Use of High and Low-Density SNP Genotypes in Genomic Selection and QTL Discovery in Dairy Cattle

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Cattle Genome Sequence

AGTCCATGGGGTTGCAGAGTCAGACACAGTGGAGTCACACACATACACACG

GCCCCACGCTGGGTTAAGGCGGGGCTGAGACAAGGGCAGGTGAGGCCTCCCA

- 30 pairs of chromosome pairs (incl. X,Y)
  - 3 billion base pairs

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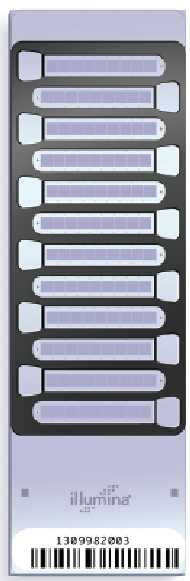
Illumina BovineSNP50 Genotyping BeadChip

FIGURE 1: BOVINESNP50 BEADCHIP



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

~ $225 per animal today

TABLE 3: BOVINESNP50 BEADCHIP CONTENT VALIDATION

BREED	SAMPLES	POLYMORPHIC LOCI*	MEAN MAF†	MEDIAN MAF†
Angus	60	41,491	0.21	0.21
Beefmaster	24	42,925	0.22	0.21
Bos indicus Gir	24	23,971	0.11	0.02
Bos indicus Nelore	21	25,814	0.11	0.02
Brahman	25	30,284	0.13	0.08
Brown Swiss	24	36,347	0.19	0.17
Charolais	26	42,589	0.22	0.21
Guernsey	21	38,632	0.19	0.17
Hereford	32	42,992	0.20	0.23
Holstein	64	42,730	0.22	0.22
Jersey	28	35,976	0.18	0.14
Limousin	45	42,821	0.22	0.22
N'Dama	25	29,049	0.14	0.08
Norwegian Red	21	42,782	0.22	0.21
Piedmontese	24	42,185	0.22	0.21
Red Angus	15	40,188	0.21	0.20
Romagnola	24	38,830	0.20	0.19
Santa Gertrudis	24	42,064	0.22	0.21
Sheko	20	35,726	0.17	0.12
Outgroup‡	18	11,206	0.05	0.00
Overall	565	47,545	0.25	0.24

*MAF > 0.05
†Across all 54,001 loci
‡*Bos bison, Bos gaurus, Bos grunniens, Bos javanicus, Bubalus depressicornis*, and *Syncerus caffer*.

Source: USDA-ARS

Dairy Cattle Genotyping

(as of January 2009)

Countries	Animals
United States and Canada	22,344
France	8,500
Netherlands, New Zealand[1]	6,000
New Zealand and Ireland	4,500
Germany	3,000
Australia	2,000
Denmark, Finland, Sweden	2,000

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CDDR Contributors

(Cooperative Dairy DNA Repository)

taurus-service inc.

Accelerated Genetics

ABS

SEMEX

Alta Genetics

Genex Cooperative, Inc.

CRI AgSource • Genex • Central Livestock

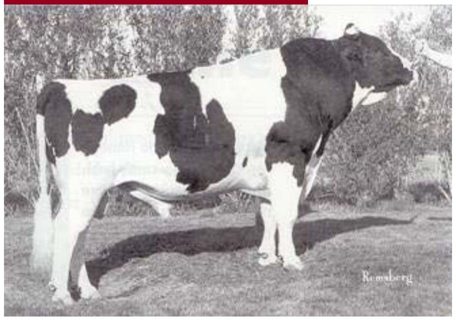
SELECT SIRES Inc.

Source: USDA-ARS

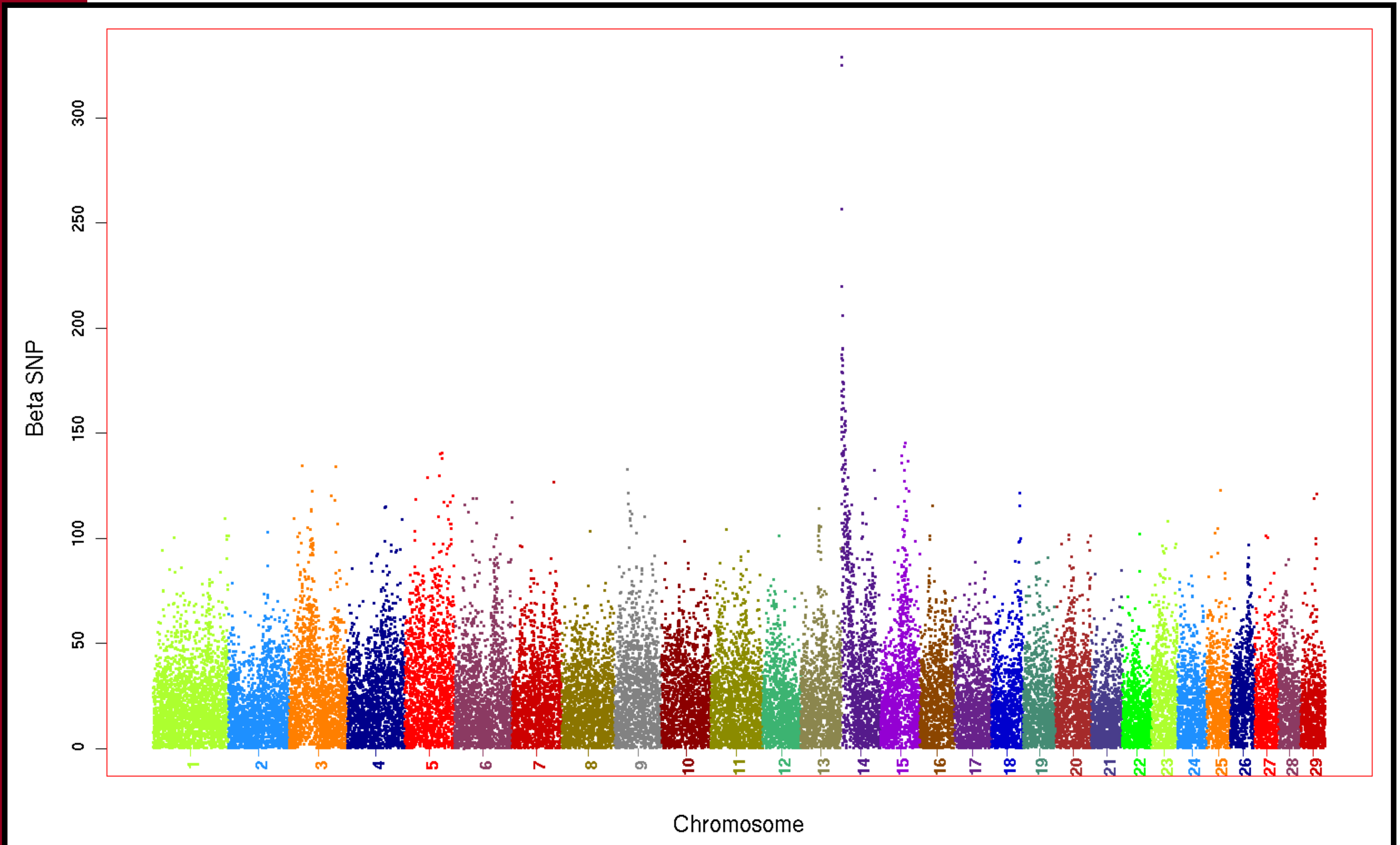
SNP Genotype of Elevation

(chromosome 1)

