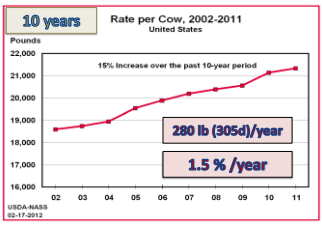
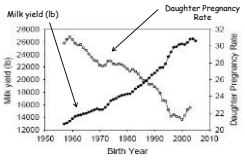
Genomic Selection for Improved Fertility of Dairy Cows with Emphasis on Cyclicity and Pregnancy

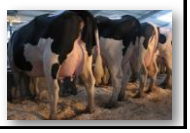
P.J. Pinedo, J.E.P. Santos, W.W. Thatcher, K.N. Galvão, R.C. Bicalho, R.O. Gilbert, G. Schuenemann, G. Rosa, S. Rodriguez-Zas S, C. Seabury, R.C. Chebel, J. Fetrow

NIFA-USDA 2013-68004-20361

Milk Production per Cow in the US

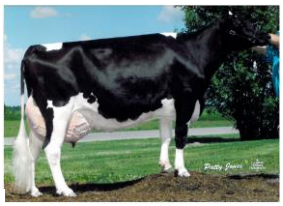






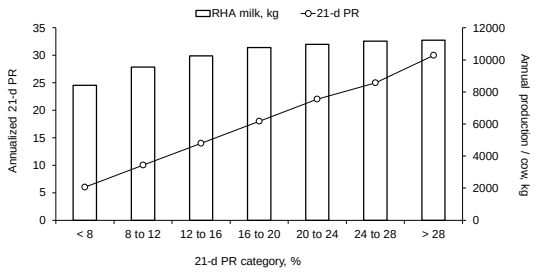
Current World Records

Hartje Meyer Beacon 9792 **33,665 kg** (74,064 pounds) in 365 d



Smurf - **216,891 kg** (478,163 pounds) over 15 years

21-d Pregnancy Rate and Milk Production of USA Herds



Source : DRMS, DairyMetrics, April 26th , 2011

Biological Impediments to Reproduction

- Delayed return to postpartum estrous cyclicity
- Reduced intensity and duration of estrous expression
- Reduced fertilization
- Increased pregnancy loss

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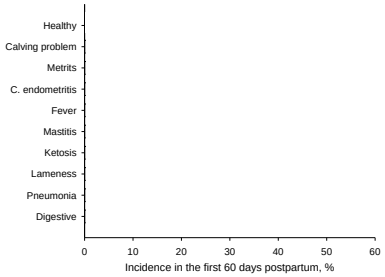
Incidence of Health Disorders in the First 60 d in Milk in High-Producing Holstein Herds



5,719 postpartum dairy cows evaluated daily for health disorders from eight experiments in seven dairy farms in the US.

Santos *et al.* (2010) Soc. Reprod. Fertil. 67:387-403

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Health Problems in the First 60 DIM and Resumption of Estrous Cyclicity in Dairy Cows

Category	Cyclic, %	Adjusted OR (95% CI)	*P*
Healthy	84.1	1.00	---
1 case of disease	80.0	0.97 (0.72 – 1.30)	0.83
> 1 case of disease	70.7	0.60 (0.44 – 0.82)	0.001
Type of health problem			
Calving problem	70.5	0.52 (0.40 – 0.68)	< 0.001
Metritis	63.8	0.37 (0.28 – 0.50)	< 0.001
Clinical endometritis	68.9	0.51 (0.37 – 0.71)	< 0.001
Fever postpartum	80.0	0.55 (0.40 – 0.74)	< 0.001
Mastitis	81.5	0.87 (0.55 – 1.36)	0.53
Clinical ketosis	77.7	0.71 (0.47 – 1.07	0.10
Lameness	85.0	0.82 (0.52 – 1.30)	0.40
Pneumonia	88.9	1.78 (0.22 – 14.34)	0.59
Digestive problem	60.7	0.54 (0.25 – 1.17)	0.12

5,719 postpartum dairy cows evaluated daily for health disorders in seven dairy farms in the US.

