Genetic Selection of Dairy Cattle for Improved Immunity

Professor Bonnie Mallard, PhD

Ontario Veterinary College

Centre of Genetic Improvement of Livestock

University of Guelph, Ontario, Canada

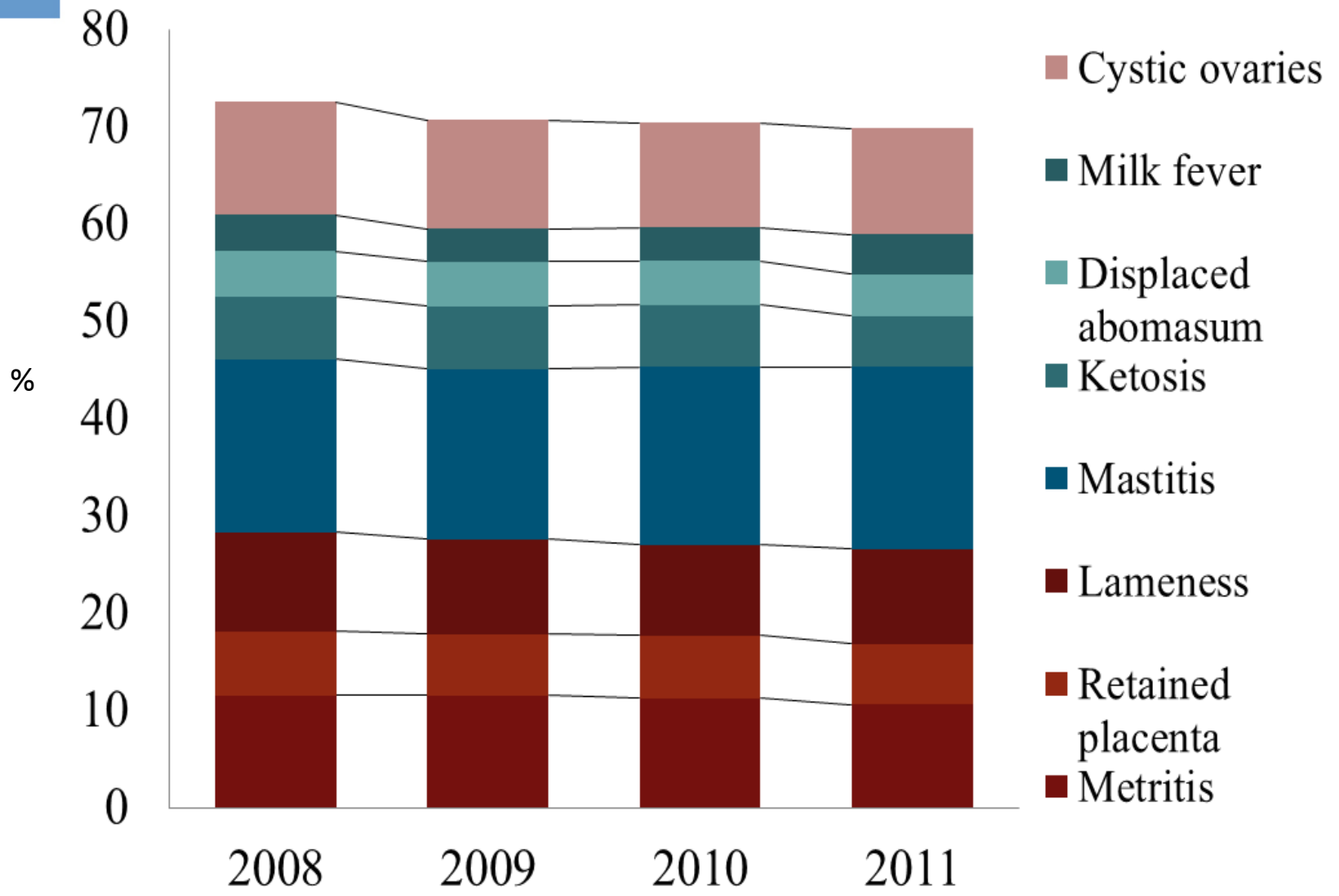
EAAP Meeting – Session 25: Improving Udder Health and Fertility

Warsaw, Poland, Sept 1, 2015

Why are dairy health traits so difficult to improve?

- Difficult to improve genetically - low heritability
- Few direct measures of disease in selection indices, Canada just added mastitis in Aug 2014
- Poor data quality & inconsistency in disease diagnosis and recording
- Selection to fight one disease may be counter-productive to other diseases

Disease Trends in Canada 2008-2011



Canadian National Health Collection System: CDN 2012- Courtesy of Dr. F. Miglior

Could Genetic Approaches be used to Improve Immunity in Livestock

We focussed on selecting for

broad-based disease resistance

based on Estimated Breeding Values (EBVs)

of immune response traits

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Why Focus on the Immune System?

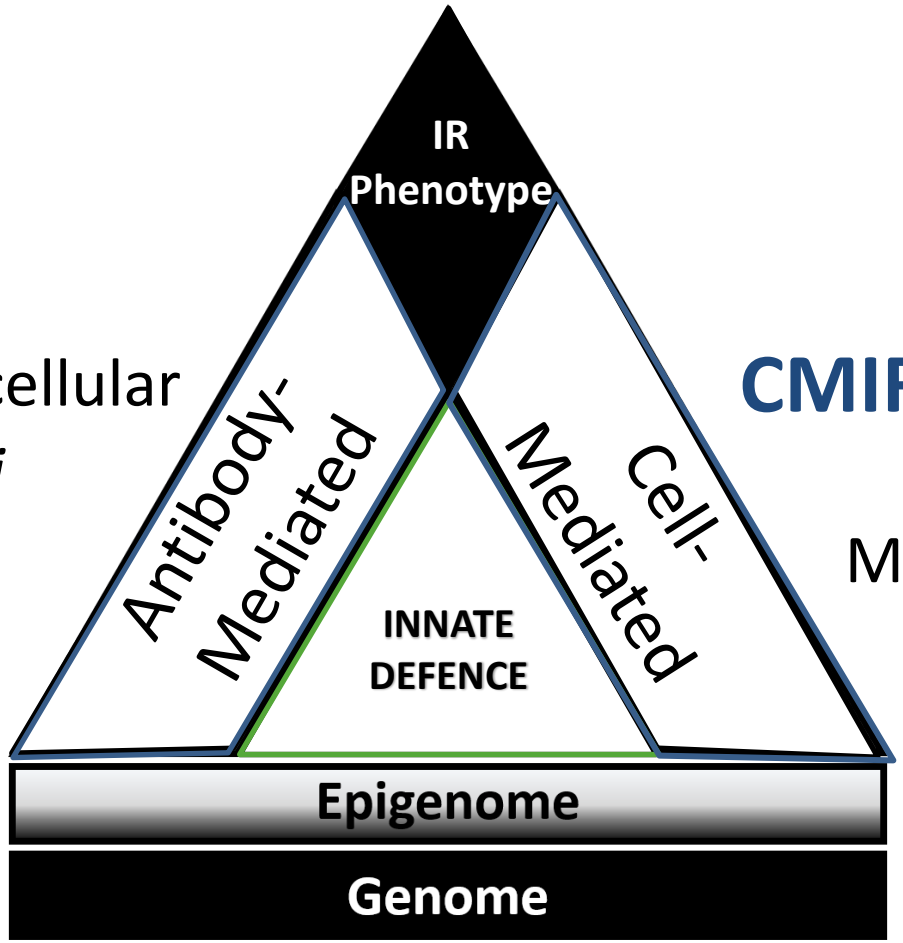
A strong chain of protection against a wide range of pathogens

Selecting for improved immune response the concept behind our research and

High Immune Response Technology

Immuno-Genetic Approach

AMIR – Extracellular
eg. *E. coli*
Mastitis



CMIR – Intracellular
eg. Virus,
Mycobacteria
Johne's

Adopted from Wilkie, B. and Mallard, B. 1999 *Vet Immunol Immunopath* 72:231-235

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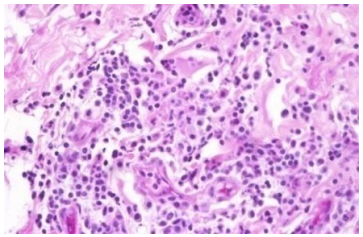
Capture Broad-based Disease Resistance

