IRISH CATTLE BREEDING FEDERATION

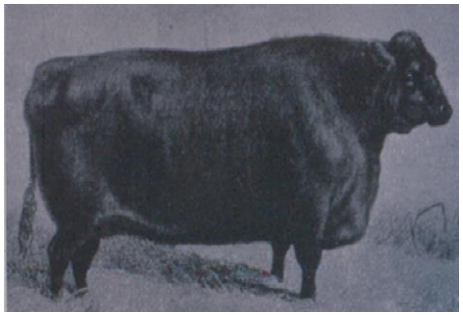
Bovine Genomic Improvements Realized from the Application of SNP Chips

Matthew McClure, PhD

National Development Plan
Transforming Ireland

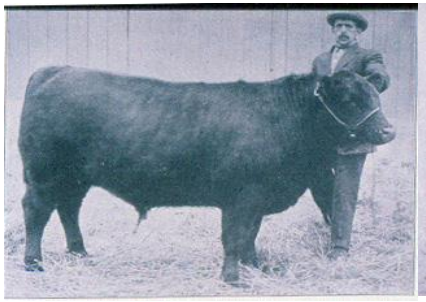
National Institute of Animal Science Symposium.
Suwon, South Korea September 6th, 2013

Select the Best



1867

1885



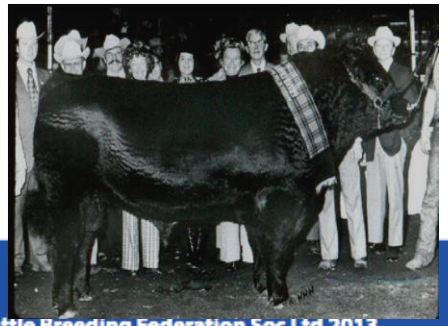
1902

1916

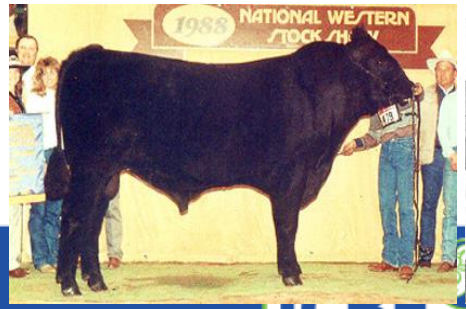
1938

1953

1964



1972

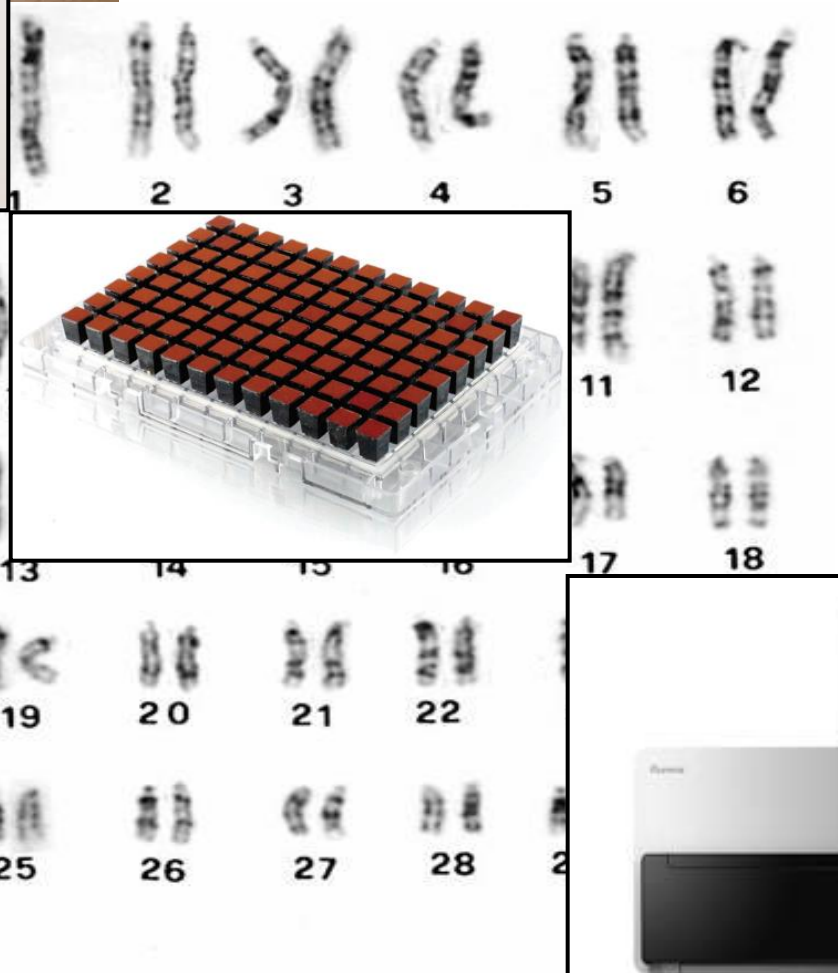


1988

1994

2007

Select the Best



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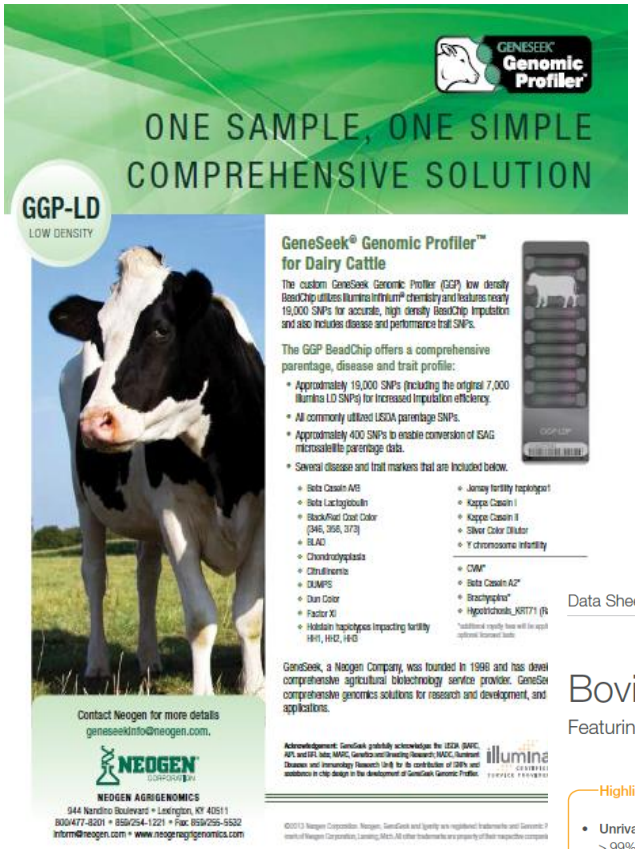
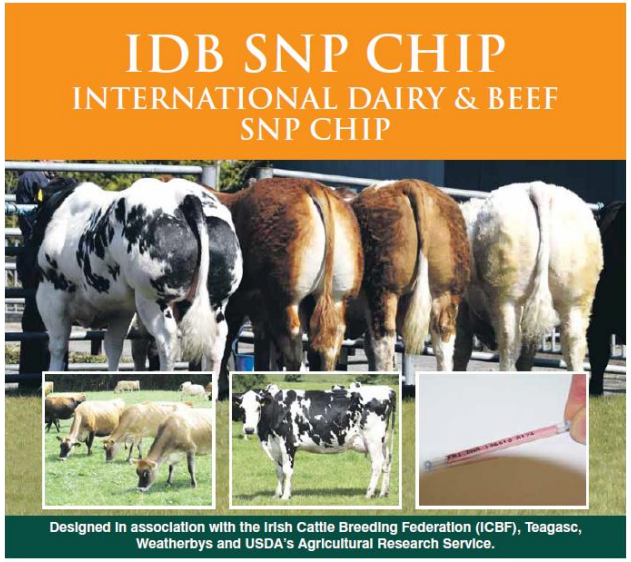
Genomic Selection Commercial Chips





Data Sheet: DNA Analysis

BovineSNP50 Genotyping BeadChip

Featuring 54,609 evenly spaced SNP probes that span the bovine genome.

illumina

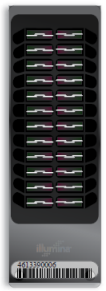
is the very latest design catering for both Beef and Dairy.
of the Illumina LD (7K) base content plus a further 10,000 (10K)
cted to ensure very high imputation accuracy to HD & to convert
ta for parentage verification. This extra panel of SNPs provides
product for both Beef & Dairy breeds.
additional ISAG recommended SNP parentage panels are
ins a comprehensive selection of genetic markers to screen for
major genes.

etails Contact: Weatherbys Ireland DNA Laboratory
3(0)45875521
ynn@weatherbys.ie
WEATHERBYS
Ireland

Highlights

- **Unrivaled Call Rates and Accuracy**
  > 99% average call rates and 99.9% reproducibility
- **Comprehensive and Uniform Coverage**
  Evenly distributed polymorphic SNPs with a mean gap of 49.4 kb
- **Simple Workflow**
  PCR- and ligation-free protocol
- **High-Throughput Format**
  Up to 24 samples can be interrogated in parallel

Figure 1: BovineSNP50 BeadChip



The BovineSNP50 BeadChip features more than 54,000 evenly spaced SNPs across the entire bovine genome.