Santos *et al.* (2010) Soc. Reprod. Fertil. 67:387-403

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Impact of Clinical Diseases on Proportion of Single Ovulating Dairy Cows with Embryos as Embryos Grades 1 & 2

Health problem (n = 476)	% of cows	Grades 1 & 2, %	AOR (95% CI)	P
Healthy	56.3	71.8	1.00	
Clinical disease	43.7	59.1	0.57 (0.34-0.94)	0.03
Multiple diseases	24.3	56.0	0.56 (0.30-1.05)	0.07
Type of clinical disease				
Healthy	56.3	71.8	1.00	
Uterine disease	18.9	50.0	0.42 (0.22-0.80)	<0.01
Ketosis	11.1	40.0	0.29 (0.12-0.67)	<0.01
Mastitis	21.6	63.3	0.82 (0.43-1.55)	0.54

Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

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Impact of Clinical Diseases on Percentage of Embryos as Elongated Embryos on Day 15 after AI in Lactating Dairy Cows

Health problem (n = 145)	% of cows	Elongated, %	AOR (95% CI)	P
Healthy	61.4	83.9	1.00	
Clinical disease	38.6	28.6	0.10 (0.02-0.35)	<0.01
Multiple diseases	15.2	16.7	0.10 (0.07-0.66)	<0.01
Type of clinical disease				
Healthy	61.4	83.9	1.00	
Uterine disease	12.4	0.0	0.05 (0.01-0.30)	<0.01
Mastitis	11.7	40.0	0.29 (0.04-1.93)	0.19

Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

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Health Problems in the First 60 DIM and Pregnancy in Dairy Cows

Category	Pregnant, %	Adjusted OR (95% CI)	*P*
Healthy	51.4	1.00	
1 case of disease	43.3	0.79 (0.69 – 0.91)	0.001
> 1 case of disease	34.7	0.57 (0.48 – 0.69)	< 0.001
Type of health problem			
Calving problem	40.3	0.75 (0.63 – 0.88)	< 0.001
Metritis	37.8	0.66 (0.56 – 0.78)	< 0.001
Clinical endometritis	38.7	0.62 (0.52 – 0.74)	< 0.001
Fever postpartum	39.8	0.60 (0.48 – 0.65)	< 0.001
Mastitis	39.4	0.84 (0.64 – 1.10)	0.20
Clinical ketosis	28.8	0.50 (0.36 – 0.68)	< 0.001
Lameness	33.3	0.57 (0.41 – 0.78)	< 0.001
Pneumonia	32.4	0.63 (0.32 – 1.27)	0.20
Digestive problem	36.7	0.78 (0.46 – 1.34)	0.38

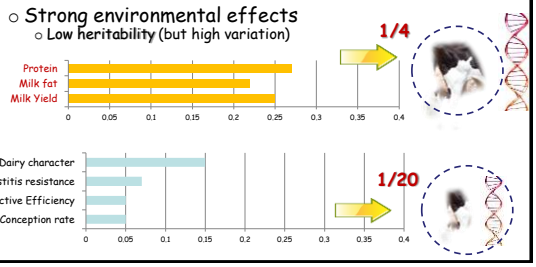
5,719 postpartum dairy cows evaluated daily for health disorders in seven dairy farms in the US

Santos *et al.* (2010) Soc. Reprod. Fertil. 67:387-403 10

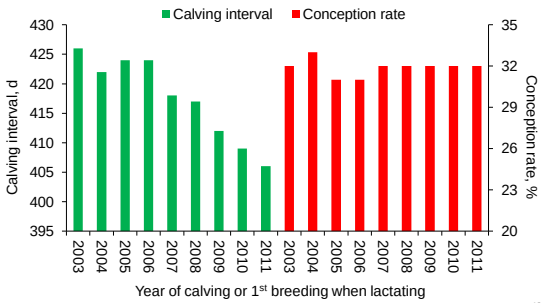
Would genetic selection work?

Genetics & Fertility?

