Genomics – A New Era for Cattle Breeding.

ICBF & Teagasc Genomics Conference.

Killeshin Hotel Portlaoise.

14th November 2012.

Objective of conference.

- An opportunity to understand genomics, from the basic concepts through to it’s role in parentage identification and future genetic improvement programs.

Session 1. Genomics & parentage identification (10 am – 1 pm)

- Chair: Gerard Brickley, beef farmer and herdbook representative on board of ICBF.
- Introduction to animal breeding, including genomics – Dr. Sinead McParland, Teagasc.
- Genomics and parentage verification – Dr. Matt McClure, US Department of Agriculture.
- Developing a customised chip for Ireland – Dr. Mike Mullen, Teagasc.
- Implementation of genomic services – Mary McCarthy, ICBF and Dr John Flynn, Weatherby’s Ireland.
- Role of genomics in Irish dairy and beef breeding programs (Part 1) – Dr. Andrew Cromie, ICBF.
- Discussion.

Session 2. Genomics & genetic improvement (2-5 pm).

- Chair: John O’Sullivan, dairy farmer and chairman of board of ICBF.
- Role of genomics in Irish dairy and beef breeding programs (Part 2) – Dr. Andrew Cromie, ICBF.
- Developments in beef genomics – Dr. Donagh Berry, Teagasc
- Developments in dairy genomics – Dr. Francis Kearney, ICBF
- Where next for genomics and cattle breeding – Dr. Matt McClure, US Department of Agriculture.
- Discussion.

IRISH CATTLE BREEDING FEDERATION

Role of Genomics in Irish Dairy and Beef Breeding Programs. Part II. Genetic Gain.

Andrew Cromie, ICBF.

12th November 2012.

Genomics & Breeding Programs

- Genetic improvement (€);
  - Quality & quantity of data (***ID, ancestry*** & performance).
  - Profit based genetic indexes (EBI & €uro-Stars),
  - ***Selecting the best*** to breed the next generation.
- Focus on two areas; (i) parentage verification and ***(ii) genetic gain.***

Genetic gain – role of parentage.

- Parentage verification is vital.
  - 5-10% parentage errors for sires.
  - What level on dams? Low in pedigree beef herds, but a further 5-10% in large dairy herds.
- Impacts on accuracy of evaluations and on genetic gain.
  - 10% parentage errors = ~5% loss in gain (UK, US, NLD……)

Genetic gain – Importance of genetic defects.

- System to identify and “purge” out genetic defects.
  - Establish clear protocol, e.g., (i) Identification of defect, (ii) collect DNA on calves & contemporaries, (iii) genotype on HD, (iv) identify and sequence region(s), and (iv) identify causal mutation.
- Key infra-structure is now in place.

Genetic gain – the Theory.

- Extensive work undertaken in breeding programs.
  - Veerkamp, 2001, Meuwissen 2008, McHugh 2010 & Amer 2011.
- Original Veerkamp work, 100 bulls * 100 daughters = €12.5/cow/year *(EBI terms)*
  - Genomics (selection intensity) = 50% more gain (Meuwissen, 2008).
  - Genomics (accuracy of selection) = further 50% gain (McHugh 2010 & Amer 2011).

Genetic Gain – the practice.

	ALL Bulls		Daughter Proven		Genomic Young Bulls	
Year	No. Bulls	EBI	No. Bulls	EBI	No. Bulls	EBI
2007	75	€131.6	75	€131.6		
2008	75	€130.1	75	€130.1		
2009	75	€174.0	53	€168.2	22	€188.8
2010	75	€196.5	40	€192.0	35	€201.8
2011	75	€205.1	45	€200.7	30	€211.8
2012	75	€220.0	42	€216.3	33	€224.8

- Genetic gain = €12.7/annum.
- Inclusion of GS bulls and average EBI of list has increased by €5, compared to DP only (~+40%).
- Switch to all GS bulls and average EBI would increase by €12. (~+100%).

Genetic Gain – the Value.

- Genomics = +€5/calf/year.
- 150k AI bred calves.
- EBI * 2 = profit/lactation.
- 4.5 lactations.
- €6.75 million/annum (cumulative).
- Since launch in 2009, has/will generate additional €67 m for Irish dairy industry.
- Annual cost of ~10k “elite” males @ €40/animal = €400k.
  - Active AI bulls and Stock bulls (average EBI of stock bulls is €100.

Genetic Gain – Potential to identify the best.

Ranked on PA EBI	Parent Ave EBI	Genomic EBI	Genomic EBI of Top 50.
Top 100	€225	€224	€251
Top 500	€211	€213	€267
Top 1000	€204	€206	€272
Top 2000	€194	€196	€276
All 4,540	€170	€171	€277

- Males genotyped in 2011 & 2012. Selected on PA EBI and then genotyped. Moving from 1000 -> 2000, cost of €50k, but benefit of €5/female = further €6m/annum.
- Opportunity to cull bottom 20% from herd, herdbook….

Genetic Gain – The future.

- Widespread genotyping (all breeding stock). Increased profitability of Irish dairy and beef herds.
  - AI bulls, stock bulls, replacement females.
- Identifying the best animals worldwide for Ireland.
  - Genotype -> compute genomic index.
- Exporting animals worldwide.
  - Genotype -> compute genomic index.

Summary

- Genomics is adding €6-7m annually to profitability of our dairy industry. Opportunity to increase further in future.
  - Consistent with original theoretical work.
- Same opportunities exist for beef.
- Combination of; (i) accurate parentage, and (ii) opportunity to identify best.
- Costs are minimal relative to potential benefits (~50:1).
- Move to widespread genotyping. Cost:benefits are clear.

Acknowledgements

- Research Stimulus Fund (RSF-06-353; 11/S/112)
- SFI (G20416)
- Breed Societies and AI stations
- ICBF & Teagasc

Developments in beef genomics

Donagh Berry[1], Mike Mullen[2],
Mary McCarthy[3], Sinead Waters[2],
John McCarthy[3] and Andrew Cromie[3]

[1] *Teagasc, Moorepark,* [2] *Teagasc, Athenry,* [3] *ICBF*

donagh.berry@teagasc.ie

Genomics – a new era for cattle breeding. Portlaoise, November 2012

Genomic selection steps

- Step 1:
  - Estimate genetic marker (SNP) effects
  - Need a very large *reference* population
    - Proven AI sires will give best value for money (>1000 AI sires)
  - Is this possible within all breeds?
- Stage 2
  - Genotype candidates and apply pertinent prediction equations
  - (Accurately) select superior animals

Beef ≠ Dairy

- Less use of AI in beef
  - Pursuing natural mating bulls rather than AI bulls
- Smaller population size per breed
  - *Acrossbreed genomic predictions*
- Lots of crossbreeding
- Considerably different reliability for each trait
  - Milk and fertility so important yet lack reliable phenotypes