Introduction

Illumina, in collaboration with the USDA ARS, University of Missouri, and the University of Alberta, has developed the second generation of a proven high-density, genome-wide genotyping array for the interrogation of genetic variation in cattle. The BovineSNP50 v2 BeadChip (Figure 1) features 54,609 informative SNP probes that uniformly span

Irish Cattle Breeding Federat

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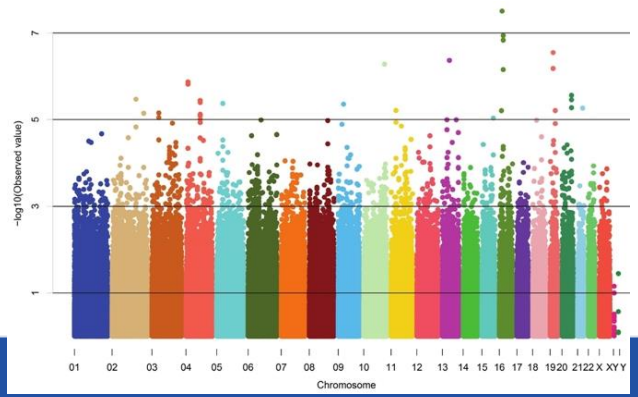
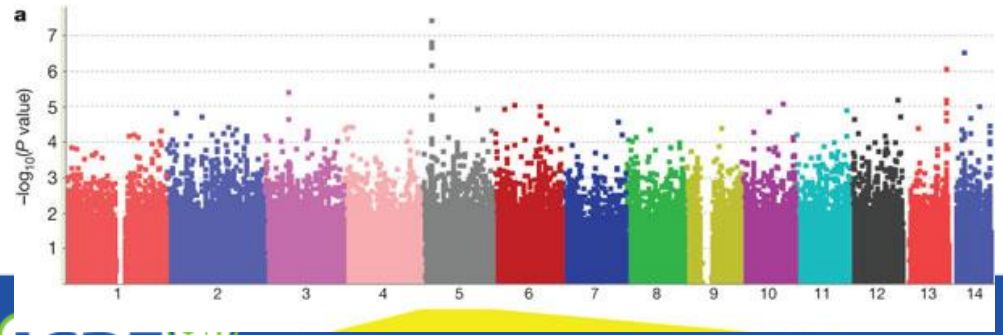
$$\begin{bmatrix} \hat{\mu} \\ \hat{\alpha} \end{bmatrix} = \begin{bmatrix} \iota^t\iota & \iota^t X \\ X^t\iota & X^tX+I\phi \end{bmatrix}^{-1} \begin{bmatrix} \iota^t y \\ X^t y \end{bmatrix}$$

$$f(\beta|\mathbf{y},\sigma_e^2) \propto \exp\left\{-\frac{1}{2}\frac{(\beta-\hat{\beta})'(\mathbf{X}'\mathbf{X})(\beta-\hat{\beta})}{\sigma_e^2}\right\}$$

		Mixture Model	
		All	Only (1-π) SNPs
Variance Ratio	Equal Known λ	"P	
	Equal Unknown λ	yesC0	BayesC BayesCπ
	Variable Unknown λ	yesA	BayesB





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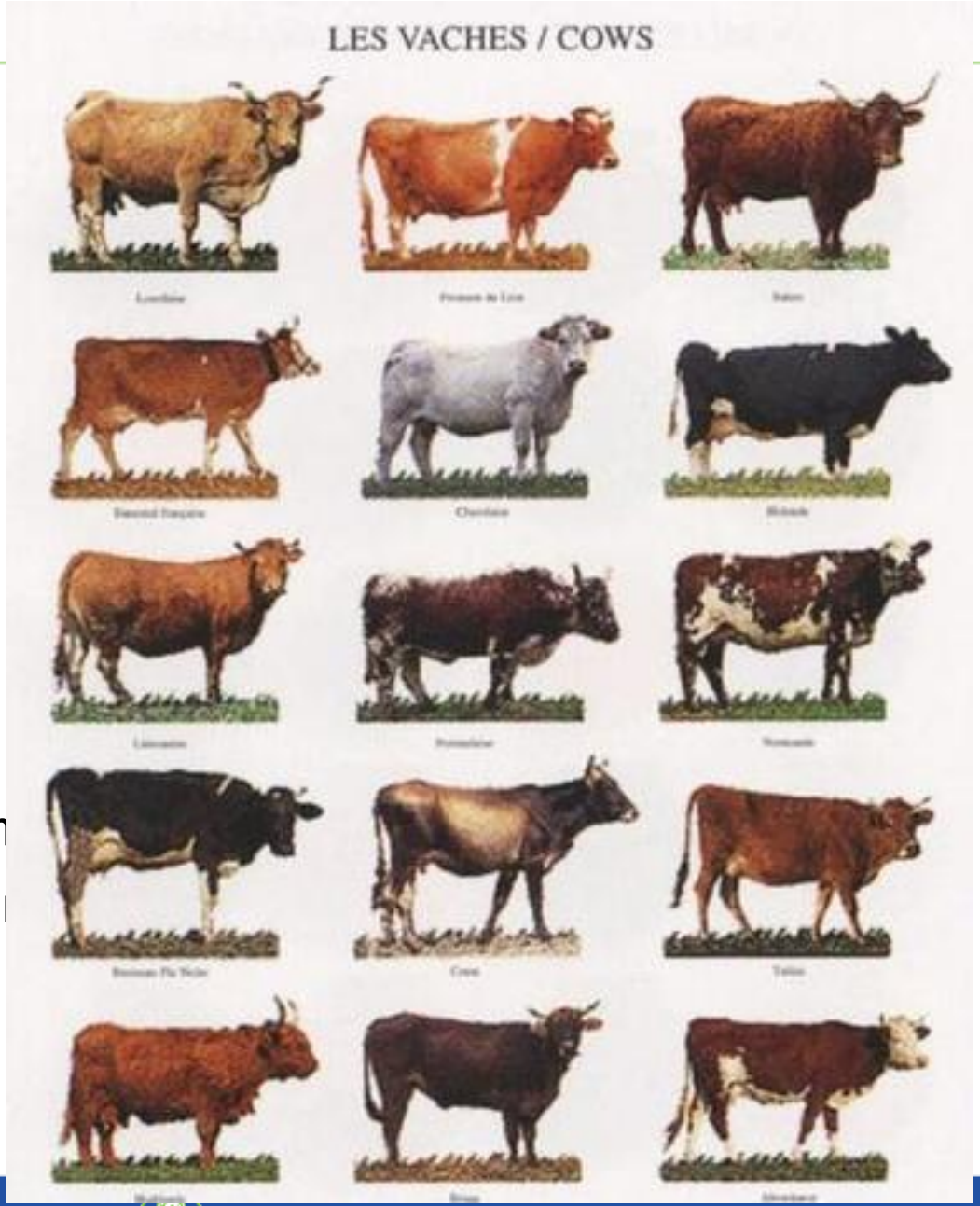
- Genomic Selection
  - Dairy
  - Beef
- Genetic Disease
  - Causative mutation
  - Haplotypes
- Identification
  - Parentage identification
  - Breeding stock selection
  - Breed identification
- Future
  - Disease resistance



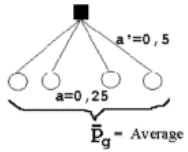
Genomic Improvements

- Visual Selectio

- Breeding Values

Breeding value index for ■ based on n measurements ○

Example: 20 daughters with an average of 7500 kg milk



a and a' coefficients of relationship

$\bar{P}_g$ = Average measurements

$h^2 = 0{,}30$, $c^2 = 0$ og $\bar{P} = 7000$

$$I = \bar{A} + \frac{n \cdot h^2 \cdot a'}{1+(n-1)t}(\bar{P}_g - \bar{P}) = 7000 + \frac{20*,30*,5}{1+19*,30*,25}\,500 = 7618$$

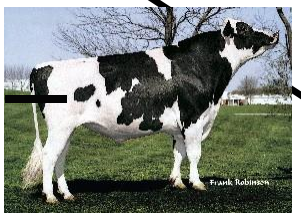
$$r^2_{AI} = \frac{n \cdot h^2 \cdot a'}{1+(n-1)t}\,a' = \frac{20*,30*,5}{1+19*,30*,25}\,0{,}5 = 0{,}618$$

- Genomic Selectio

$$\begin{bmatrix} \hat{\mu} \\ \hat{\alpha} \end{bmatrix} = \begin{bmatrix} \iota^t\iota & \iota^t X \\ X^t\iota & X^tX+I\phi \end{bmatrix}^{-1} \begin{bmatrix} \iota^t y \\ X^t y \end{bmatrix}$$

Lifecycle of dairy bull

Parents Selected



Dam Inseminated

~60% reliability

~$300

Bull Born

Genomic Test

Daughters Born (9 m later)

Semen collected (1yr)

Daughters have calves (2yr later)

~80% reliability

~$50,000

Bull Receives Progeny Test (5 yrs)

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Does Genomics Work – USA Dairy

Trait	Heritability	Daughter equivalents: Parent average	Daughter equivalents: Genomic prediction	Daughter equivalents: Gain from genomic prediction compared with parent average
Net merit	0.20	8	20	12
Milk yield	0.30	6	16	10
Fat yield	0.30	6	24	18
Protein yield	0.30	6	15	9
Fat percentage	0.50	3	22	19
Protein percentage	0.50	3	13	10
Productive life	0.08	18	39	21
SCS	0.12	14	32	18
Daughter pregnancy rate	0.04	32	67	35
Sire calving ease	0.09	16	24	8
Daughter calving ease	0.06	21	41	20
Final score	0.29	4	8	5
Stature	0.42	3	8	5
Strength	0.31	3	10	7
Body depth	0.37	3	9	6
Dairy form	0.29	4	12	8
Foot angle	0.15	7	14	7
Rear legs (side view)	0.21	5	14	9
Rear legs (rear view)	0.11	10	19	9
Rump angle	0.33	3	11	8
Rump width	0.26	4	12	8
Fore udder	0.29	4	14	10
Rear udder height	0.28	4	10	6
Udder depth	0.28	4	18	14
Udder cleft	0.24	5	10	5
Front teat placement	0.26	4	13	9
Teat length	0.26	4	14	10
All	0.25	8	19	11

Vanraden et al. 2008, J. Dairy Science

Does Genomics Work – Irish Beef Index

€uro Stars	€uro Index
5 Stars	€87
4 stars	€63
3 stars	€50
2 stars	€36
1 star	€10
Diff	**€154**

→

Weanling	
Wt kg	Value €
377	€727
358	€691
357	€676
350	€652
346	€645
	€82

→

Finisher		
Age	CWt kg	Value €
565	323	€1,204
571	311	€1,150
573	305	€1,111
578	297	€1,078
581	288	€1,038
		€166

→

Retailer		
HVC kg	VHVC kg	Value €
55.8	25.4	€1,820
53.6	24.7	€1,747
52.1	24.0	€1,703
49.6	23.1	€1,632
47.4	22.2	€1,559
		€261

€150/Cow difference between un-engaged and fully engaged herds in Cattle Breeding Activities

Worth €100m/annum at an Irish industry level.