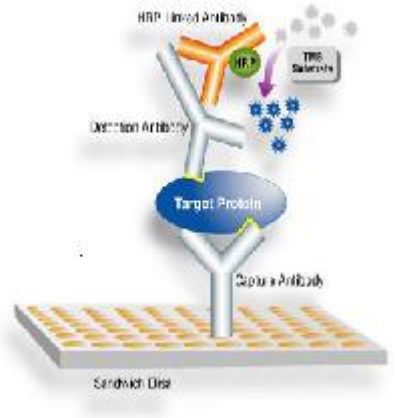
Performance of Two Tests

+

CELL-MEDIATED IMMUNE RESPONSE



ANTIBODY-MEDIATED IMMUNE RESPONSE



Photos and figures courtesy of Dr. B. Mallard

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The HIR test requires 3 farm visits:

Immunization and sampling takes ~ 5 min/animal

Individuals with a robust and balanced IR are called High Immune Responders and the method is Identified as the HIR Technology

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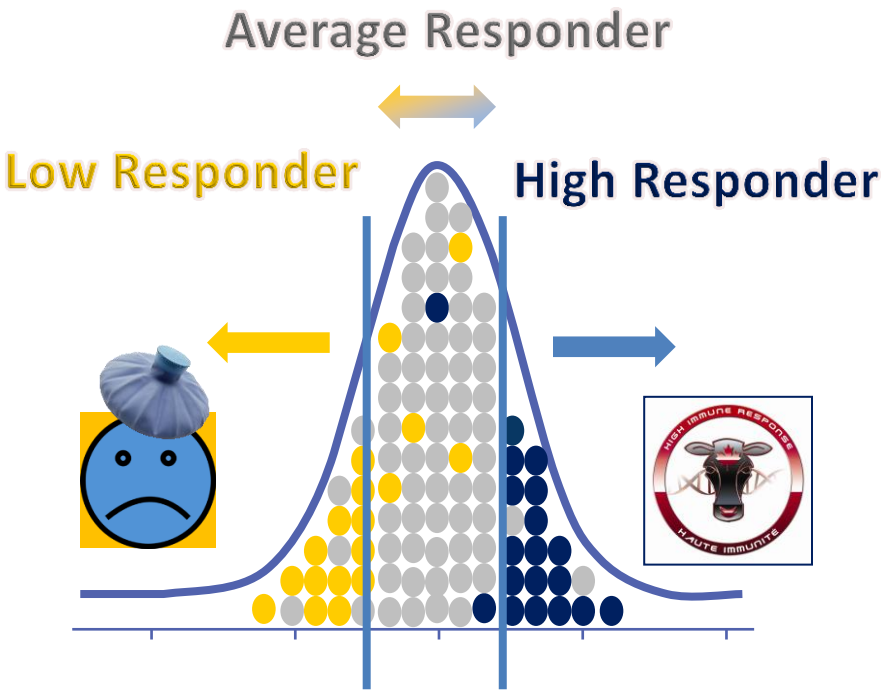
HIR Classifies Cattle as High, Average Or Low Immune Responders



Selection for Immune Response is Based on

Estimated Breeding Values

Significance of being a High Immune Responder

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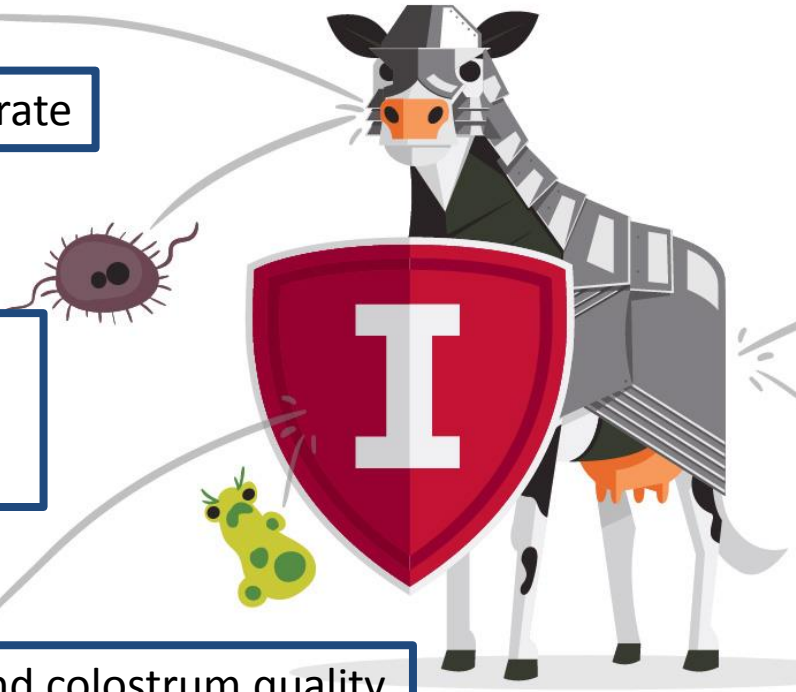
Decreased occurrence of mastitis, metritis, ketosis, retained placenta

Less likely to be seropositive for paratuberculosis

Faster growth rate



Beneficial associations with herd life and some reproductive traits

Better hoof health – digital dermatitiis

Improved milk and colostrum quality

Improved response to vaccine

Refs – Wagter et al JDS 2000, Pinedo et al , Proc. Int. Colloq. Paratb., Mn, Aug 9-14, 2009, Thompson-Crispi K. 2012. JDS. 95(1):401

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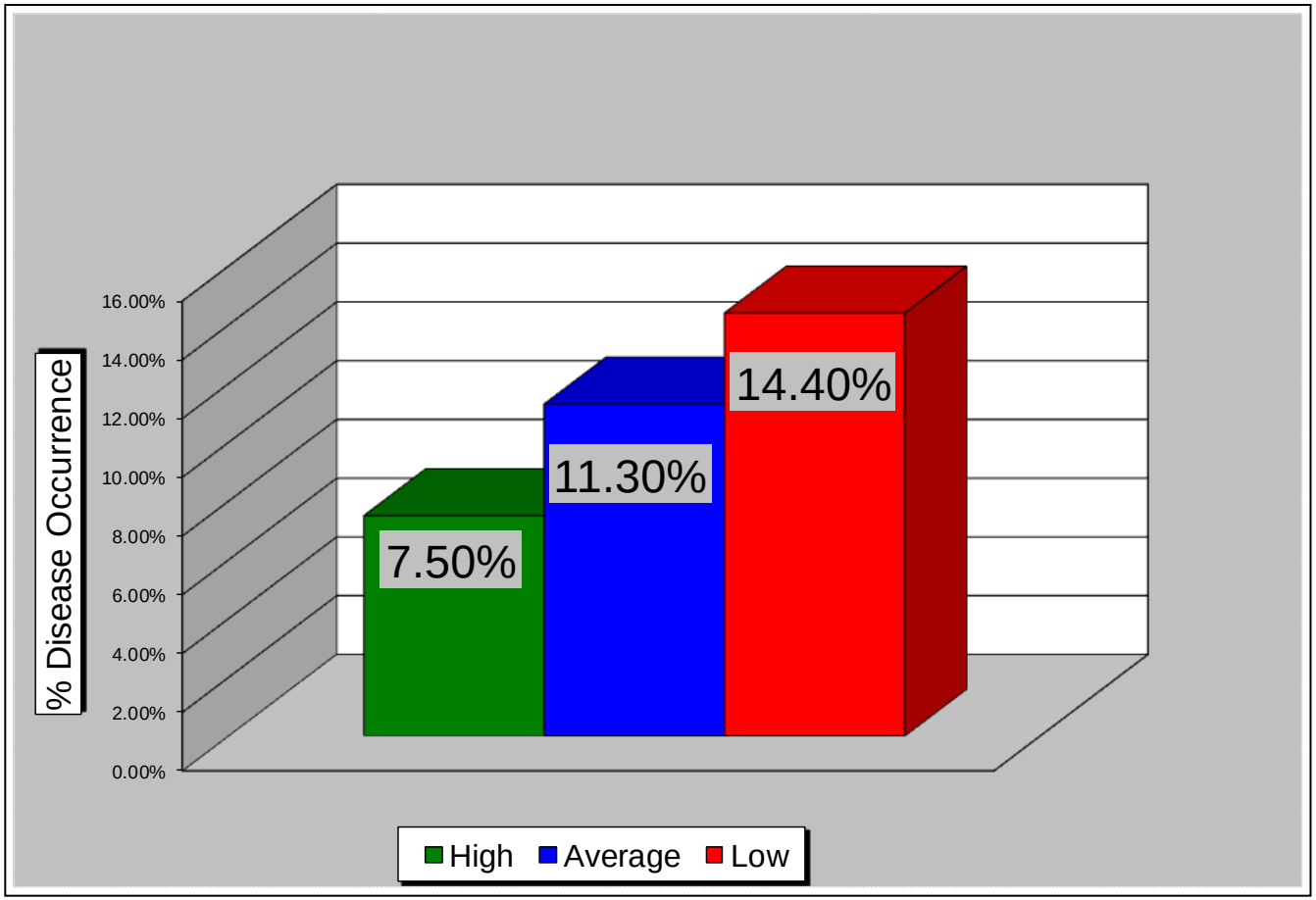
Benefit #1 - Lower Disease Incidence