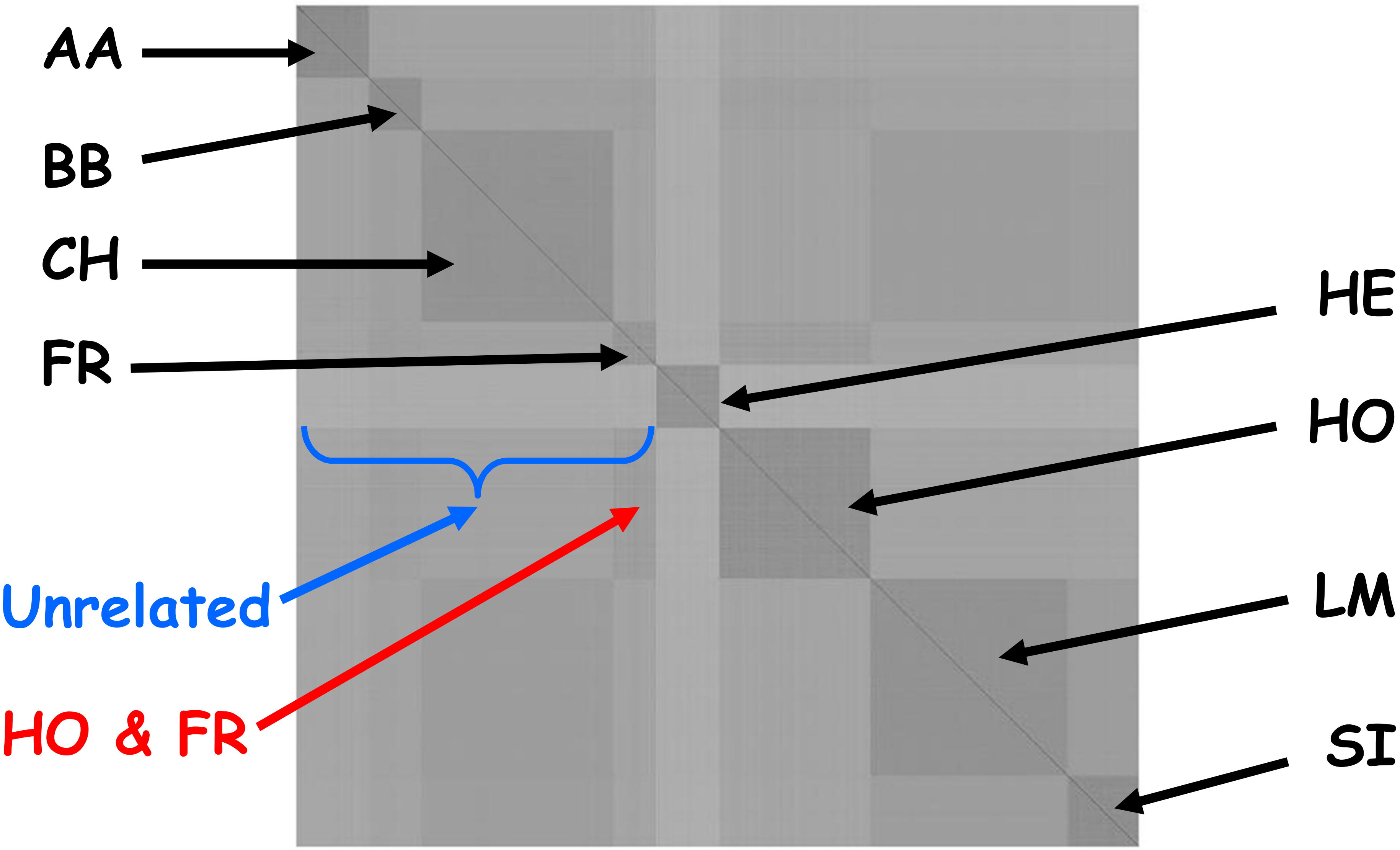
What is genomic selection doing?

Recombination ≈ f(distance + n generations)

Genotyping status

Breed	Total	Carcass wt	Direct calv. Diff.	Fertility
LM	730	672	709	167
CH	710	674	684	140
BB	196	157	190	45
HE	234	201	222	58
HF	721	701	707	145
SI	264	239	248	81
AA	269	235	256	48
TOTAL	3124	2879	3016	684

Fifty shades of grey



Testing

1. Assume the youngest proven bulls are calves with no information
2. Develop genomic SNP keys from older population
3. Genomically predict "calves" based only on DNA
4. Compare DNA/genomic predictions to actual proofs

Testing

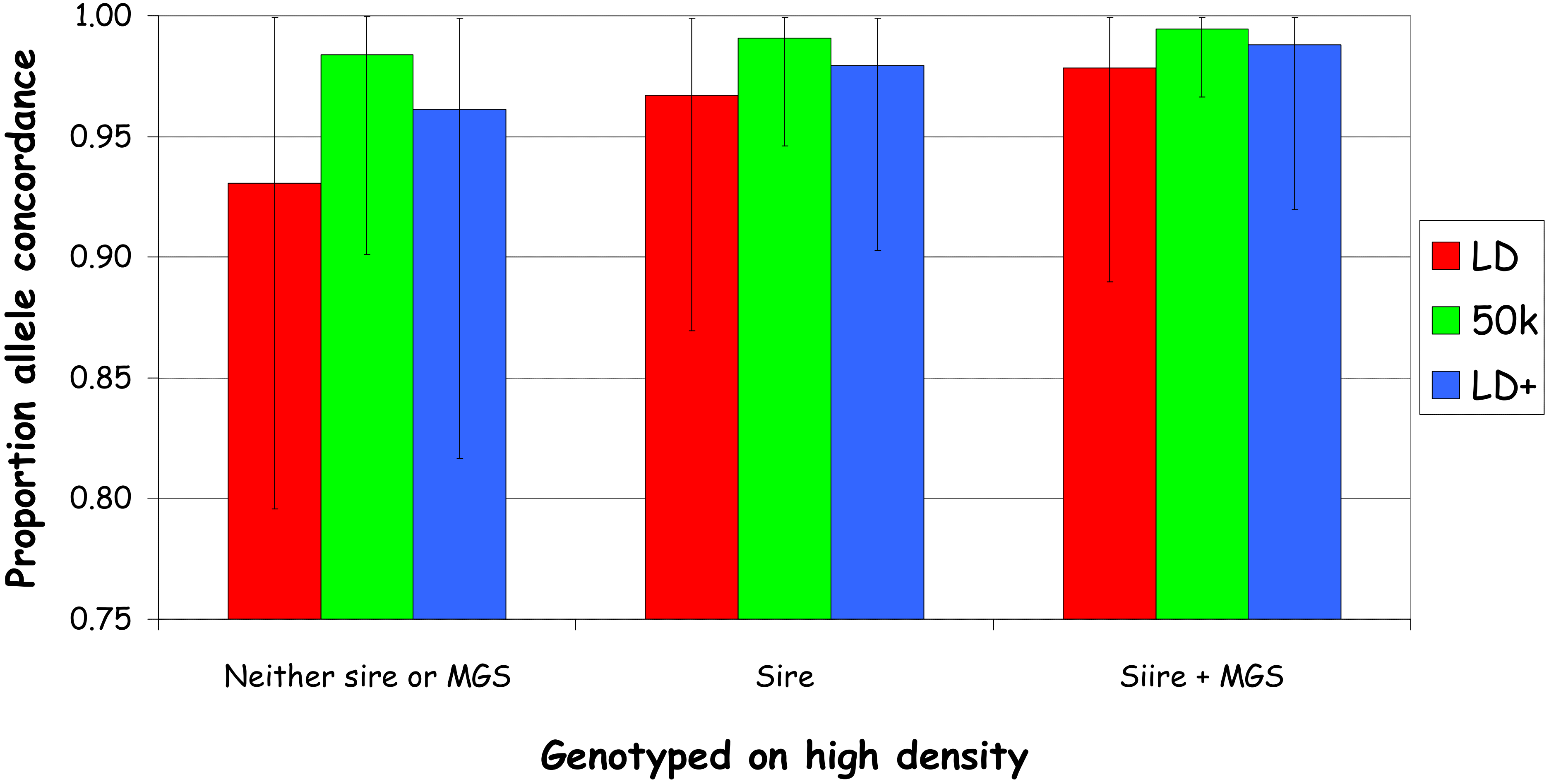
- Accuracy of genomic SNP key increases with population size
- LM & CH > SI >> AA & HE
- Little information to be gained from other breeds
  - Consistent with other international studies
- LM & CH are border-line okay to implement for some traits (~5% improvement)
  - Insufficient genotyped animals for other breeds

Conclusions

- Need a larger training population size per breed
  - DNA (hair/blood/semen) + phenotypes
  - High density genotypes (~€121 each)
- Impute (expensive) high density genotypes from (cheaper) lower density genotypes

- Make a big push to collect more genotypes in 2013

Imputing high density from 50K or low density



Way forward

- Funding
  - 4-year researcher dedicated to multi-breed (beef) genomics
- Genotype influential back-pedigree on high density (~€121 per animal)
- Genotype current proven bulls on “50k” (i.e., dairy) genotyping platform
- Move parentage to SNPs and up the testing rate
- Collaborate internationally

Collaborate internationally

- UK
  - 716 high density Limousin genotypes
- Canada
  - 480 HD and 560 50K each for AA, LM, CH, SI, & HE (Oct 2013)
  - Full sequence data
- US
  - Few thousand genotypes
- Australia
  - ~1,300 AA, LM, CH, SI, HE
- Who else?

10,000 by end 2013

Genomics in the US

Trait	Red AA (6,412)	AA (3,500)	SI (2,800)	LM (2,400)	HE (1,050)
BirthWt	0.75	0.64	0.65	0.58	0.43
WeanWt	0.67	0.67	0.52	0.58	0.32
Milk	0.51	0.51	0.34	0.46	0.22
Fat	0.90	0.70	0.29		0.40
REA	0.75	0.75	0.59	0.63	0.36
CED	0.60	0.69	0.45	0.52	0.43

Dorian Garrick

Conclusions

We need more genotypes!!

