GWAS to Identify Genes that Influence Calf Health from Holstein and Crossbred Dairy Cows and Calves

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Outline

- **Background on University of Minnesota dairy cattle breeds and herds**

- **Holstein and 1964 Holstein**

- **Crossbred cow and heifer analysis**

- **Calf health GWAS and ROH**

- **Future research**

West Central Research and Outreach Center

Conventional Dairy Herd

Organic Dairy Herd

Ideal Dairy Cow
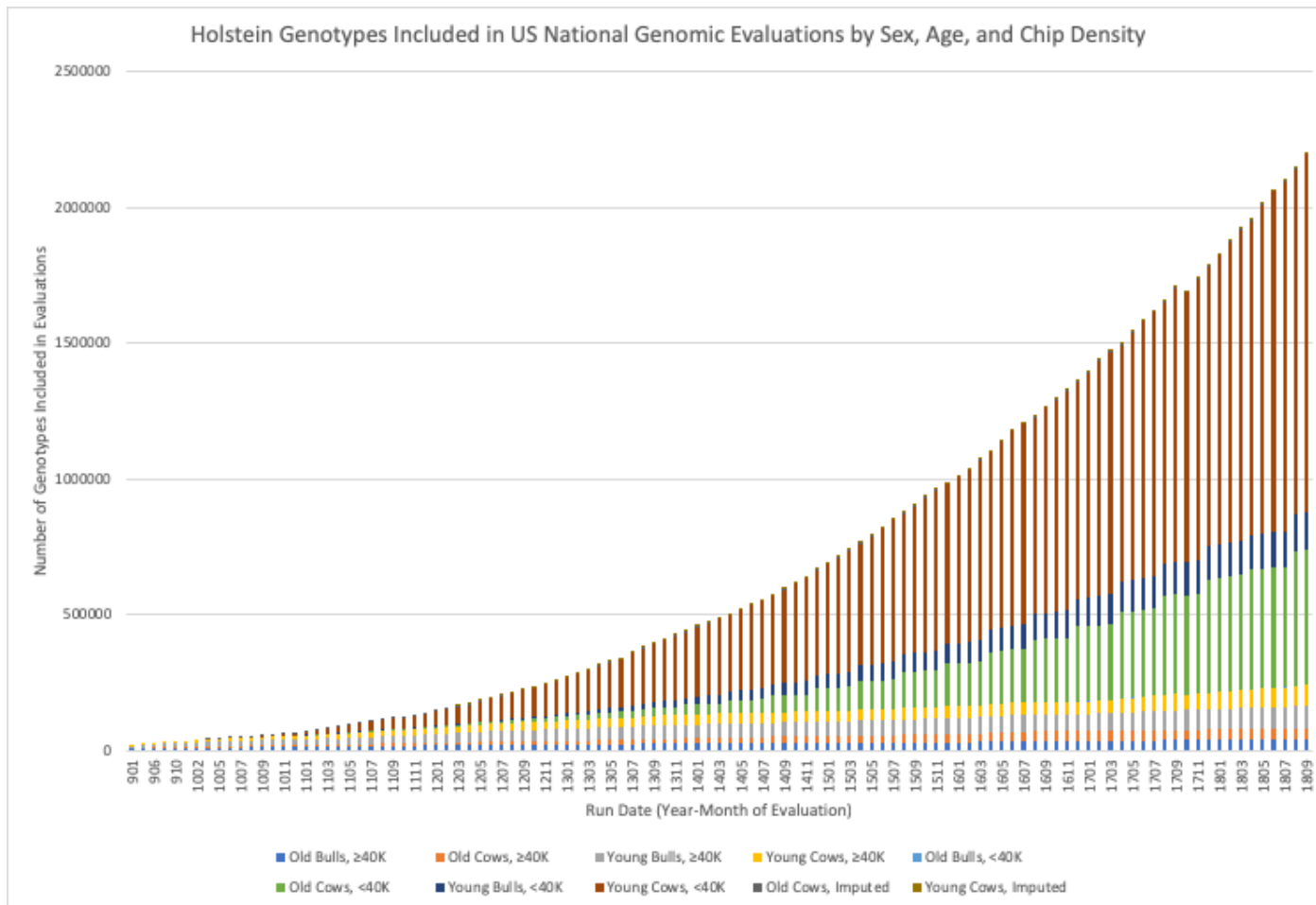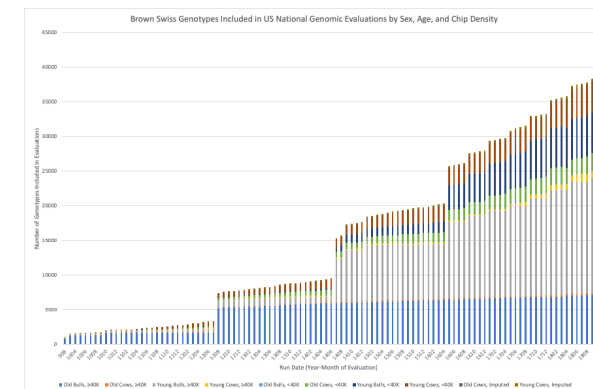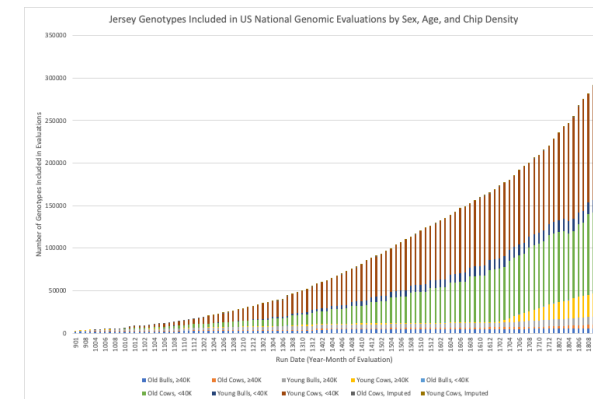
- **High fat and protein**

- **Excellent fertility and ability to produce a calf regularly**

- **Longevity and few health problems (~5 to 7 years)**

- **Low somatic cell count**

- **Smaller and functional cow**

- **Efficiently converts feed to milk**

- **Breed depends on each producer's management system**

Genotypes are plentiful

Source: Council on Dairy Cattle Breeding (2019).

Genomic Selection and Crossbreeding for Health in Organic Dairy Cattle

- Establish associations of mastitis and cow health with genomic evaluations for specific diseases

- Establish associations of respiratory disease, general health, and growth in organic dairy calves with genomic predictions of respiratory disease resistance, and breed composition

- Evaluate the influence of genetic merit and breed composition on pasture behavior and associated health outcomes

Genomic testing

- **Number of animals tested**
  - **GGP 50K**
    - **424 crossbreds**
    - **165 Holstein**
    - **86 Control Holstein**
  - **GGP HD 150K**
    - **127 crossbreds**
    - **51 Holstein**
   - **24 Control Holstein**

1964 genetic control Holstein

- **Started in 1964 a the Southern Research Center in Waseca, MN**

- **Moved to West Central Research Center in 2003 to a low-input and grazing environment**