IR vs Disease Incidence (Combined Diseases)



Disease data from: Wagter, et al. 2000 J. Dairy Sci. 83:488-498; Thompson-Crispi, et al. 2012. J. Dairy Sci. 95:3888-3893; Thompson-Crispi, et al. 2013. Clin Vacc Immuno. 20:106-112.

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Disease Incidence - Large US Dairy

Research carried out on 700 cows
In 3,000 cow dairy in North Florida

- 27% less Mastitis
- 17% less Metritis
- 32% less Retained Placenta
- No adverse production effects

High

Versus

Entire Herd

Reference - Thompson-Crispi and Mallard et al. 2012 JDS 95:3888

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Mastitis Incidence on Canadian Farms

Incidence of clinical mastitis per 100 cow-years by EBV Low, Average and High AMIR

PATHOGEN *E. coli*, *S. aureus* + others	LOW AMIR *n=86*	AVE AMIR *n=289*	HIGH AMIR *n=83*	ALL COWS
Incidence Rate	30.7[a]	27.9[a]	17.1[b]	26.3
High Severity	6.15[c]	1.98[d]	2.13	2.72

Reduction in Mastitis by High AMIR = (26.3 - 17.1)/ 26.3 = 35%

Reference: Thompson-Crispi et al Clin Vaccine Immunol 2013 vol 1 106-112

Incidence of Pneumonia

Herd A – 265 head

	Pneumonic	Nonpneumonic	Percent	P value
High Responders	2	34	**5.6%**	
Vs.				p = 0.09
Herdmates	35	194	**15.3%**	

Herd B – 1267 head

	Pneumonic	Nonpneumonic	Percent	P value
High Responders	11	149	**6.9%**	
Vs				p = 0.22
Herdmates	101	1006	**9.1%**	

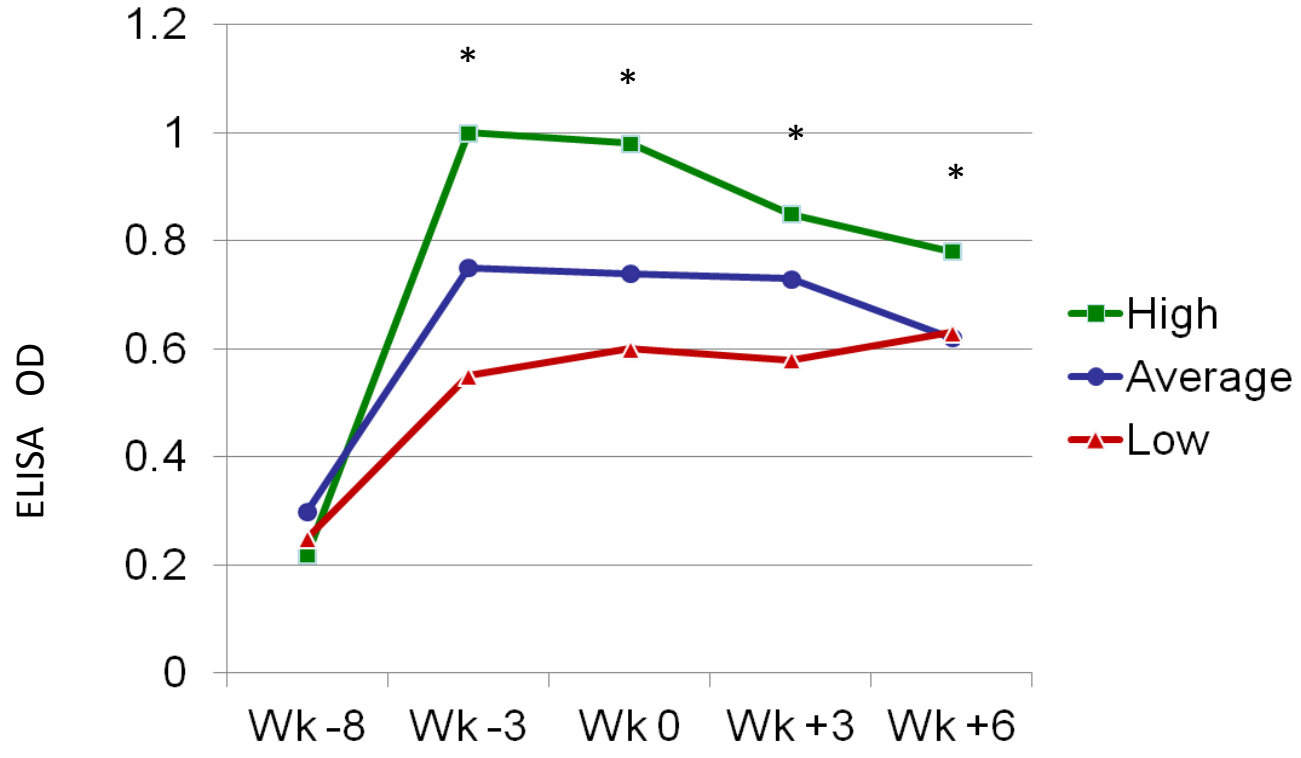
Herd C – 2724 head

	Pneumonic	Nonpneumonic	Percent	P value
High Responders	45	186	**19.5%**	
Vs.				p = 0.005
Herdmates	683	1810	**27.4%**	

