



IRISH CATTLE BREEDING FEDERATION

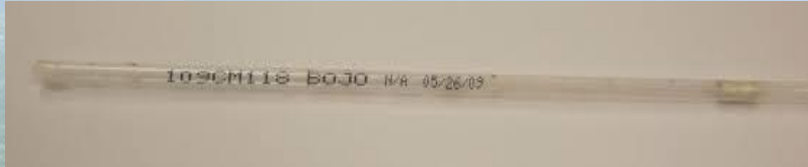
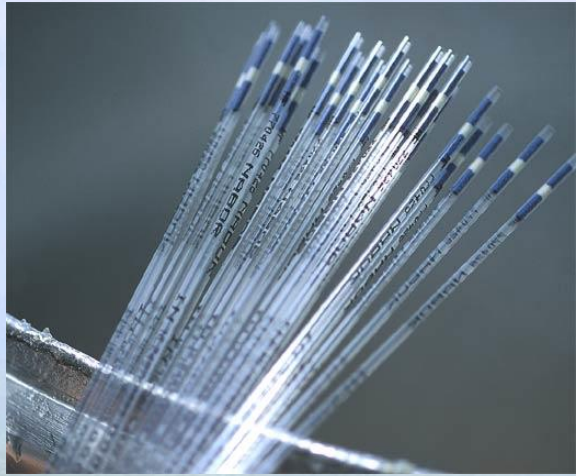
Genomics in Ireland with the IDB SNP chip:
Parentage, Breeding Values, and Disease Status



Matthew McClure, ICBF
Holstein UK 12/05/2015



Parentage Validation/Prediction



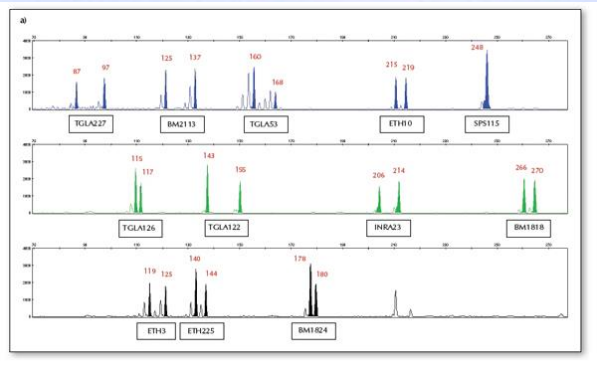
Parentage Validation/Prediction

How many needed?

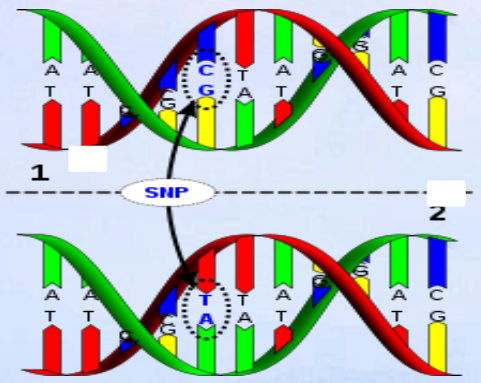
Recipient's blood			Reactions with donor's red blood cells			
ABO antigens	ABO antibodies	ABO blood type	Donor type O cells	Donor type A cells	Donor type B cells	Donor type AB cells
None	Anti-A Anti-B	O				
A	Anti-B	A				
B	Anti-A	B				
A & B	None	AB				

Compatible Not compatible

Blood Typing



Microsatellite Markers



SNPs

Microsatellites

ISAG Panel: BM1824, BM2113, INRA023, SPS115, TGLA122, TGLA126, TGLA227, ETH10, ETH225, ETH3, SPS115, TGLA53

Additional panel of MGTG4B, CSRM60, SPS113, ILSTS006, RM067, CSSM66

SNP: ISAG100
ISAG200
Some labs use more



121 Validation
2000 Prediction

Small SNP Sets: Genotype Errors

- Fail Sire A with 121 SNP (ISAG200 subset)
 - ≥2 misconcordance = fail
- Predict Sire A with 2,000 SNP
 - ≤10 misconcordance = pass



Why validate with small and predict large SNP

Unsort	C	1	G	3
Map	itt	sire_itt	ARS-USMARC-PARENT-EF093511-RS2901	
1	HERAUSM00000GRKA584		1	B_B
2	HERIRLM141607070601	HERAUSM00000GRKA584		
3	HERIRLM151225330379	HERAUSM00000GRKA584		A_A
4	HERIRLM151225340413	HERAUSM00000GRKA584		A_A
5	HERIRLM151225360423	HERAUSM00000GRKA584		A_A
6	HERIRLM151225370399	HERAUSM00000GRKA584		A_A
7	HERIRLM151225380425	HERAUSM00000GRKA584		A_A
8	HERIRLM151225380441	HERAUSM00000GRKA584		A_A
9	HERIRLM191141760568	HERAUSM00000GRKA584		A_A
10	HERIRLM231305310207	HERAUSM00000GRKA584		A_A
11	HERIRLM241245190385	HERAUSM00000GRKA584		A_A
12	HERIRLM331493150493	HERAUSM00000GRKA584		A_A
13	HERIRLM361055830685	HERAUSM00000GRKA584		A_A
14	HERIRLM361055880665	HERAUSM00000GRKA584		A_A
15	HERIRLM121182590084	HERAUSM00000GRKA584		A_B
16	HERIRLM121201450915	HERAUSM00000GRKA584		A_B
17	HERIRLM121201460899	HERAUSM00000GRKA584		A_B
18	HERIRLM141643520372	HERAUSM00000GRKA584		A_B
19	HERIRLM151225310435	HERAUSM00000GRKA584		A_B
20	HERIRLM151225330412	HERAUSM00000GRKA584		A_B
21	HERIRLM151225390376	HERAUSM00000GRKA584		A_B
22	HERIRLM151313160329	HERAUSM00000GRKA584		A_B
23	HERIRLM151654470902	HERAUSM00000GRKA584		A_B
24	HERIRLM211463520049	HERAUSM00000GRKA584		A_B
25	HERIRLM211463580046	HERAUSM00000GRKA584		A_B
26	HERIRLM231305370204	HERAUSM00000GRKA584		A_B
27	HERIRLM241842660174	HERAUSM00000GRKA584		A_B
28	HERIRLM281110080573	HERAUSM00000GRKA584		A_B
29	HERIRLM291166240641	HERAUSM00000GRKA584		A_B
30	HERIRLM301207290630	HERAUSM00000GRKA584		A_B
31	HERIRLM311122080052	HERAUSM00000GRKA584		A_B
32	HERIRLM311317670240	HERAUSM00000GRKA584		A_B
33	HERIRLM331340371248	HERAUSM00000GRKA584		A_B
34	HERIRLM331358460991	HERAUSM00000GRKA584		A_B
35	HERIRLM121182560081	HERAUSM00000GRKA584		B_B
36	HERIRLM141607090603	HERAUSM00000GRKA584		B_B
37	HERIRLM151225340421	HERAUSM00000GRKA584		B_B
38	HERIRLM151225370424	HERAUSM00000GRKA584		B_B
39	HERIRLM151313130326	HERAUSM00000GRKA584		B_B