- **Herd is maintained between 20 to 40 cows and heifers.**

- **100+ years of semen remain**

1964 Holstein selection

1964 Holstein selection

Manhattan Plot: FPC

EMMAX-IBS

Significance = log10(1/p)
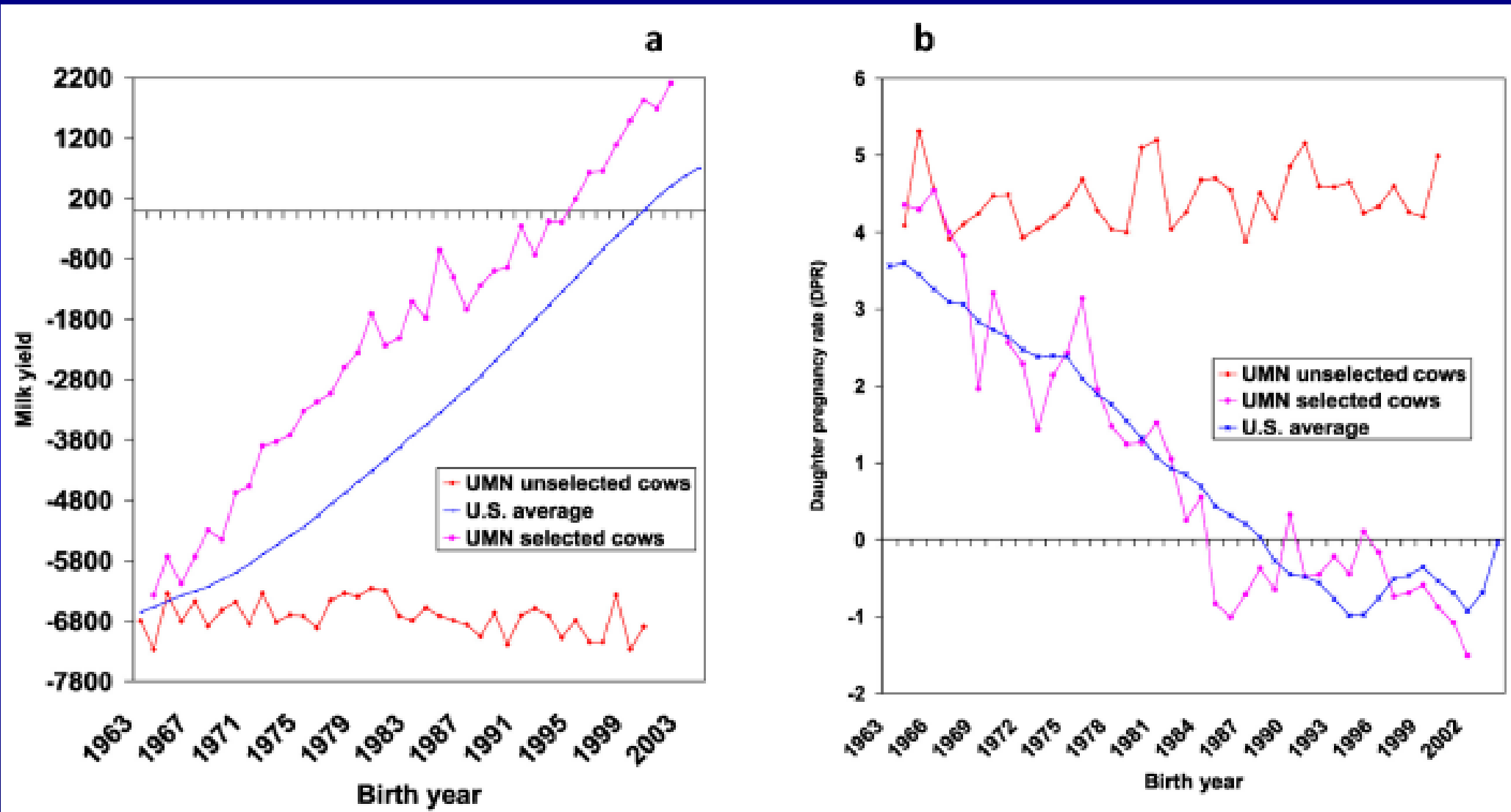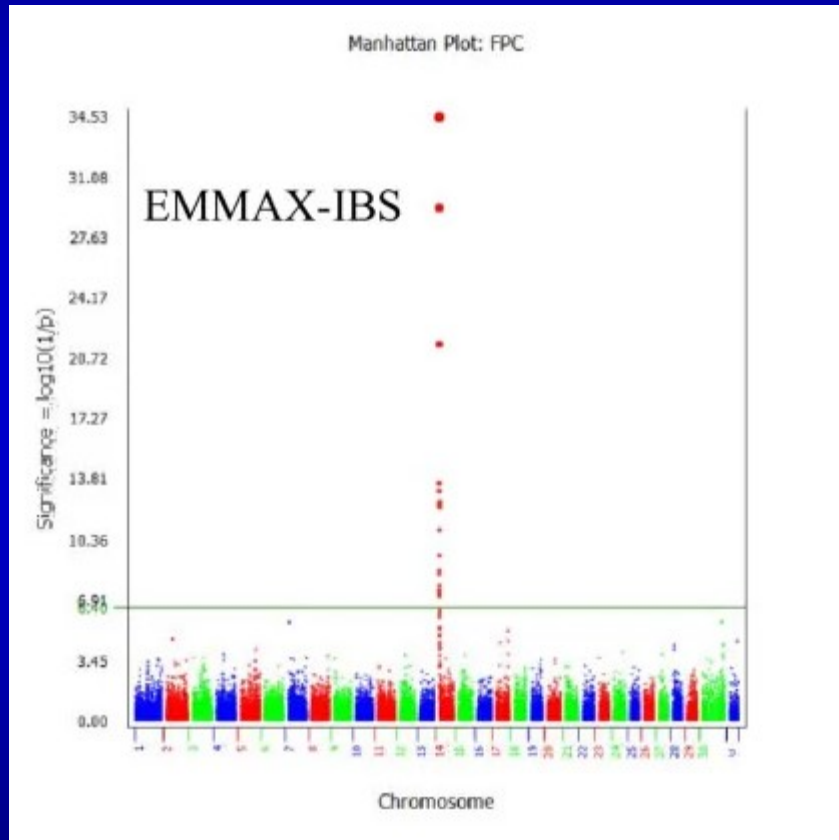
Chromosome

Additional file 11: Table S4. Immunity genes in or near chromosome regions subjected to genetic selection since 1964.

Chr	Selection signature	Gene symbol	Gene name	Documented immunity function
1	12964810-17425222 (3Mb sliding windows)	NCAM	neural cell adhesion molecule 1	affects the innate immune system in the lung [1]
1	63951419-65580210	IGSF11	immunoglobulin superfamily member 11	a novel target for cancer immunotherapy of gastrointestinal and hepatocellular carcinomas [2]
		CD80	cluster of differentiation 80	costimulatory signals for T cell proliferation, cytokine production, and generation of CTL[3]
		GSK3B	glycogen synthase kinase-3 beta	negatively regulate IFN-ß Production by TLR4-stimulated innate immune cells [4]
1	85294656-88698235 (2Mb sliding windows)	SOX2	SRY-box 2	a sequence-specific DNA sensor in neutrophils to initiate innate immunity against microbial infection [5]
		USP13	ubiquitin specific peptidase 13	negatively regulates antiviral responses by deubiquitinating STING [6]
2	79257749-80298164	STAT1	signal transducer and activator of transcription 1	targeted disruption of the mouse STAT1 gene results in compromised innate immunity to viral disease [7]
		STAT4	signal transducer and activator of transcription 4	mediated immune mechanisms in protection against plague [8]
2	84373550-86035295	SLC39A10	solute carrier family 39 member 10	controls humoral immunity by modulating B-cell receptor signal strength [9]
2	91221891-92326427	CD28	cluster of differentiation 28	promote T cell survival [10]
2	120914934-121503634	TRIM64	tripartite motif containing 64	Trim62-deficient mice had increased susceptibility to fungal infection [11]
2	128695085-129554709	GRHL3	grainyhead like transcription factor 3	A GRHL3-regulated repair pathway suppresses immune-mediated epidermal hyperplasia [12]
		IFNLR1	interferon lambda receptor 1 interleukin 22 receptor	expression of Ifnlr1 on intestinal epithelial cells is critical to the antiviral effects of interferon lambda against norovirus and reovirus [13]
		IL22RA1	subunit alpha 1	critical role of IL-22/IL22-RA1 signaling in pneumococcal pneumonia [14]

1964 Holstein Genetics

Purebred Holstein

Petes Photo

Number of observations

Variable	1964 Control	Holstein
Number of cows	45	64
305-d milk (kg)	4,973	7,358
305-d fat (kg)	155	266
305-d protein (kg)	150	238
Somatic cell score	3.2	2.5

Clarifide Plus results

Variable	1964 Control	Holstein
Number of cows	45	64
Future inbreeding (%)	1.46	6.87
Fat + protein	-183	36
DPR	7.1	2.1
Livability	-0.3	1.2
Final Score Type	-4.5	-0.3
NM$	-837	276
DWP$	-746	403

Net Merit ($)