Benefit #2 - HIR and Vaccination

Better response to commercial vaccines

LsMEANS OF SERUM ANTIBODY TO J5 *E. coli* VACCINE



Reference: Wagter & Mallard et al 2000 JDS 83:488

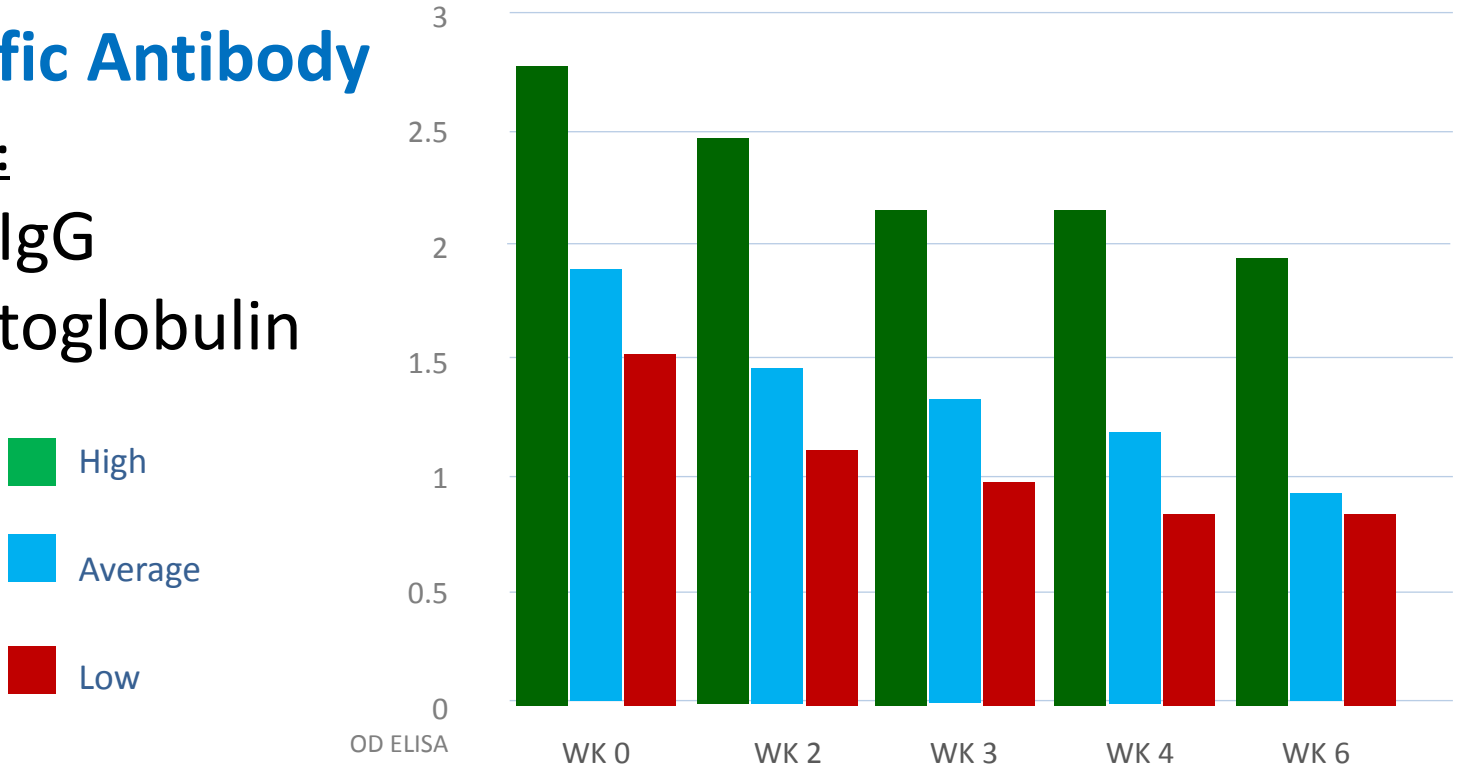
Benefit # 3 - Better Quality Colostrum

Specific Antibody

Also:

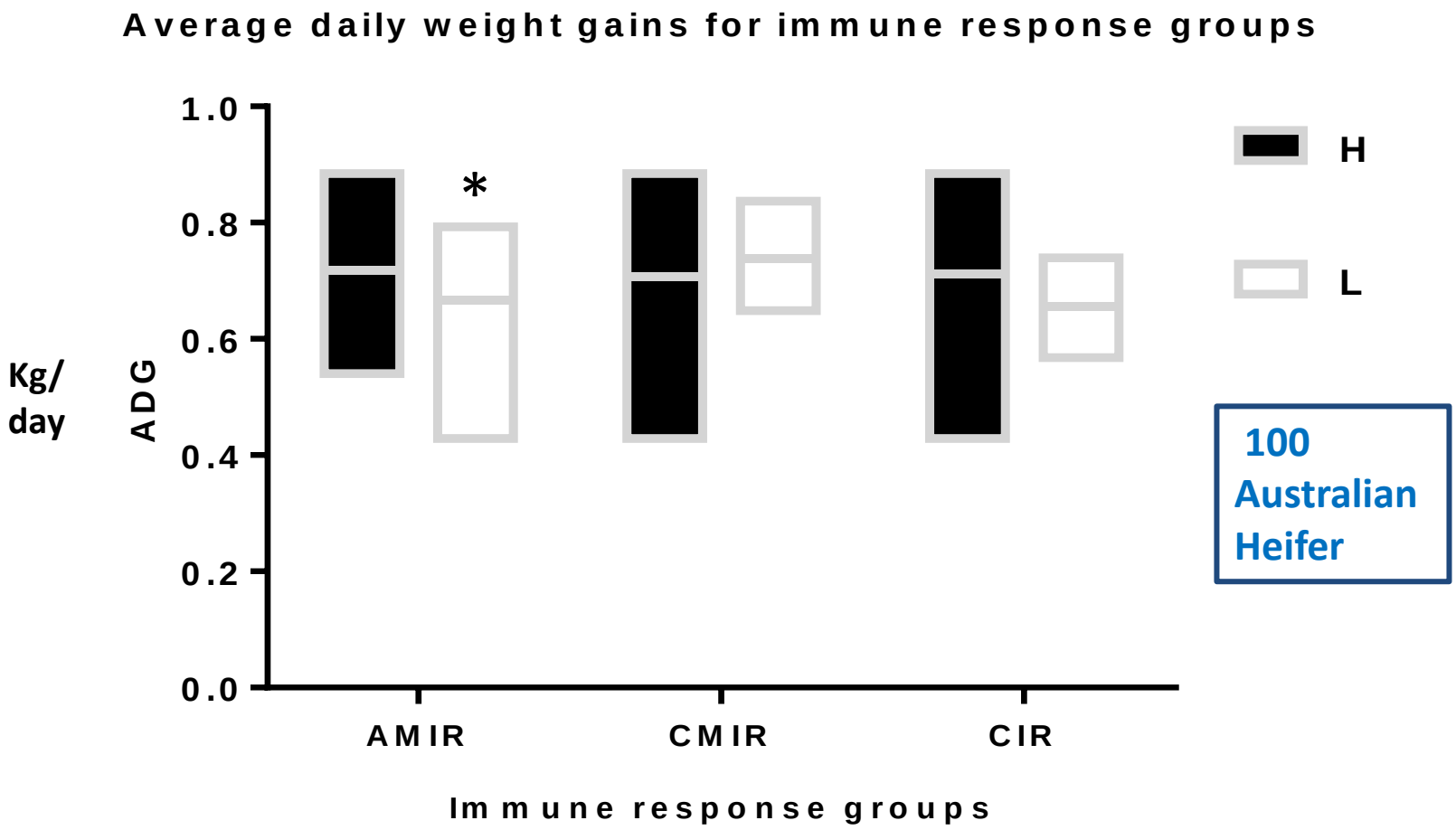
Total IgG

B-Lactoglobulin



Ref - Wagter & Mallard et al JDS 83:488, 2000;
Fleming MSc Thesis, 2014

Benefit # 5 – Better Growth of Heifers



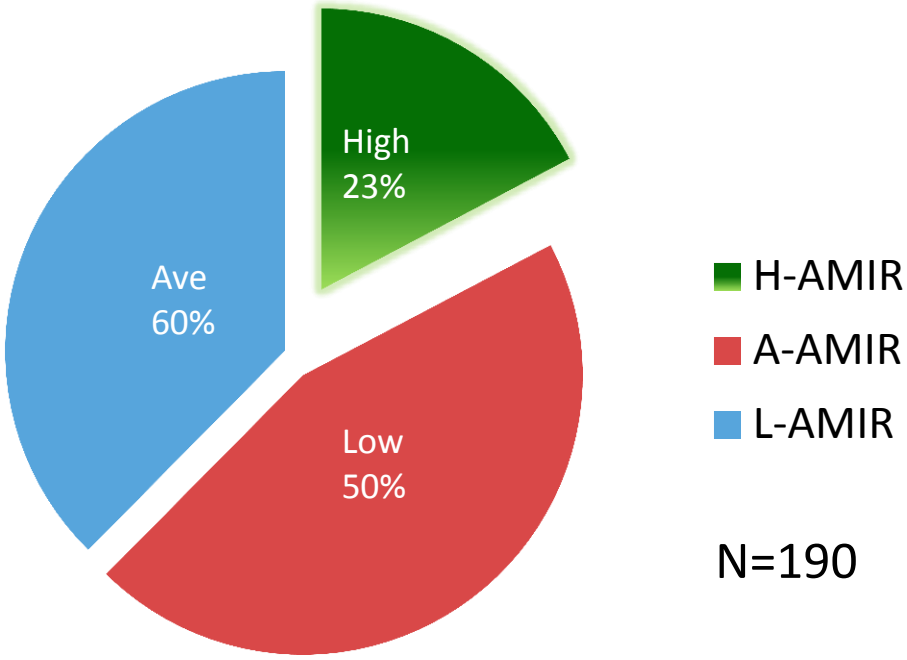
REFERENCE - IMMUNE FUNCTION AS A PREDICTOR OF DAIRY CATTLE HEALTH AND DISEASE
J.W. Aleri, B.C. Hine, M.F. Pyman, P.D. Mansell, W.J. Wales, B.A. Mallard and A.D. Fisher
Australian cattle and sheep Veterinarians Conference 11-13 Feb, 2015 Hobart, Australia.