Funding acknowledgements

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IRISH CATTLE BREEDING FEDERATION

Developments in Dairy Genomics

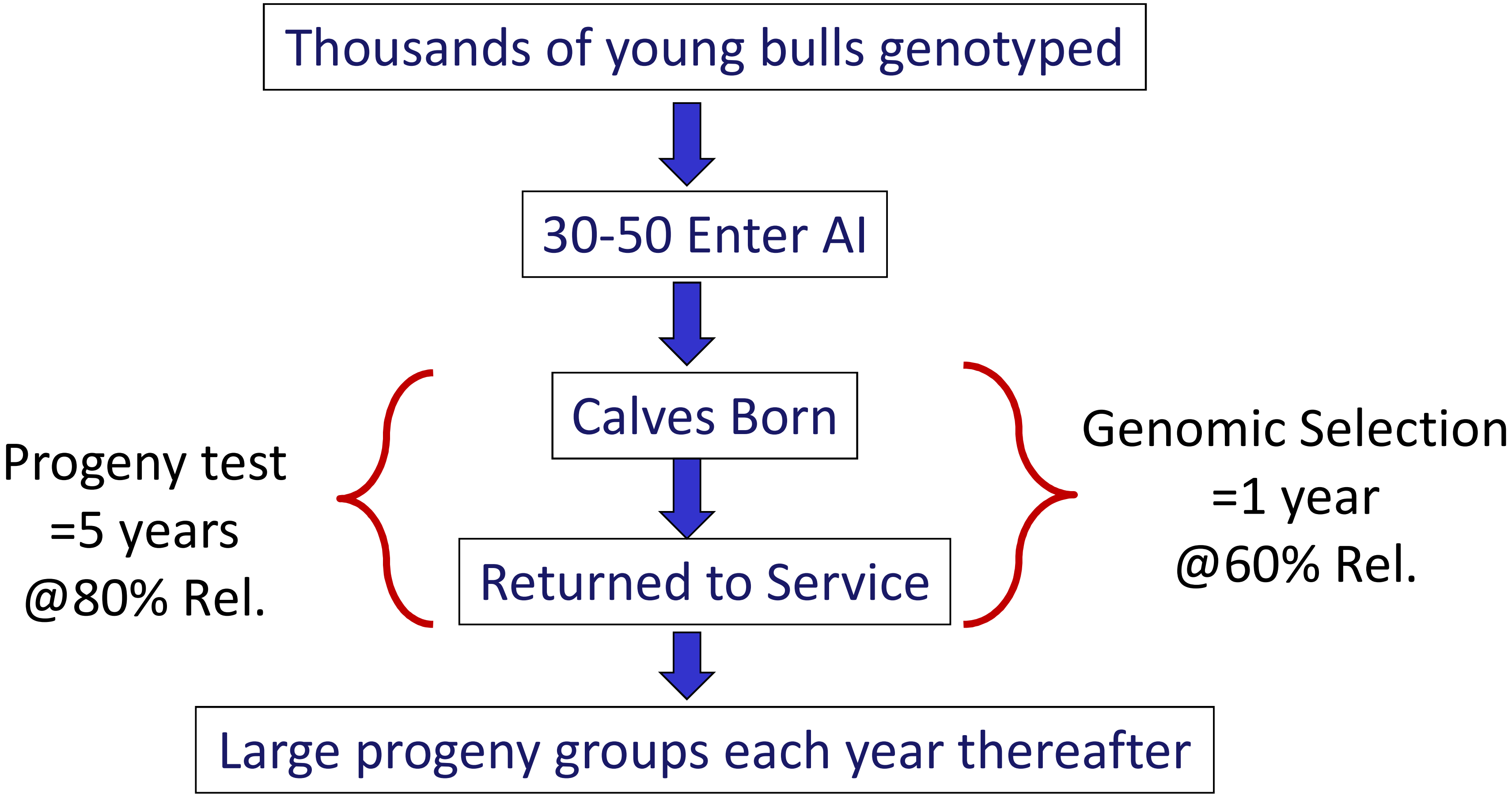
Francis Kearney[1] and Donagh Berry[2]
[1]ICBF, [2]Teagasc Moorepark

National Development Plan
Transforming Ireland

Genomic Selection

- Has revolutionised dairy cattle breeding
- Estimate EBI for a young animal based on a DNA profile
- Combine DNA & parentage information to generate a higher reliability EBI
- A genomic EBI is equivalent to having 10-15 daughters milking
- National Genomic evaluations introduced in Ireland in Spring 2009 (15 EBI traits, 20 type traits)

Genetic Gain



Thousands of young bulls genotyped

30-50 Enter AI

Calves Born

Returned to Service

Large progeny groups each year thereafter

Progeny test
=5 years
@80% Rel.

Genomic Selection
=1 year
@60% Rel.

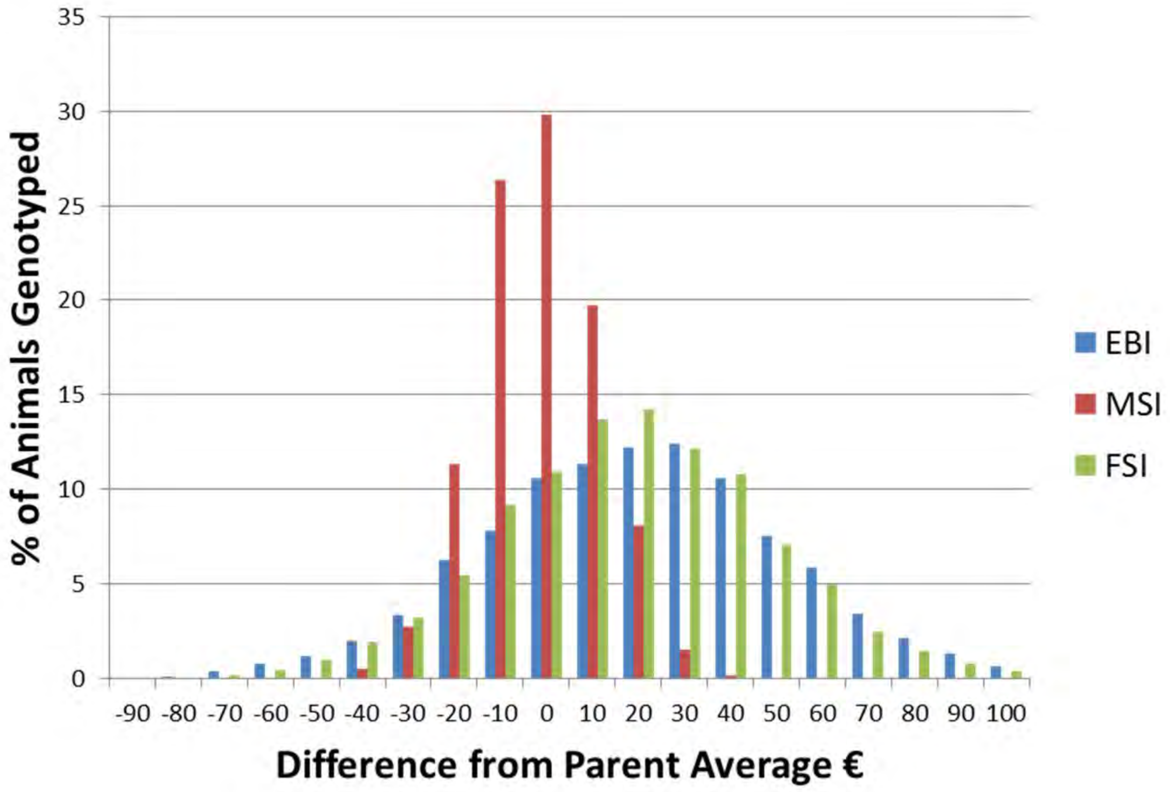
Genetic Gain

- In past waiting 10+ years to get high fertility & survival reliability
- With use of genomics we can get bigger daughter groups faster
  - higher reliability at a much younger age
- Only best quality proven bulls kept
- High quality GS & proven bulls to choose from