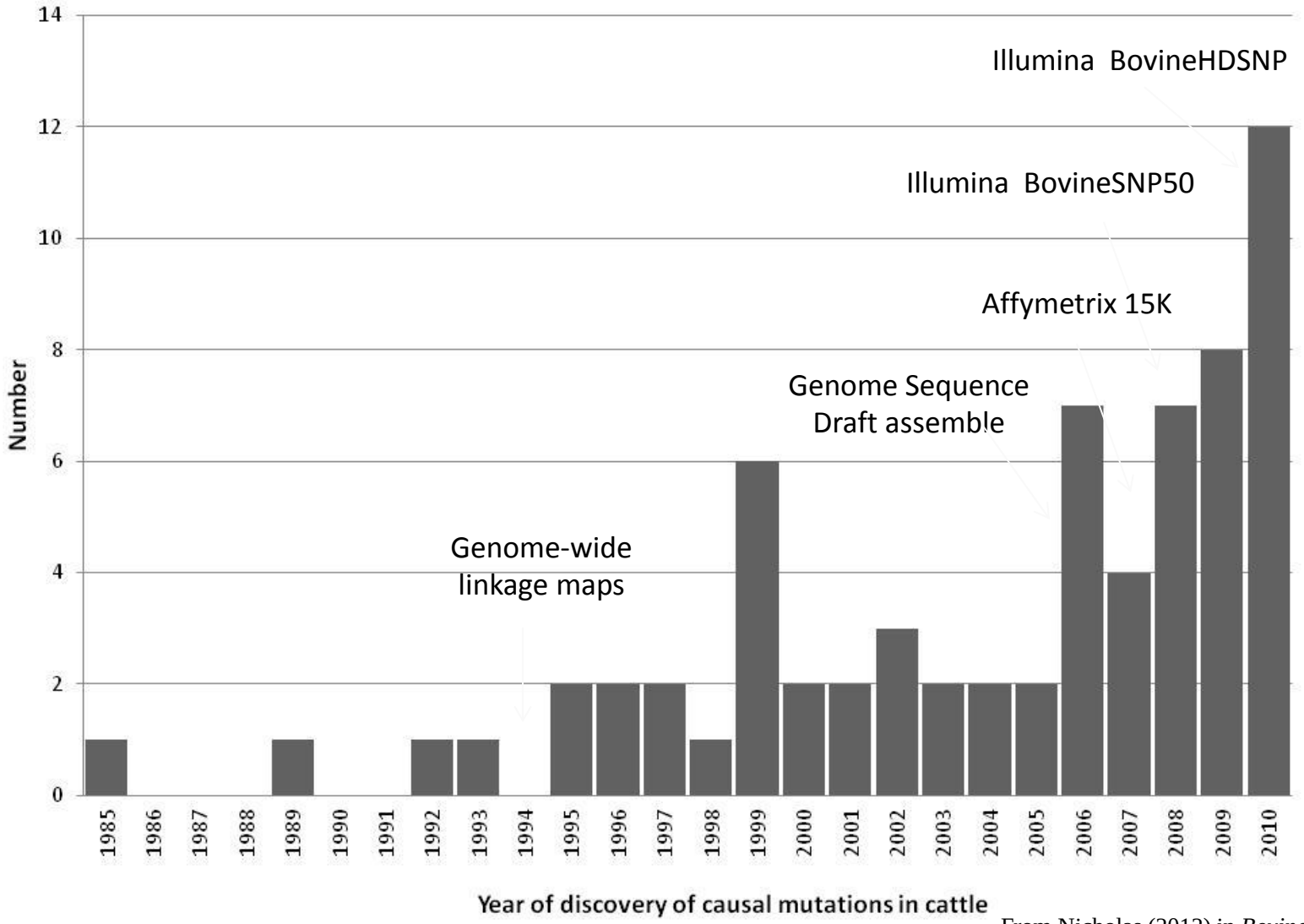
Genomic Improvements

- 1) Genomic Selection

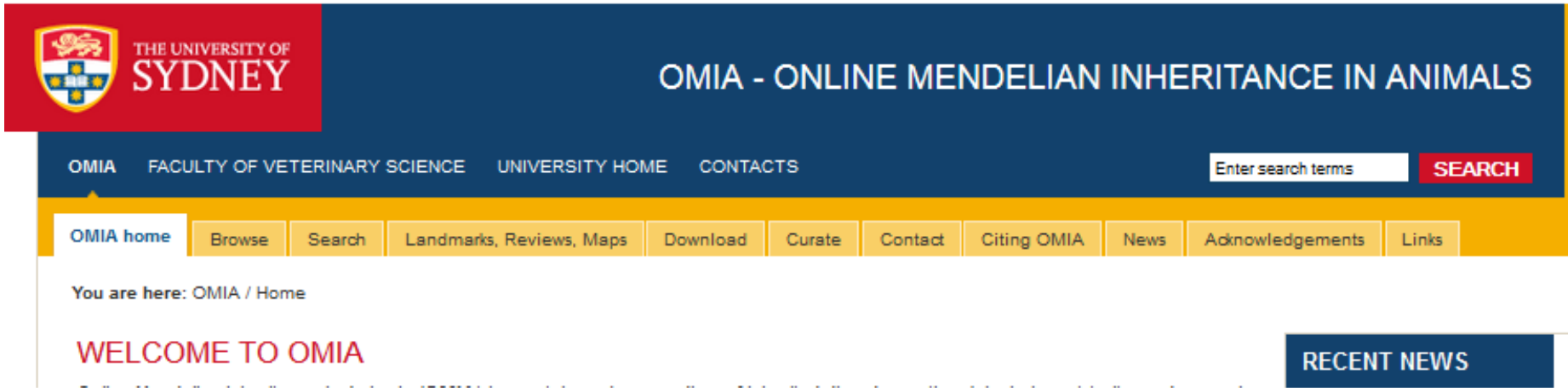
$$\begin{bmatrix} \hat{\mu} \\ \hat{\alpha} \end{bmatrix} = \begin{bmatrix} \iota^t\iota & \iota^tX \\ X^t\iota & X^tX+I\phi \end{bmatrix}^{-1} \begin{bmatrix} \iota^ty \\ X^ty \end{bmatrix}$$

- 2) Genetic Diseases

Mendelian Diseases



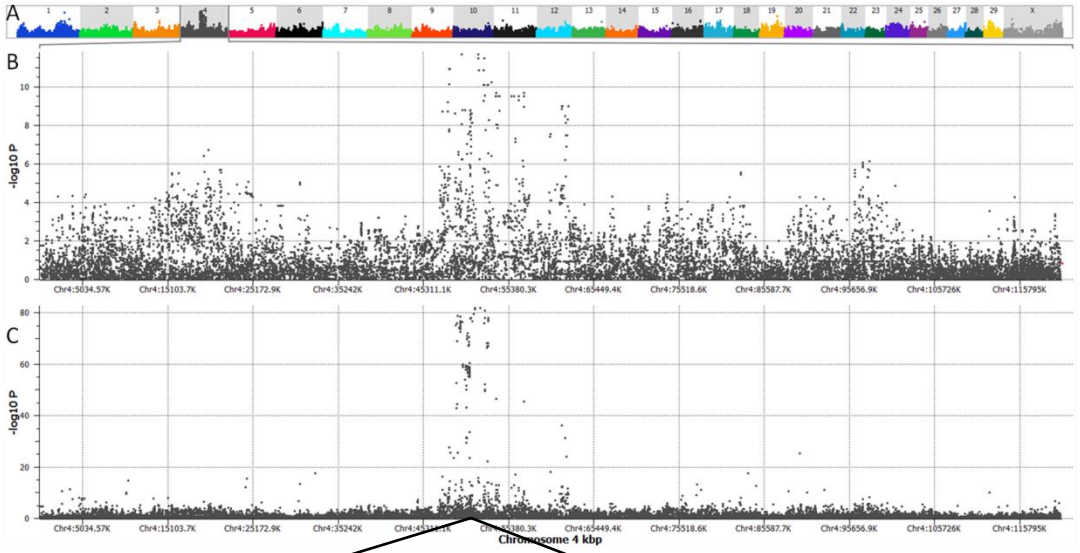
From Nicholas (2012) in *Bovine Genomics* (ed. Womack). Wiley-Blackwell, Ames, Iowa (in p

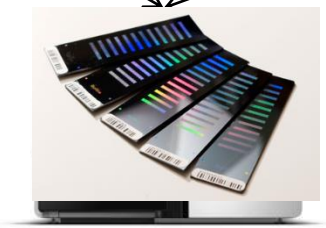


Summary

	dog	cattle	cat	sheep	pig	horse	chicken	goat	rabbit	Japanese quail	golden hamster	Other	TOTAL
Total traits/disorders	620	443	315	229	226	219	206	74	61	43	40	501	2977
Mendelian trait/disorder	241	179	79	96	50	41	125	13	30	32	28	159	1073
Mendelian trait/disorder; key mutation known	166	86	45	42	23	29	38	8	7	9	3	65	521
Potential models for human disease	330	156	179	98	83	115	42	30	37	11	14	255	1350

