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
  - 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





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





Blood collection



Deep  
pharyngeal  
swab  
collection

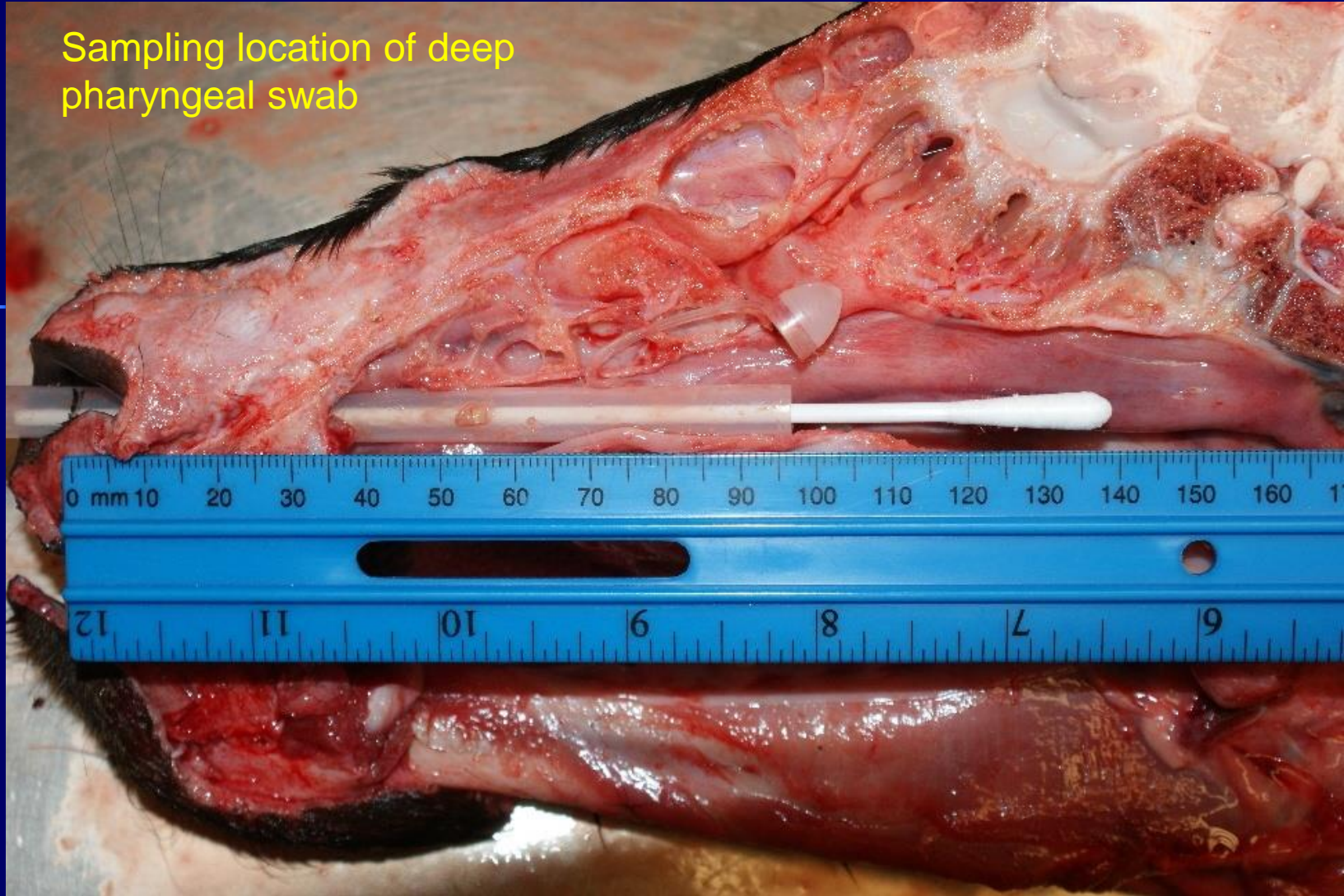


Nasal swab

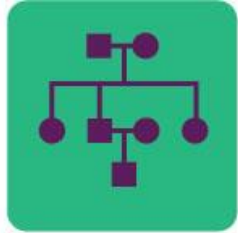




Sampling location of deep  
pharyngeal swab



To culture organisms associated with BRD, pharyngeal swabs offer a less invasive, less stressful and more rapid alternative to bronchoalveolar lavage.