Genomic Evaluations

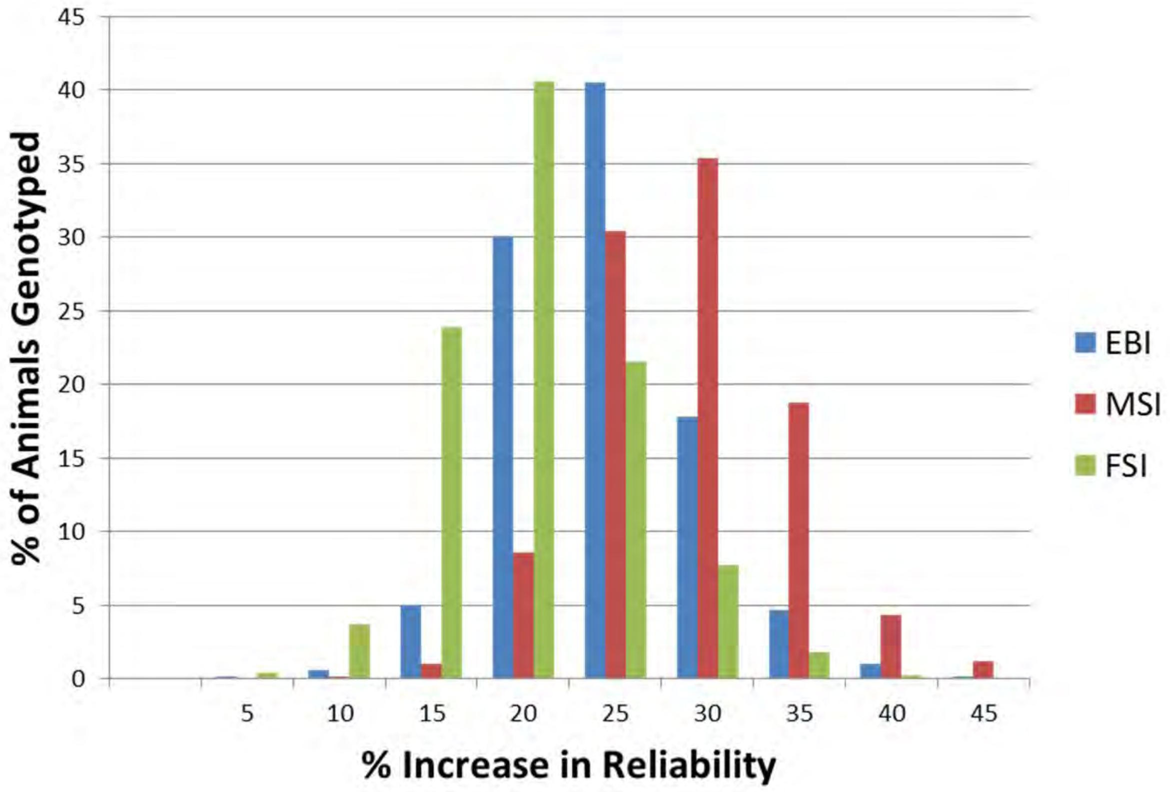
- Official Genomic Evaluation is a combination of parent average and genomic information
- Weighting given to the genomic component depends on the amount of the back pedigree that is genotyped and in the training population

Expected Change



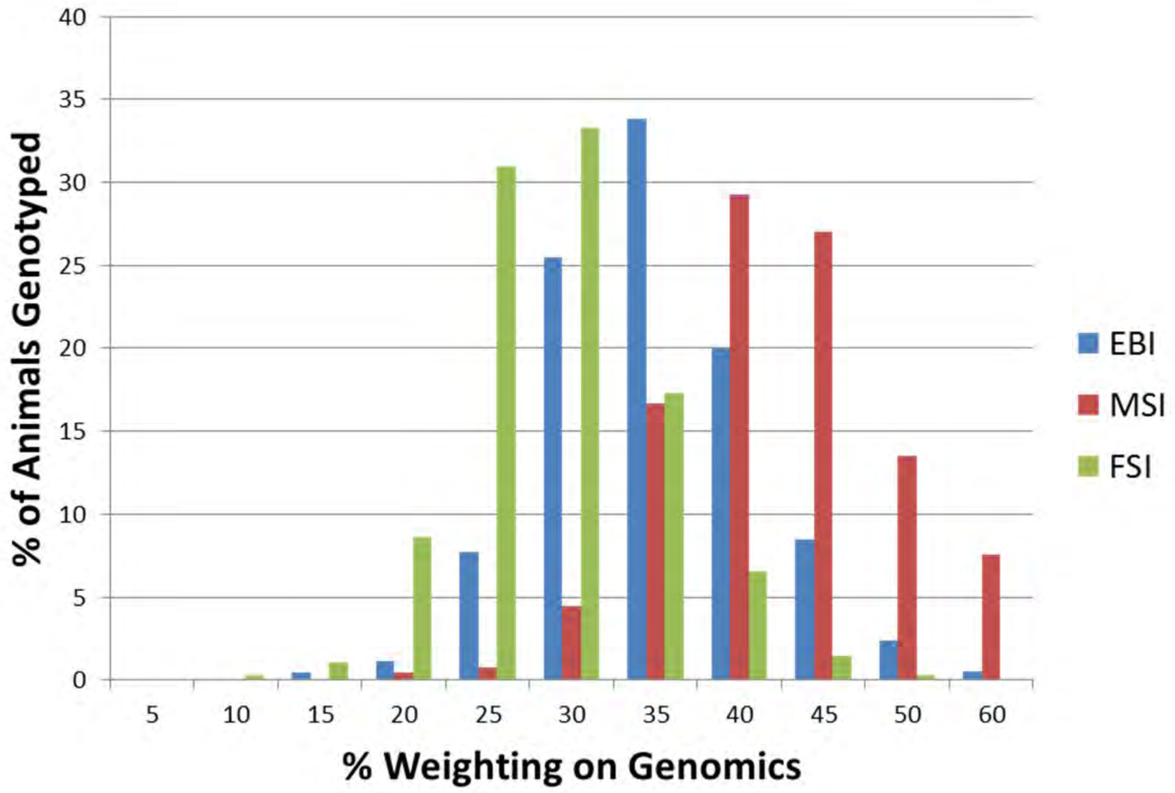
Average Diff. EBI	Diff. MSI	Diff. FSI
€5.90	€-6.8	€13

Reliability



↑ EBI Rel	↑ MSI Rel	↑ FSI Rel
22%	27%	18%

Weighting



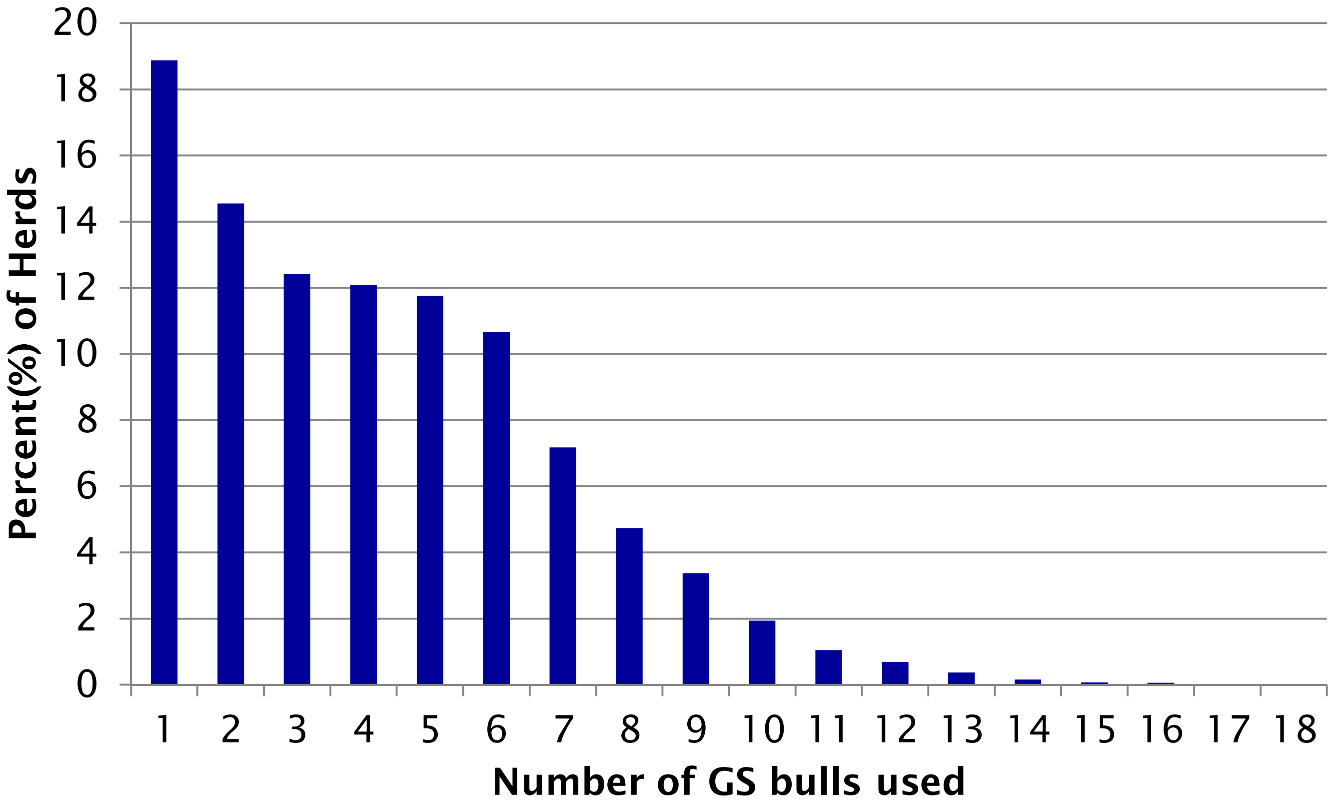
Weighting EBI	Weighting MSI	Weighting FSI
33%	40%	27%