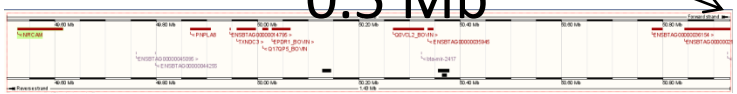
Mapping to Diagnostic





153 SNP

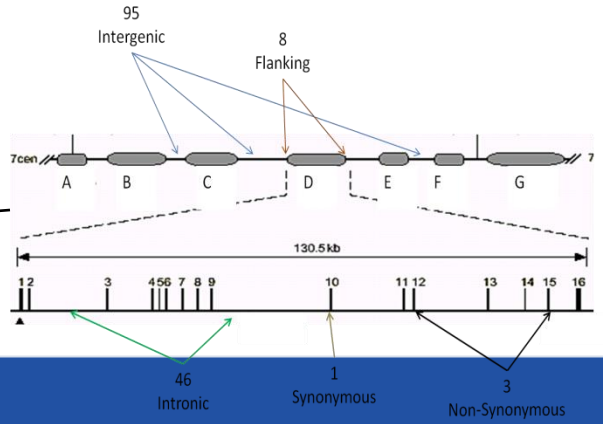
0.5 Mb



NRCAM PNPLA8 CTTNBP2

41 SNP

1 Haplotype

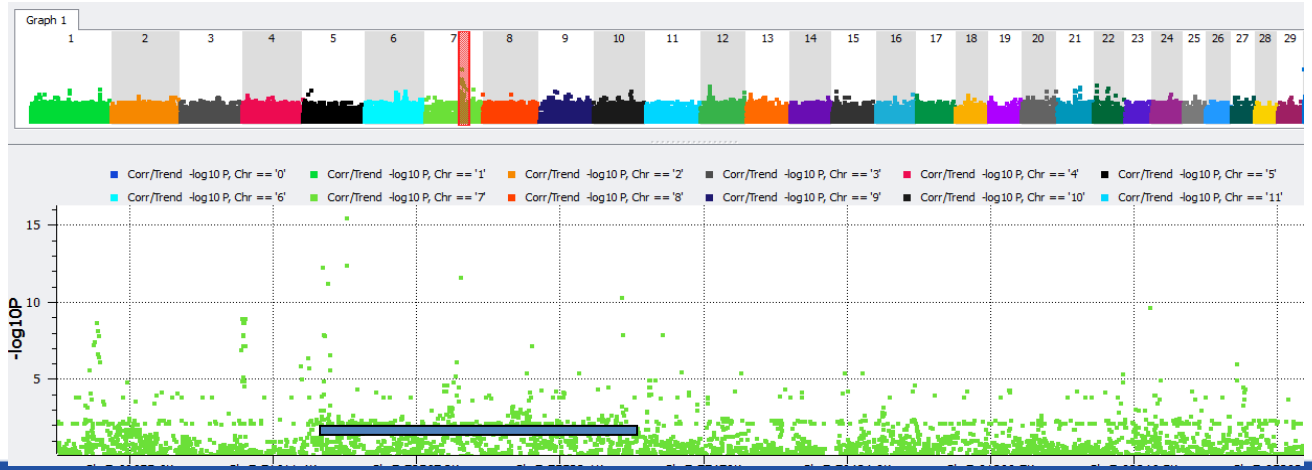


Rectovaginal Constriction

Identified in USA Jersey's 1970's

Progeny identified carriers

Mapped with SNP ~3 months



Haplotype Diseases

J. Dairy Sci. 94:6153–6161
doi:10.3168/jds.2011-4624

Harmful recessive effects on fertility detected by absence of homozygous haplotypes

P. M. VanRaden,*[1] K. M. Olson,† D. J. Null,* and J. L. Hutchison*
*Animal Improvement Programs Laboratory, Agricultural Research Service, USDA, Beltsville, MD 20705-2350
†National Association of Animal Breeders, Columbia, MO 66205-1033

OPEN ACCESS Freely available online

PLOS | ONE

Detection of Haplotypes Associated with Prenatal Death in Dairy Cattle and Identification of Deleterious Mutations in GART, SHBG and SLC37A2

Sébastien Fritz[1,2], Aurelien Capitan[1,2], Anis Djari[3], Sabrina C. Rodriguez[2,3], Anne Barbat[2], Aurélia Baur[1,2], Cécile Grohs[2], Bernard Weiss[2], Mekki Boussaha[2], Diane Esquerré[4], Christophe Klopp[3], Dominique Rocha[2], Didier Boichard[2]*

Genomic evaluation of Ayrshire dairy cattle and new haplotypes affecting fertility and stillbirth in Holstein, Brown Swiss and Ayrshire breeds

T.A. Cooper, G.R. Wiggans, P.M. VanRaden, J. L. Hutchison, J. B. Cole, and D. J. Null*
Animal Improvement Programs Laboratory, Agricultural Research Center, USDA, Beltsville, MD 20705-2350

ICBF.com

Manage

Genetic Improvement with Disease Risk

PUBRUN=1308

Bull	Sire	Dam	Birth	Ped_Comp%	Itb_ID
HO 135746776	HO 122358313	HO 130677626	2004/04/30	100	3

Alias=

Bull Name

LONG-LANGS OMAN OMAN-ET

Recessive Codes: TV TL TY TD

Reg St		Inbrd	Exp_Fut Inbrd	Dau_Inbrd
**	Pedigree	5.4	6.5	5.7
	Genomic	8.7	7.8	

Current Status	Cntrl Stud	Sampling Status	Orig Stud	Entered AI Yr Mo	Short Name	Primary Stud Code
I	14	S	14	05/12	MAN-O-MAN	014HO04929

Eval Breed HO

	PTA	Rel	Daus	Herds	Src Mean	DauDev	PA	RelPA
Milk	1190	.99	3048	1404	29004	1242	405	.47
Fat	78				1129	85	48	
Prot	71	.99	3048	1404	917	75	38	.47
PL	1.9	.91	977	533	28.8	3.3	0.9	.46
SCS	2.93	.98	3193	1472	2.33	-0.07	2.86	.46
DPR	0.9	.94	1238	451	22.9	-1.1	0.2	.45
CCR	2.3	.90	1035	591			0.5	.45
HCR	1.4	.89	2184	959			0.2	.42
NM$	633	.95					352	.46
FM$	513							
CM$	784							

Yield Rel	0.99
Fat PTA%	0.13
Prot PTA%	0.13
Age wt	0.40

Percentile 97

Genomics Ind = 1

Chip = 2 50K2

SCR Not available

Most Daus Lac/Dau	Herd	Daus	%US	%OS	Ctry	#Ctries	Mgt Gp	First Lactation Age	%RIP	DIM
1.3	35360080	30	100	1	USA	1	36	25	41	235

Identification

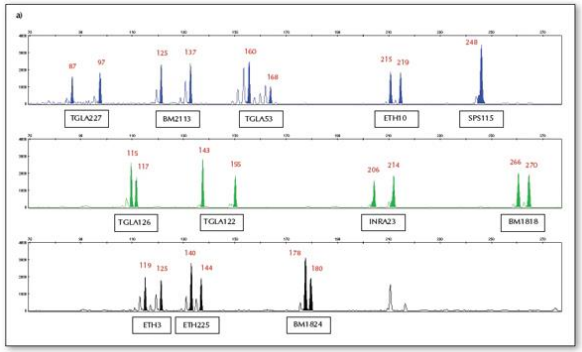
- Parent Verification

<1990's

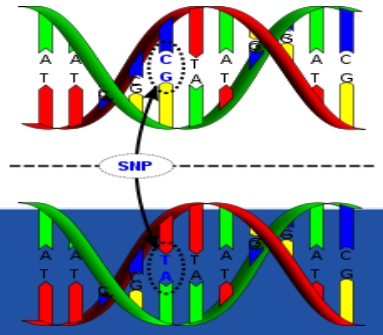
Recipient's blood			Reactions with donor's red blood cells			
ABO antigens	ABO antibodies	ABO blood type	Donor type O cells	Donor type A cells	Donor type B cells	Donor type AB cells
None	Anti-A Anti-B	O				
A	Anti-B	A				
B	Anti-A	B				
A & B	None	AB				