Benefit # 6 – Improvement in Lameness

- ✓ **High AMIR** cows had less Infectious Digital Dermatitis, but more Non-Infectious Hoof Lesions
- ✓ **High CMIR** cows tended to have less Interdigital hyperplasia

Leading Cause of Culling

Infectious Digital Dermatitis



2014 Data from Mallard Group

2012 HIR Licensed from University of Guelph

Semex Approach

- Test all marketable proven bulls & the latest genomic bulls
- >1500 HO bulls tested, all Semex bulls are tested
- Top 10% for overall immune response qualify for Immunity+

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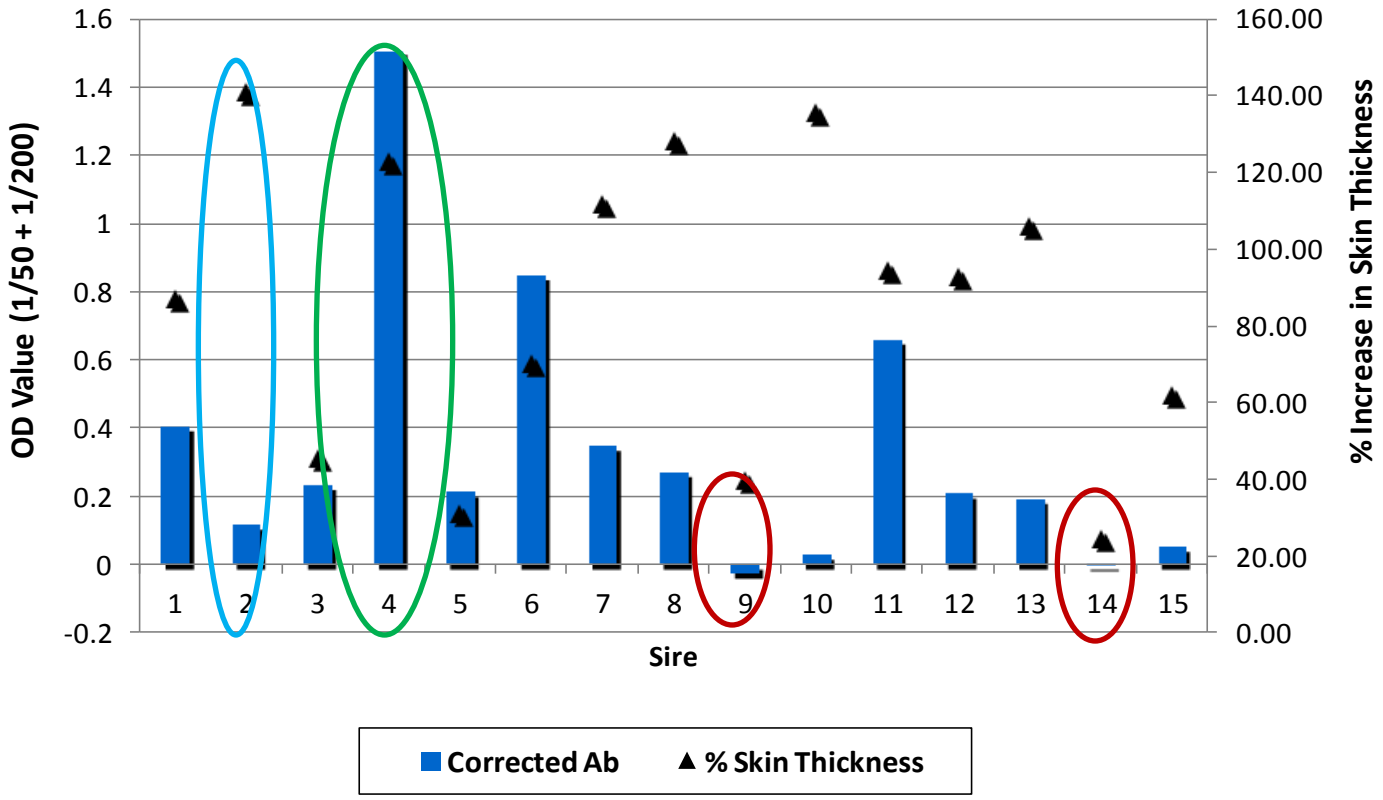
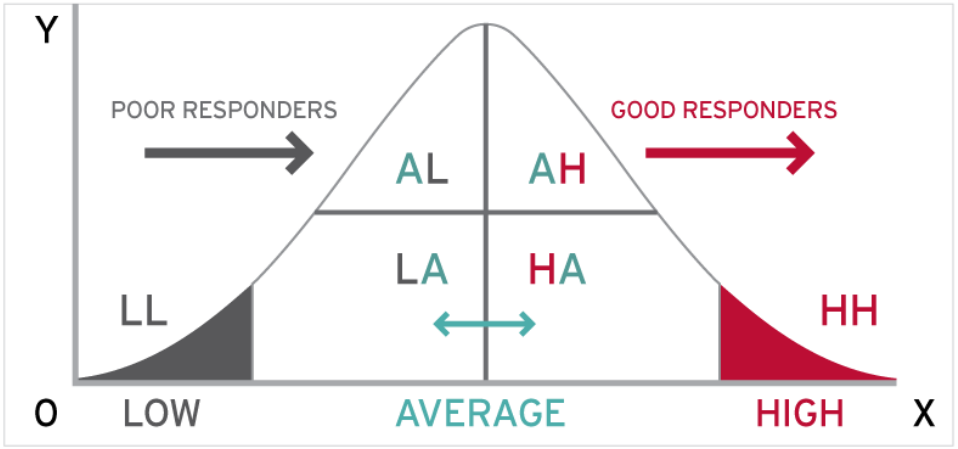
Sample of Test Results

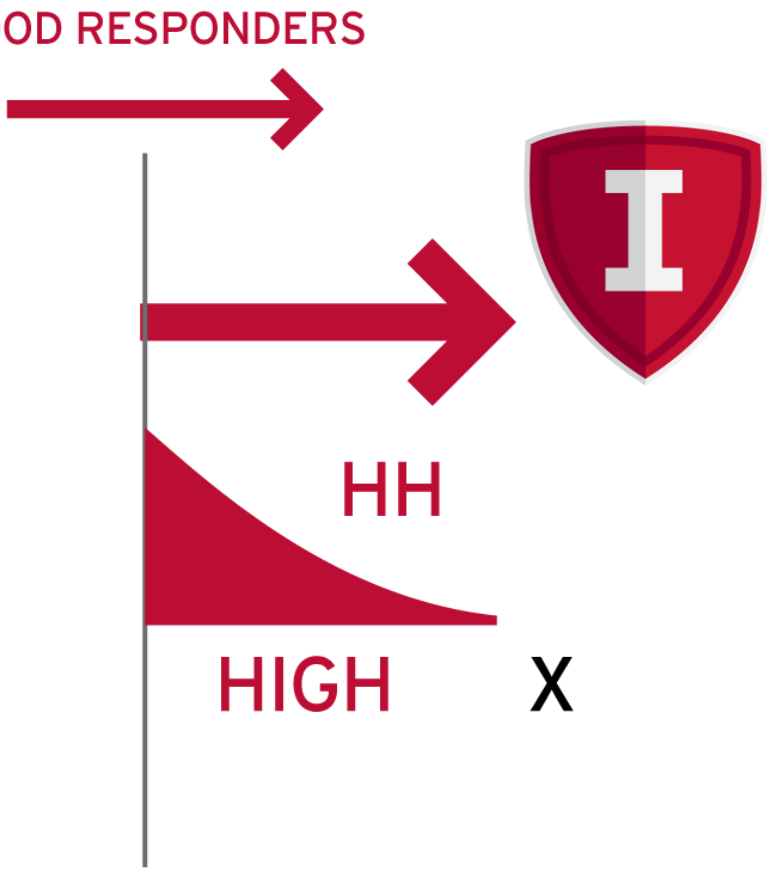


No adverse reactions or CFIA cross-reactivity were found before and after HIR testing.