Small SNP Sets: Validate Wrong Sire

Animal	Listed sire		
LIMIRLF.....554	LIMIRLM.....050		
SNP set	#_mismatches	#SNP_both_genotyped	%_SNP_mismatch
121 SNP	0	118	0.00%
LD_base	267	6848	3.90%
CHAIRLF.....639	CHAIRLM.....163		
SNP set	#_mismatches	#SNP_both_genotyped	%_SNP_mismatch
121 SNP	1	113	0.88%
LD_base	336	6729	4.99%
CHAIRLF.....355	CHAIFRAM.....993		
SNP set	#_mismatches	#SNP_both_genotyped	%_SNP_mismatch
121 SNP	1	114	0.88%
LD_base	227	6761	3.36%
LIMIRLF.....500	LIMIRLM.....959		
SNP set	#_mismatches	#SNP_both_genotyped	%_SNP_mismatch
121 SNP	0	112	0.00%
LD_base	0	6711	0.00%

Sire Validation Errors with Small SNP Sets

- Fail with 121 then predict with 2,000 SNP
- Validate the wrong sire?
- **Why validate with small and predict large SNP**



How Many SNP to Predict 1 Correct Sire

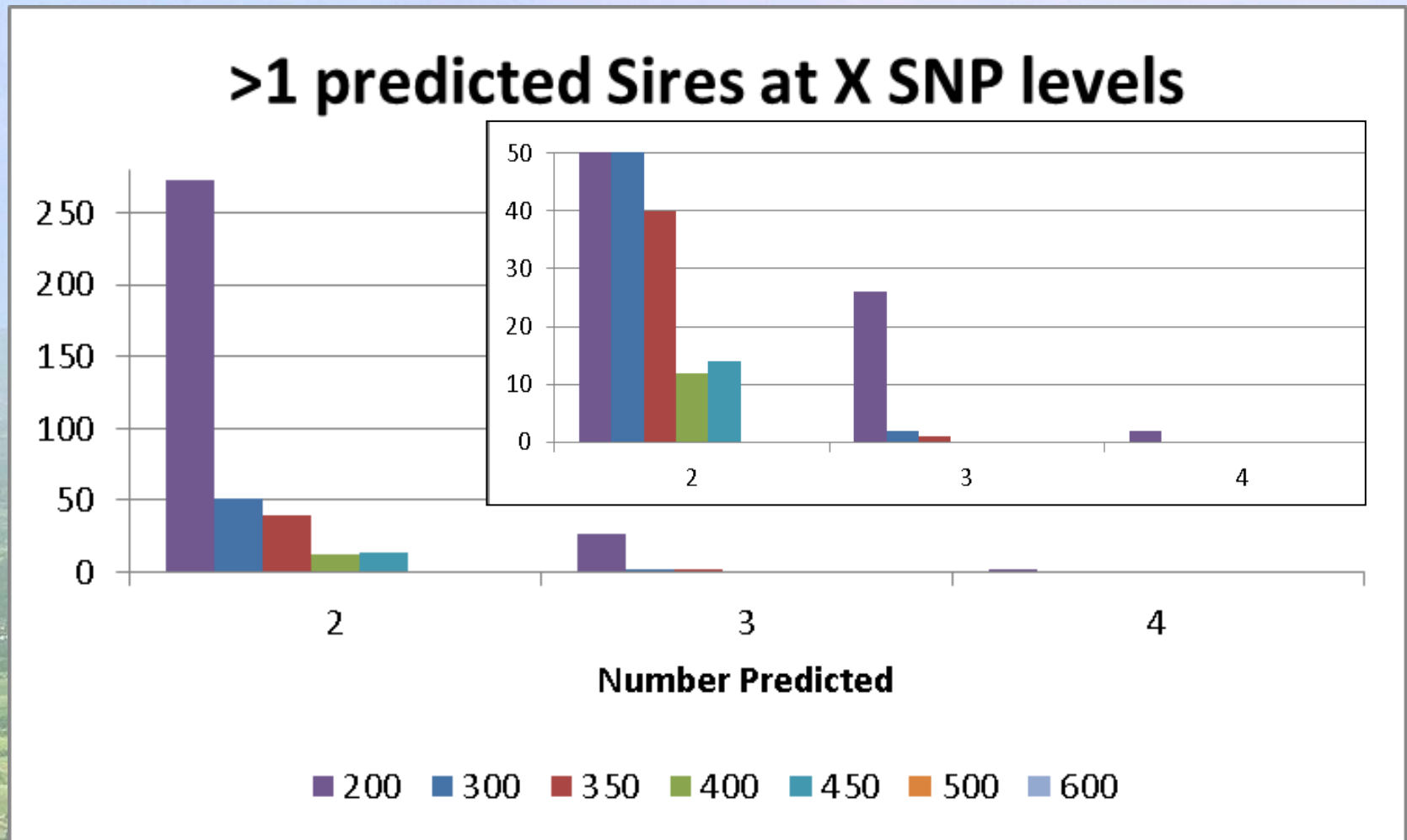


How Many SNP to Predict 1 Sire

- 56,000 genotyped animals
- SNP densities tested
 - ISAG200
 - Plus top 100, 200,1800 MAF SNP
- 9,000 sire validated animals
- Predict sire/dams

Animals	56,000
breed	Jun-14
HOL	68.65%
LIM	7.94%
CHA	7.41%
AAN	4.42%
SIM	2.35%
HER	3.06%
BBL	1.01%
MSH	0.06%
SAL	0.04%
JER	0.17%
PAR	0.17%
LMS	1.91%
BAQ	0.04%
AUB	0.00%
CHL	1.68%
PIE	0.55%
HFD	0.17%
MON	0.14%
IRM	0.00%
NWR	0.09%
RED	0.01%