Histogram of Animal Traits

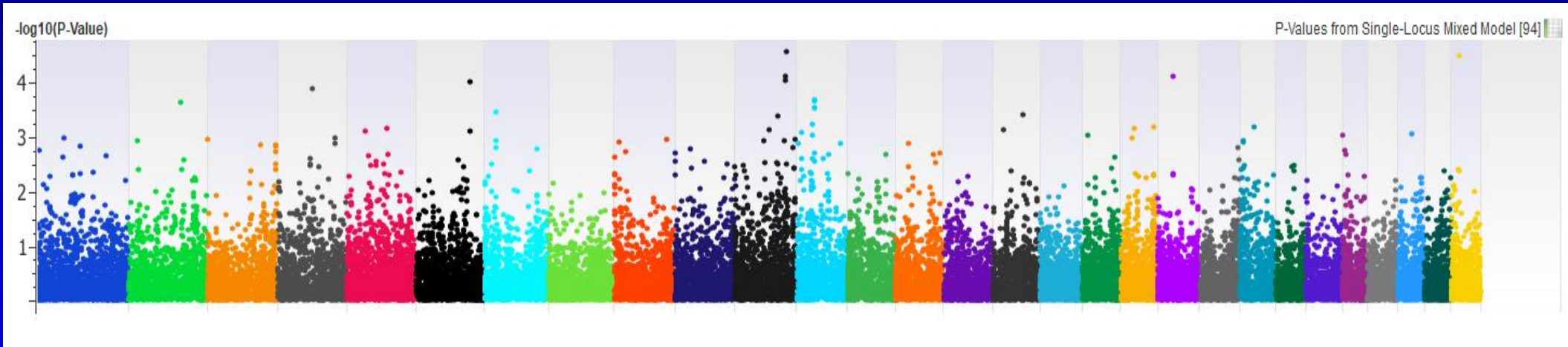NM$ for University of Minnesota West Central (Animal Count = 242)
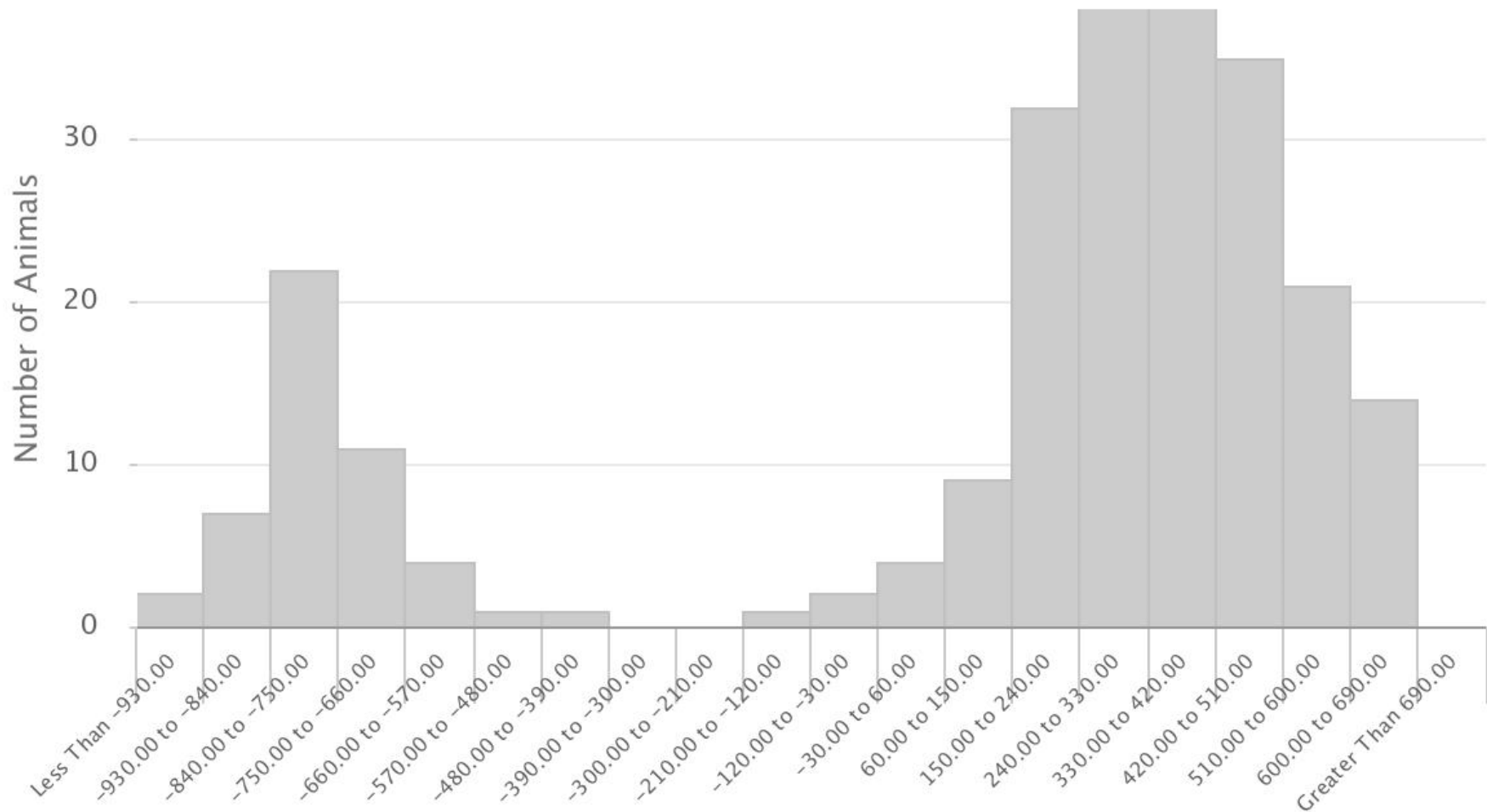
Holstein
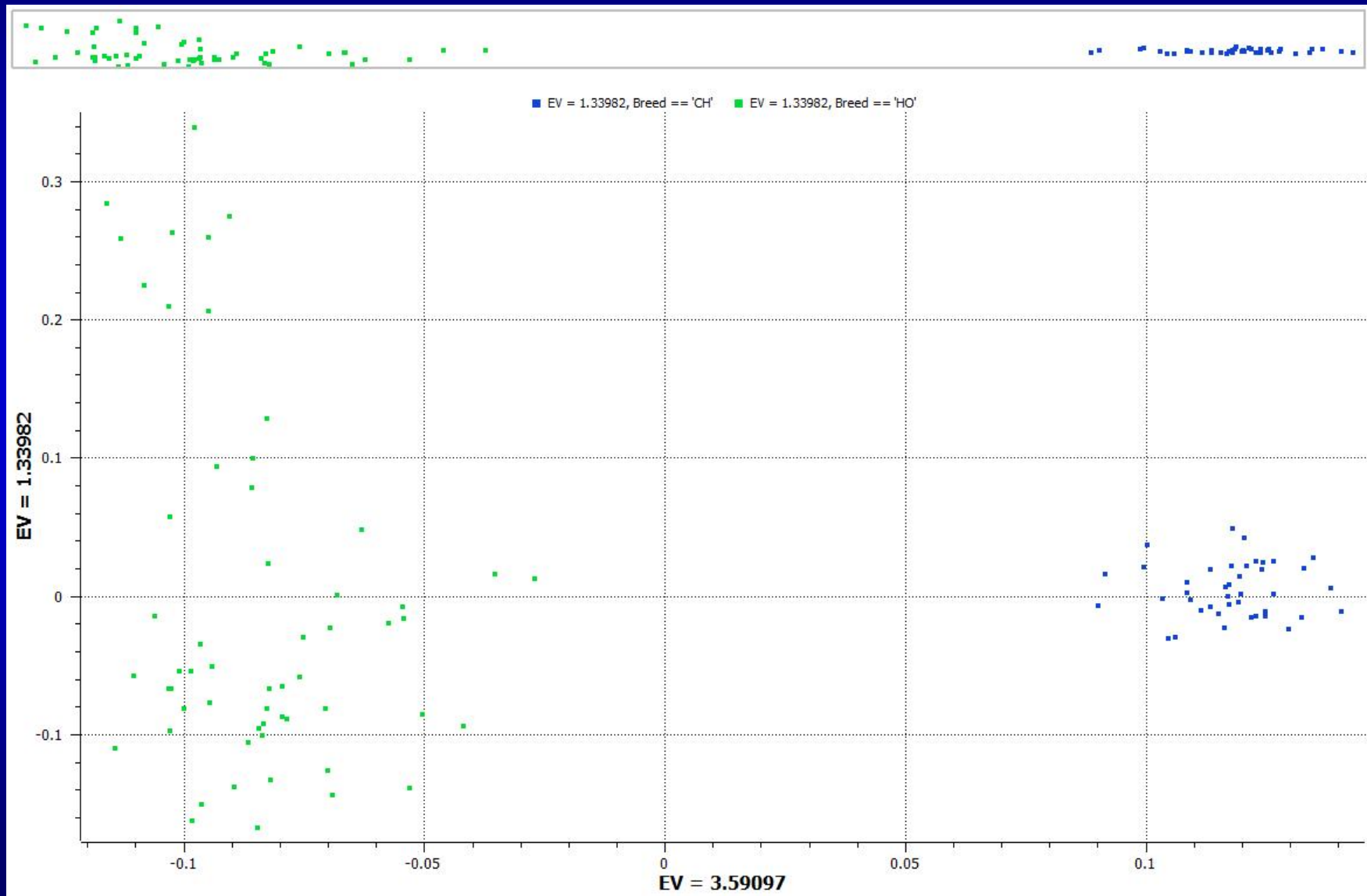
Holstein
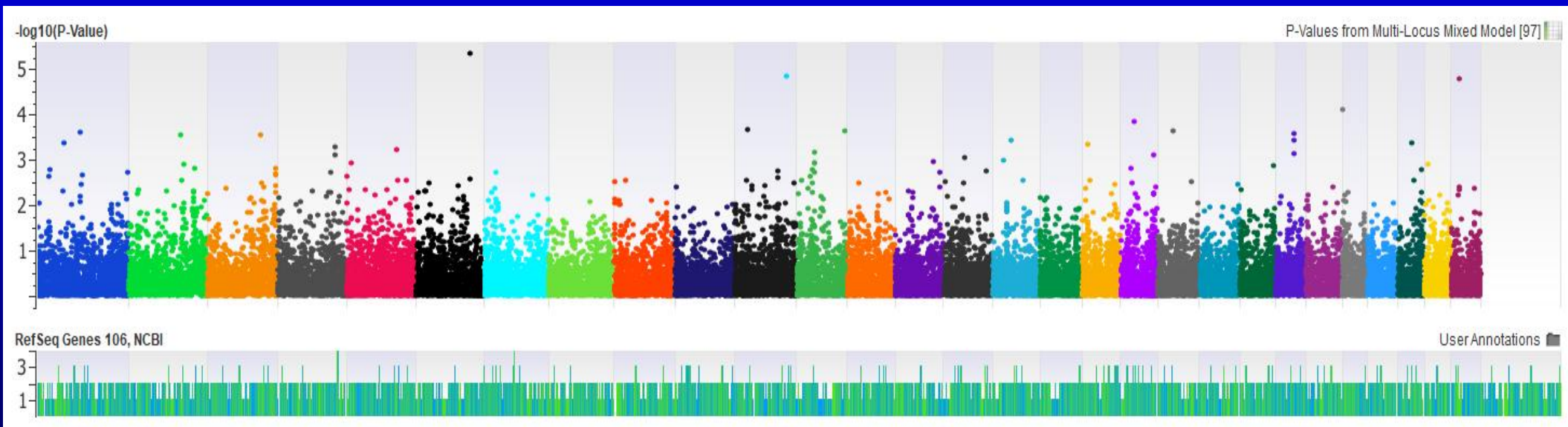
KIT proto-oncogene, receptor tyrosine kinase– Chr 6

Manhattan Category (After Step 2)	Actual Sample Size	Minor Allele (Test Allele)	Major Allele	Minor Allele D Frequency	Major Allele d Frequency	Style
Chr 6	98	G	A	0.423469387755102	0.576530612244898	Chr 6
Cofactor	98	G	A	0.433673469387755	0.566326530612245	Chr 6
Chr 6	98	A	C	0.454081632653061	0.545918367346939	Chr 6

RAN binding protein 2– Chr 11

Minor Allele (Test Allele)	Major Allele	Minor Allele D Frequency	Major Allele d Frequency	Style
A	G	0.0969387755102041	0.903061224489796	Cofactor
A	G	0.137755102040816	0.862244897959184	Chr 11
G	A	0.428571428571429	0.571428571428571	Chr 11
A	G	0.443877551020408	0.556122448979592	Chr 11
G	A	0.443877551020408	0.556122448979592	Chr 11
G	A	0.443877551020408	0.556122448979592	Chr 11
G	A	0.357142857142857	0.642857142857143	Chr 11

University of Minnesota crossbreeding research

- **Crossbreeding initiated in 2000 with two research herds of Holsteins — the campus herd at St. Paul and the low input research herd at Morris, MN**