AI Usage

	2012			2011
Proof Type	% Use	Bulls/hrd	EBI (Rel)	EBI (Rel)
DP-IRL	30	2.6	177(78)	143(75)
DP-INT	22	3.0	180(56)	155(47)
GS	48	4.2	215(57)	209(57)

- Based on > 570,000 Technician serves
- Usage of GS bulls has from 34% to 48% since 2009
- Farmers still using more GS bulls to spread their risk

AI Usage

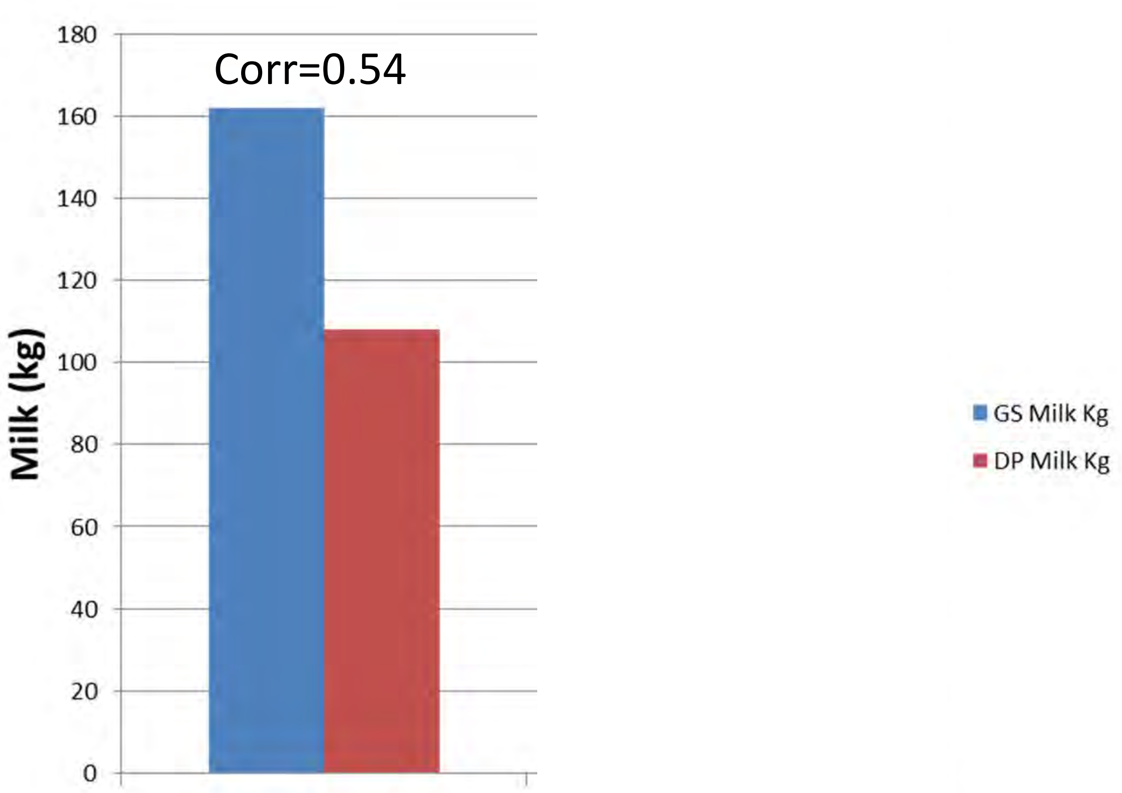


Percent(%) of Herds
20
18
16
14
12
10
8
6
4
2
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
Number of GS bulls used

Predictions

- 182 bulls marketed on GS now with daughter proof > 80% rel
  - 35 in 2009, 40 in 2010, 63 in 2011, 50 bulls in 2012
- Correlation between GS & DP > PA & DP
  - 10-20% greater depending on trait
- In 2011 we made a correction for bias in GS proofs
  - Production
    - Milk 50kg, fat 1.7kg, protein 1.9kg = Subtracted from each traits (-€9 from MSI)
  - Fertility no evidence of bias – no adjustment required

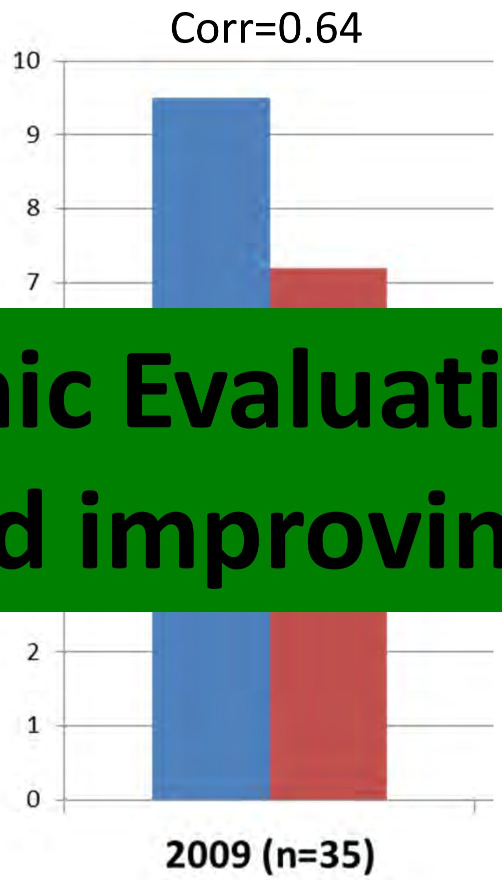
Bias



2009 (n=35)

Training = 1000

Bias



Training = 1000

Genomic Evaluations are working and improving each year!

New Developments

- Moving from BovineLD to LD plus (~19k SNPs)
- Increasing the reference population to improve the reliability of genomic proofs
  - Genotyping females
  - Sequencing of founder animals
  - Access to other populations ? (Nth American Consortium, Eurogenomics, other countries)
- Improving the methods used for estimating genomic EBI

Evaluation Methods

- Two-Step Evaluation
  1. Calculate traditional evaluations
  2. Calculate genomic evaluation using only genotyped animals
  - No trickling effect of information from genotyped animals to related non-genotyped animals (except for young animals)
- One-Step Evaluation
  1. All available information is used at the same time – trait observations, pedigrees, genotypes

Evaluation Methods

- One-Step Evaluation
  - Increased reliability and less bias (e.g., New Zealand, Harris et al., 2012)
  - Not trivial to introduce for all traits in EBI !

Evaluation Method	Trait	KiwiCross	HF	Jersey
Two-Step				
	Milk volume	0.51	0.34	0.39
	Fat	0.32	0.31	0.36
	Protein	0.63	0.46	0.40
Single-step				
	Milk volume	0.53	0.40	0.43
	Fat	0.35	0.43	0.39
	Protein	0.64	0.51	0.48

6 -12% increase

Other Dairy Breeds

- Need a large number (min 700) of well proven bulls to be able to conduct genomic selection
- Currently very small number of AI bulls for other breeds e.g., Jersey & Norwegian Red
- Discussion under way to get access to genotypes of bulls of these breeds
- If successful will supplement with cows

Interbull

- Irish GEBV have passed Interbull validation
- Interbull will provide International genomic evaluations for young bulls
- Each country submits their GEBVs to Interbull
- AI companies can use this to screen for foreign bulls with high GEBI
- For selected animals a genotype would be obtained and used directly in Irish evaluation