100011122002001211101111211110111100112110002012200222011112021012002111221100211120011110010110110102200110022011011200201101020222121122102010011100011220221222112021120120201002022020000211000112020112211121110220111100002122020002210120200022112201110121001112111021121100201021000220002201000201100002202211022112101121110122220012112122200200020020202012221100222222200221211112100211112001101110112002022200011120110102111212111020221002112012110011110211121102111220001011011102022002211101020111211110112021021021211011022122001211011211012022011002220021002110001110021102110111000222002022121211000222010200222212122112111200201102020012222221122120212112101100121101102002200020010020001111011001211021212111201010121202210101011111021102112211111121211121011012001111102111101111122012101212110102220202121122212022200212121012121020110011122212110



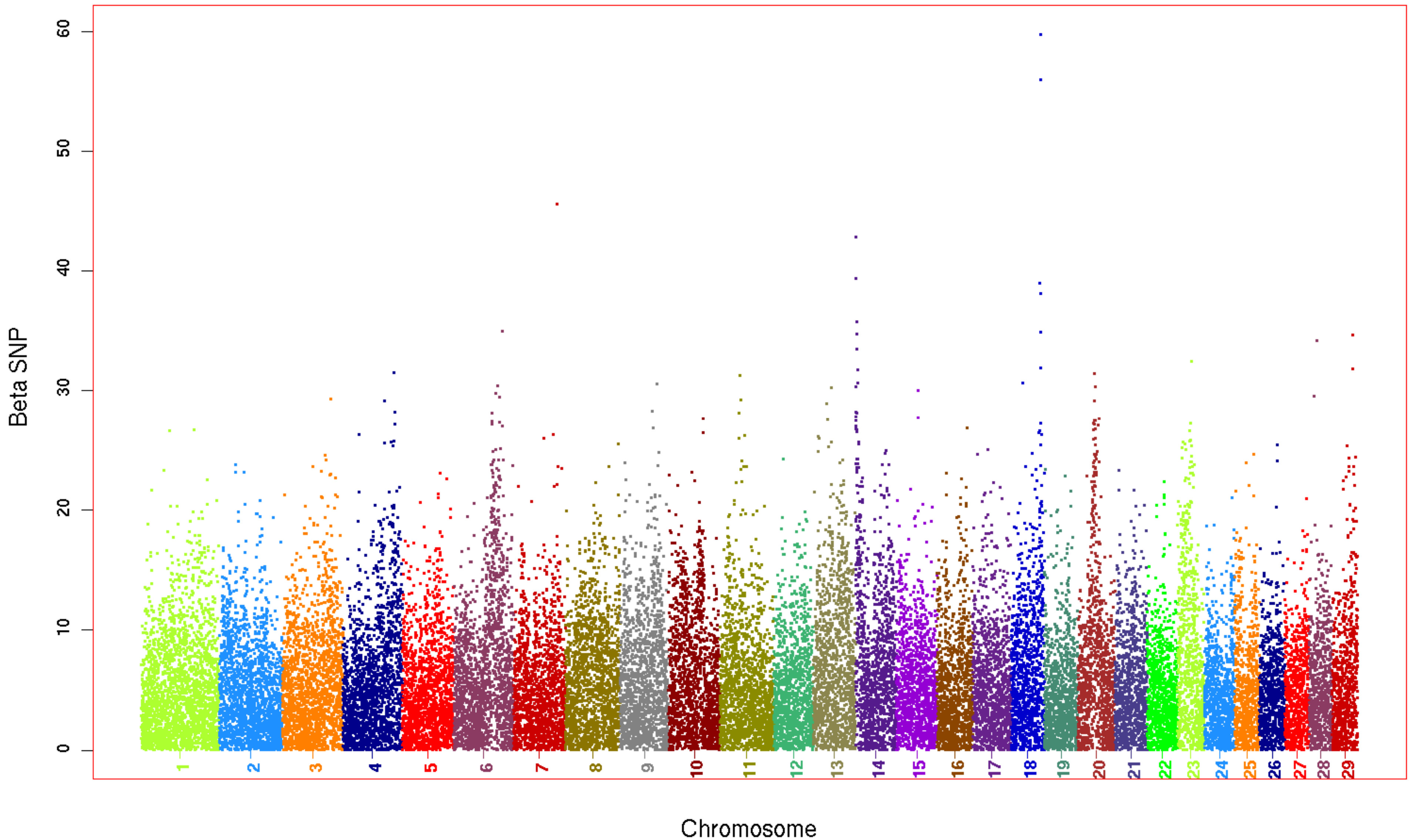
SNP Effects for Milk Yield



O'Connell, 2008

Source: USDA-ARS (O'Connell)

SNP Effects for Net Merit



What is a Genomic PTA?

- Approximately 40,000 genetic markers (SNPs) are evaluated
- For each SNP, the difference in predicted transmitting ability (PTA) between animals with 0, 1, or 2 copies of a specific allele is estimated
- Genomic evaluations combine SNP effect estimates with the existing parent average (PA) or PTA for each animal

Source: USDA-ARS (VanRaden)

Validation Study

(2004 data were used to predict 2009 data)

	HOL	JER	BSW
Predictor:			
Bulls born <2000	4,422	1,149	472
Cows with data	947	212	40
Total	5,369	1,361	512
Predictee:			
Bulls born >2000	2,035	388	150

Source: USDA-ARS (VanRaden)

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Reliability Gains by Trait

(gain above parent average reliability ~35%)

	HOL	JER	BSW
Lifetime Net Merit	24%	8%	9%
Milk Yield	26%	6%	17%
Fat Yield	32%	11%	10%
Protein Yield	24%	2%	14%
Fat %	50%	36%	8%
Protein %	38%	29%	10%

Source: USDA-ARS (VanRaden)