- **2000 to 2002:**
  - **½ bred to Holstein AI sires**
  - **½ bred to Jersey AI sires**

- **2003 to 2007:**
  - **Pure Holsteins bred to Holstein and Montbeliarde AI sires**
  - **Jersey x Holstein crossbreds bred to Montbeliarde AI sires**

- **2008 forward:**
  - **Viking Red replaced Jersey in the 3-breed rotation**

Profit per day from California study
(ignoring differences in health cost)

	Cows	Production income/day	Profit/day
Holstein	165	$11.47	$4.17
VR×HO and NR×HO	369	−$.22 **	+$.15 **
		−2 %	+4 %
MO×HO	218	−$.22 **	+$.22 **
		−2 %	+5 %

** Difference from Holstein $P < 0.01$

Holstein sire
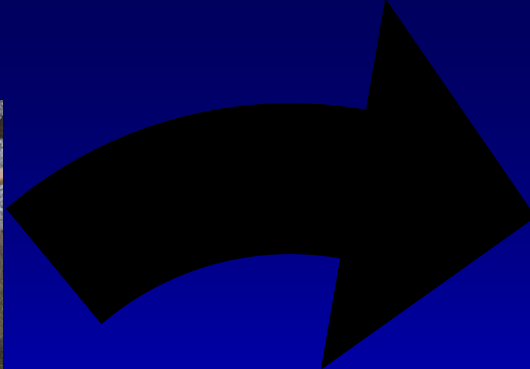
Viking Red sire
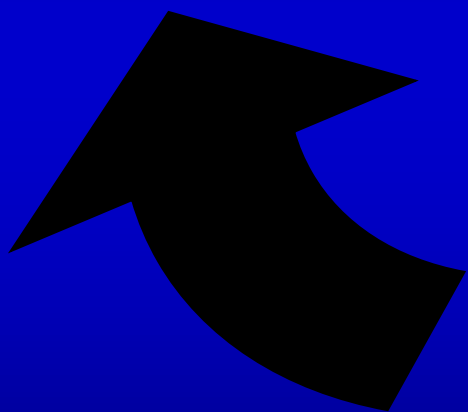
Montbeliarde sire

Pro Cross at the U of MN

22

Jersey

Viking Red

Normande

GrazeCross
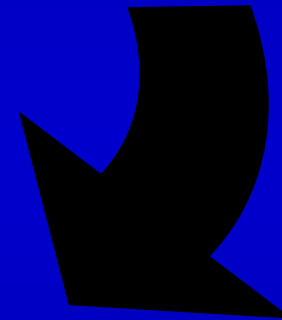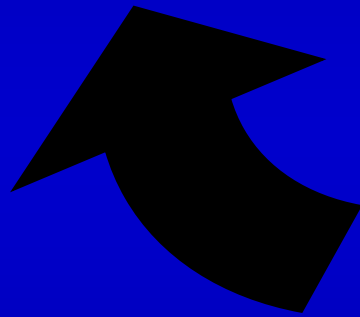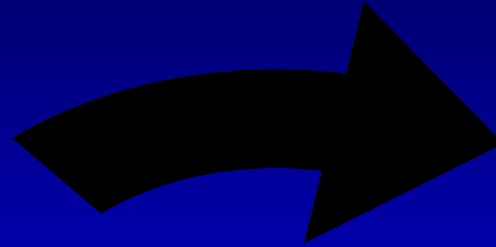
Viking Red x Holstein x Montbéliarde

Petes Photo

Normande x Viking Red x Jersey

Petes Photo

Jersey x Normande x Viking Red

Petes Photo

Montbéliarde x Holstein x Viking Red

Petes Photo

A2 Genetics WCROC

Breed group	N	A1/A1	A1/A2	A2/A2
		----------%----------		
Holstein	50	16	36	48
1964 Holstein	37	27	41	32
Holstein-sired	65	17	34	49
Jersey-sired	51	8	45	47
Montbéliarde-sired	98	17	47	36
Normande-sired	56	5	45	50
Viking Red-sired	136	15	40	45
Overall	493	15	41	44