Summary

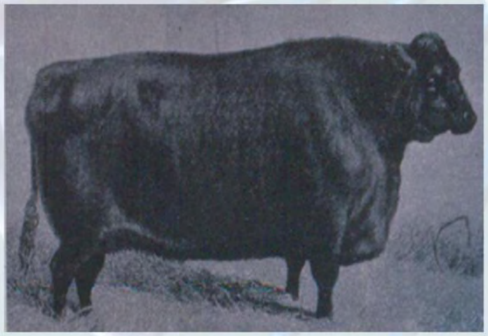
- Genomics is a vital for increasing genetic gain
- Use extensively in Ireland
- Farmers are spreading their risk
- Bias is reducing
- Increase in reference population (males & females) and new methods will improve genomic predictions further
- International proofs for young bulls next year

Future Vision of Cattle Genomics

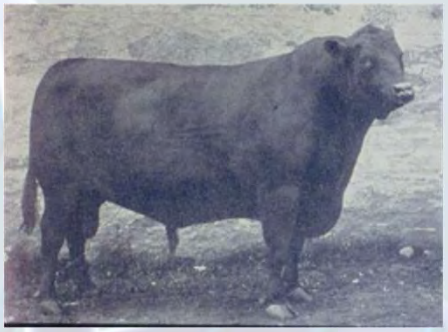
Matthew McClure, PhD

USDA-ARS, Bovine Functional Genomics Lab

ICBF Producer Meeting



1867

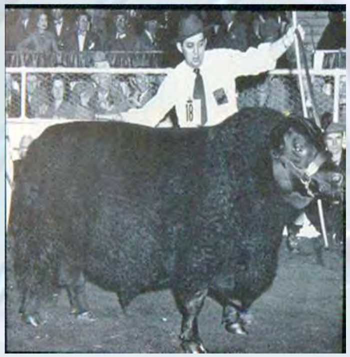


1885

1902

1916

1938



1953

1964

1972

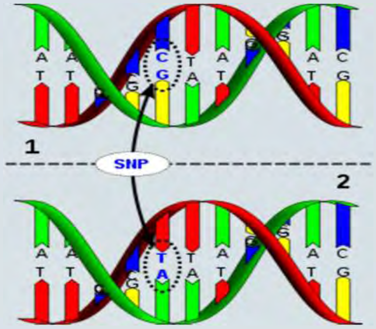
1988

1994

2007

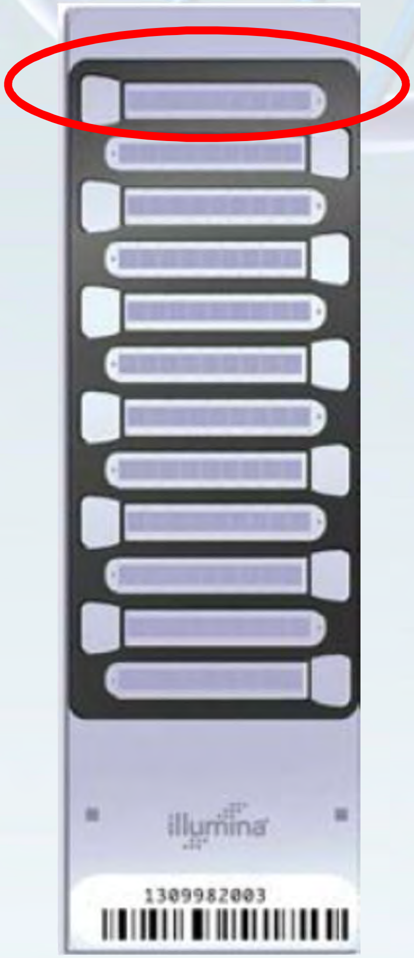
Select the Best*

Future Vision

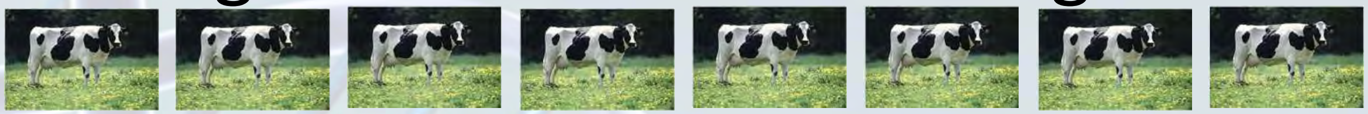


- **Genomic Selection**
- Quicker Genetic Disease Diagnosis
- Manage Breeding Value + Genetic Disease Risk
- New traits
- Breed ID

Genomic Selection in US Dairy

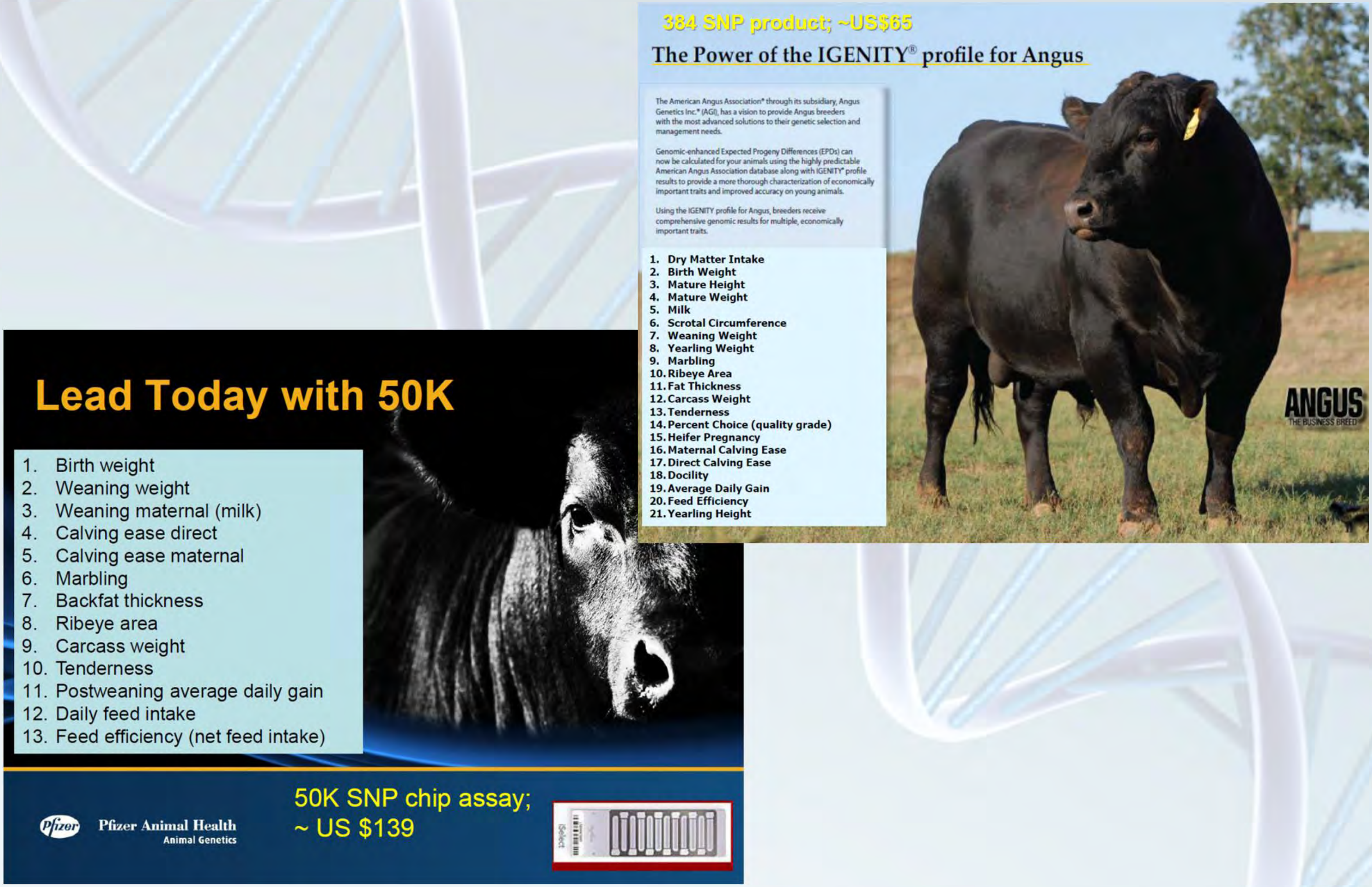


- Pedigree information ~7 daughters



- SNP information: ~34 daughters

Genomic Selection in US Beef



384 SNP product; ~US$65

The Power of the IGENITY® profile for Angus

The American Angus Association® through its subsidiary, Angus Genetics Inc.® (AGI), has a vision to provide Angus breeders with the most advanced solutions to their genetic selection and management needs.

Genomic-enhanced Expected Progeny Differences (EPDs) can now be calculated for your animals using the highly predictable American Angus Association database along with IGENITY® profile results to provide a more thorough characterization of economically important traits and improved accuracy on young animals.