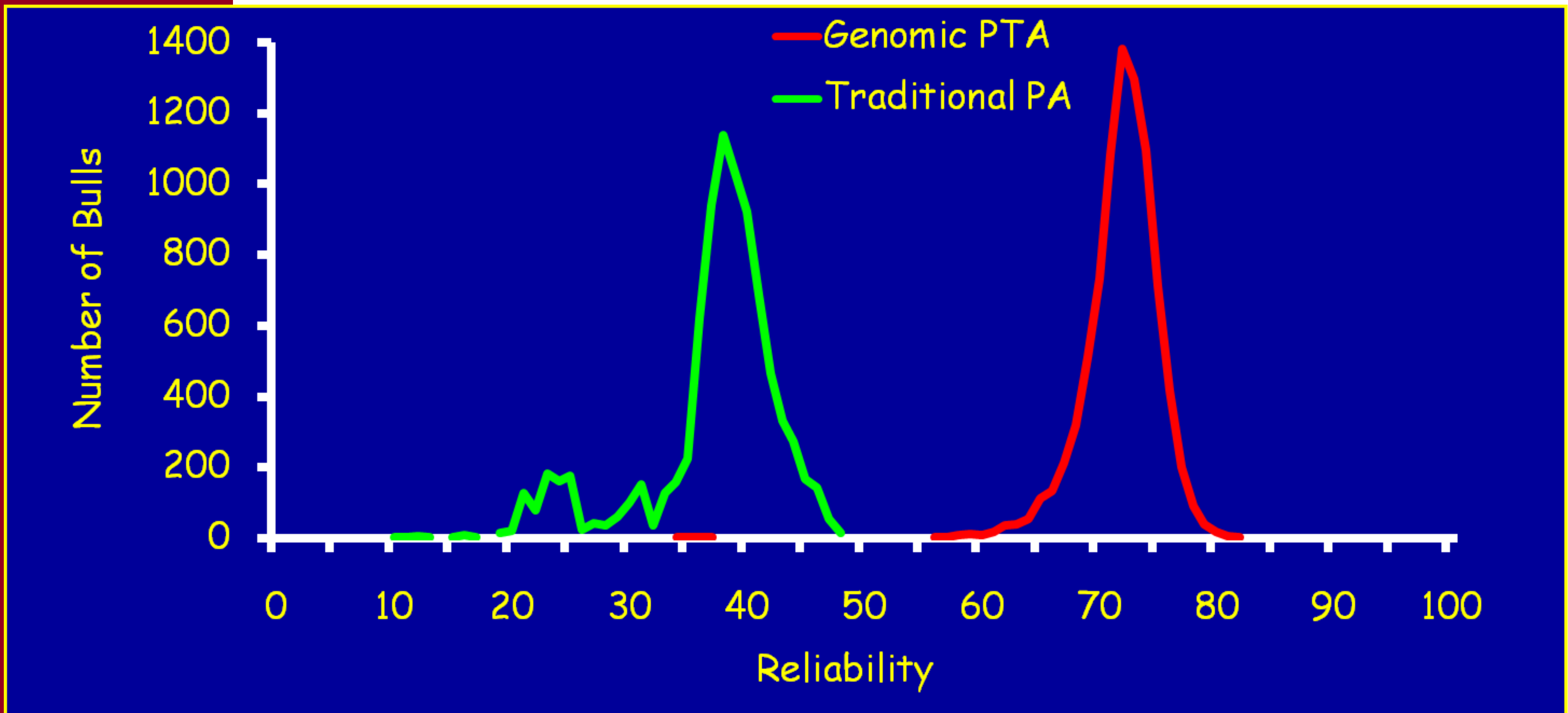
Reliability Gains by Trait

(gain above parent average reliability ~35%)

	HOL	JER	BSW
Productive Life	32%	7%	12%
Somatic Cell Score	23%	3%	17%
Daughter Pregnancy Rate	28%	7%	18%
Final Score	20%	2%	5%
Udder Depth	37%	20%	8%
Foot Angle	25%	11%	(1%)

Source: USDA-ARS (VanRaden)

Reliabilities for Young Bulls
Parent Average vs. Genomic PTA



Source: USDA-ARS

Adoption of Genomic Testing

(young bulls in US AI studs, April 2009)

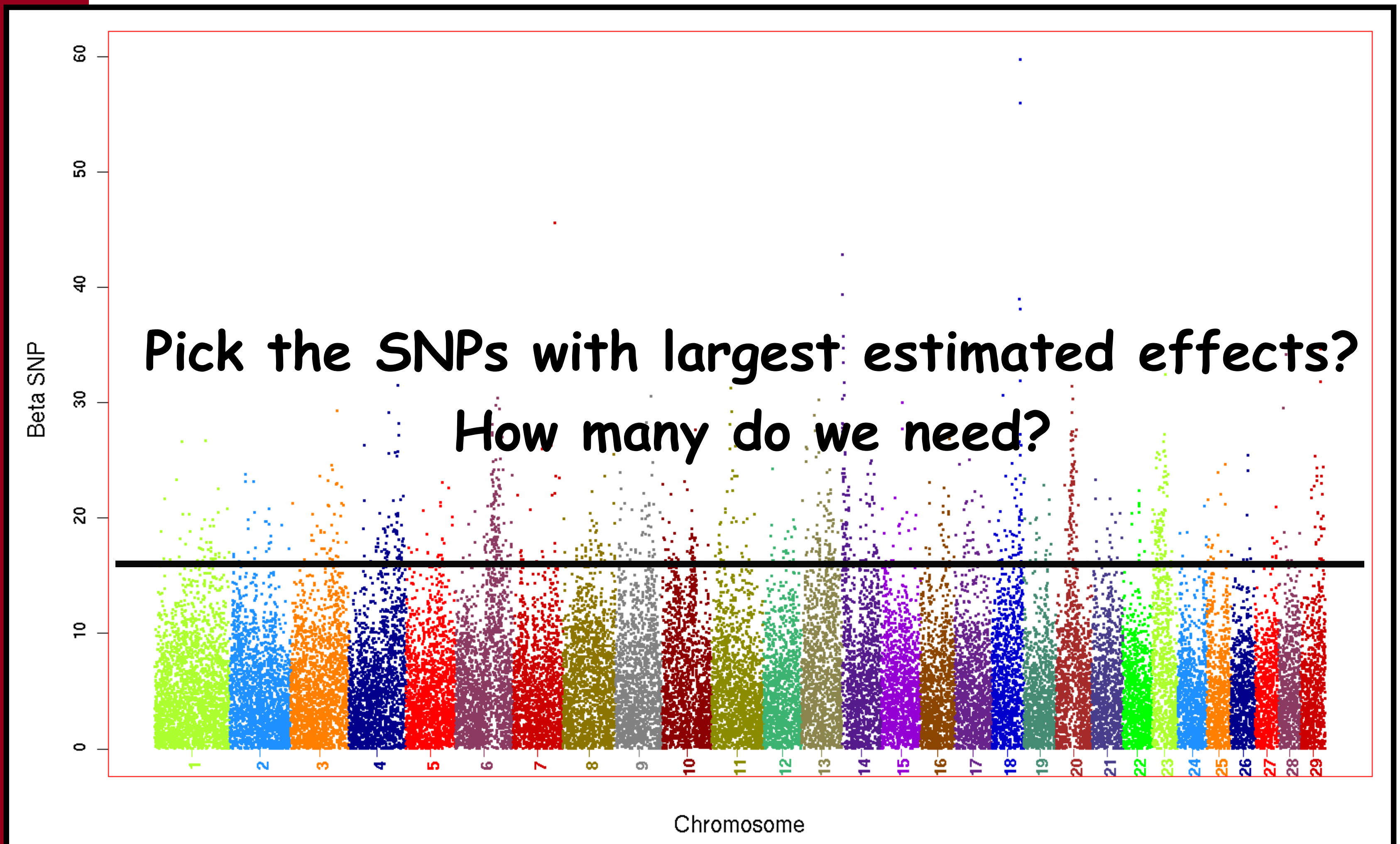
Birth Year	No. Bulls Sampled	No. Bulls Tested	Percent Tested
2008*	649	615	95%
2007*	1548	1172	76%
2006	1726	1118	65%
2005	1677	1217	73%
2004	1655	991	60%