Sire Prediction with 200, 300,... SNP



Space between Validation and Fail

2000 SNP

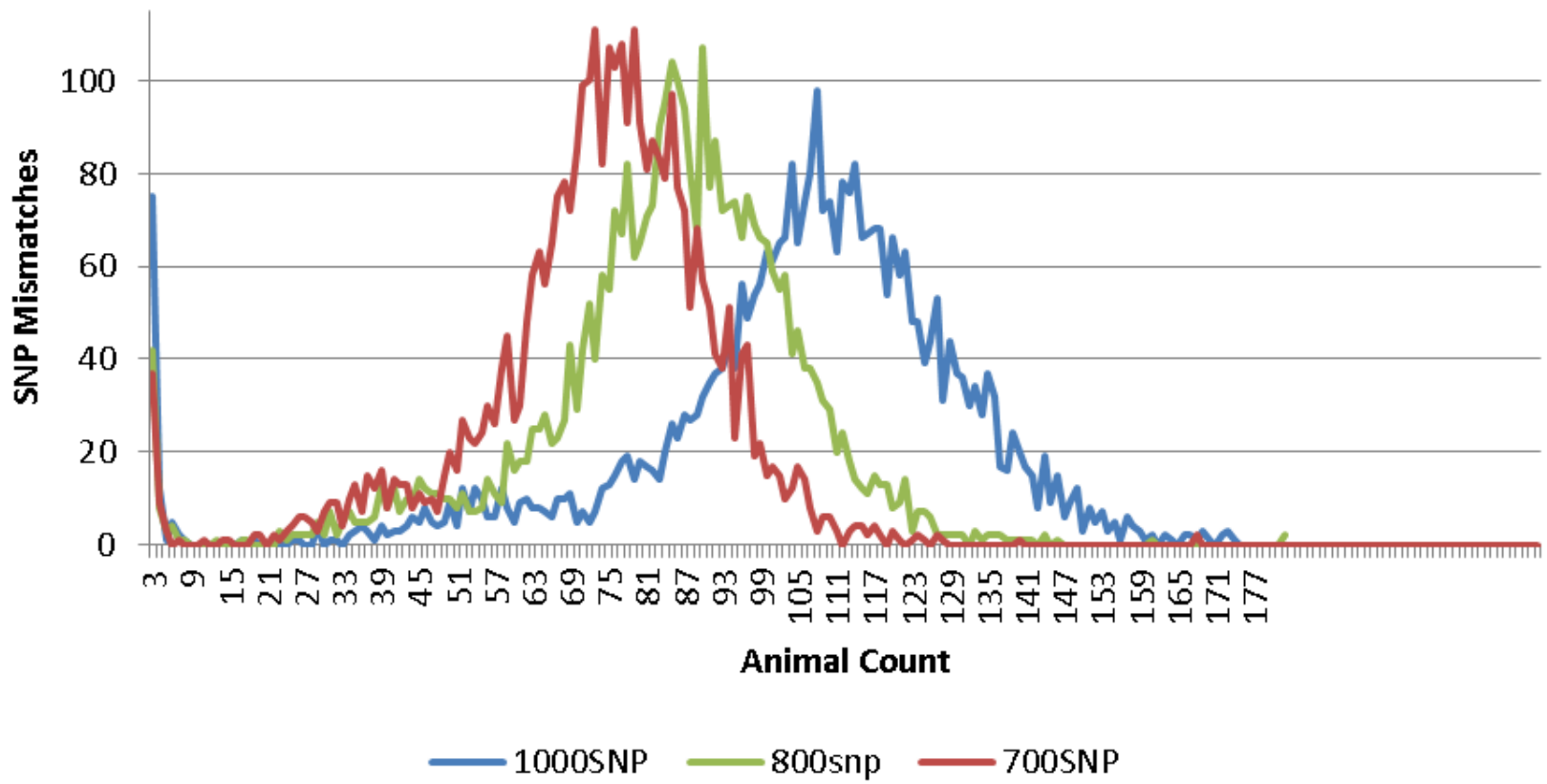
Validate

Fail

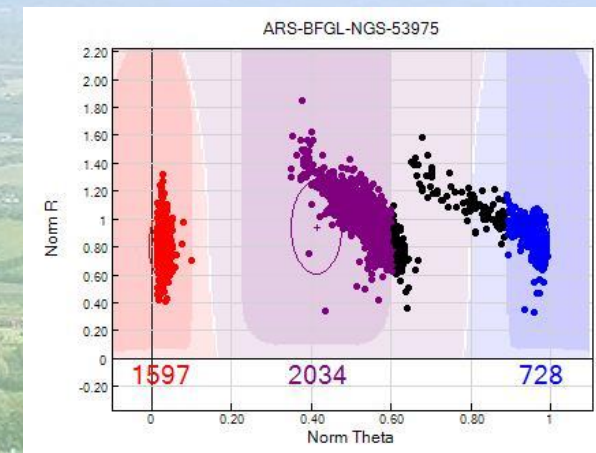