Compatible Not compatible

Present

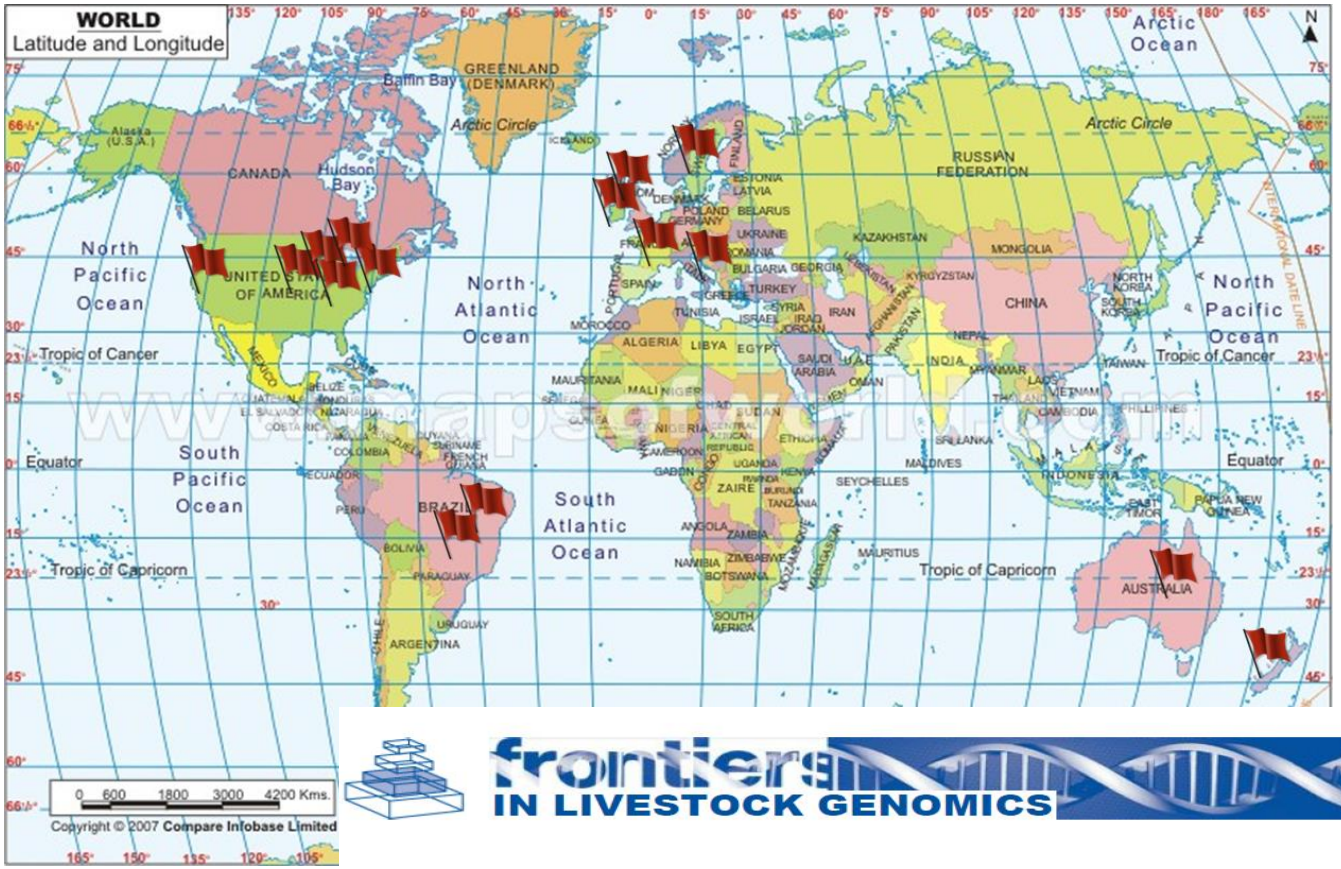


Future



Microsatellite Imputation

Breed	SNP	SNP+MS
Abondance	172	165
Angus	623	235
Aubrac	239	234
Ayshire	523	86
Bazadaise	80	53
Beefmaster	36	36
Belmont Red	40	
Belgian Blue	210	12
Blonde D'Aquitain	225	201
Brahman	410	364
Brangus	13	13
Braunvieh	17	17
Bretonne Pie Noire	27	16
Brown Swiss	91	64
Brune Des Alpes	109	109
Charolais	1449	1109
Chiangus	19	0
Crossbred	506	3
Devon	16	16
Dexter	15	15
Fresian	163	35
Gasconne	142	142
Gelbvieh	44	0
Gir	209	101
Guernsey	110	18
Hereford	853	243
Holstein	2596	678
Jersey	87	131
Kerry	1	0
Limousin	2171	1572
Longhorn	13	13
Maine Anjou	38	16
Montbeliarde	257	251
Murray Grey	22	
N'Dama	24	0
Nelore	2659	135
Normande	256	242
Parthenaise	291	218
Pie Rouge Des Plaines	160	116
Piedmontese	24	17
Red Angus	61	47
Red Pie (italial)	2	0



frontiers IN LIVESTOCK GENOMICS

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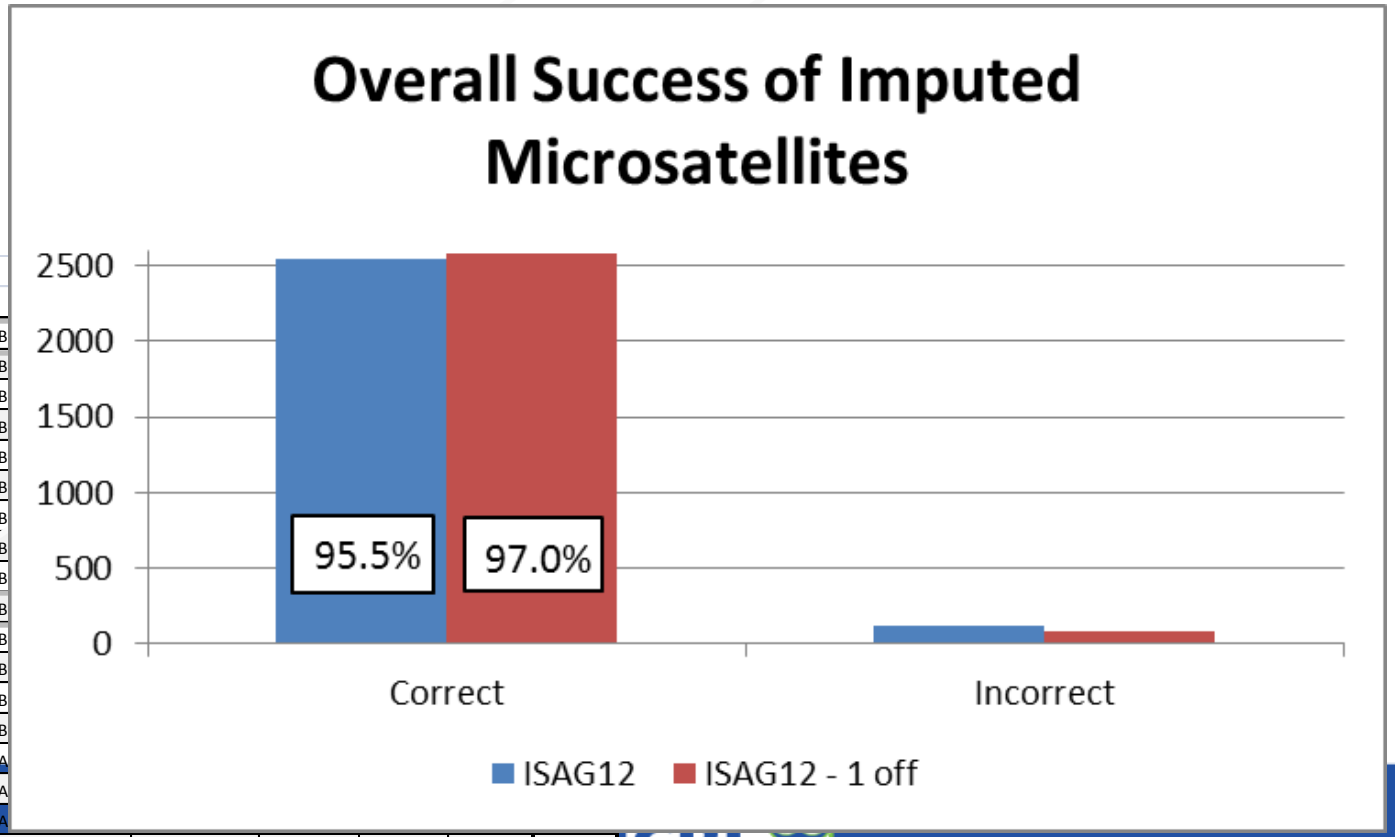
Imputation of Microsatellite Alleles from Dense SNP Genotypes for Parentage Verification Across Multiple Bos taurus and Bos indicus breeds

Matthew Charles Mcclure, Tad Stewart Sonstegard, George R Wiggans, Alison Louise Van_Eenennaam, Kristina L Weber, M. Cecilia Torres Penedo, Donagh Berry, John Flynn, Jose Fernando Garcia, Adriana Santana Carmo, Luciana C.A.

Microsatellite Imputation

BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	BovineHI	Bovin
B	A	B	B	A	B	B	A	A	A	B	B	A	B	A	A
B	A	B	B	B	B	B	A	A	B	B	B	A	B	B	B



BM1824					
Haplotype					
BABBAABBAAAABBBAABABAB					
BAABAABBAAAABBBAABABAB					
BBBBAABBAAAABBBAABABAB					
BABBAABBAAAABBBAABABAB					
BABBAABBAAAABBBAABABAB					
BAABBAABBAAABBBAABABAB					
BAABABABBAAABBAABAABAB					
BAABABABBAAABBAABA/ GAB					
AABBAABBBAAABBAABAABAB					
AAAABAAABBABBAAABAABAB					
AAAABAAABBABBAAABAABAB					
AAAABAAABBABBAAABAABAB					
BAABBAABBBABBBAABBABAB					
AAAABAAABBABBAAABAABAB					
BABBAABBAABAABBBBBBABA					
BAAABABBAABAABBBBBBABA					
BAABAABBAABAABBBBBBABA					
AABBAABBAABAABBBBBBABAAAABABBBBAB	188			188	188
AAAABABBAABAABBBBBBABAAABABBBBAB	188	188	188_190	188_190	188_190