*count for birth year is incomplete

Low-Cost Genotyping Assays

- At the current price, the BovineSNP50 BeadChip is limited to applications involving males and elite females
- An with 300-1000 selected SNPs might deliver a substantial portion of the gain for a fraction of the price
- Applications may include: parentage discovery, selection of replacement heifers, preliminary screening of young bulls, and genomic mating programs

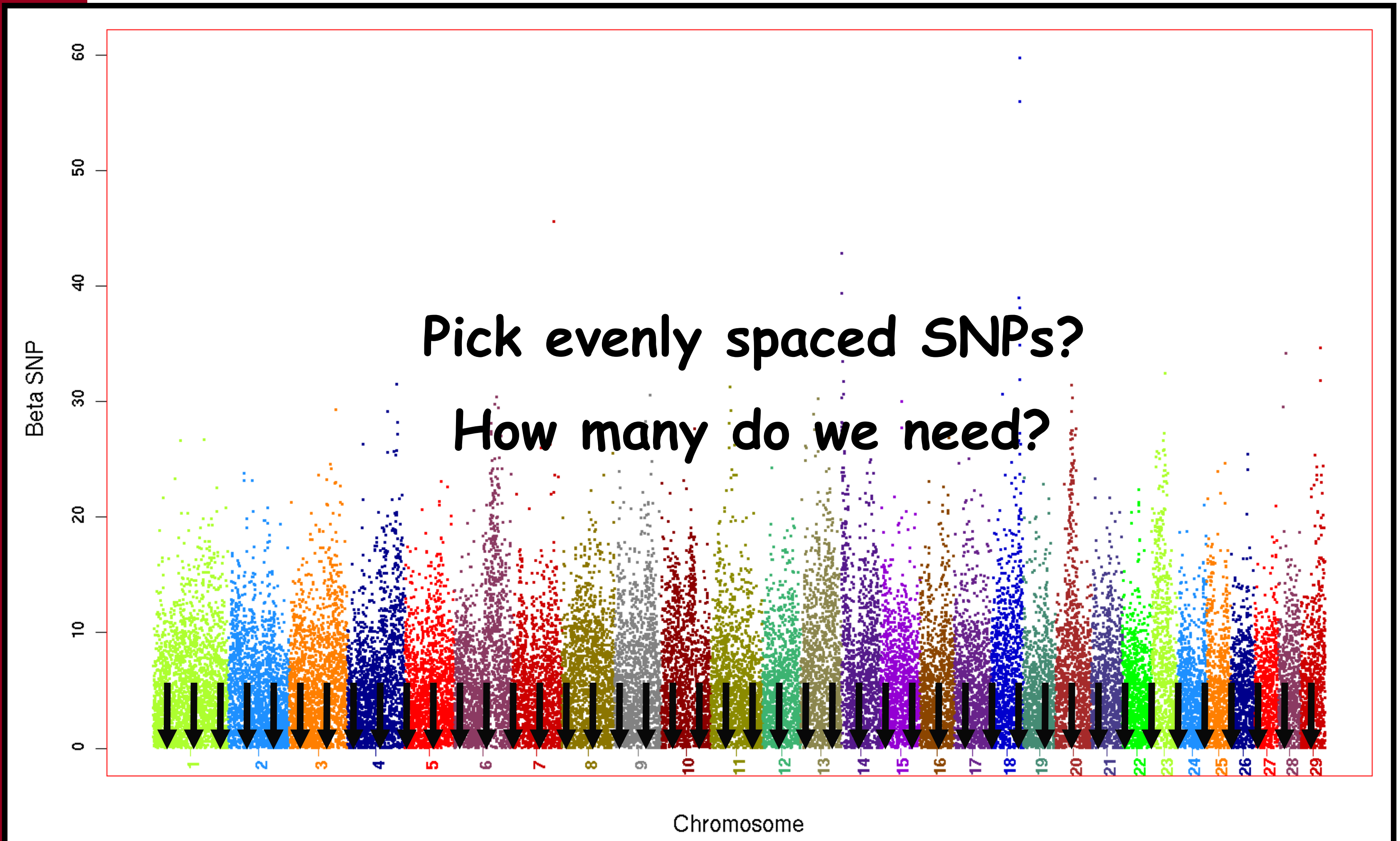
Which SNPs to Select?



Pick the SNPs with largest estimated effects?

How many do we need?

Which SNPs to Select?