- Strong environmental effects
  - Low heritability (but high variation)



Recent Evolution of Reproductive Parameters in Holsteins



http://aipl.arsusda.gov/publish/dhi/current/reproall.html

Many Sires Have Improved Daughter Fertility and Increased PTA Milk

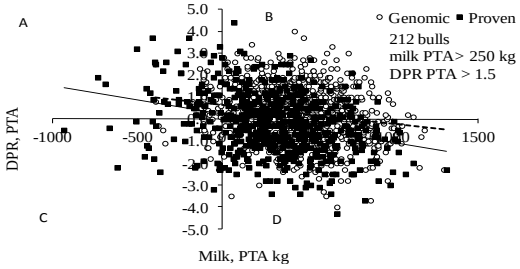


Fig. 2. Milk PTA (kg) and DPR of genomic and proven sires released in December 2011 (AIPL-USDA)

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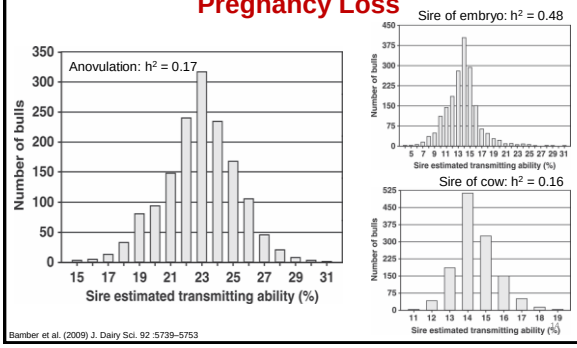
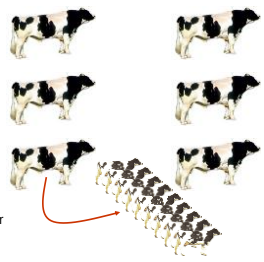
Heritability of Anovulation and Pregnancy Loss



Bamber et al. (2009) J. Dairy Sci. 92 :5739–5753

Traditional Genetic Selection *Progeny Testing*



Don't know the genes responsible for the trait (milk yield)

We know that bulls with daughters that produce more milk are more likely to have the genes that confer higher milk production

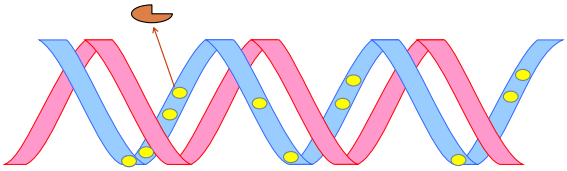
Estimated genetic value - - - - - - - - reliability - - - - - - - - True genetic value

P.J. Hansen

ILLUMINA Bovine SNP50 Bead Chip

Development of Genomics in 2009 Changed Genetic Selection

For the first time, can identify the genes responsible for the trait or genetic markers close to the genes



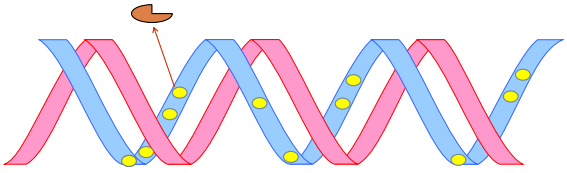
Gene – a blueprint that tells the cell how to make a protein (~22,000 in cow)

Protein – the main work horses in a cell or animal

Mammary Gland

- Secreted to feed the neonate (milk protein)
- Synthesize milk fat, sugars
- Cause contraction of alveoli to allow milk ejection
- Prevent bacterial growth