Irish Parent Verification Process

Herdbook

Certificate Issued

Rules Applied

Report Generated

Exclusion Report

DNA Typed

Wrong Sire

No Sire MS

Calf

Failed

Test against all Sires in DB

Verified

MS - Sire Verified

Verified

Verify Result

Full MS Test

Verified

Failed

Verified by MS

Single Mismatch

Multiple Mismatch

SNP - Sire Check

Verified

SNP Imputed to MS

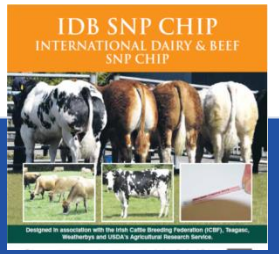
Imputed MS

ICBF Database

Weatherbys

Hair Roots

Genotyped



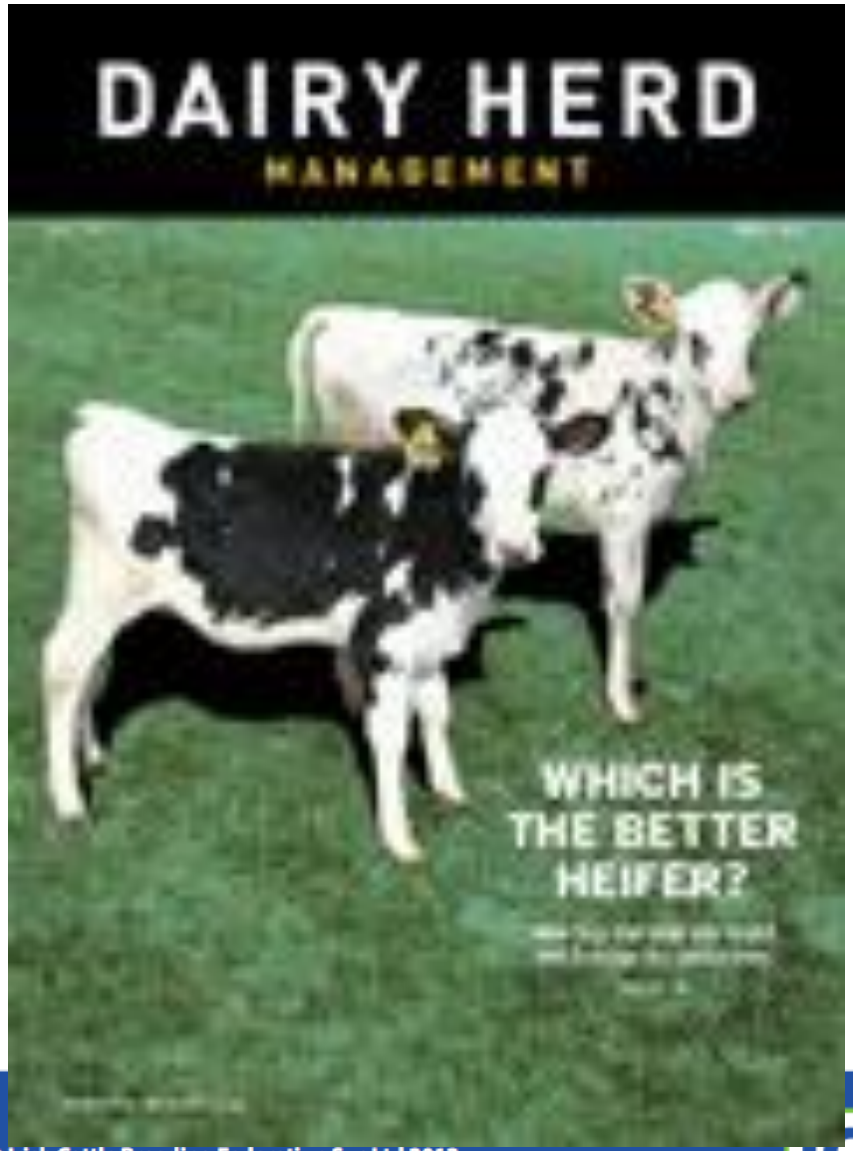
ICBF.com

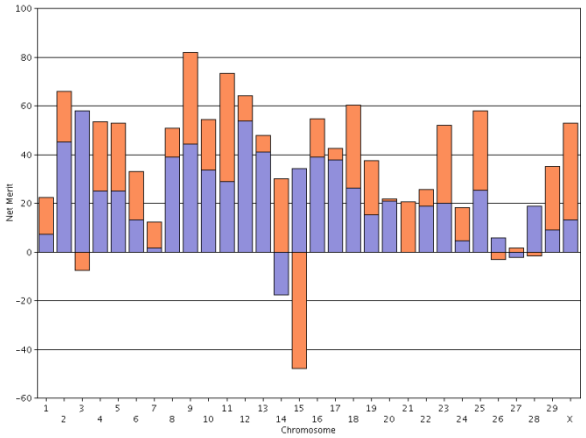
Identification

- Parent Verification
- Replacement Selection

Choose the Best Replacement?

Now we know which heifer is best

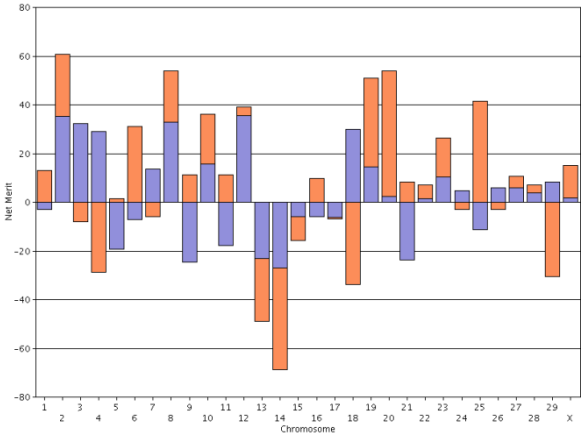




The best has a PTA NM$ of +868 and a REL of 73%.

PLANET has 3,783 genotyped daughters - which one do you want in your herd?

The worst has a PTA NM$ of +48 and a REL of 68%.



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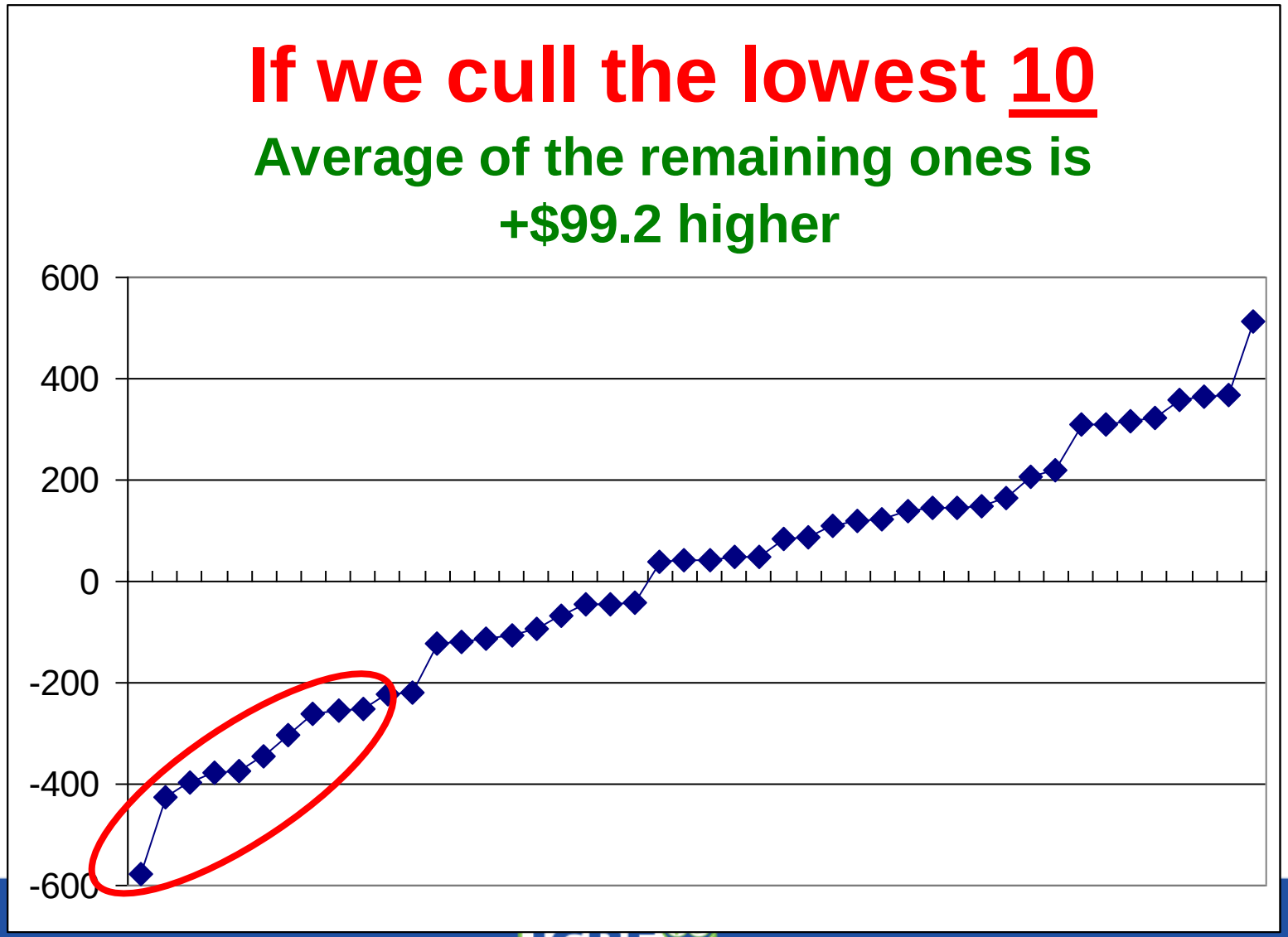
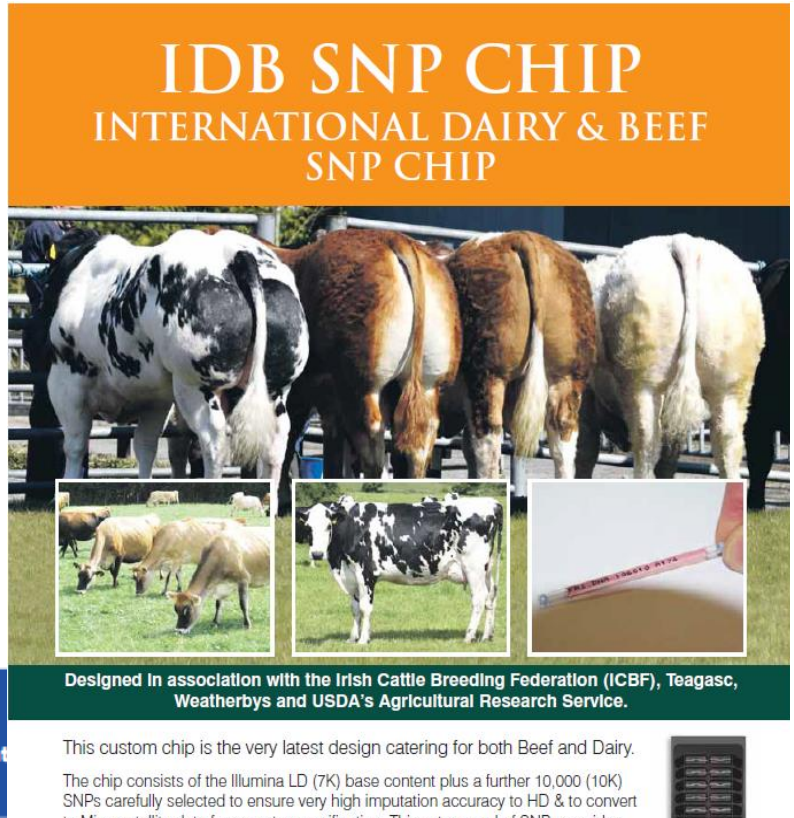
John Cole, USDA-ARS-AIPL