Validation of Low-Density Genomic PTAs

- Compute parent averages and genomic PTAs using 2003 data from 3,305 Holstein bulls born in 1952-1998

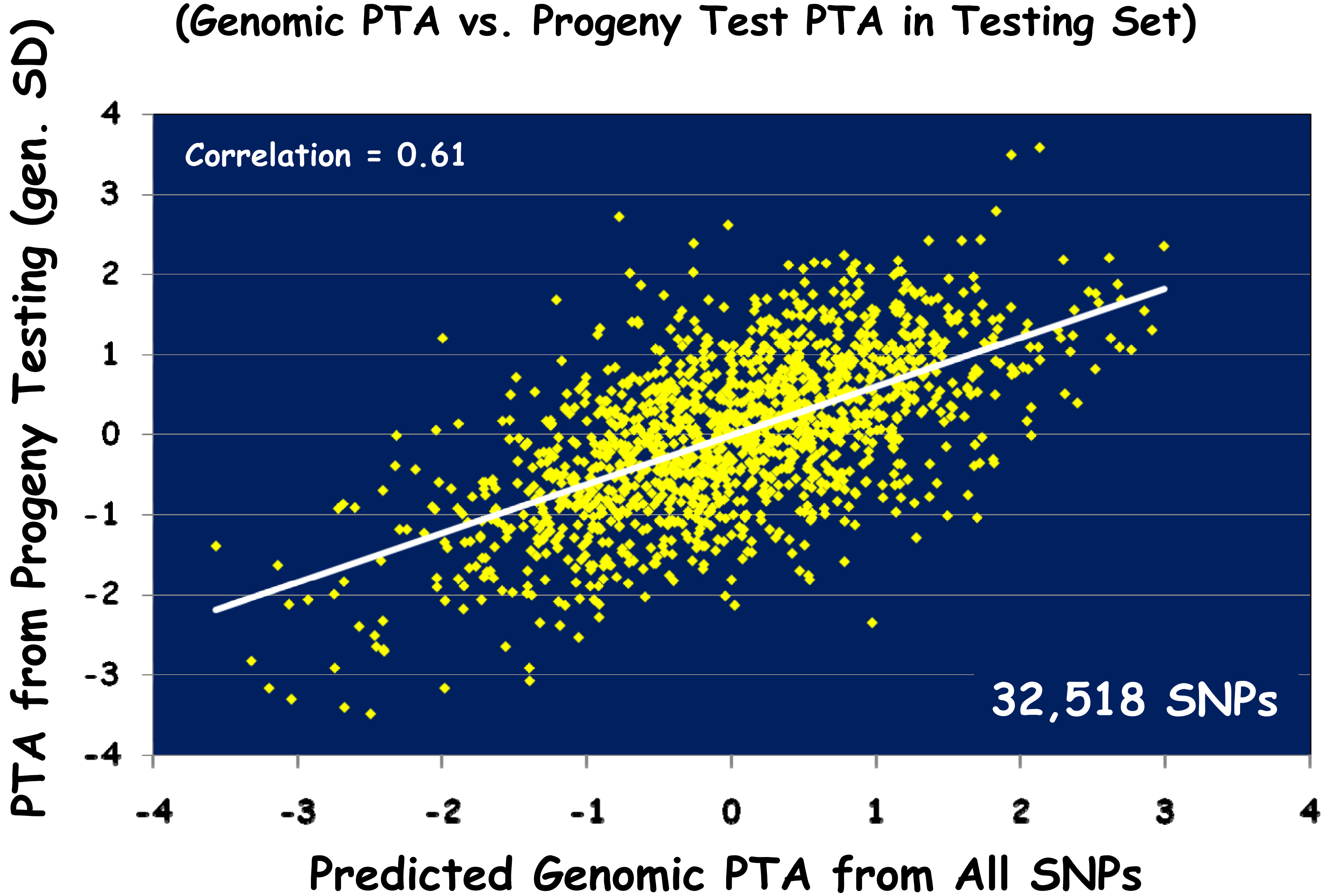
  → "Training Set"

- Compare ability to predict daughter deviations in 2008 data for 1,398 bulls born from 1999-2002

  → "Testing Set"

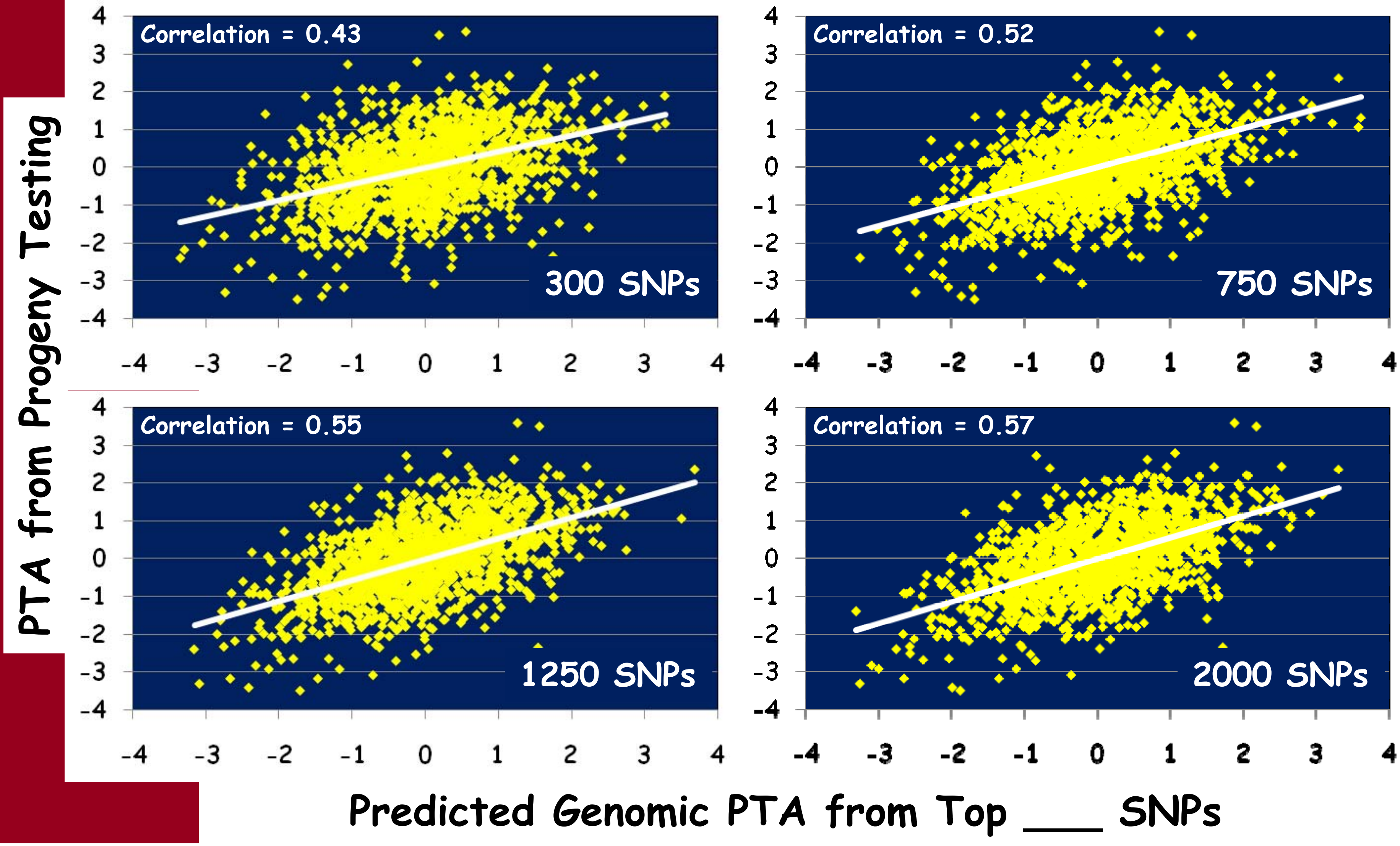
Predictive Ability for Net Merit

(Genomic PTA vs. Progeny Test PTA in Testing Set)