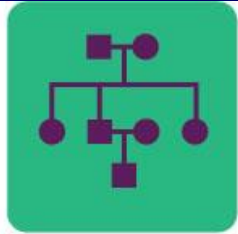
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# Control Calves

- Score control in same way as cases (score of 4 or less)
- Try to select animals in the adjacent hutch, same dairy of origin, and same sex
- Collect samples for control animals in same way as case

Try to identify cases and controls in a relatively constant environment, subjected to the same exposure and stresses, to decrease the environmental “noise” of these field BRD datasets





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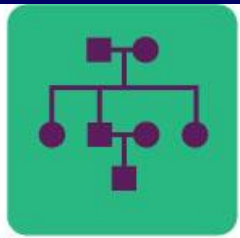
# Overarching Research Aims

1. Identify genomic regions associated with BRD resistance/susceptibility in beef and dairy cattle.
2. Identify the interaction of the cattle genome with the pathogens responsible for BRD.
3. Identify novel pathogens present in animals with BRD, and develop pathogen diagnostic panel
4. Develop BRD Genetic Selection Panel.
5. Develop genomic estimates of breeding values for resistance to BRD.
6. Assess how animal welfare is affected by BRD in cattle.



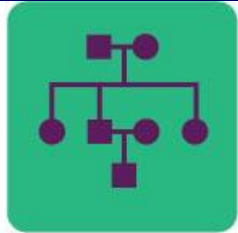


# BRD Coordinated Agricultural Project: PD: Jim Womack



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**Our goal is to integrate research, education, and extension activities to develop cost-effective genomic and management approaches to reduce the incidence of BRD in beef and dairy cattle**

The objective of this multi-institutional project is to reduce the incidence of bovine respiratory disease by:

- Capitalizing on recent advances in genomics to enable novel genetic approaches to select for disease-resistant cattle
- Developing improved DNA-based tests for disease diagnosis
- Producing and delivering a variety of educational materials for beef and dairy cattle producers, and feedlot personnel on best management practices to reduce disease incidence
- Providing educational opportunities for undergraduate, graduate and veterinary students to generate a future human resource for the continued reduction in bovine respiratory disease incidence



http://www.brdcomplex.org/ 

About



## Bovine Respiratory Disease Complex

### Coordinated Agricultural Project

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Teaching Materials](#) [Links  
Resources](#) [About  
Our Research](#)

We are a collaborative group of researchers whose goal is to reduce the prevalence of bovine respiratory disease complex in beef and dairy cattle for the improvement of animal welfare and profitability. The "Integrated Program for Reducing Bovine Respiratory Disease Complex (BRDC) in Beef and Dairy Cattle" Coordinated Agricultural Project is supported by [Agriculture and Food Research Initiative Competitive Grant no. 2011-68004-30367](#) from the USDA National Institute of Food and Agriculture. Our project is led by [Dr. James Womack](#) of [Texas A&M University](#) and includes scientists and educators from the University of California-Davis, Colorado State University, the University of Missouri, New Mexico State University, Washington State University and USDA's Agricultural Research Service.



United States Department of Agriculture  
National Institute of Food and Agriculture

[Research Plan \(PDF 6MB\)](#)  
[Our Researchers](#)  
[Our Advisory Board](#)  
[Calendar of Events \(PST\)](#)

### Grant Announcements

[USDA Announcement](#)  
[GenomeWeb Daily News](#)  
[Texas A & M](#)

### Researchers

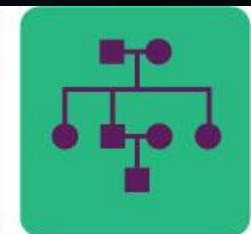
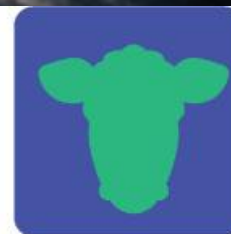
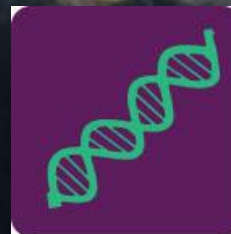
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