Crossbreds
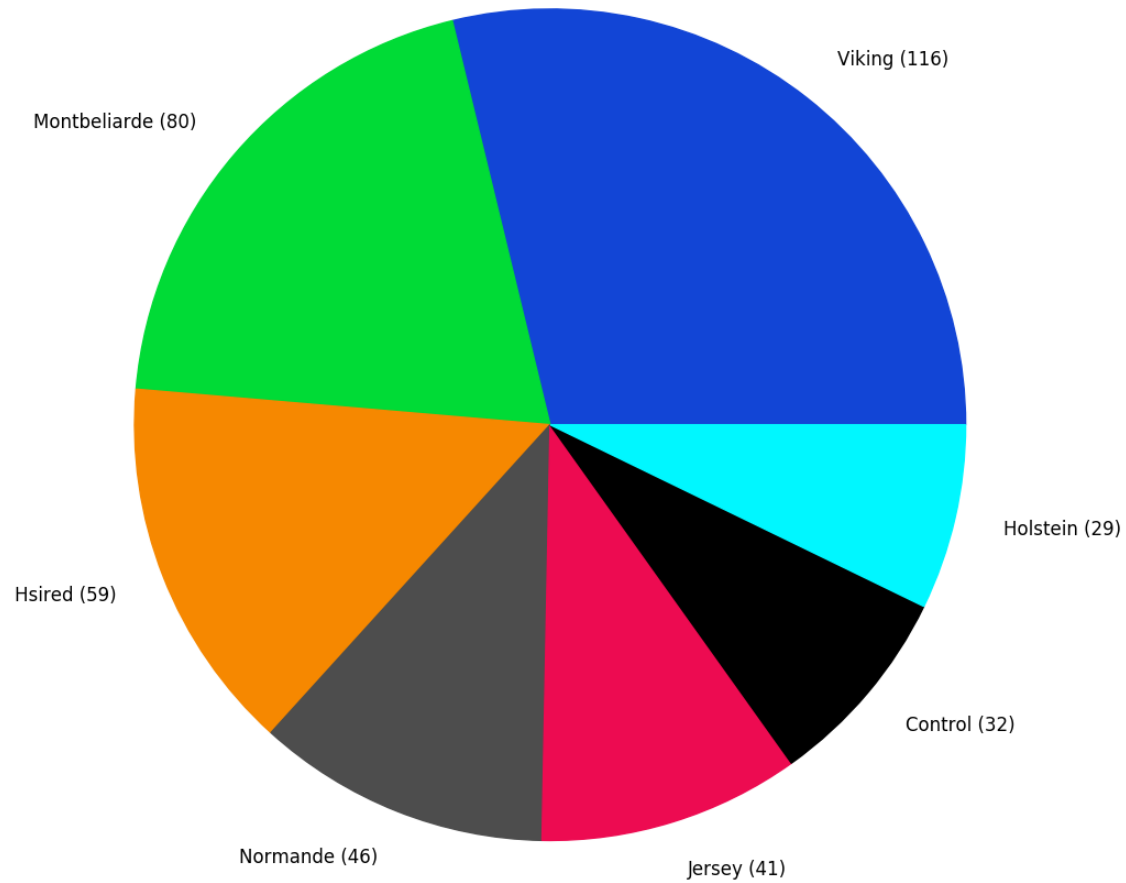
Crossbreds
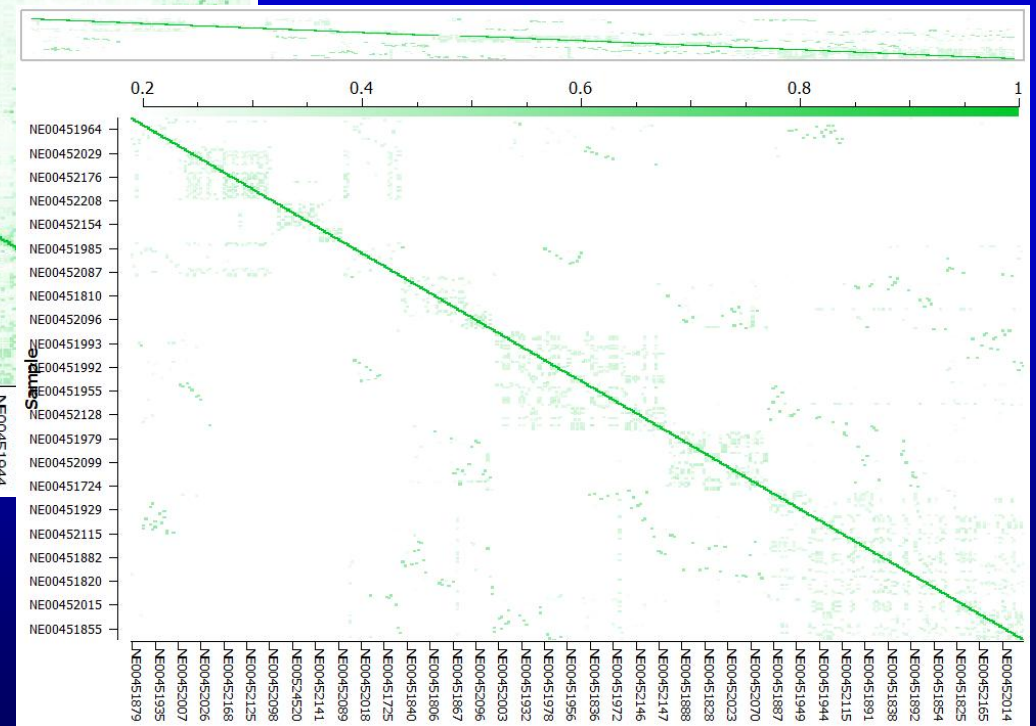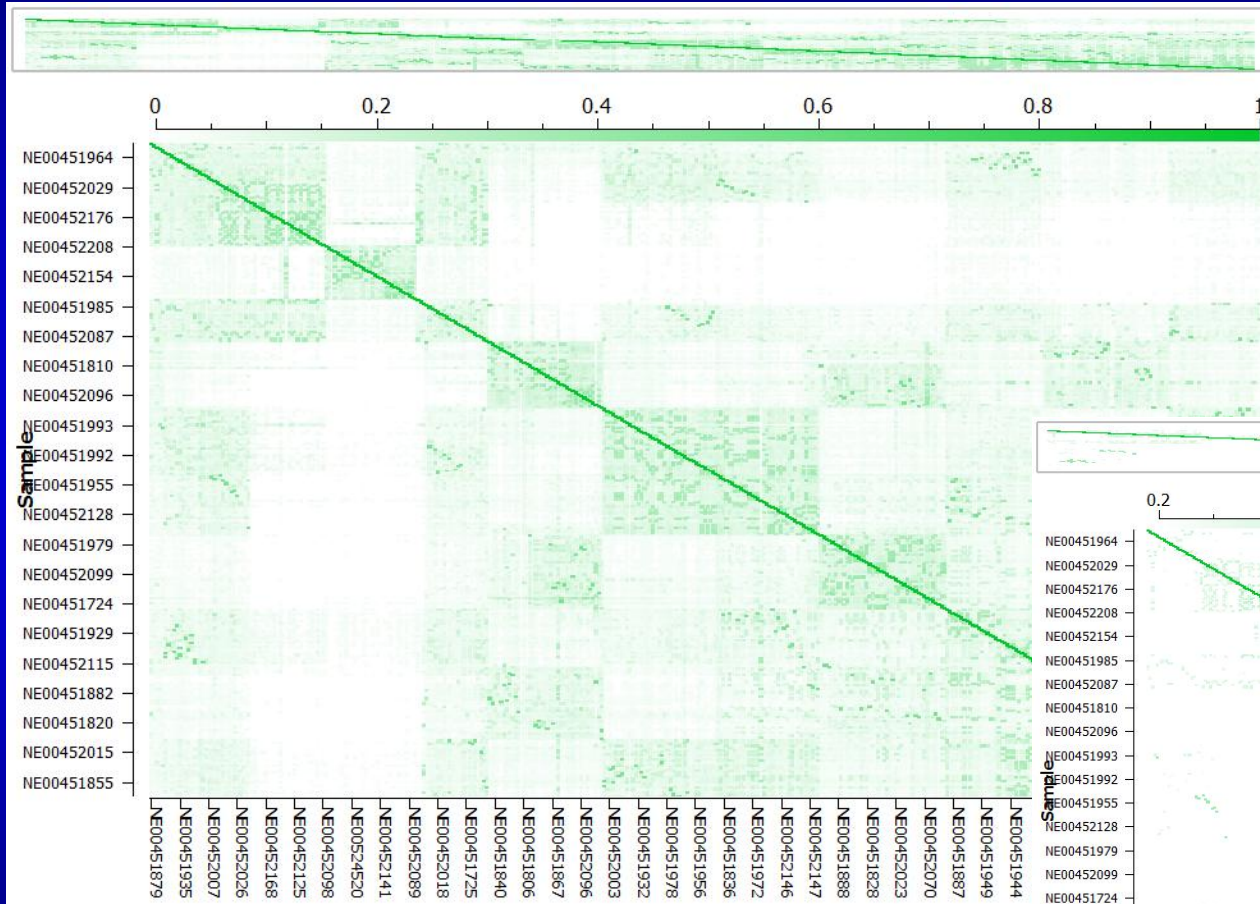
Crossbred Population Stratification
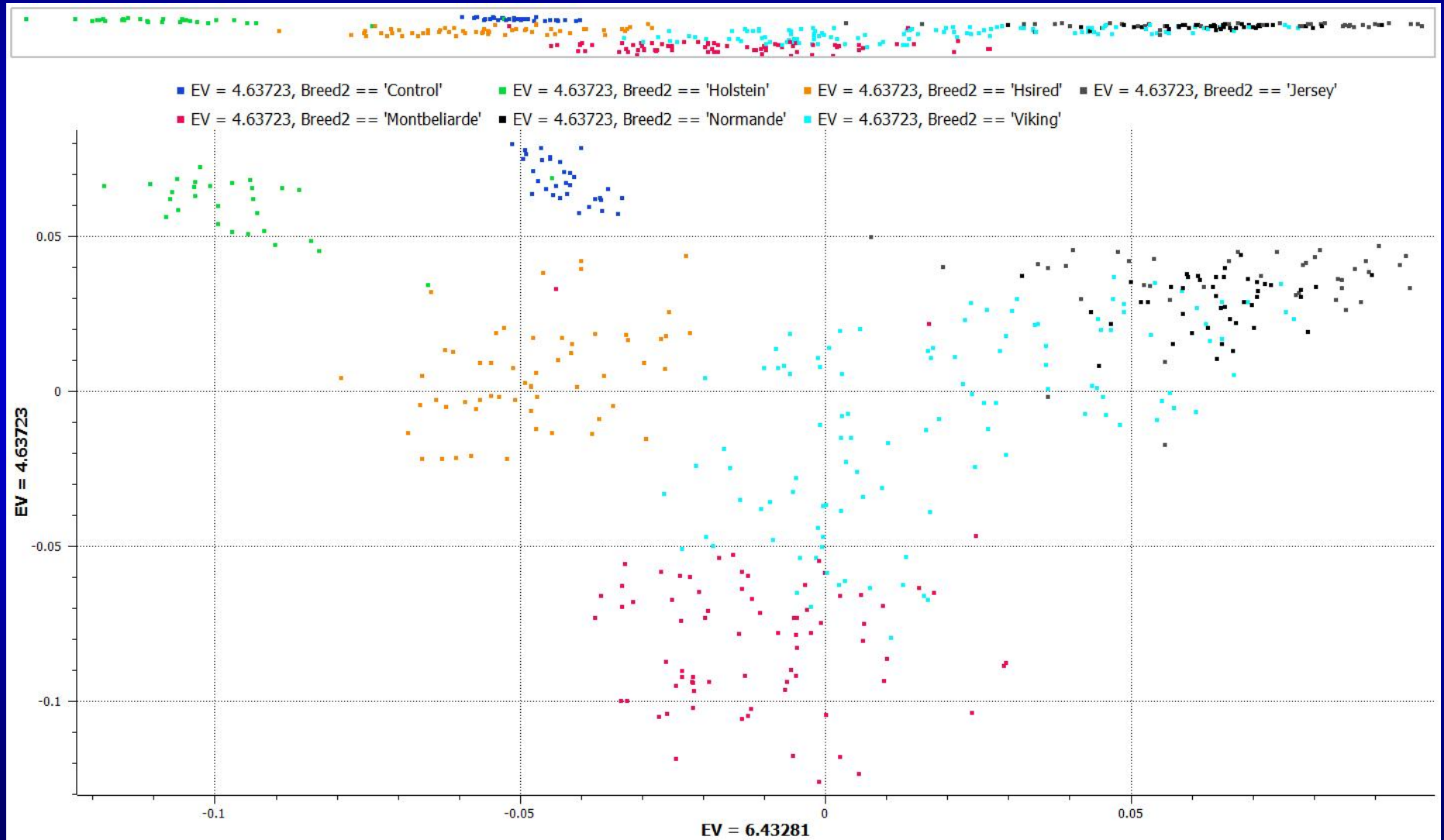
Crossbreds
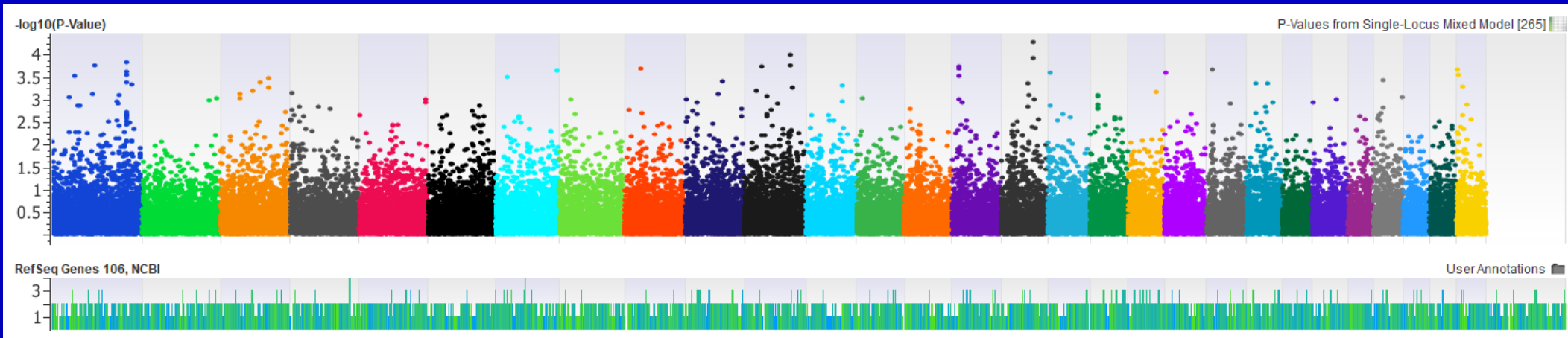
Calf Health - Holm and Laue HL 100 feeder

Health scores for feeding groups

Trait	Milk	Replacer
Nose score	0.00	0.02
Eye score	0.03[a]	0.01[b]
Ear score	0.01	0.00
Cough score	0.01	0.00
Fecal score	0.89[a]	1.54[b]
Navel score	0.00	0.02
Joint score	0.00	0.00

Means within a row without common superscripts are different at P < 0.05.