Bulls Designated as Immunity+

Approximately 10% of sires





Disease Occurrence of *Immunity+* Daughters

US Herd Milking 1500 Cows in 2013

Disease	Cattle	Immunity+ Daughters	All Other Daughters	Disease Reduction
Mastitis	1st lactation	8.8%	15.8%	**44.3%**
All Recorded Disease	1st lactation	16.7%	18.2%	**8.5%**
Pneumonia	Heifers	6.8%	9.1%	**25.3%**

Disease reduction calculated as: (Disease incidence in all other daughters - disease incidence Immunity+ daughters) / Disease incidence in all other daughters * 100%

(Data Courtesy of Jay Shannon, Semex Alliance)

DISEASE IN 35,000 COW DAIRY IN SAUDI ARABIA USING *IMMUNITY+* & *NON-IMMUNITY+* SEMEN

JUNE 2015 FROM DC305

By SID	Name	# Heifers	PNEUM	PNEUM Rate	Scours	Scours Rate	PinkEye	PinkEye Rate
200H5755	Alltop	336	10	3.0%	30	8.9%	38	11.3%
200H5565	Longtime	324	16	4.9%	21	6.5%	33	10.2%
200H5678	Maritime	334	1	**0.3%** *	32	**9.6%** *	1	**0.3%** *
200H5611	Sailing	301	5	1.7%	38	12.6%	37	12.3%
200H3559	Sleeman	625	7	1.1%	50	8.0%	37	5.9%
Herd Average	**All Sires**	**18730**	**268**	**1.4%**	**2543**	**13.6%**	**593**	**3.2%**

Slide courtesy of Dany Peirre Rondeau – Sales Manager: Middle East, North Africa, Pakistan & Vietnam

Proof Data (August 2013) - *Immunity+* Sires

Compared to all other Sires Tested for Immune Response using the HIR Method

Trait of Interest	Average Proof for Immunity+ Sires	Difference between Immunity+ & all other Sires Tested	
TPI	+ 2305	+186	Favorable
Net Merit	+$708	+$165	Favorable
Productive Life	+4.7	+1.6	Favorable
Daughter Preg Rate	+0.8	+0.70	Favorable
Somatic Cell Score	2.69	-0.11	Favorable
Daughter Calving Ease	5.7	-0.70	Favorable

(Data Courtesy of Jay Shannon, Semex Alliance)

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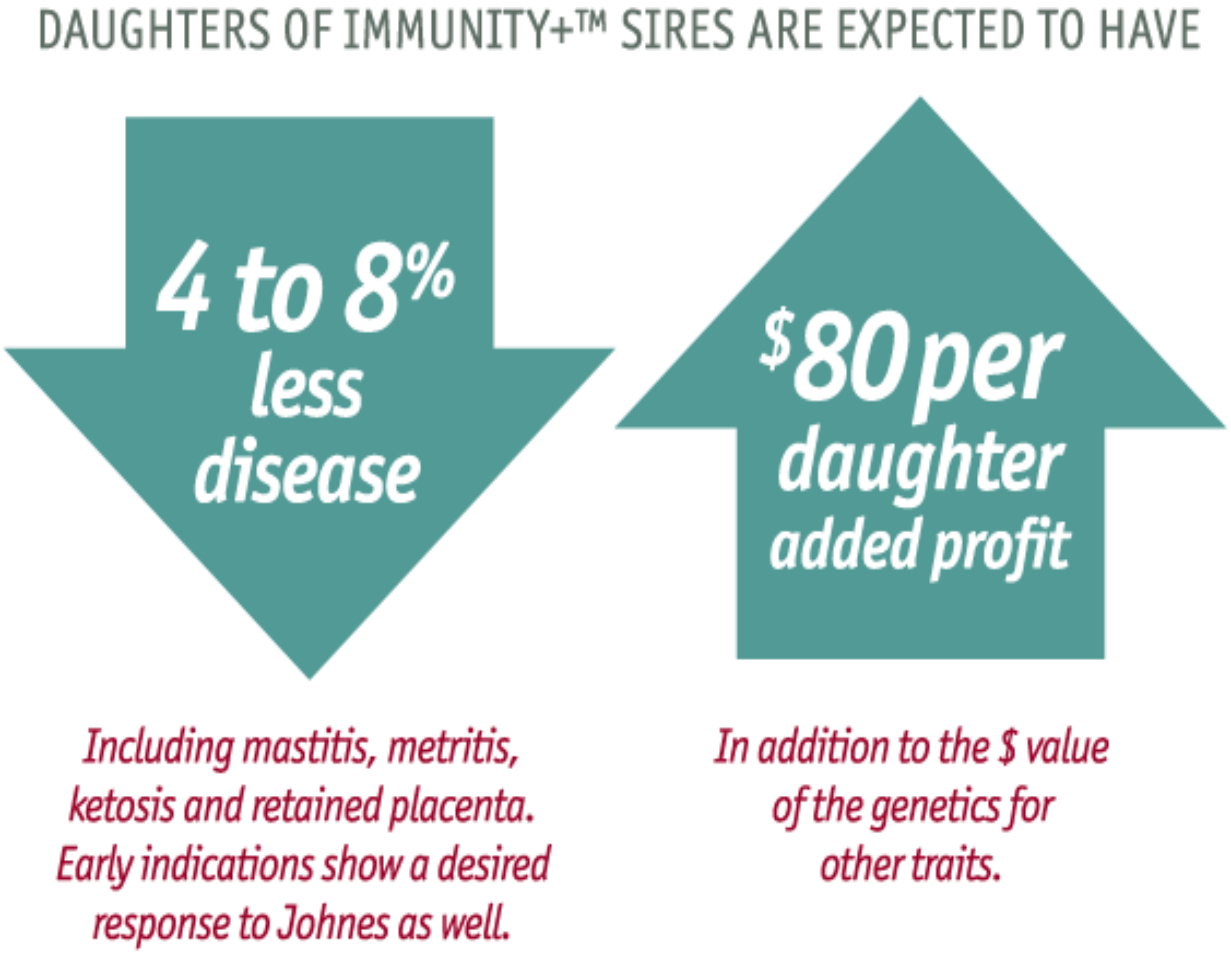
Building a Stronger Herd