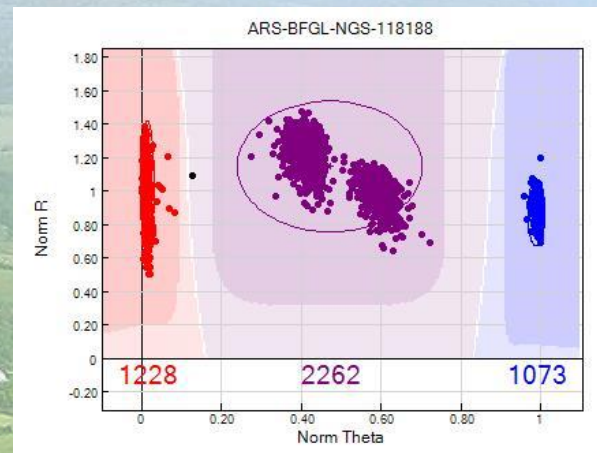
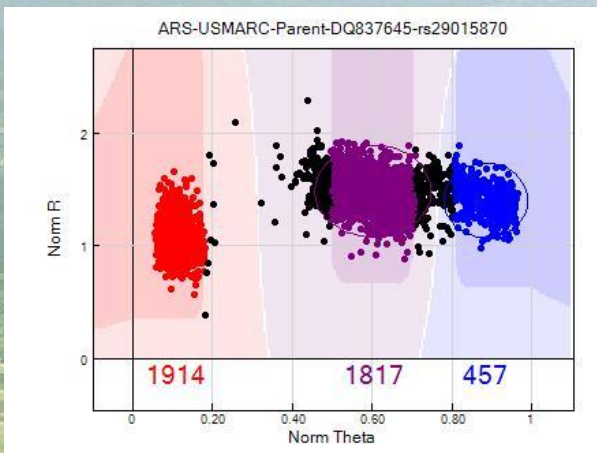
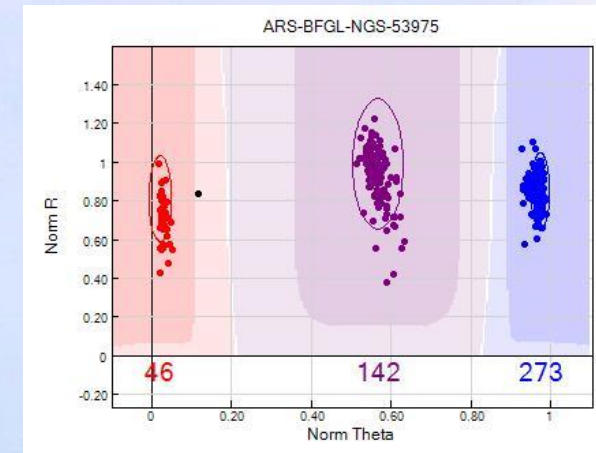
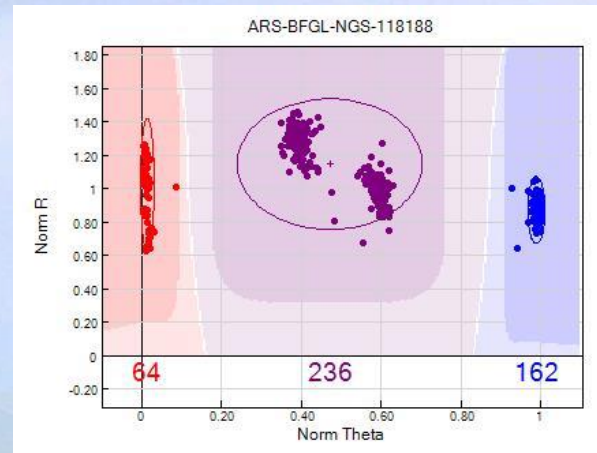
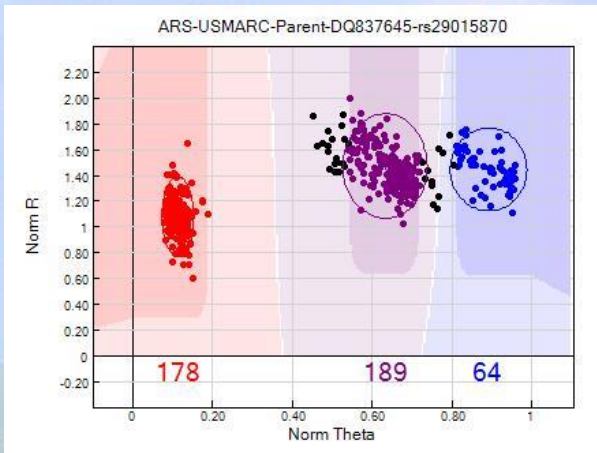