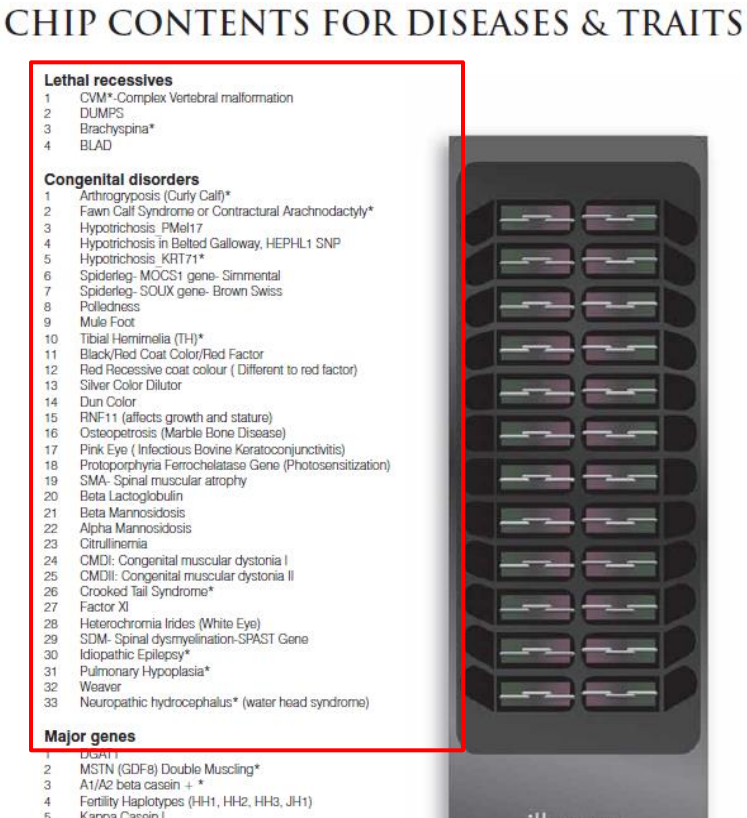
46 Holstein Heifers with Genetic Net Merit



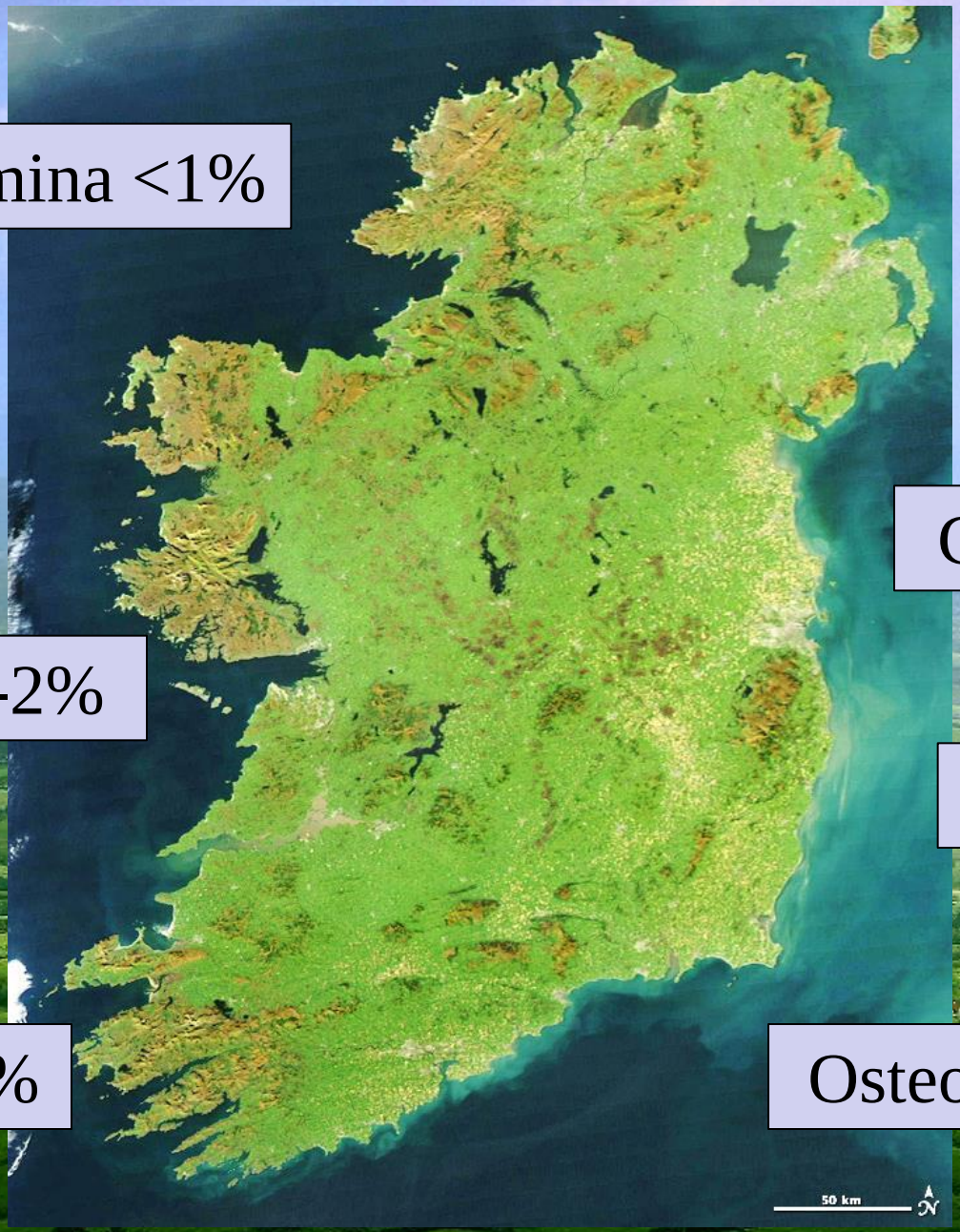
Identification

- Parent Verification
- Replacement Selection
- National Disease Surveillance





National Genetic Disease Overview



Citrullinaemina <1%

DUMPs 0%

CVM-4%

Branchspina-2%

Curly Calf 0%

Mulefoot <1%

Osteopetrosis <1%

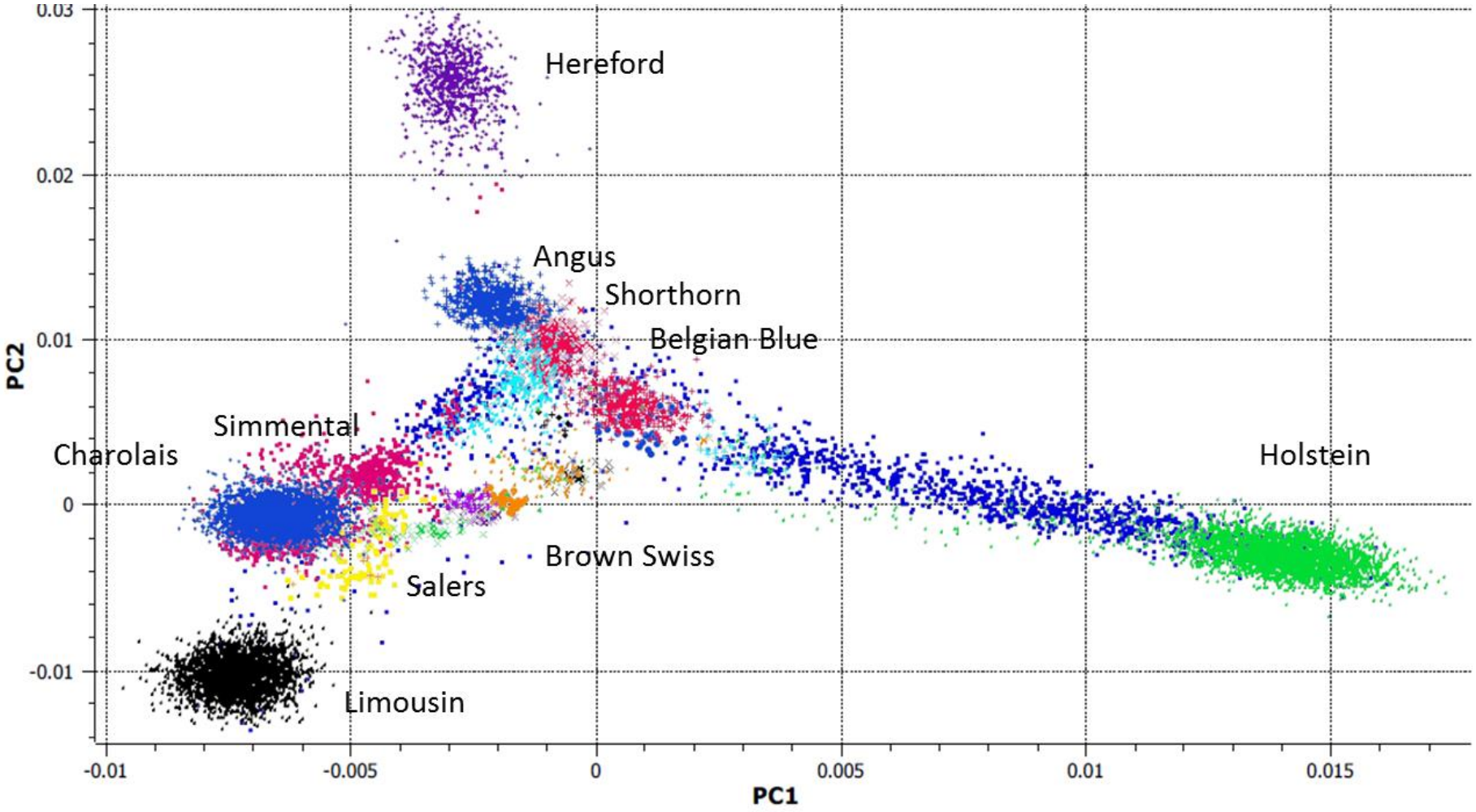
Identification

- Parent Verification
- Replacement Selection
- National Disease Surveillance
- Breed Composition