Dr Chesnais, Senior Geneticist, Semex

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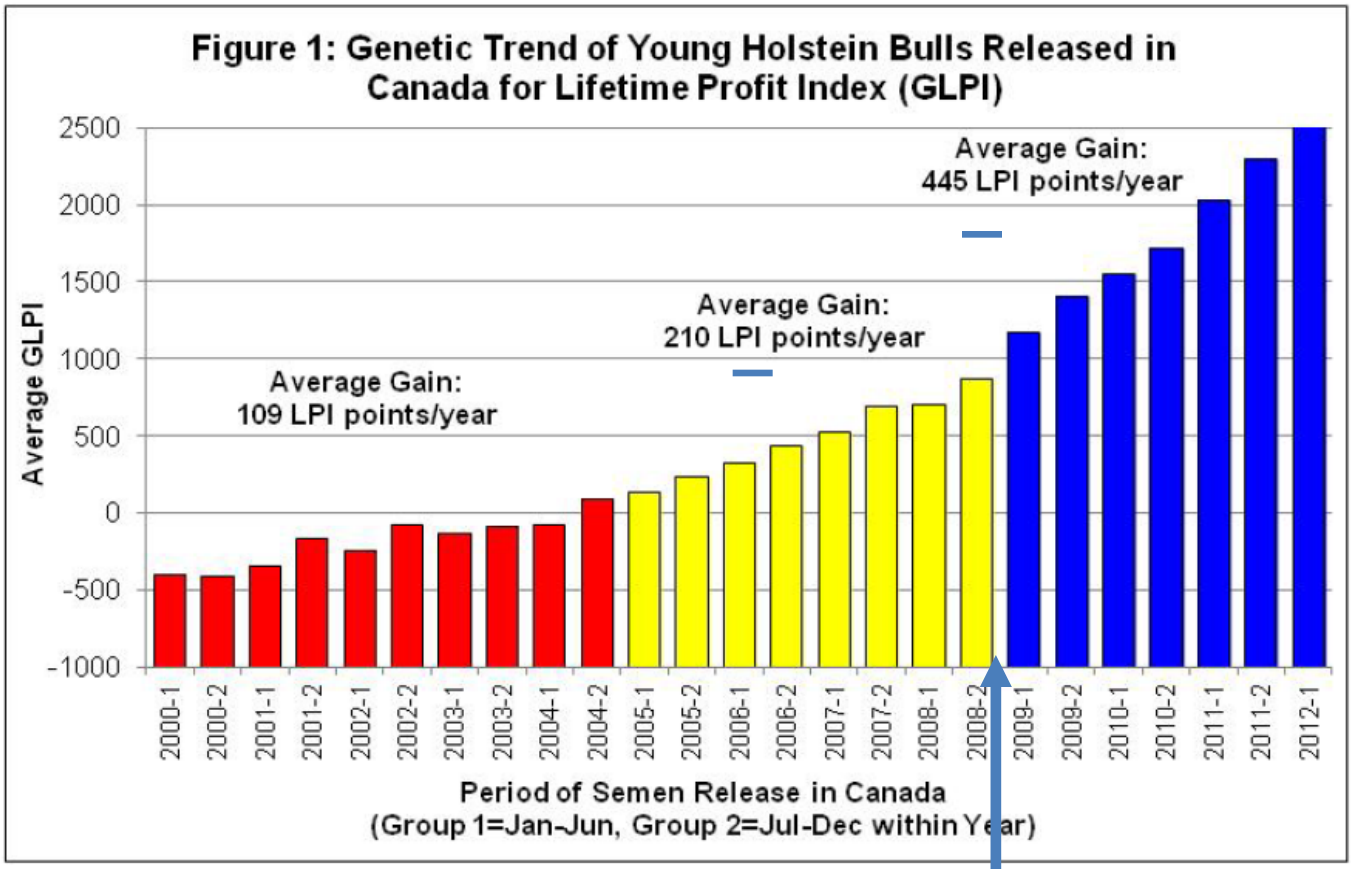
Our Current Research on Genomics of Immune Response

The Power of Genomics

Genetic Gain in Dairy Cattle

CANADA LPI



Official adoption of Genomics 2008

B. Van Doormaal, Canadian Dairy Network, July 2012,
Increased Rates of Genetic Gain with Genomics

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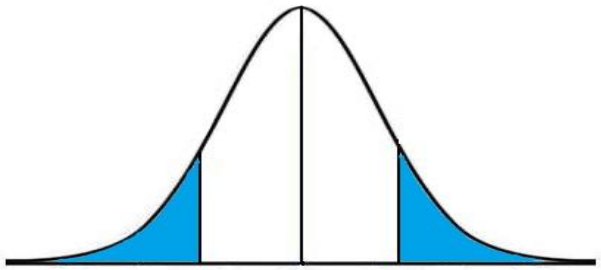
Genomics and Immune Response

GWAS was performed on Holsteins (**n=680 cows, 543 bulls**) classified on IR and **selective genotyping** of **High** or **Low** responder using the SNP50