Predictive Ability for Net Merit

(Genomic PTA from SNPs vs. Progeny Test PTA in Testing Set)



Animal ID Applications

(96+ SNPs in the parentage panel)

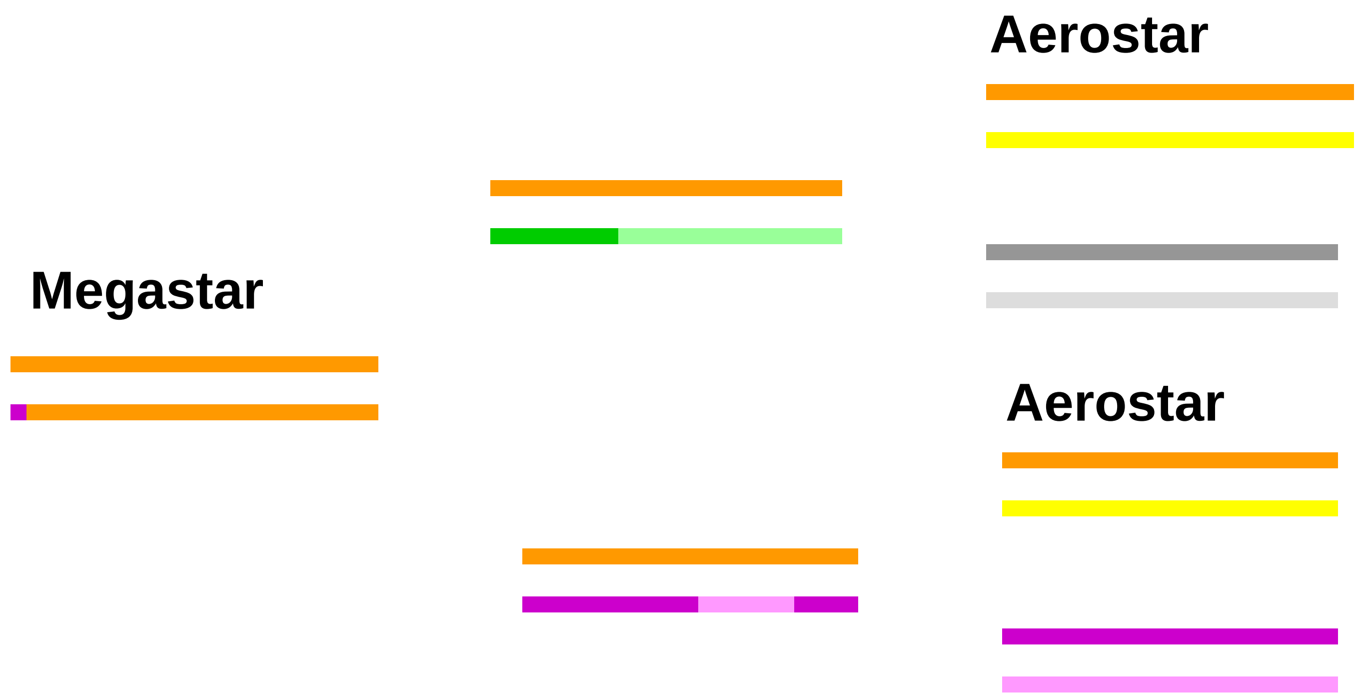
Original graphic obtained from Michael Heaton, USDA, ARS, Meat Animal Research Center (MARC). Used with permission.

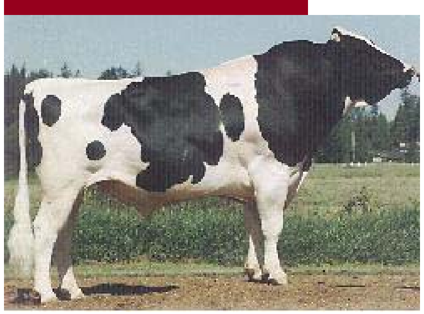
- Verify reported parents
- Discover parents if unknown or incorrect
- Trace animals or animal products

Close Inbreeding (F=14.7%)

Double Grandson of Aerostar

(Chromosome 24)





VanRaden, 2008

SNP Genotype of Megastar
(chromosome 24)

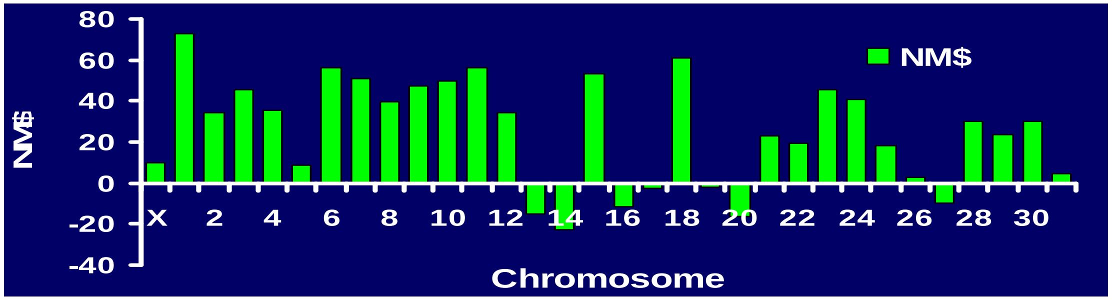
1021222101021021011102110112112211211002202000222020002020220
0000220020222202202000020020222222000020222200000220200002002
2002000000222200022220000000000020222022002000222020222220002
2022222222200002002202022202000200022000000002202220000002200
2020002222002020020020202220222222202220200020220220222220202
2202020202200022002220220022200000220200002002002000200222220
0022220202002220022202000020200000022222020200002002002222000
2022022220022000222022002222020200022022022220022200220002000
2202000002200220222000022000022000222020022220002200200202020
2020002220002220022202202200000220220020020020220002000222202
2002220020220200222202220000020220002020020202000220022000002
2022200202220200022002000200022002002000200220222220022022000
2000020002000020220020220200200002220000222002000200222000022
0220020022002202202020202020200022202000220200202202222020220000
2020200002020200022222200222200020022022220000020220020200202
022022020200002000200220220002200