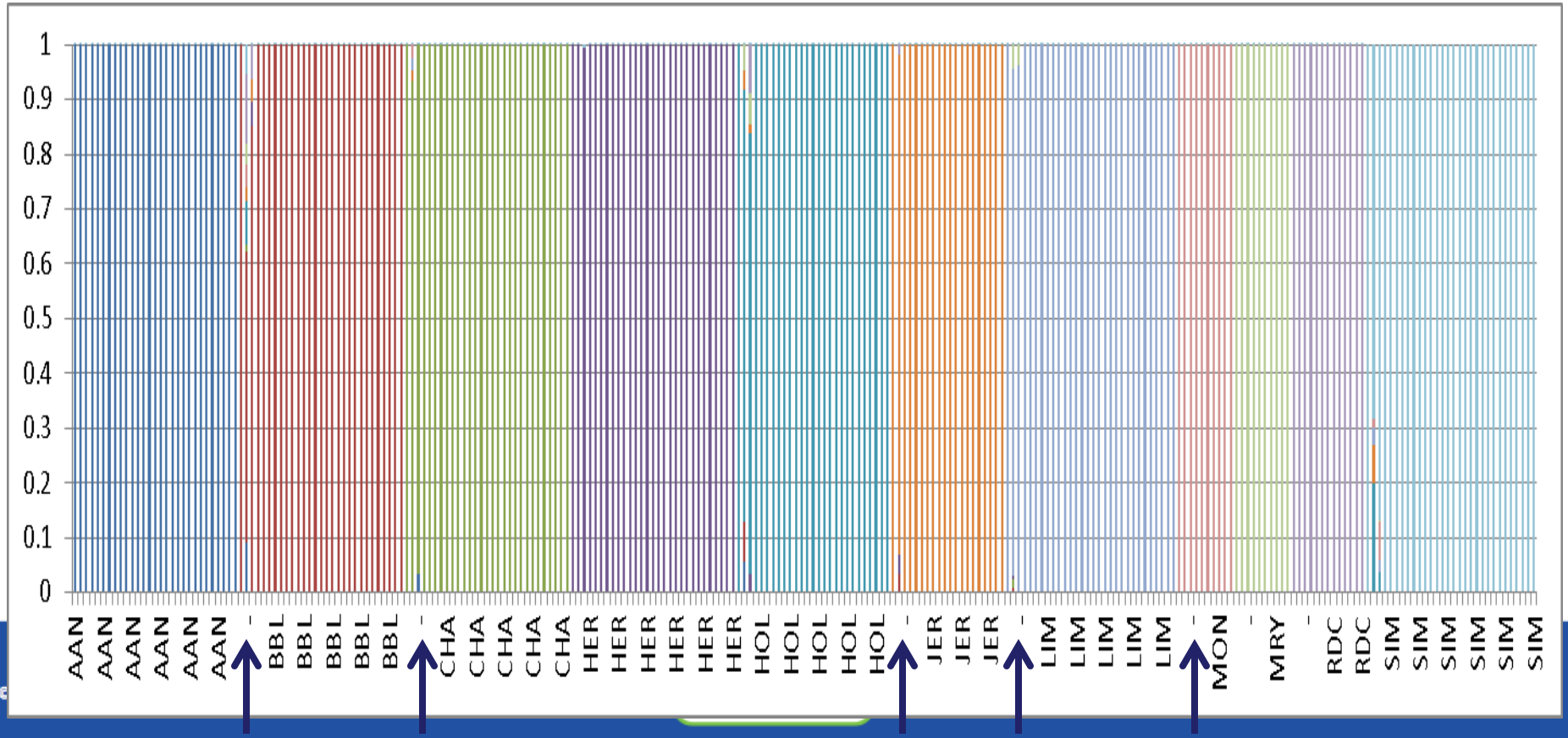
Breed ID

?

PCA analysis of 45 breeds



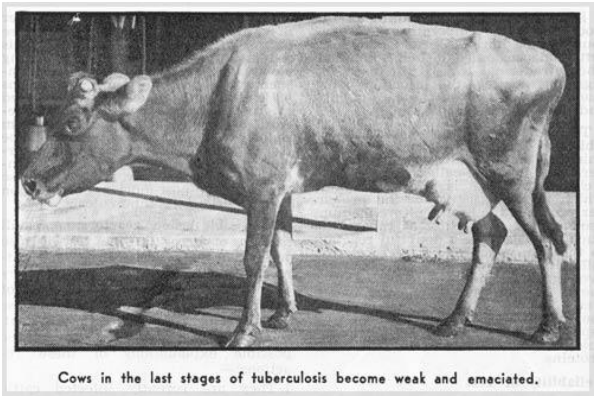
Breed ID


1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
AAN
BBL
CHA
HER
HOL
JER
LIM
MON
MRY
RDC
SIM

Disease Resistance

- Mendelian
- Infectious

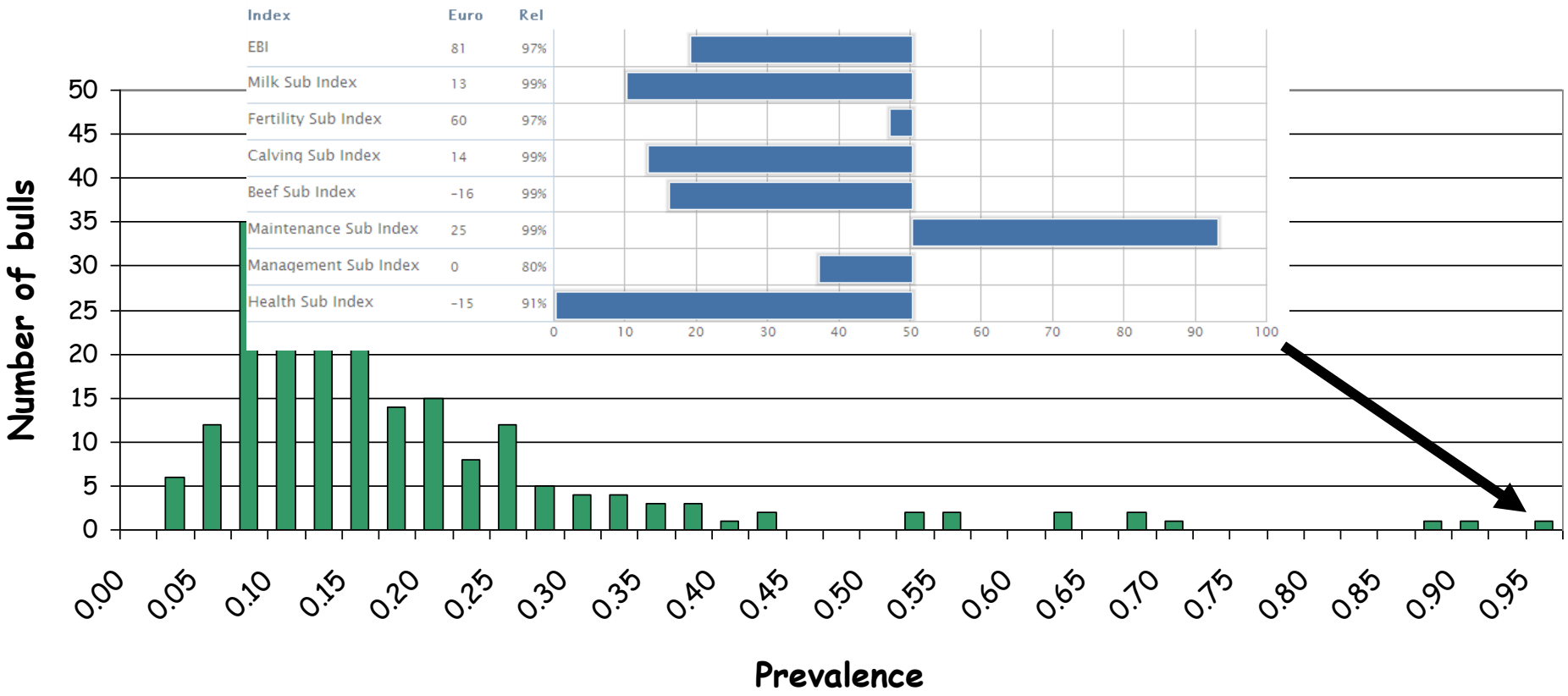
Health



Cows in the last stages of tuberculosis become weak and emaciated.

?

TB – sire prevalence



Ian Richardson

Thank You

- BFGL (USDA-ARS)
  - Curt Van Tassell
  - Tad Sonstegard
  - Heather Huson
  - Larry Shade
  - George Liu
  - Derek Bickhart
  - Steve Schroeder
  - Alicia Beavers
  - Euisoo Kim
  - Lakshmi Matukumalli
- AIPL (USDA-ARS)
  - Paul VanRaden
  - Dan Null
  - John Cole
  - George Wiggans
  - Tabatha Cooper

- Univ. of Missouri
  - Jeremy Taylor
  - Robert Schnabel
  - Stephanie McKay
  - Jae Woo Kim
  - Jared Decker
  - Megan Rolf
  - Tasia Taxis
  - Sarah Gregg
  - Rich Chapple
  - Yao Ping
- Weaver-Italian Brown Swiss
  - Paolo Ajmone
  - Licia Colli
  - Enrico Santus

- Industry / Breed Associations
  - Sally Northcutt (Angus Assoc)
  - Cari Wolfe (Jersey Assoc)
  - Holstein Assoc
  - Brown Swiss Assoc
  - Cofactor Genomics
    - Jon Armstrong
    - Jarret Glasscock
  - Illumina
    - Cindy Lawley
- Microsatellite
  - Bovine HapMap
  - Breed Associations
    - Sue Denise
  - Alison Van Eneenaam
  - Cecilila Penedo
  - John Keele
  - Mike Coffey
  - Marie-Yvonne Boshcher
  - Donagh Berry
  - Andrew Cromie
  - Fernando Garcia
  - Milla Albuquerqu
  - Luciana Regitano

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Questions