Lo - Cows
82 = L-AMIR
65 = L-CMIR

Un-related Bulls
81 = L-AMIR
72 = L-CMIR



Low Responders

High Responders

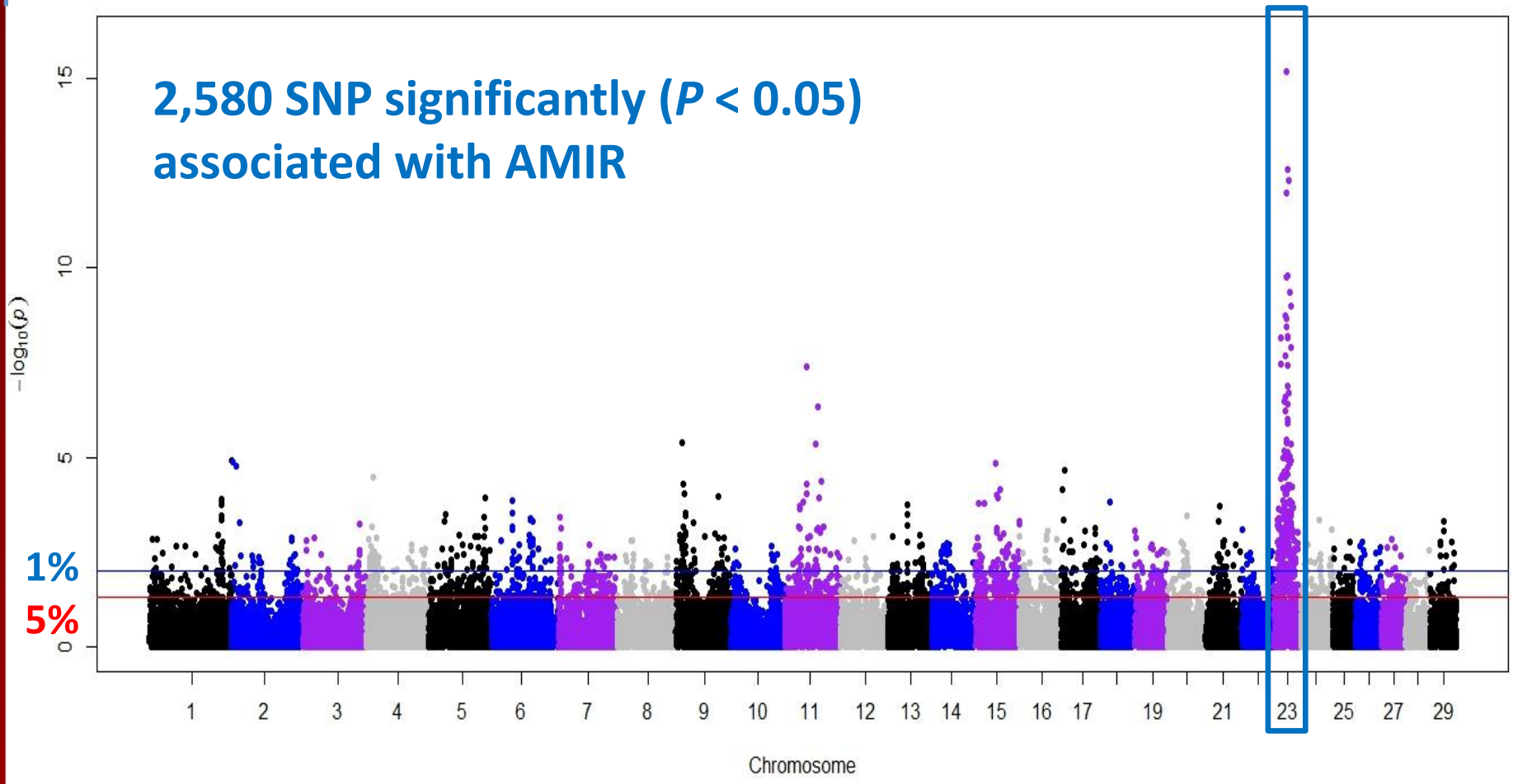
Hi - Cows
81 = H-AMIR
75 = H-CMIR

Un-related Bulls
83 = H-AMIR
74 = H-CMIR

Thompson-Crispi et al 2014 BMC Genomics. 15(1):559

Manhattan Plot for AMIR

Markers and Chromosomal Regions of Interest



Result: 186 SNP following 5% correction for false discovery rate

Thompson-Crispi et al 2014 BMC Genomics. 15(1):559

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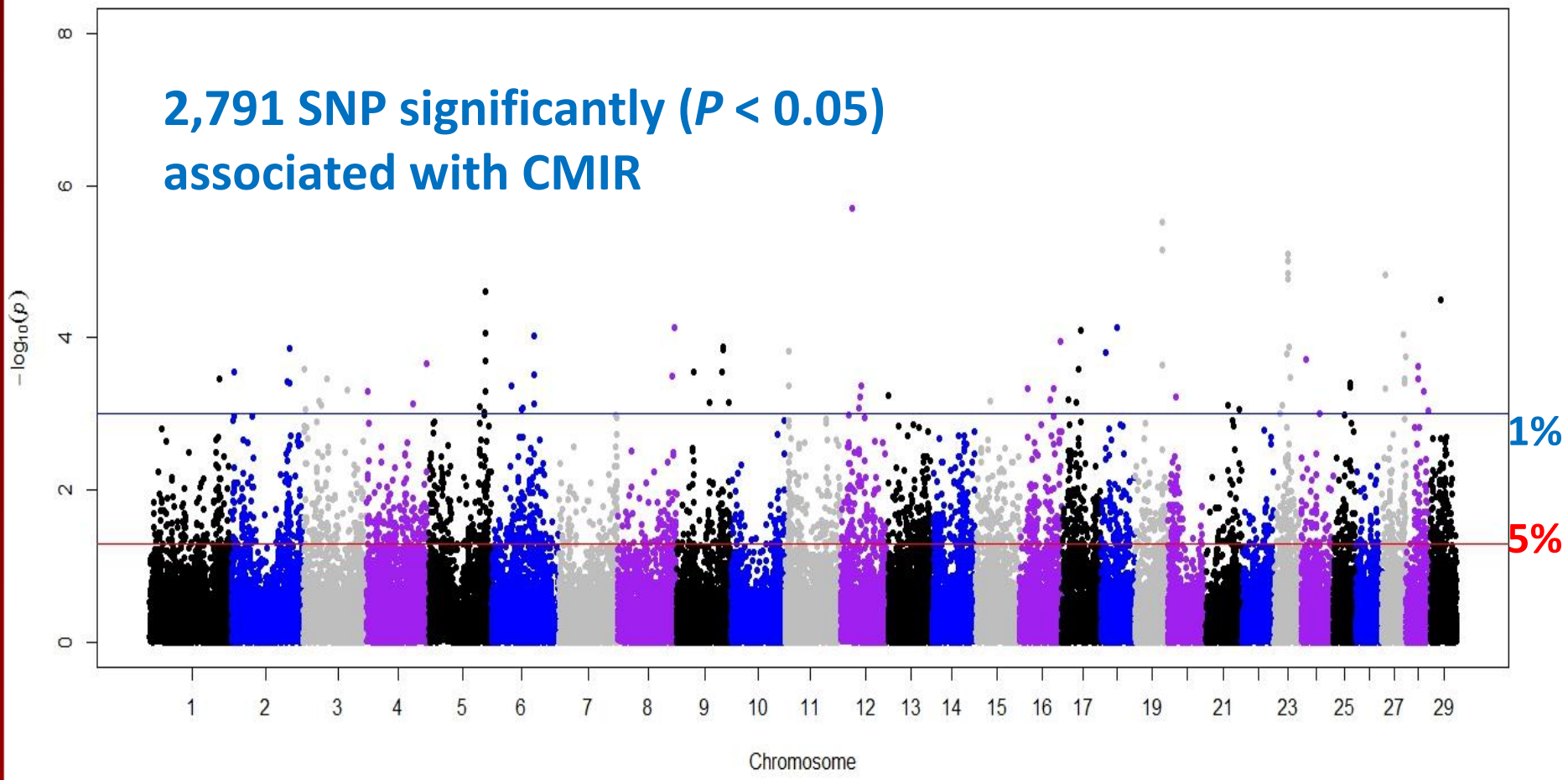
Manhattan Plot for CMIR

Markers and Chromosomal Regions of Interest



Result: 21 SNP following 5% correction for false discovery rate

Thompson-Crispi et al 2014 BMC Genomics. 15(1):559

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Next Step with Genomics of Immune Response Project

Establish a large reference population of 5000 cows and >2000 Semex bulls within Canada

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First GWAS for Adaptive Immune Responses in Cattle

- Knowledge of **HIR gene profiles** should enhance selection for **disease resistance**
- Allow **broader application** of the HIR technology by inclusion IR traits in genomic evaluations

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Genetic Selection for Immune Response

can Improve Dairy Health Management -

- Via Improved Breeding & Culling Decisions
- Via Improved Vaccine Protocols
- Via Improved Colostrum Management
- Via Improving other Fitness Traits

Our Current Research also shows Epigenetic Influences on the Bovine Immune System

Ref – Hussey, Paibomesai and Mallard, CJVR 77:54, 2013

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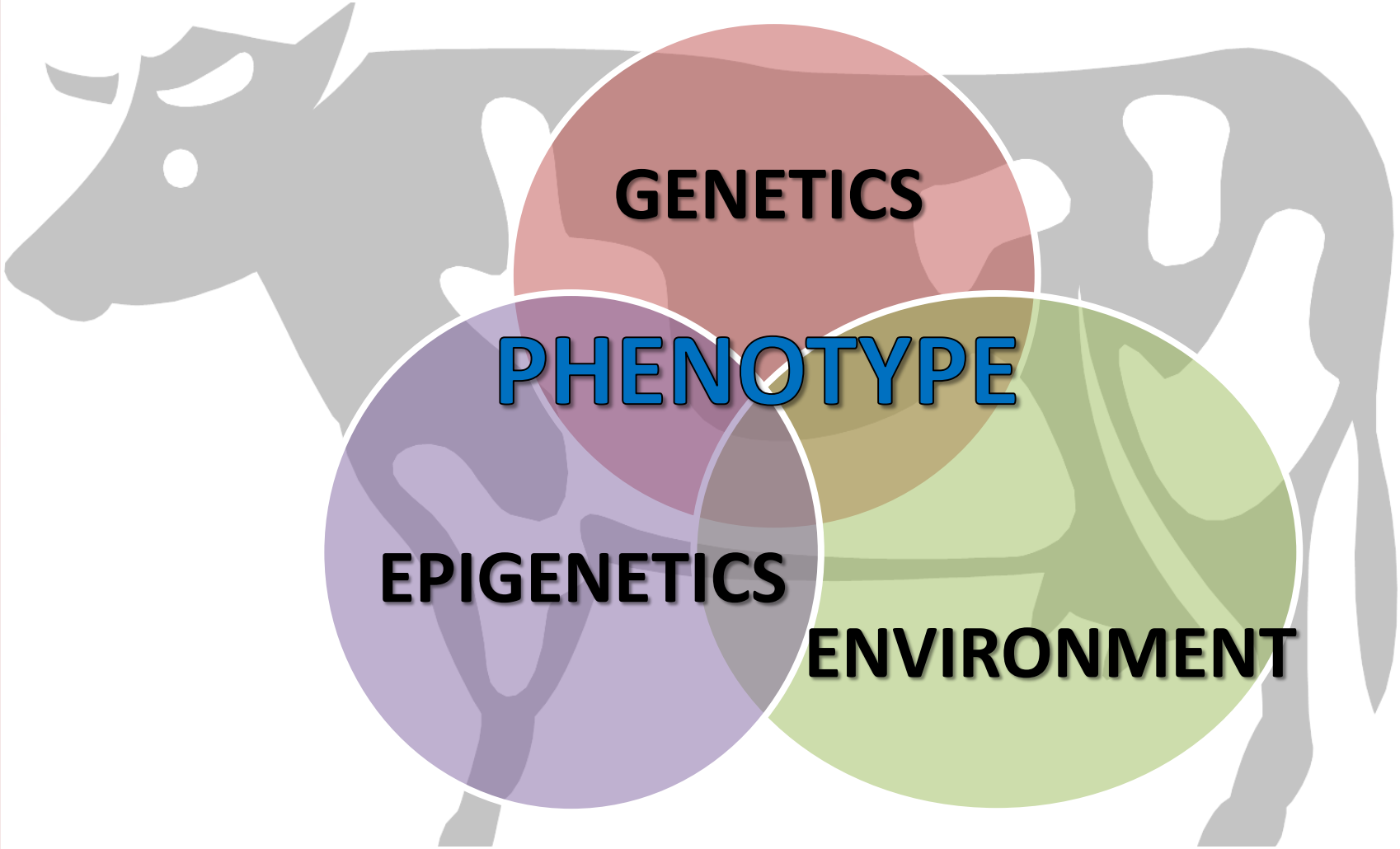
TAKE HOME - What you do today can effect the generations of tomorrow



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Questions

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NSERC

OMAFRA

CDN

Dairy Gen

Semex Alliance