Using the IGENITY profile for Angus, breeders receive comprehensive genomic results for multiple, economically important traits.

1. **Dry Matter Intake**
2. **Birth Weight**
3. **Mature Height**
4. **Mature Weight**
5. **Milk**
6. **Scrotal Circumference**
7. **Weaning Weight**
8. **Yearling Weight**
9. **Marbling**
10. **Ribeye Area**
11. **Fat Thickness**
12. **Carcass Weight**
13. **Tenderness**
14. **Percent Choice (quality grade)**
15. **Heifer Pregnancy**
16. **Maternal Calving Ease**
17. **Direct Calving Ease**
18. **Docility**
19. **Average Daily Gain**
20. **Feed Efficiency**
21. **Yearling Height**

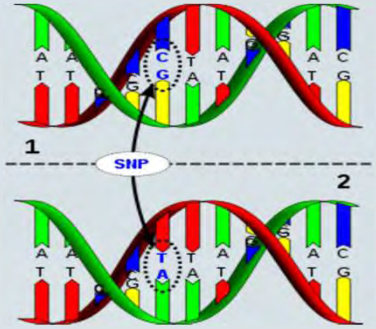
Lead Today with 50K

1. Birth weight
2. Weaning weight
3. Weaning maternal (milk)
4. Calving ease direct
5. Calving ease maternal
6. Marbling
7. Backfat thickness
8. Ribeye area
9. Carcass weight
10. Tenderness
11. Postweaning average daily gain
12. Daily feed intake
13. Feed efficiency (net feed intake)

Pfizer Animal Health
Animal Genetics

50K SNP chip assay;
~ US $139

Future Vision



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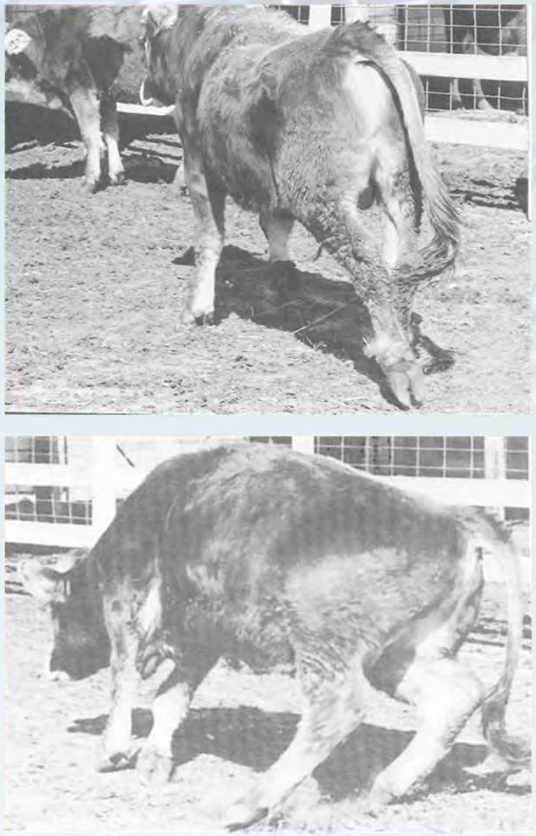
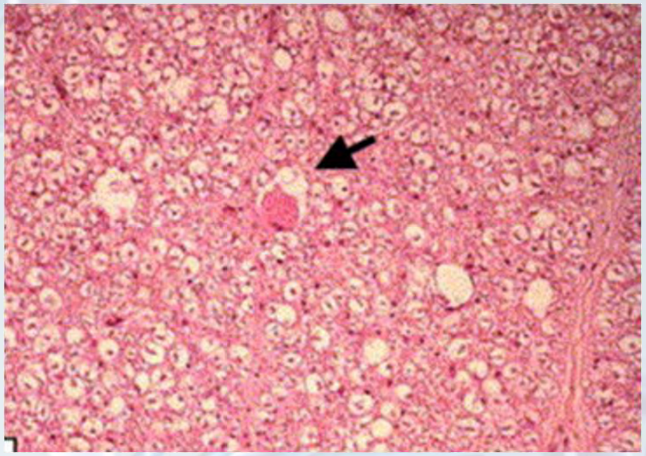
BFGL Research