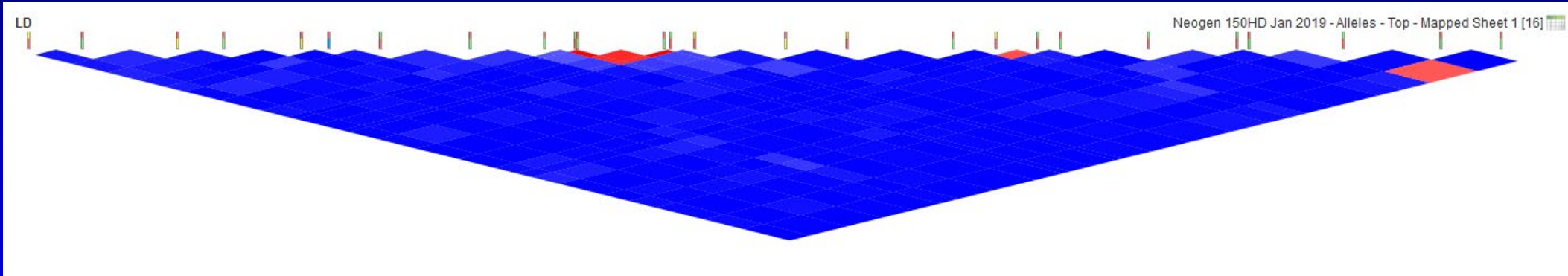# Calf breed distribution
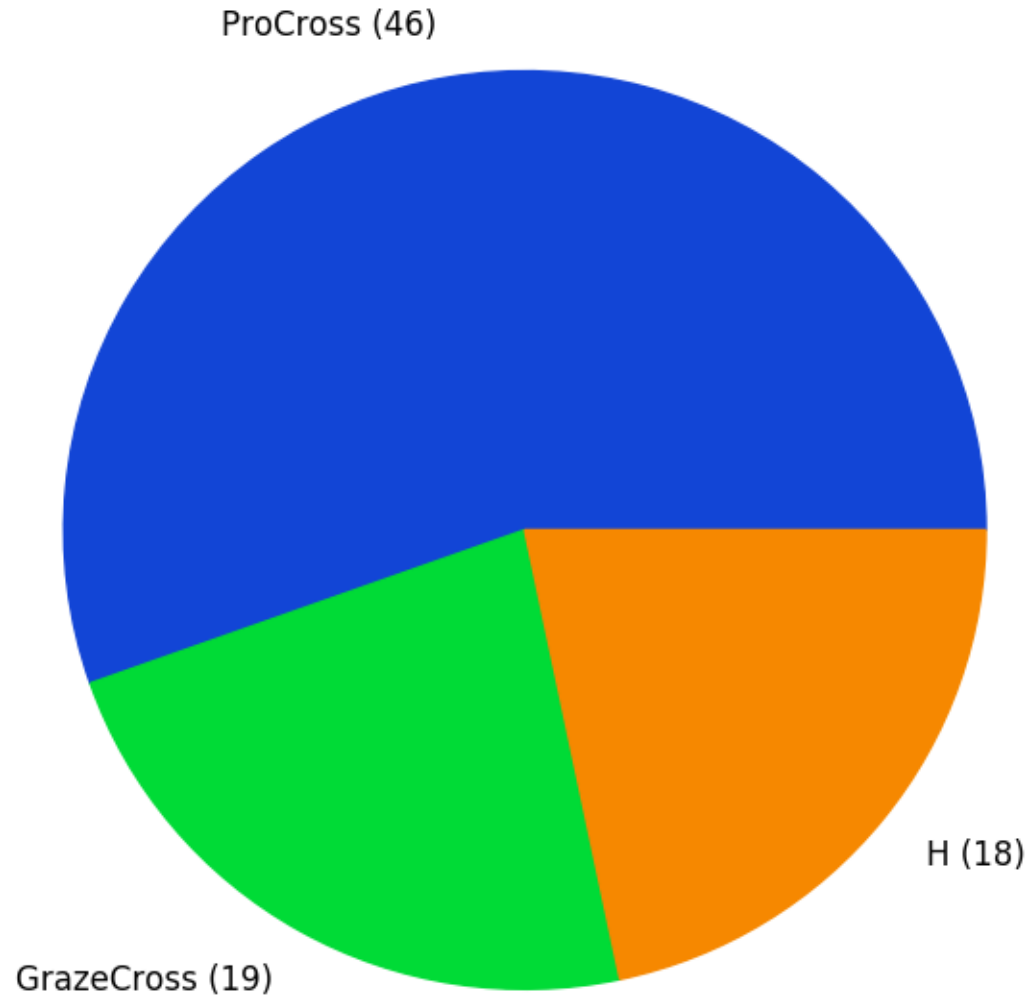
Calf call rate
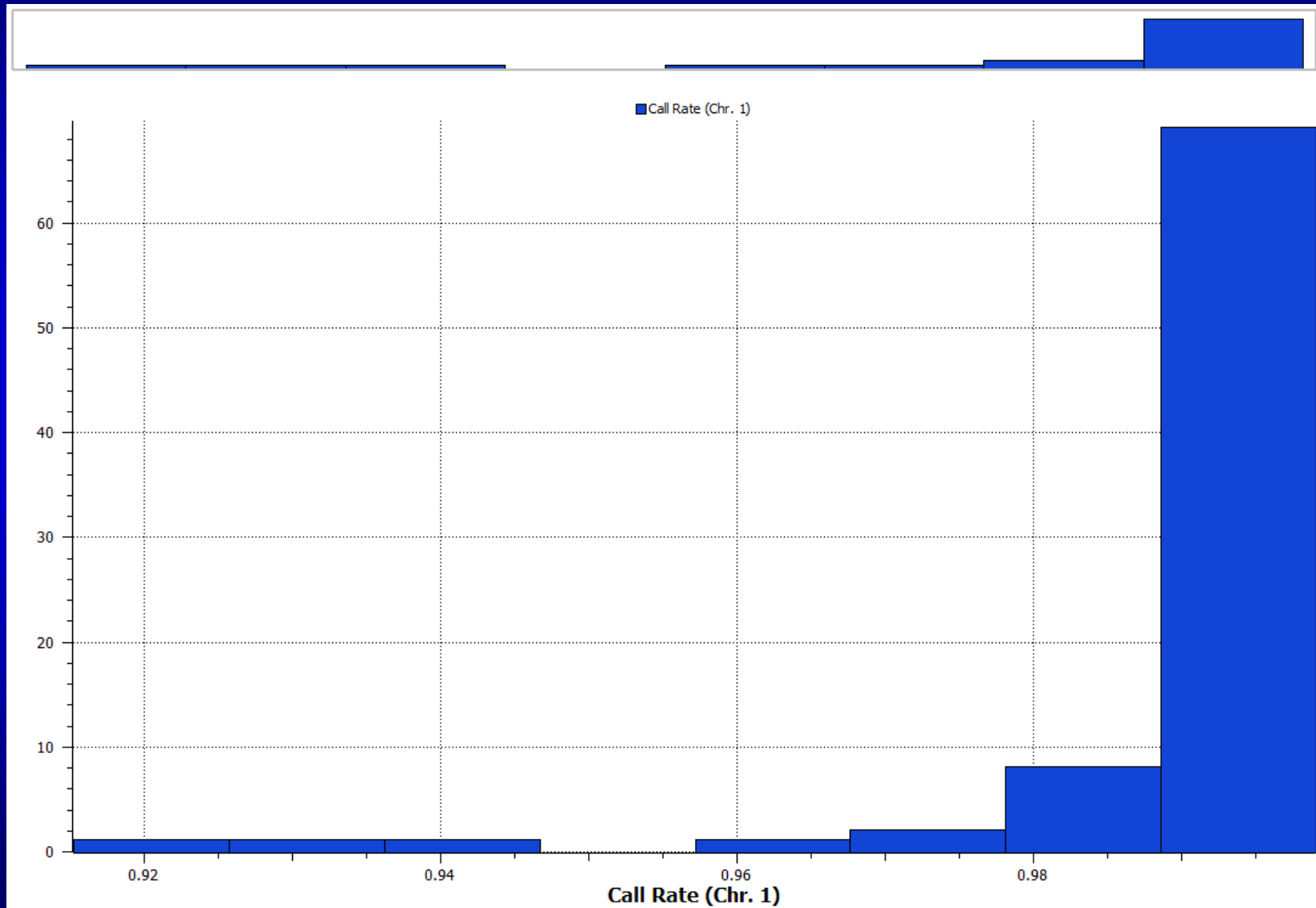
Calf Cryptic Relatedness
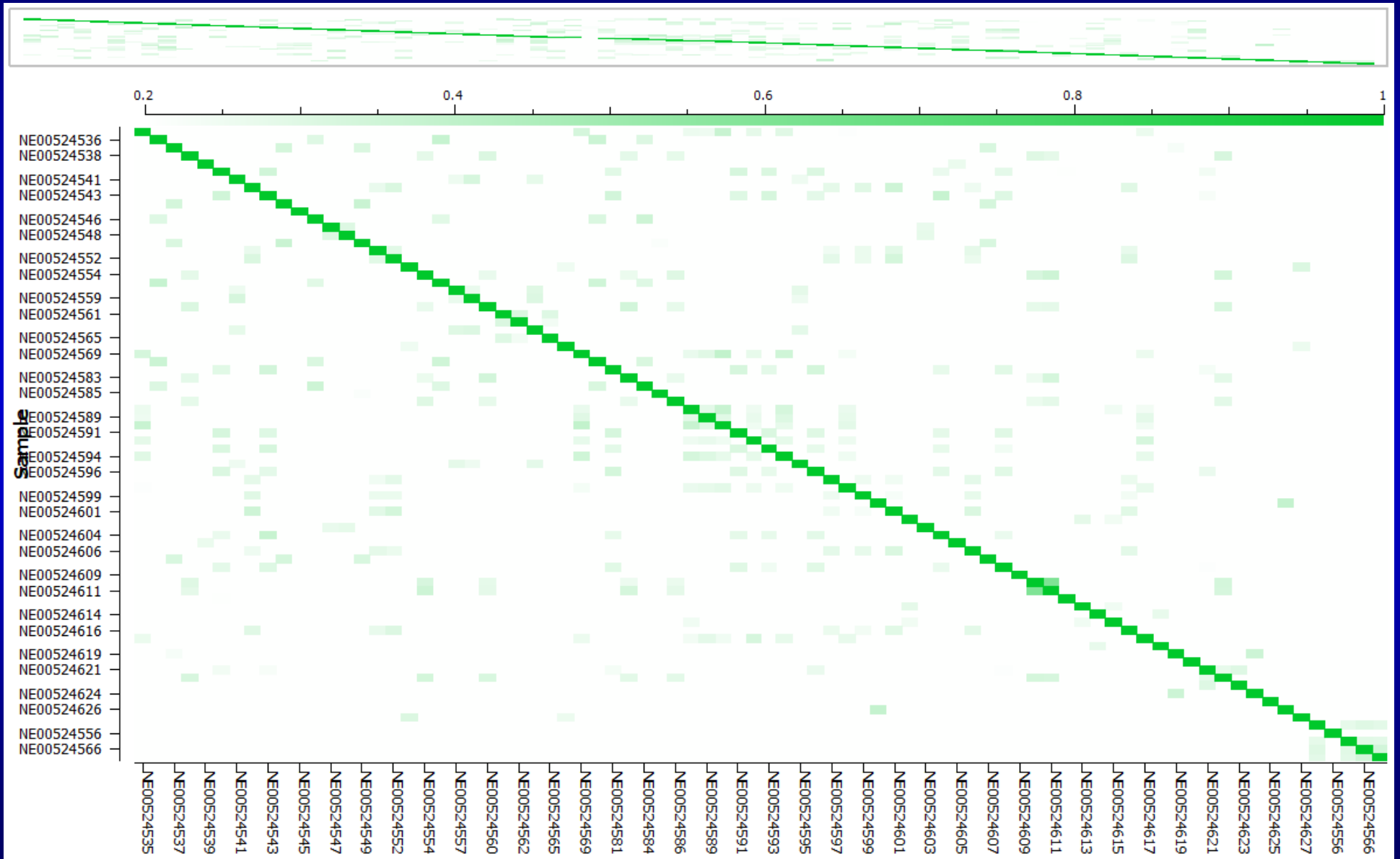