P.J. Hansen



Mutation – a change in the blueprint so the protein is made differently

Protein – functions better, functions worse, or doesn't function at all

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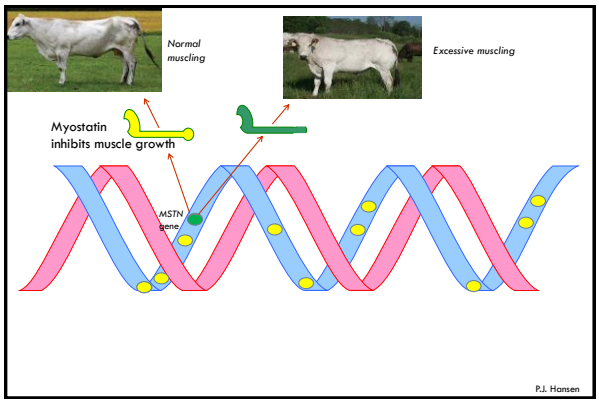
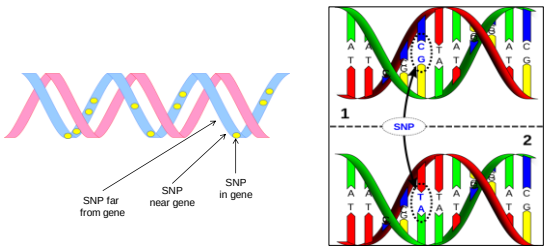
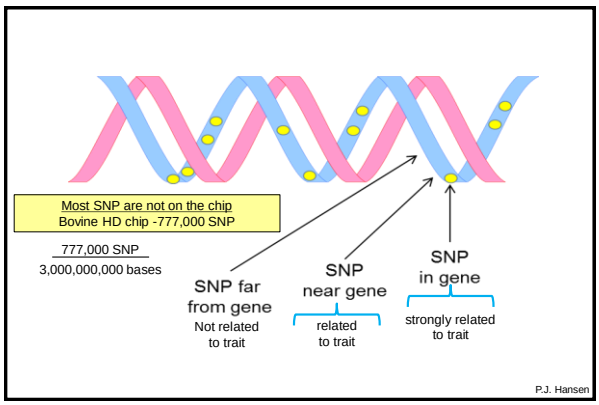


Single Nucleotide Polymorphism (SNP)

- Occurs when one of the base pairs making up the DNA is changed – 3 billion base pairs in cattle)
- Most common mutation - estimated to account for 84% of the variation in gene expression in animals
- Most SNPs do not occur in genes but in regions of the DNA between genes





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

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Translational Genomics for Improved Fertility of Animals

Genomic Selection for Improved Fertility of Dairy Cows with Emphasis on Cyclicity and Pregnancy

http://agrilife.org/efridairycowfertility/

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NIFA AFRI Translational Genomics for Improved Fertility of Animals

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Texas A&M AgriLife Research, Texas A&M University, University of Florida, Cornell University, University of Minnesota, University of Wisconsin, University of Illinois at Urbana-Champaign, The Ohio State University

Objectives

Main objective is to identify molecular markers for genomic selection to improve fertility of dairy cattle

1. Develop a fertility database with genotypes and phenotypes based on direct measures of fertility in Holstein cows
2. Identify SNPs associated with fertility traits by use of genome-wide analyses (GWAS)
3. To obtain genomic-estimated breeding values (GEBV) that can be applied in selection for improved fertility
4. Incorporate these findings in available platforms
5. Extend the knowledge to the dairy industry
6. Educate students on animal health, reproduction, and genetics

Approach

Phenotypes:

12,000 cows
2,400 cows/state
2 - 4 farms/state
Cool / hot season

Approach

Phenotypes:

- Calving problems (dystocia, RP, stillbirth)
- Uterine health
  - ✓ Metritis
  - ✓ Clinical endometritis
- Resumption of postpartum ovulation
- Subclinical ketosis
- Detection of estrus

Direct Measures of Fertility

Approach

Phenotypes:

- Body condition and lameness score
- Pregnancy per artificial insemination in the first two AI
- Maintenance of pregnancy to d 60 of gestation
- Interval to pregnancy

Plus:

- ✓ Production data
- ✓ Other diseases in the first 60 DIM
- ✓ Survival
- ✓ Management

Direct Measures of Fertility

Table 4. Incidence (%) of diseases in the first 60 days postpartum in 11,400 dairy cows from 16 herds according to region of the country and season of calving