Space between Validation and Fail

**SNP Mismatches for sire validations
114,000 animals**

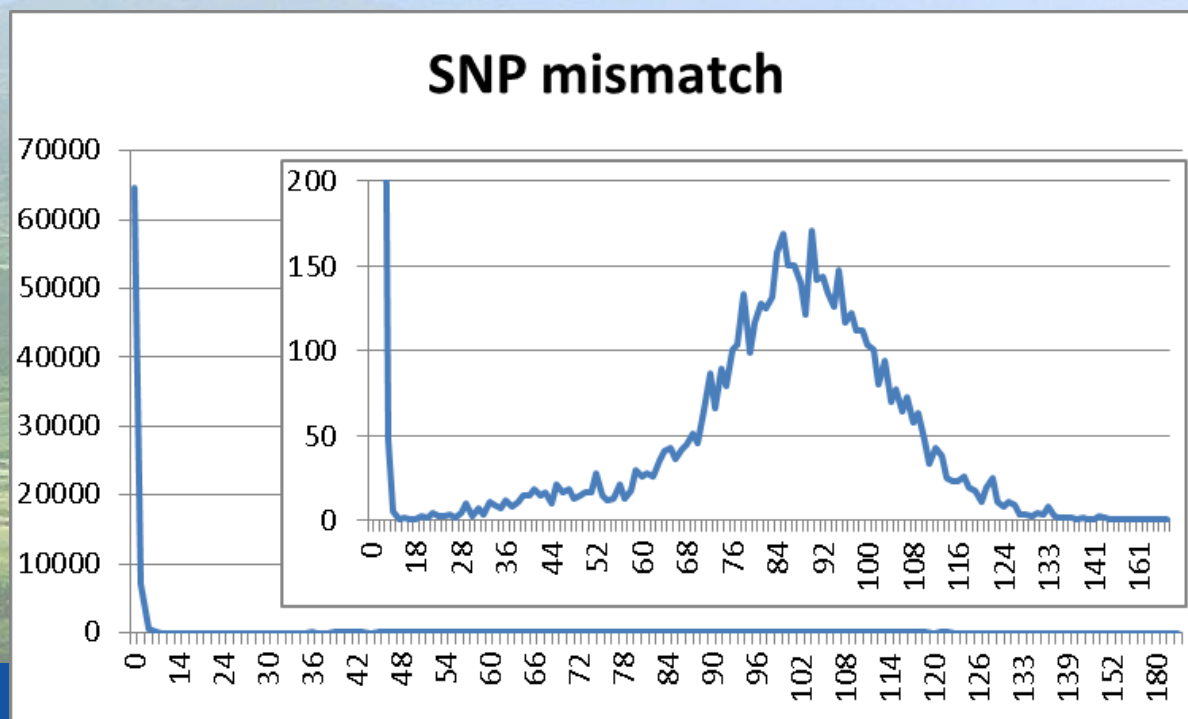


SNP Refinement QC Quality: Clusters when processing 400 vs 4K / week



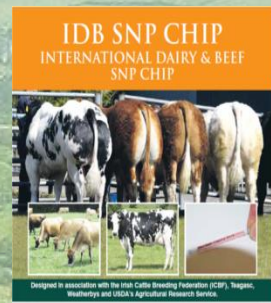
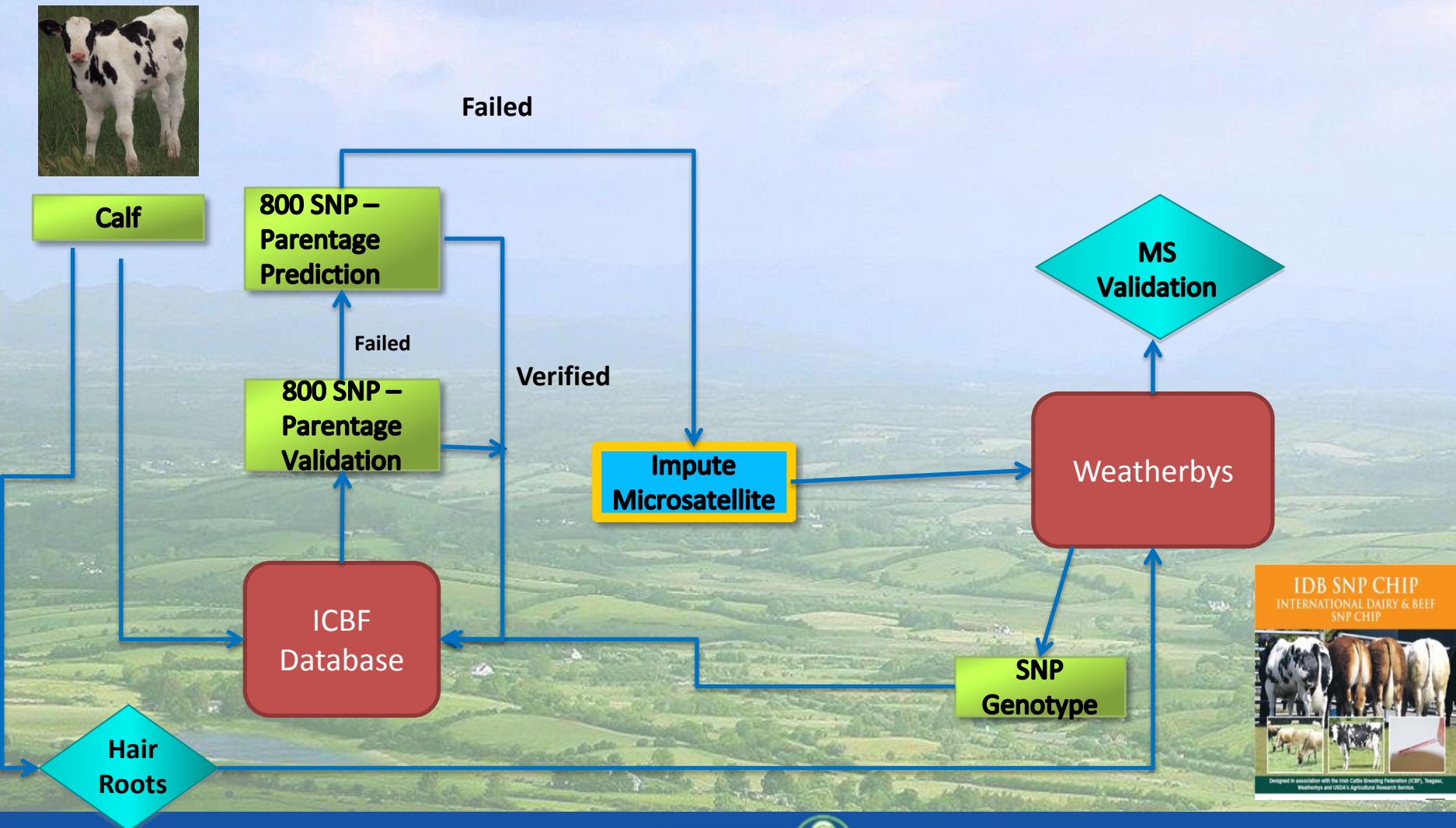
Recommend: Use >500 SNP for Validation

- ICBF Switched to 800 SNP July 2014
- Refinement in February 2015



Animals	56,000	180,000
breed	Jun-14	Feb-15
HOL	68.65%	30.08%
LIM	7.94%	22.34%
CHA	7.41%	18.68%
AAN	4.42%	7.22%
SIM	2.35%	6.77%
HER	3.06%	4.66%
BBL	1.01%	2.75%
MSH	0.06%	1.57%
SAL	0.04%	0.92%
JER	0.17%	0.67%
PAR	0.17%	0.64%
LMS	1.91%	0.59%
BAQ	0.04%	0.59%
AUB	0.00%	0.53%
CHL	1.68%	0.52%
PIE	0.55%	0.17%
HFD	0.17%	0.07%
MON	0.14%	0.05%
IRM	0.00%	0.03%
NWR	0.09%	0.03%
RED	0.01%	0.03%

Irish Parent Verification Process



Microsatellite Imputation

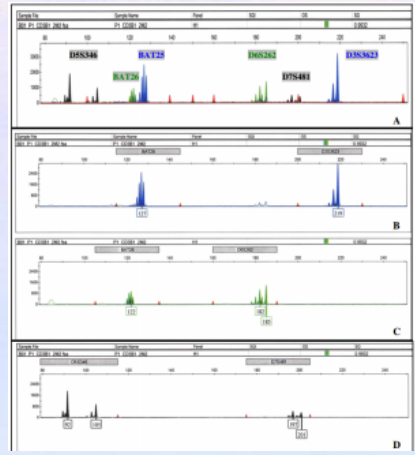
Initial reference population:

7,076 *Bos taurus* MinSNP = 892

Current reference population

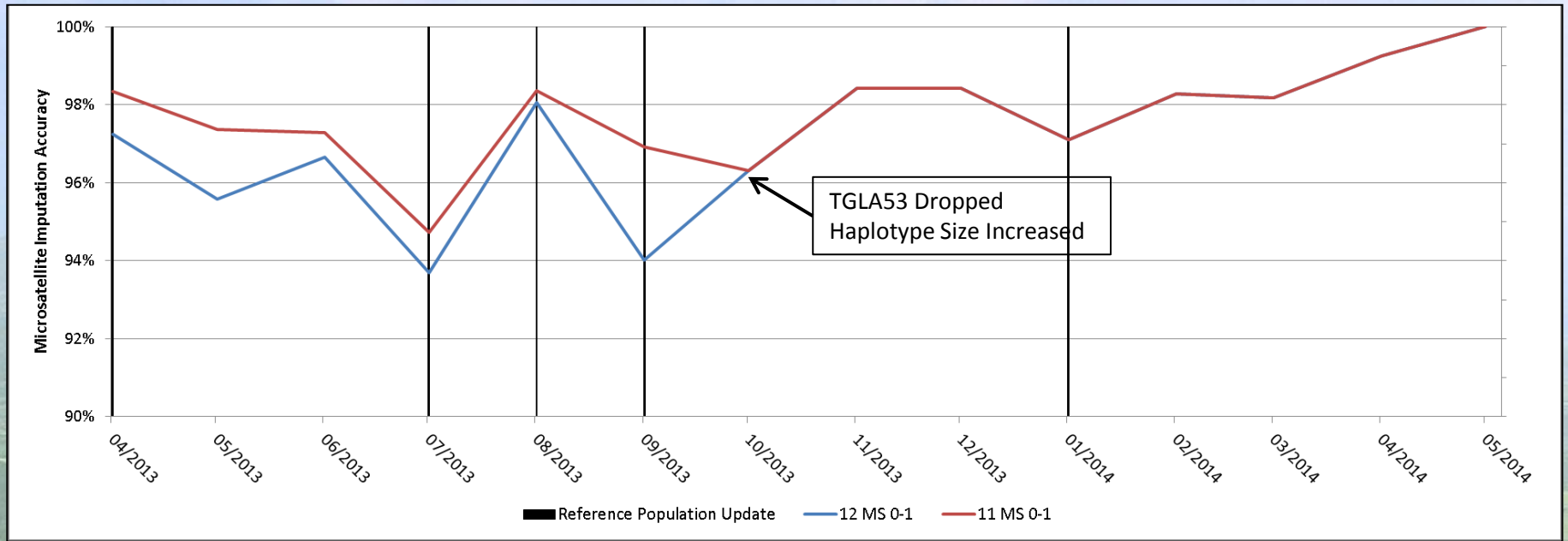
N= 8,483

MinSNP = 920



Haplotype	Angus	Ayshire	BelgianBlue	Charolais	Guernsey	Hereford	Holstein	Jersey	Limousin	RedAngus	Shorthorn	Simmental	Overall
AAABABBAABBAABBBBBAABBAABBAABAA/		266	266	266		266			266	266	266	266	266
BBBBBAAAABBAABBBBAABBAABBAABAA/													262
AABBABBAABBAABBAABBAABBAABBAAB/							270						270
BBBBBAAAABBAABBBBAABBAABBAABAA/								262					262
AABBABBAABBAABBBBBAABBAABBAABA/					280					280			280
AABBABBAABBAABBAABBAABBAABBAAB/													286
AABBABBAABBAABBAABBAABBAABBAAB/												268	268
AABBABBAABBAABBBBBAABBAABBAABA/						262							262
AABBABBAABBAABBBBBAABBAABBAABA/													268
BBBBBAAAABBAABBBBBAABBAABBAABA/				272				272					272
AABBABBAABBAABBBBBAABBAABBAABA/		260											260
AABBABBAABBAABBAABBAABBAABBAABA/											260		260
AAABABBAABBAABBBBBAABBAABBAABA/				268					268			268	268
AAABABBAABBAABBAABBAABBAABBAABA/	262										262	262	262
AABBABBAABBAABBBBBAABBAABBAABA/	258	258		258							258		258
AAABABBAABBAABBBBBAABBAABBAABA/	266		266			266	266						266
AAABABBAABBAABBBBBAABBAABBAABA/				268					268			268	268
AAABABBAABBAABBBBBAABBAABBAABA/							262						262
AABBABBAABBAABBAABBAABBAABBAABA/				266					266			266	266
AABBABBAABBAABBAABBAABBAABBAABA/						266						266	266

Irish Microsatellite Imputation Accuracy



Impact of Microsatellite Imputation

- >17,000 MS imputed Irish animals (May, 2014)
 - SNP parentage failed (small #)
 - Embryo transfer animal
 - No SNP genotype on sire (most of them)
- Saved Irish cattle farmers **>€350,000**
 - MS genotyping ~€20/animal
- >98% accuracy
 - 2+ misconcordances = MS genotyped

IDB SNP CHIP
INTERNATIONAL DAIRY & BEEF
SNP CHIP

Designed in association with the Irish Cattle Breeding Federation (ICBF), Teagasc, Weatherbys and USDA's Agricultural Research Service.

This custom chip is the very latest design catering for both Beef and Dairy.

The chip consists of the Illumina LD (7K) base content plus a further 10,000 (10K) SNPs carefully selected to ensure very high imputation accuracy to HD to convert to Microsatellite data for parentage verification. The extra panel of SNPs provides the very latest dual product for both Beef & Dairy breeds.

Both the chip and additional ISAAC recommended SNP parentage panels are present on the chip.

The IDB also contains a comprehensive selection of genetic markers to screen for genetic disorders in major genes.

For more details Contact: Weatherbys Ireland DNA Laboratory
+353(0)45875521
j.yrini@weatherbys.ie WEATHERBYS
ireland

Addition use for Microsatellite Imputation

Correcting Human Error

Bull DNA sent for HD	MS matches to
Hillcrest Jerome	Hillcrest Jerome
Lorabar Mighty Prince	Thrunton Unstoppable
Thrunton Unstoppable	Maine Dragon (FT)
Hillcrest Champion	Lorabar Mighty Prince D113 (FT)
Curaheen Tyson	Hillcrest Champion
Woodhall Dynamite	Curaheen Tyson
Sacombe Wishful Thinking	Woodhall Dynamite
Jupiter (JPR)	Jupiter (CH)
Blakestown Artiste (BZT)	Blakestown Artiste
Hurtig Fleckvigh	Hurtig
Dovea Napoleon (NAP)	Dovea Napoleon
Paulern Ulysses	Dovea Napoleon
Maine Dragon	Paulern Ulysses
Fieldson Alfy	Fieldson Alfy
Friarstown Edition	Friarstown Edition G028
Freetown Regent	Friarstown Edition G028
Exodus	No match found
Rainbow Hills Independence 46X	No match found
BUT	No match found
Bellman Of Knockadrianan	No match found

Beef Commercial herds

BGS Males	N=21,000
Sire SNP validate	55.00%
SNP Predict	4.70%
SNP Fail	2.50%
MS Validate	16.50%
MS Fail	1.50%
Sire not Genotype	20.00%
Overall Males	
Sire Validate	76%
Sire Fail	4%
Limbo	20%

Hol-UK samples

- 69 IDB genotyped with >90% call rate
 - 6 with 1 marker exclusion
 - 1 with 2 marker exclusion
 - 1 with 3 marker exclusion
 - 59 FPT or PPT