Calf PCA analysis
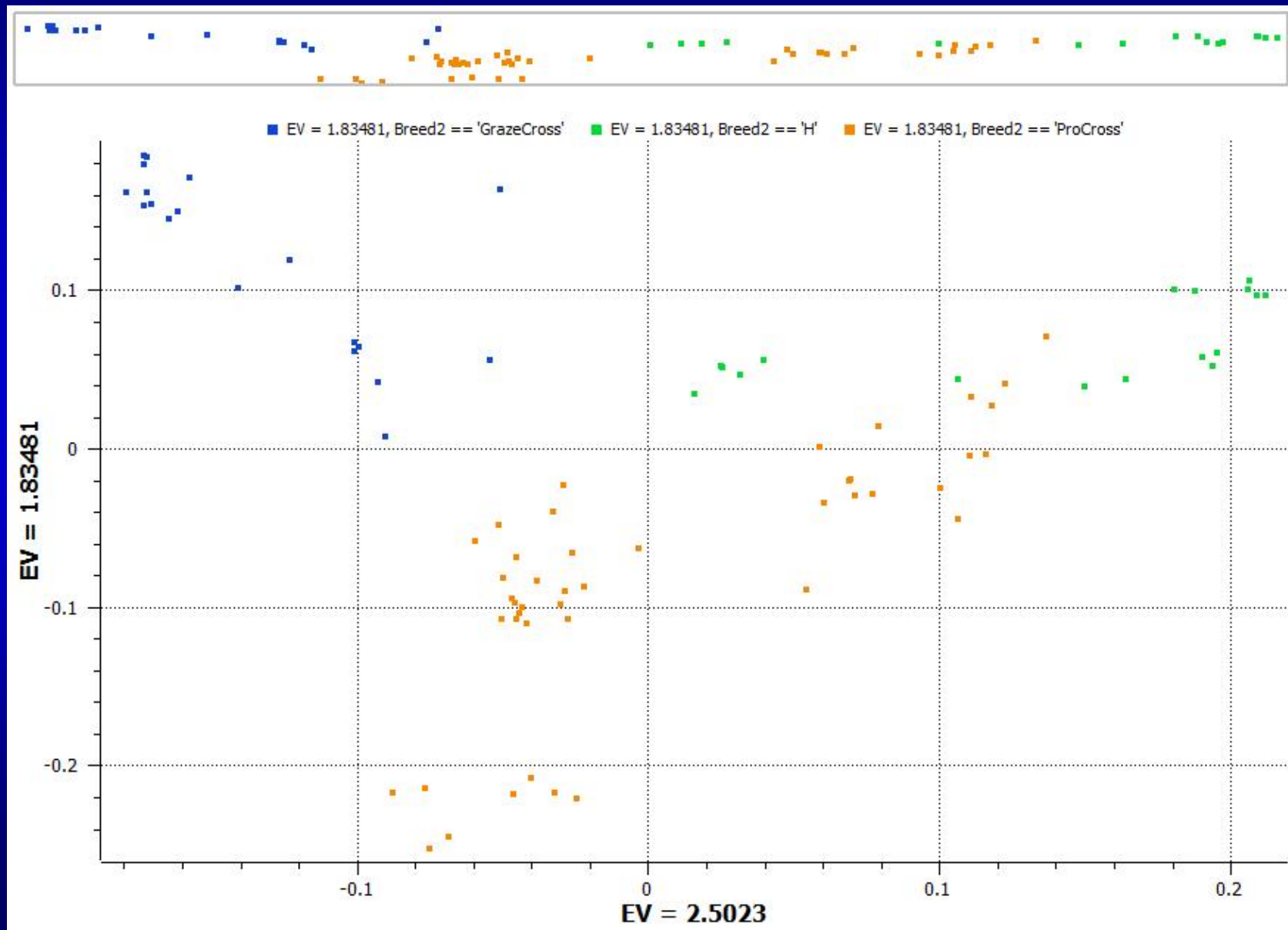
Calf Manhattan Plot
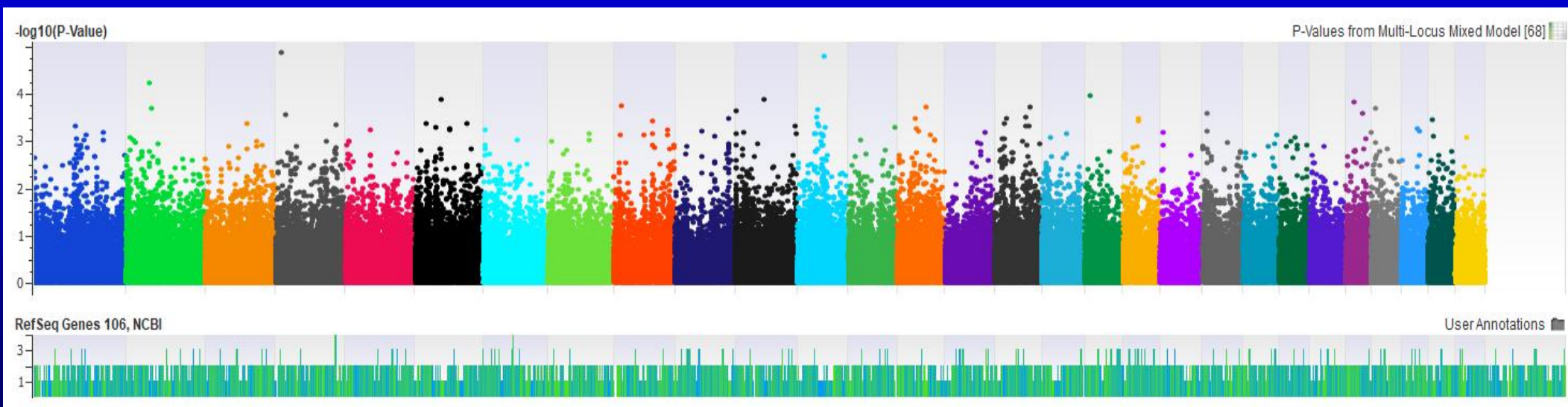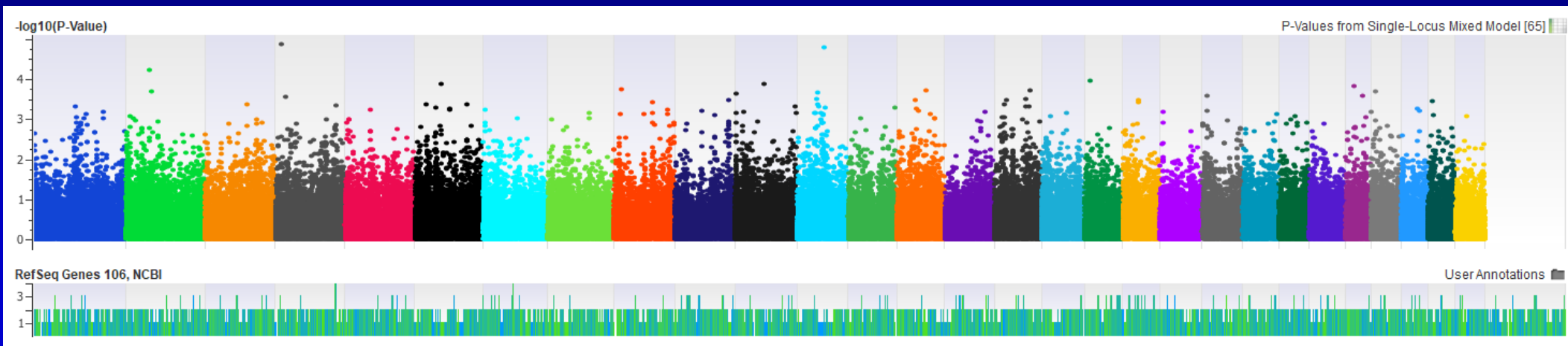
Calf LD Plot
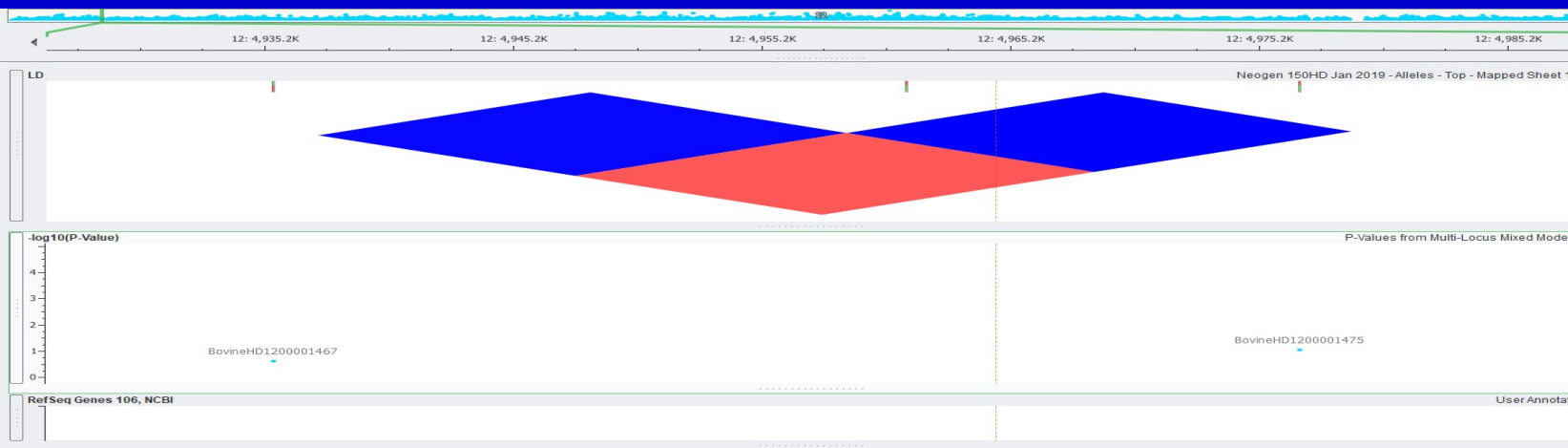
coagulation factor X