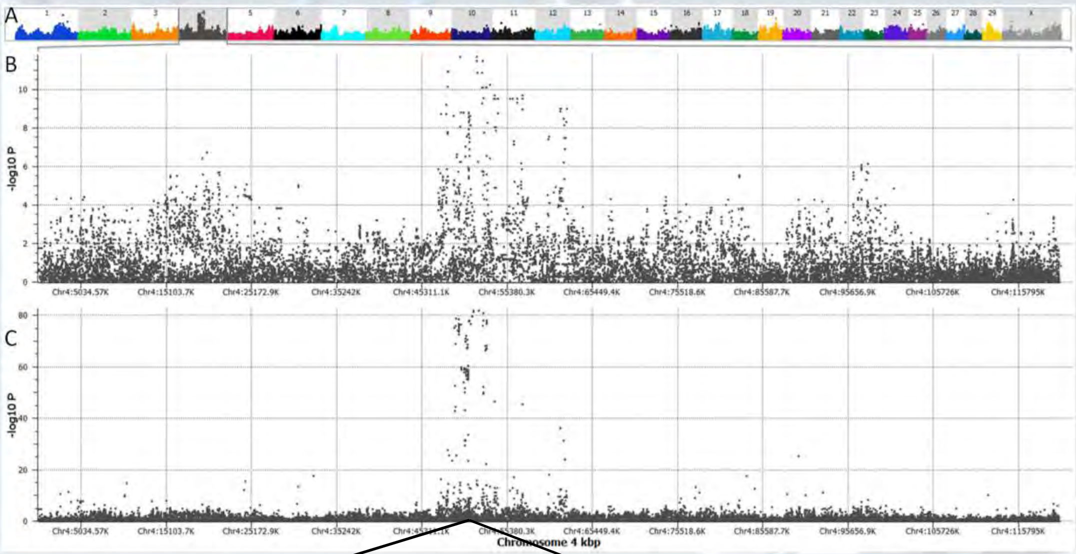
- Weaver Syndrome





Mapping to Diagnostic

5 Mb



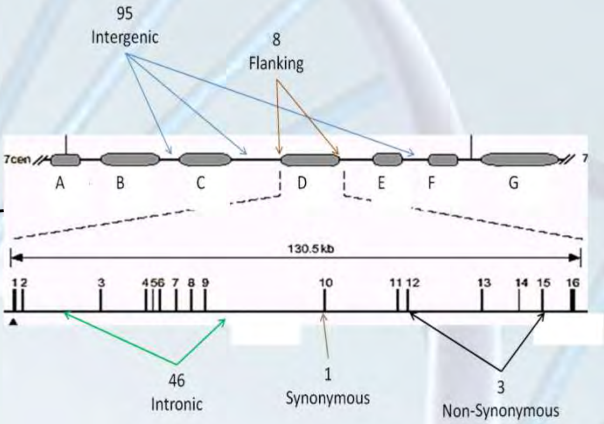
0.5 Mb

NRCAM PNPLA8 CTTNBP2

41 SNP

1 Haplotype

153 SNP

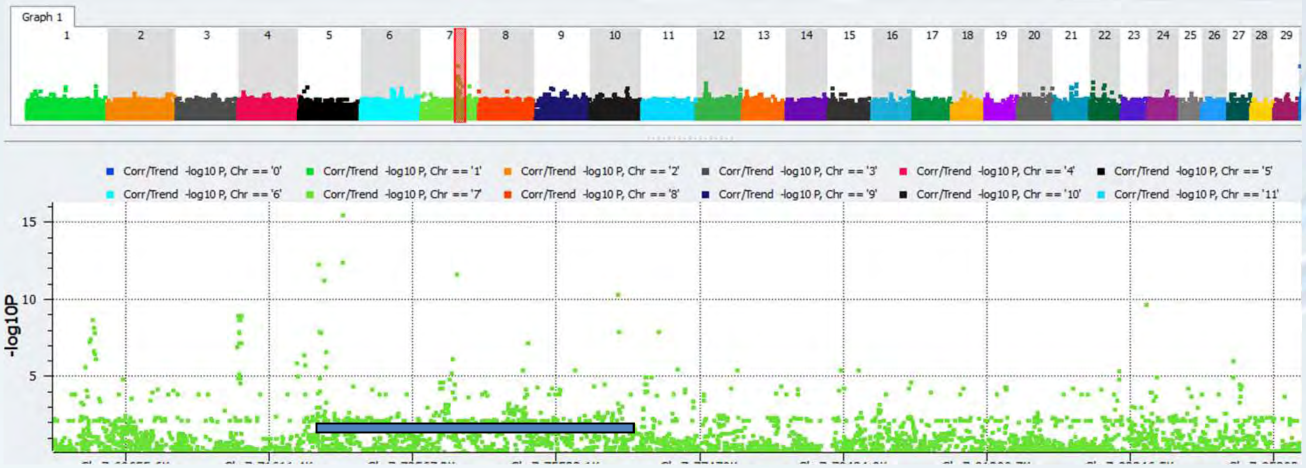


Rectovaginal Constriction

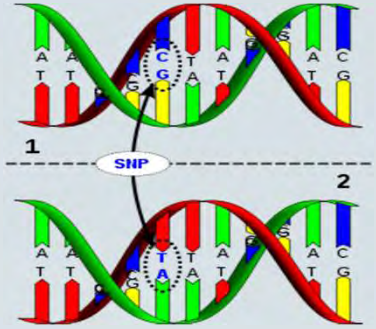
Identified in USA Jersey’s 1970’s

Progeny identified carriers

Mapped with SNP ~3 months



Future Vision



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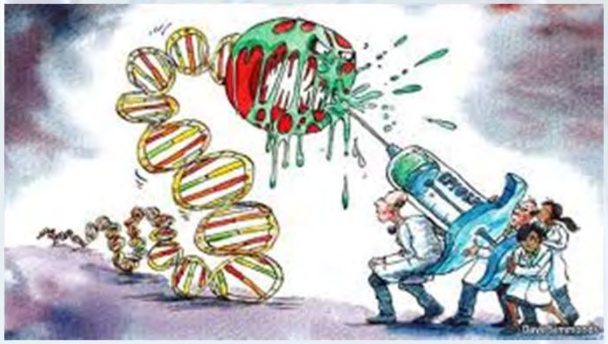
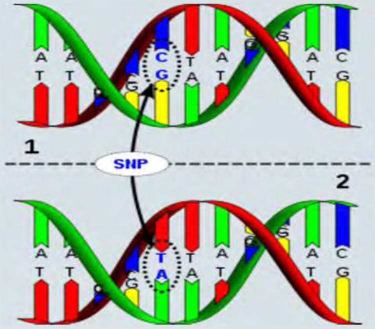
Manage

Genetic Improvement with Disease Risk

O-BEE MANFRED JUSTICE-ET (O Man)



Future Vision



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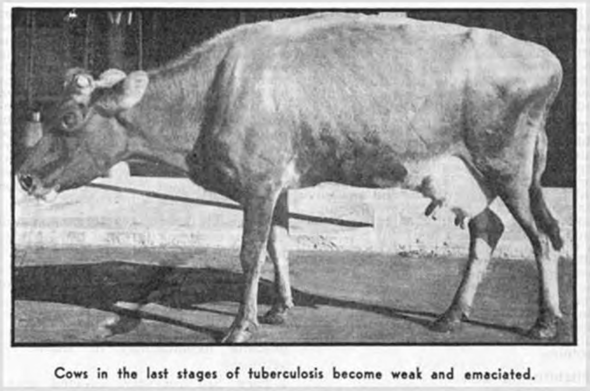
- **New traits**
- Breed ID

New Traits

Disease Resistance

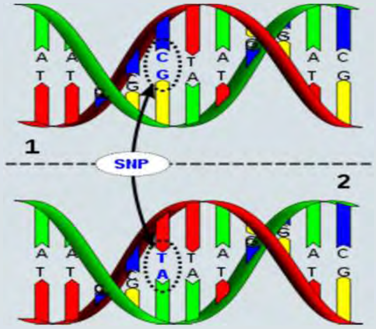

Cows in the last stages of tuberculosis become weak and emaciated.

Efficiency

Environmental Resistance

Eating Quality

Future Vision



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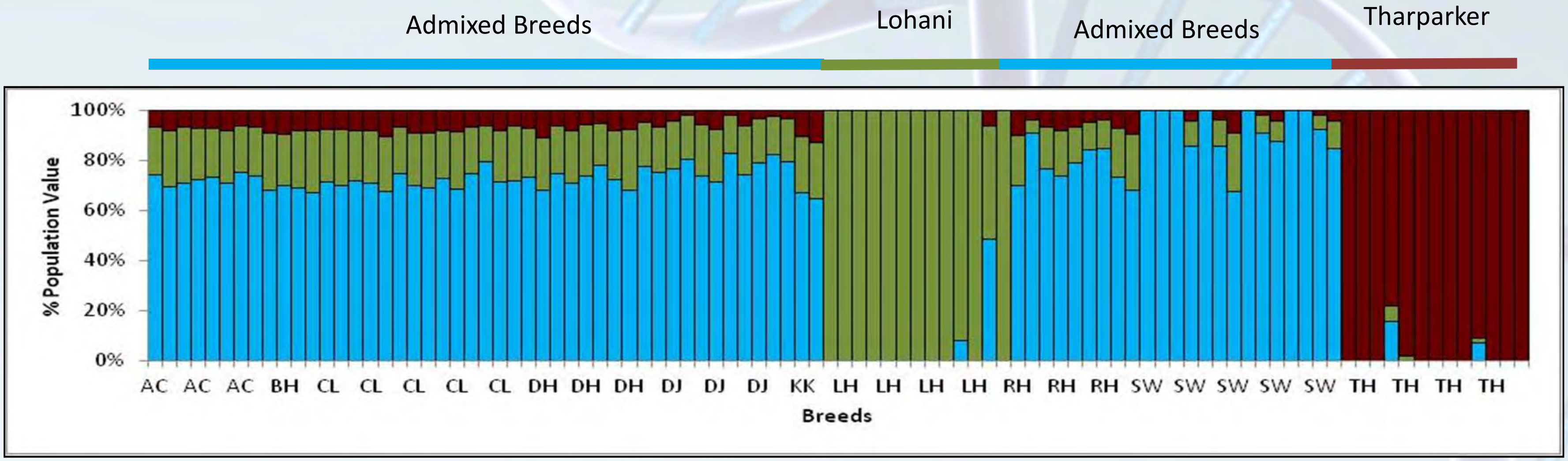
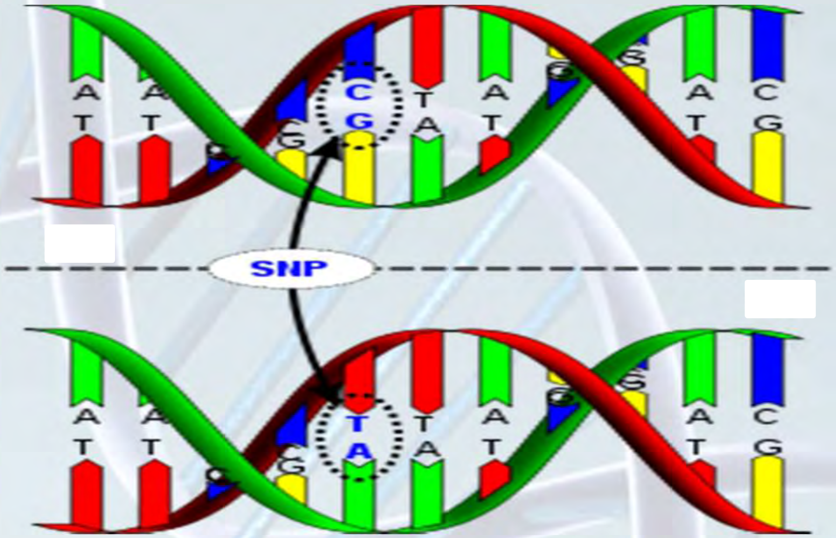
- **Breed ID**

Breed ID


Ozark Empire Fair


Admixed Breeds
Lohani
Admixed Breeds
Tharparker
100%
80%
60%
40%
20%
0%
% Population Value
AC AC AC BH CL CL CL CL CL DH DH DH DJ DJ DJ KK LH LH LH LH RH RH RH SW SW SW SW SW TH TH TH TH
Breeds

Future of Livestock Genomics



Decreasing costs and increasing information

=

More animals and livestock species being genotyped

Summary

- Beef and Dairy breeds will benefit from Genomic Selection
- Genetic Diseases
  - Quick diagnostic tests developed
  - Manage Risk
- Additional Traits

- Genotyping as a Routine Farm Practice

Thank You

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Questions