Effects on Inbreeding

- Traditional animal model evaluations favor co-selection of families or relatives
- Genomic selection allows within-family selection, which leads to less inbreeding
- Low-cost, low-density genotyping assays will allow widespread screening of families that might provide unique genetic contributions to the population
- Identification and control of inherited defects will be greatly enhanced as well

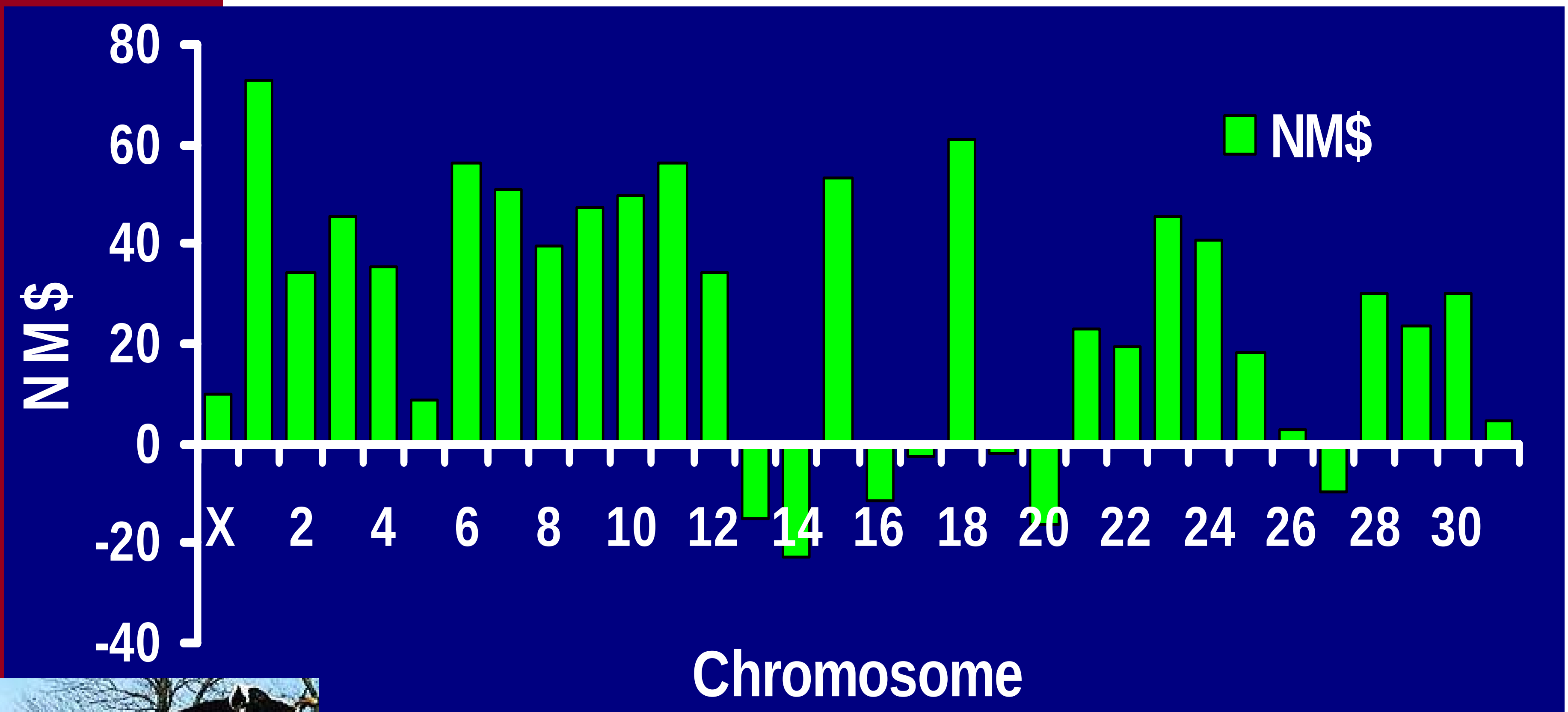
Potential for Mate Selection

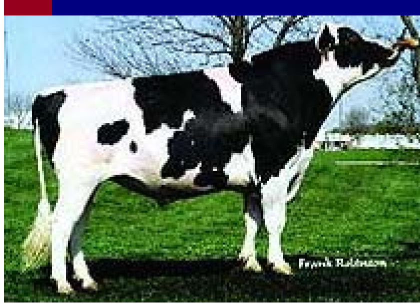
- Millions of cows are mated using computerized programs each year, based on faults in conformation or avoidance of inbreeding
- SNP genotypes of AI sires and potential mates could be used to minimize inbreeding or to identify parents with "complementary" DNA profiles