Breeding Management: Select the Best Replacement Heifer

Genomic Breeding Value

€127

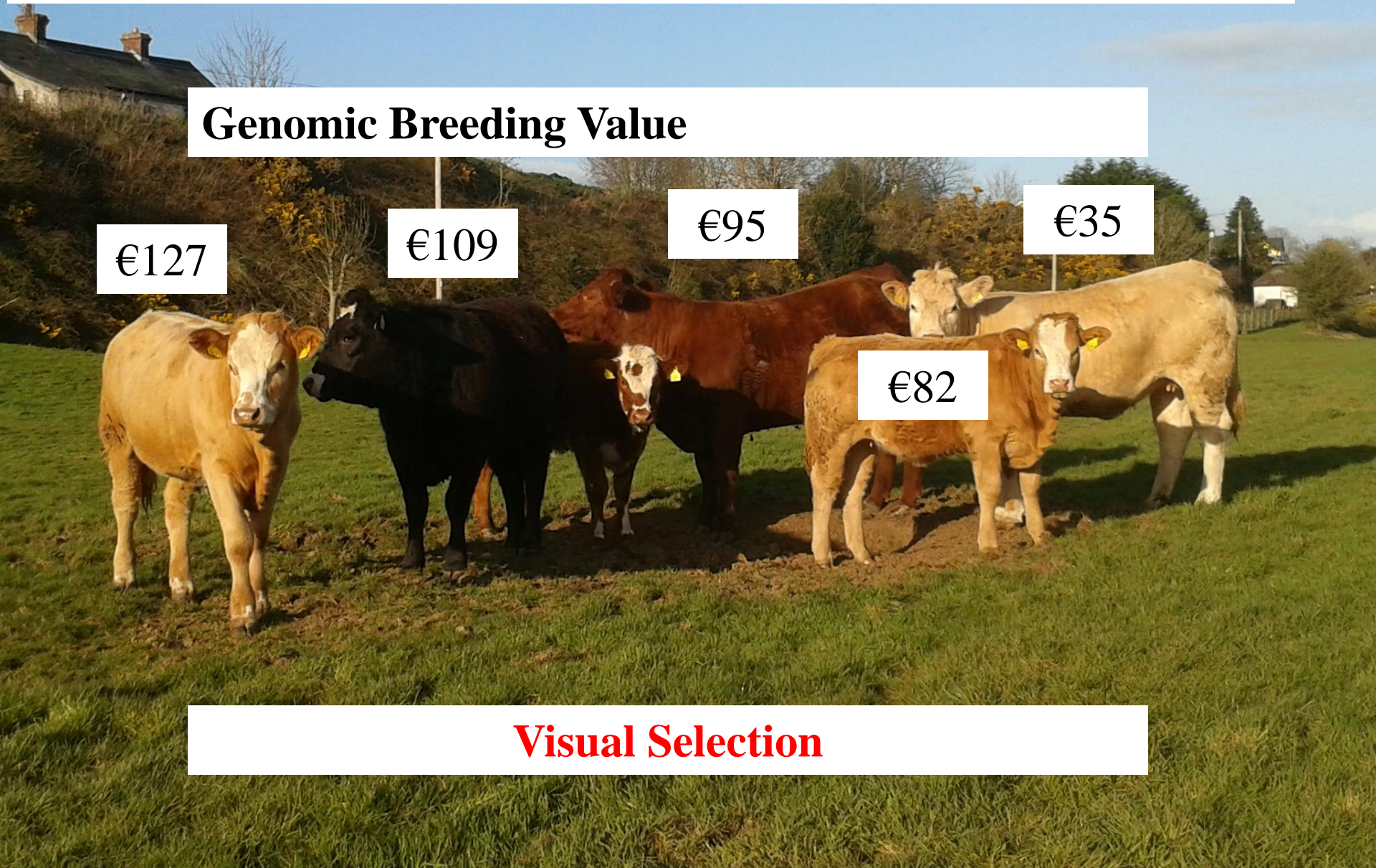
€109

€95

€35

€82

Visual Selection



Breeding Management: Sire Selection



€127

Bull	Name	HO %	Sire	EBI	EBI rel	Proof Source	Milk	Fert	Calv	Beef	Maint	Mmgt	Health
WLY	IMLEACH LUCKY WHISTLER	63	MWH	327	54	GS	85	184	44	-16	19	7	4
RBH	(IG) SRUTHAN ROBERTO	63	HYZ	309	53	GS	77	200	36	-15	14	2	-7
DBW	DOONMANAGH DSU BOWSER	75	DSU	307	51	GS	85	175	33	-10	20	1	2
	COOKSTOWN												

Genetic Disease Carrier??

Breeding Management:

Genetic Disease and Major Genes

Validated		
BLAD ★	DUN	NH
ABCG2	EBD	OS
AM_662	GH_2141	PCS
BC_A1A2	GH_2291	PHA1
BC_A3	GHR_F279Y	PHA2
Black_E	HH1 ★	PMT_491
BM	HH3 ★	PMT_632
BY ★	HH4 ★	PMT_857
CAPN1_316	HY_KRT71	POLL_C ★
CAPN1_4751	JH1	POLL_H ★
CAPN1_530	KC	PROTO
CAST_282	LGB	RED_e
CAST_2870	MC	RNF11
CAST_2959	MF	SD1
CMD1	MH2	SMA
CMD2	MSU_SH	STAT1
CSN2_A3	MYO_C313Y	STAT3_19069
CT	MYO_E226X	STAT3_25402
CTS	MYO_E291X	STAT5_13244
CVM ★	MYO_F94L	STAT5_13319
DGAT1 ★	MYO_nt821	STAT5_13516
DLT3	MYO_Q204X	TH-Improver
DUMPS ★	MYO_S105C	

In Progress		
AED	HA	MYO_nt748-78
AH1	HH2	PWCS
AM_961	HH5	SAA_MOCS1
BD1	HI	SAA_SUOX
BD2	HY_HEPHL1	SCD1
BH1	IBK	SCD2
BH2	IE	Scurs_2
BSD	LAA	SD2
CD2	MOD	STAT5_12195
ChrY_Fem	MPS_IIB	STAT5_3117
CHS	MSU_HE	TG5_257
CMS	MYO_D182N	TG5_335
CWH	MYO_nt267	TM
Dilution	MYO_nt324	Weaver
Dilutor	MYO_nt374	Xan_II
Dwarf_PRKG2	MYO_nt414	YMF
Factor_XI	MYO_nt419	

Needed	
Agouti	MYO_nt387
Albino_TYR	MYO_-nt747+11
AX	MYO_nt747+7
CD	NCL
CD1	PMEL17_A612E
Dward_GH1	PMEL17_del
DWBD	RVC
FGMA	SP
Goitre	TG5_422
IC	THR
Marfan	

IDB SNP CHIP
INTERNATIONAL DAIRY & BEEF
SNP CHIP

Designed in association with the International Dairy & Beef SNP Chip project, Weatherby's Animal Health and Research Services.