	NE		MW		SE		SW	
Disease	Warm	Cool	Warm	Cool	Warm	Cool	Warm	Cool
Retained placenta	8.0	5.9	7.4	5.4	15.0	7.6	4.3	2.9
Metritis	21.7	23.8	19.5	20.2	19.7	18.5	27.6	24.8
Subclinical ketosis	41.8	18.7	25.9	15.5	24.9	20.1	31.3	14.6
Mastitis	26.1	16.0	6.1	5.5	18.0	21.3	12.0	8.1
Displaced abomasum	3.0	5.6	2.9	1.4	6.0	4.0	1.0	1.0
Pneumonia	1.1	1.5	1.7	1.8	3.8	13.4	7.1	3.5
Clinical endometritis	15.4	32.5	25.9	20.4	23.4	42.9	24.3	26.1
Lameness	11.3	2.6	2.1	8.1	1.7	12.1	5.4	2.0

Developing a Reproductive Index Based on Factors of Increased Heritability

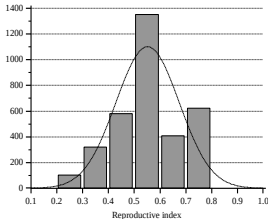

Fig. 4. Frequency distribution of the reproductive index to predict pregnancy after 2 AI in 3,500 lactating dairy cows

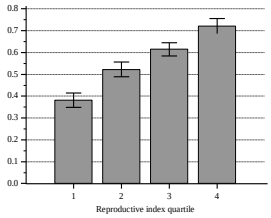

Fig. 5. Percent of cows pregnant after 2 AI according to the reproductive index quartiles

$$P(\text{pregnancy} \mid a, b) = \frac{e^{\hat{a} b_i Z_i + m\varepsilon}}{1 + e^{\hat{a} b_i Z_i + m\varepsilon}}$$

Prevalence of events that predict pregnancy after 2 AI in Holsteins

Nonpregnant in Q1 of RI (low fertility) and Pregnant of Q4 of RI (high-fertility)

	Nonpregnant cows within Quartile 1	Pregnant cows within Quartile 4	P-value
	% (n/n)		
Cows	15.7 (521/3,318)	14.1 (467/3,318)	---
Disease			
1 disease	75.1 (391/521)	13.5 (63/467)	0.0001
> 1 disease	50.3 (262/521)	0 (0/467)	0.0001
Calving problem	31.5 (164/521)	8.6 (40/467)	0.0001
Uterine disease	48.6 (253/521)	4.9 (23/467)	0.0001
Anovular cows	74.3 (387/521)	0 (0/467)	0.0001
Pregnancy loss	12.1 (63/521)*	0 (0/467)	0.0001

* Cows that became pregnant on d 32 after first or second AI, but lost pregnancy and remained open after 2 AI.

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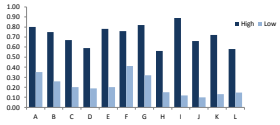
Approach

Genotyping:

Subpopulations for extreme high and low fertility:

- **High-fertility cows** (n=850): Pregnant cows on d 60 after first AI with the highest RI
- **Low-fertility cows** (n=1,750): Non-pregnant cows on d 60 after two postpartum AI with the lowest RI

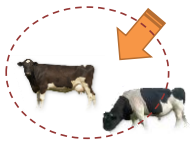
n = 2,600



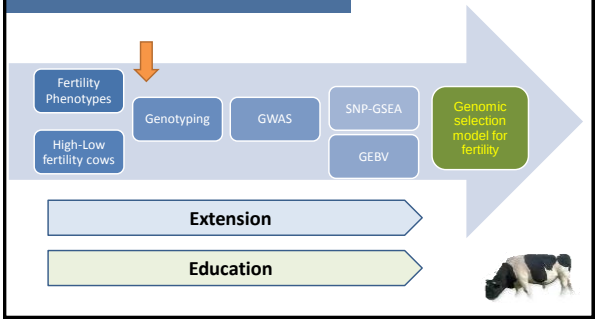
Approach

Validation:

New pool of **1,000 cows** based on high and low RI and a group of **200 AI sires** with extreme values for daughter fertility (high DPR > +1.5 vs. low DPR < -1.5).



Outline




Thank you!
jepsantos@ufl.edu
http://agrilife.org/afridairycowfertility/