Net Merit by Chromosome

7HO6417 O Man

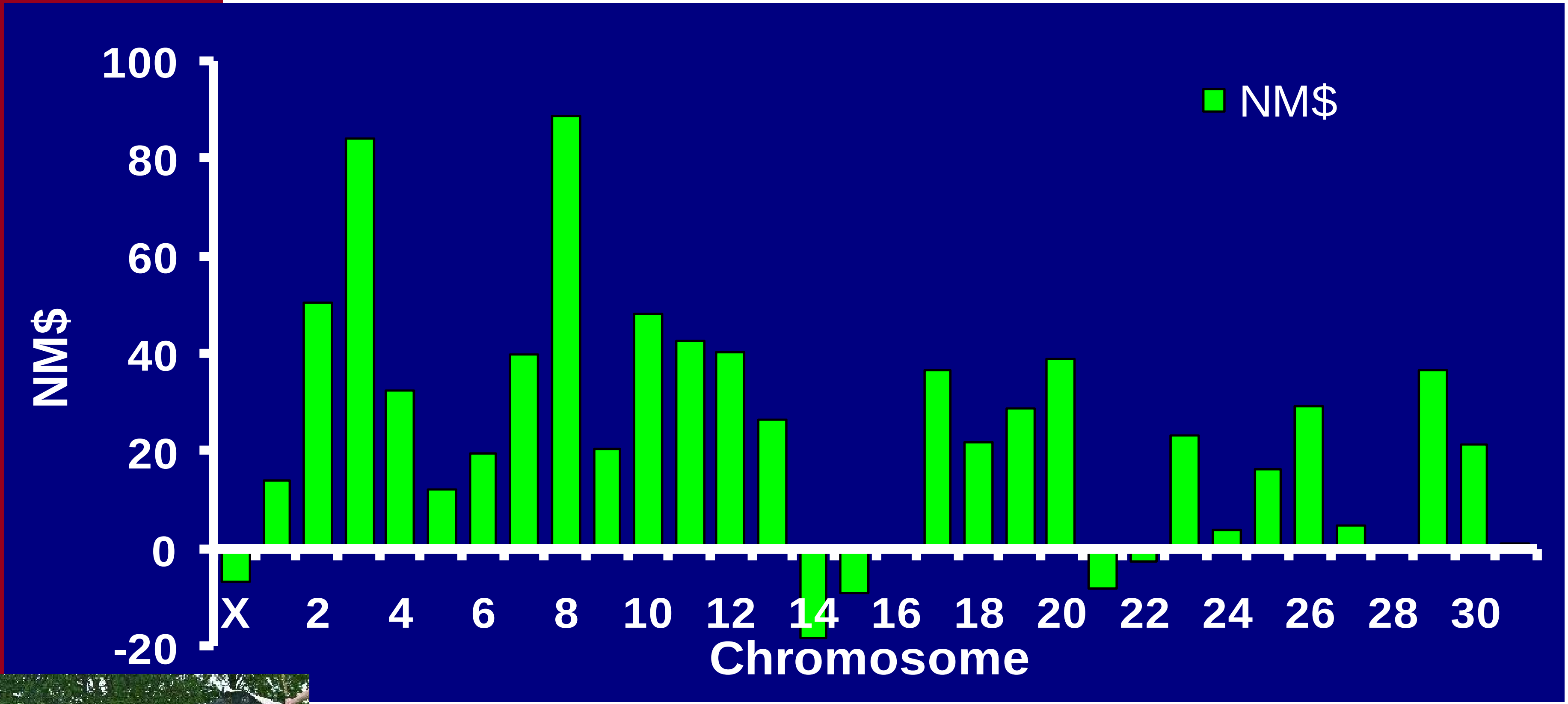




VanRaden, 2008

Net Merit by Chromosome

7HO8081 Planet



VanRaden, 2008

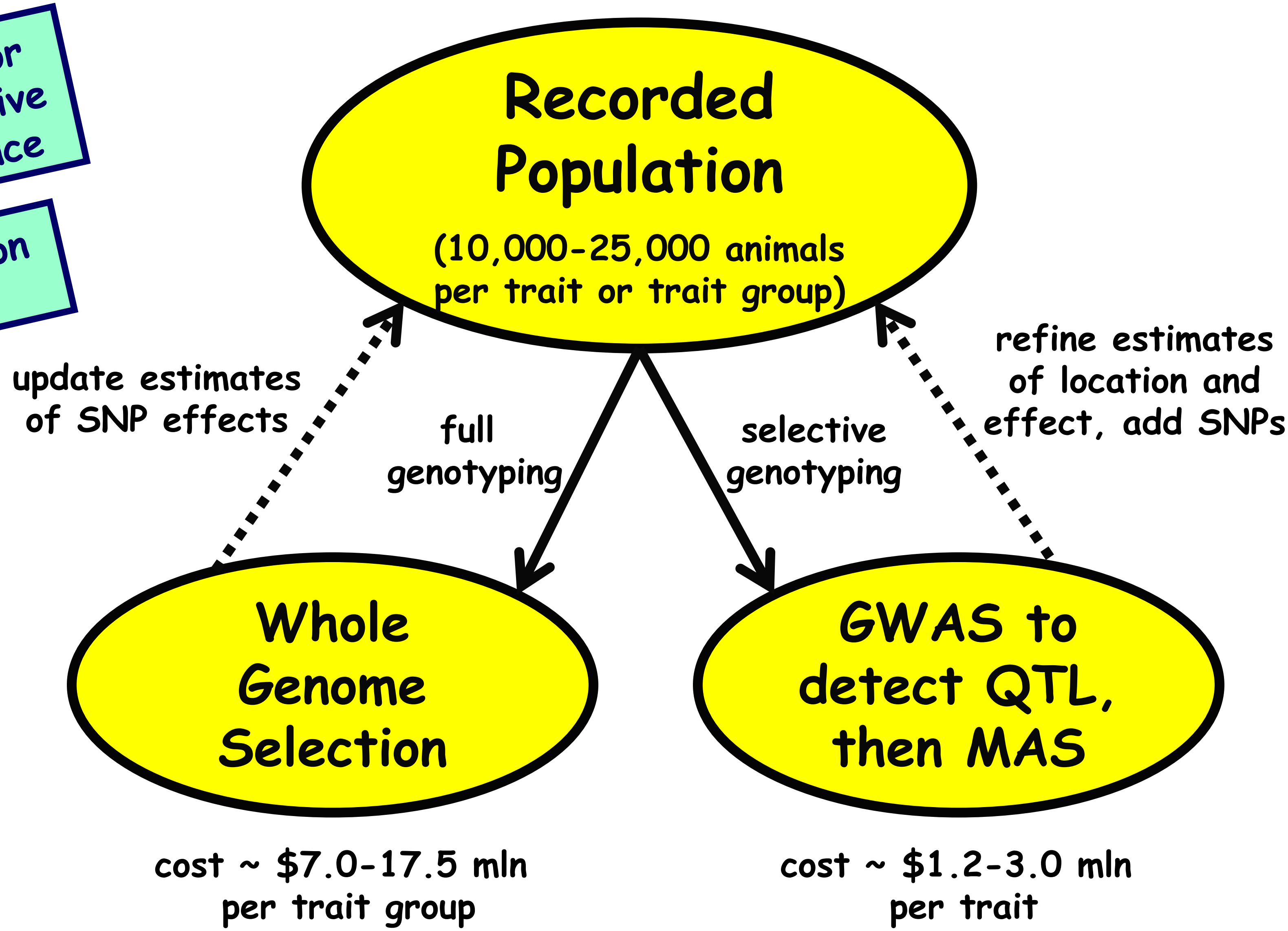
Possibilities for Novel Traits

- Opportunities to collect DNA and phenotypes for traits not routinely assessed in national recording schemes
- Examples include: feed intake, hormone level, immune function, hoof care, etc.
- Potential resource populations include: experimental herds, calf ranches, heifer growers, commercial herds with specific milking/feeding/management equipment, veterinary databases (without sire ID)

Novel Traits and Genomics

additive or non-additive inheritance

no selection bias



$200/genotype
$100/trait
5 traits/group
select high/low 10%

Synergy with Herd Management

- "Personalized medicine" is a key objective of biomedical research
- Examples include *genotype-guided* Warfarin dosing using two major *genes*
- Cost-effective applications in livestock will involve a series of small returns from enhanced vaccination programs, ration formulation, mate selection, veterinary care, and animal grouping decisions
- Integration with herd management software will be the key to success

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http://www.wisc.edu/dysci

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