This custom chip is the very latest design catering for both beef and dairy. The chip consists of the Illumina LD (75) base content plus a further 10,000 SNPs. SNPs are selected to ensure very high imputation accuracy in HD to convert to Microarray data for genotyping. The same panel of SNPs provides the very latest dual product for both Beef & Dairy breeds.

With the use of our additional GAD recommended SNP genotyping panels are present on the chip.

The IDB also contains a comprehensive selection of genetic markers to screen for genetic disorders in large genes.

For more details Contact: weatherby@weatherbys.co.uk
+353(0)45875521
www.weatherbys.co.uk

National Genetic Disease and Major Gene Overview: from >100,000 Genotyped Animals

Trait	Carrier Count	National %
ABCG2	583	0.583%
Agouti	0	0.000%
AM_662	1	0.001%
BC_A1A2	44239	44.239%
BC_A3	124	0.124%
BLACK_E	25751	25.751%
BLAD	221	0.221%
BM	17	0.017%
BY	394	0.394%
CAPN1_316	28042	28.042%
CAPN1_4751	43504	43.504%
CAPN1_530	36252	36.252%
CAST_282	42538	42.538%
CAST_2870	45252	45.252%
CAST_2959	30934	30.934%
CMD1	230	0.230%
CMD2	89	0.089%
CSN2_A3	124	0.124%
CT	63	0.063%
CTS	529	0.529%
CVM	727	0.727%
DGAT1	22061	22.061%
DLT3	7017	7.017%
DUMPS	1	0.001%
DUN	13	0.013%
EBD	0	0.000%
HH1	427	0.427%
HH3	768	0.768%
HH4	62	0.062%
HY_KRT71	336	0.336%
JH1	31	0.031%
KC	44768	44.768%
LGB	44202	44.202%



Trait	Carrier Count	National %
MC	0	0.000%
MF	33	0.033%
MH2	41	0.041%
MSU_SH	0	0.000%
MYO_C313Y	248	0.248%
MYO_E226X	54	0.054%
MYO_E291X	3	0.003%
MYO_F94L	23295	23.295%
MYO_nt821	5281	5.281%
MYO_Q204X	54	0.054%
MYO_S105C	4	0.004%
NH	0	0.000%
OS	9	0.009%
PCS	6	0.006%
PHA1	3	0.003%
PHA2	0	0.000%
PMT_491	0	0.000%
PMT_632	6	0.006%
PMT_857	7	0.007%
POLL_C	9536	9.536%
POLL_H	63	0.063%
PROTO	765	0.765%
RED_E	24979	24.979%
RNF11	277	0.277%
SD1	13475	13.475%
SMA	7	0.007%
STAT1	26176	26.176%
STAT3_19069	40188	40.188%
STAT3_25402	43496	43.496%
STAT5_13244	44630	44.630%
STAT5_13319	12206	12.206%
STAT5_13516	44725	44.725%
TH_IMPROVER	195	0.195%



Breeding Management: Avoid Carrier X Carrier Mating

€127

Bull	Name	HO %	Sire	EBI	EBI rel	Proof Source	Milk	Fert	Calv	Beef	Maint	Mmgt	Health
WLY	IMLEACH LUCKY WHISTLER	63	MWH	327	54	GS	85	184	44	-16	19	7	4
RBH	(IG) SRUTHAN ROBERTO	63	HYZ	309	53	GS	77	200	36	-15	14	2	-7
DBW	DOONMANAGH DSU BOWSER	75	DSU	307	51	GS	85	175	33	-10	20	1	2
	COOKSTOWN												

Animal 1E000000XXXXX

Disease	Abbreviation	Status
Silver_Char_Dilutor_PME1_	Silver Diluter	0
Holstein Haplotype 3_SMC2_chr8:95410507T>C	HH3	1
Holstein Haplotype 1_APAF1_chr5:6315040C>T	HH1	0
Brachyspina_FANCI_chr21:21184870del188198	BY	0
Holstein Haplotype 4_GART_chr1:1277227A<C	HH4	0
Montbellarde Haplotype 1_SHBG_chr19:27956790C>T	MH1	0
Montbellarde Haplotype 2_SLC37A2_chr29:28879810C>T	MH2	NA
Jersey Haplotype 1_CWC15_chr15:15707169C>T	JH1	0

Animal 1E000000XXXXX

Disease	Abbreviation	Status
Silver_Char_Dilutor_PME1_	Silver Diluter	0
Holstein Haplotype 3_SMC2_chr8:95410507T>C	HH3	1
Holstein Haplotype 1_APAF1_chr5:6315040C>T	HH1	0
Brachyspina_FANCI_chr21:21184870del188198	BY	0
Holstein Haplotype 4_GART_chr1:1277227A<C	HH4	0
Montbellarde Haplotype 1_SHBG_chr19:27956790C>T	MH1	0
Montbellarde Haplotype 2_SLC37A2_chr29:28879810C>T	MH2	NA
Jersey Haplotype 1_CWC15_chr15:15707169C>T	JH1	0

Animal 1E000000XXXXX

Disease	Abbreviation	Status
Silver_Char_Dilutor_PME1_	Silver Diluter	0
Holstein Haplotype 3_SMC2_chr8:95410507T>C	HH3	1
Holstein Haplotype 1_APAF1_chr5:6315040C>T	HH1	0
Brachyspina_FANCI_chr21:21184870del188198	BY	0
Holstein Haplotype 4_GART_chr1:1277227A<C	HH4	0
Montbellarde Haplotype 1_SHBG_chr19:27956790C>T	MH1	0
Montbellarde Haplotype 2_SLC37A2_chr29:28879810C>T	MH2	NA
Jersey Haplotype 1_CWC15_chr15:15707169C>T	JH1	0

Animal 1E000000XXXXX

Disease	Abbreviation	Status
Silver_Char_Dilutor_PME1_	Silver Diluter	0
Holstein Haplotype 3_SMC2_chr8:95410507T>C	HH3	1
Holstein Haplotype 1_APAF1_chr5:6315040C>T	HH1	0
Brachyspina_FANCI_chr21:21184870del188198	BY	0
Holstein Haplotype 4_GART_chr1:1277227A<C	HH4	0
Montbellarde Haplotype 1_SHBG_chr19:27956790C>T	MH1	0
Montbellarde Haplotype 2_SLC37A2_chr29:28879810C>T	MH2	NA
Jersey Haplotype 1_CWC15_chr15:15707169C>T	JH1	0

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