SLC7A1 solute carrier family 7 member 1

Calf Q Q Plot
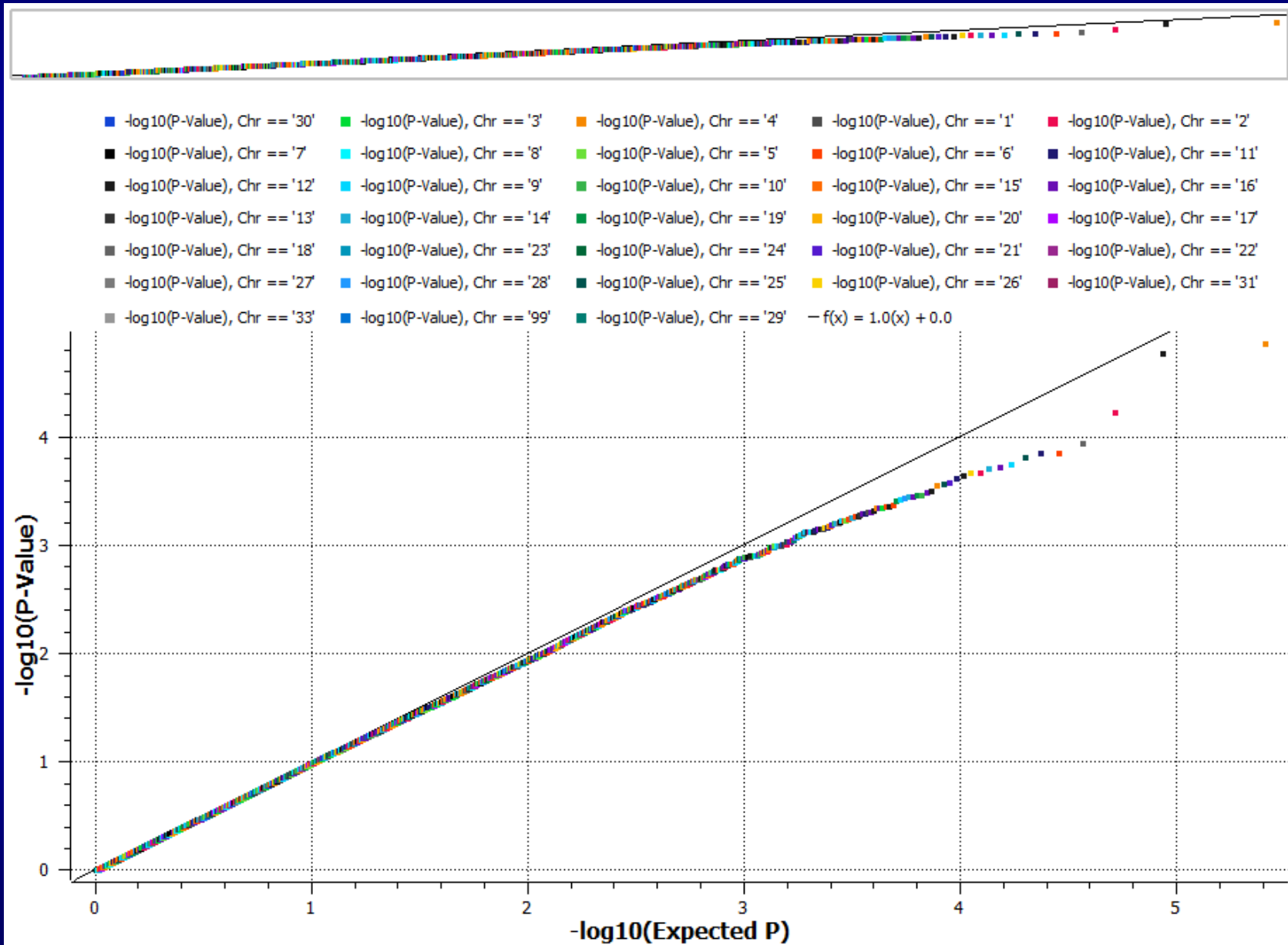
Calf ROH
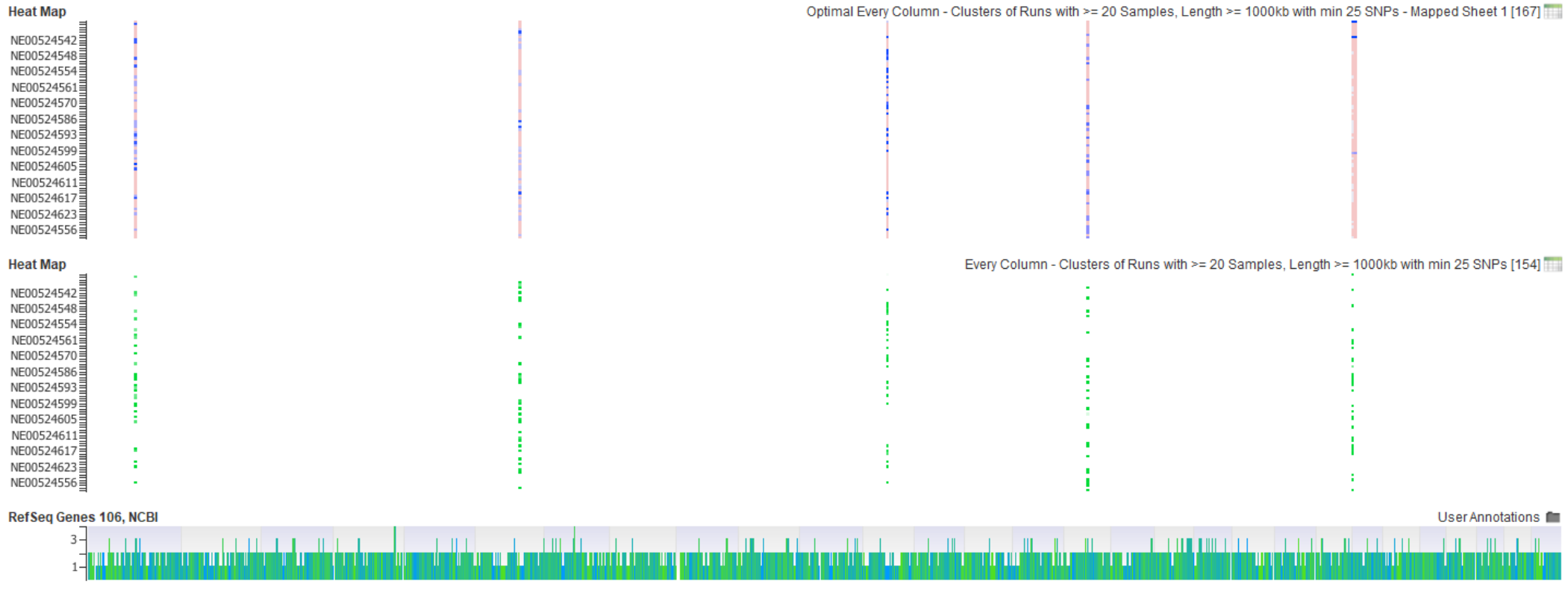
Calf ROH
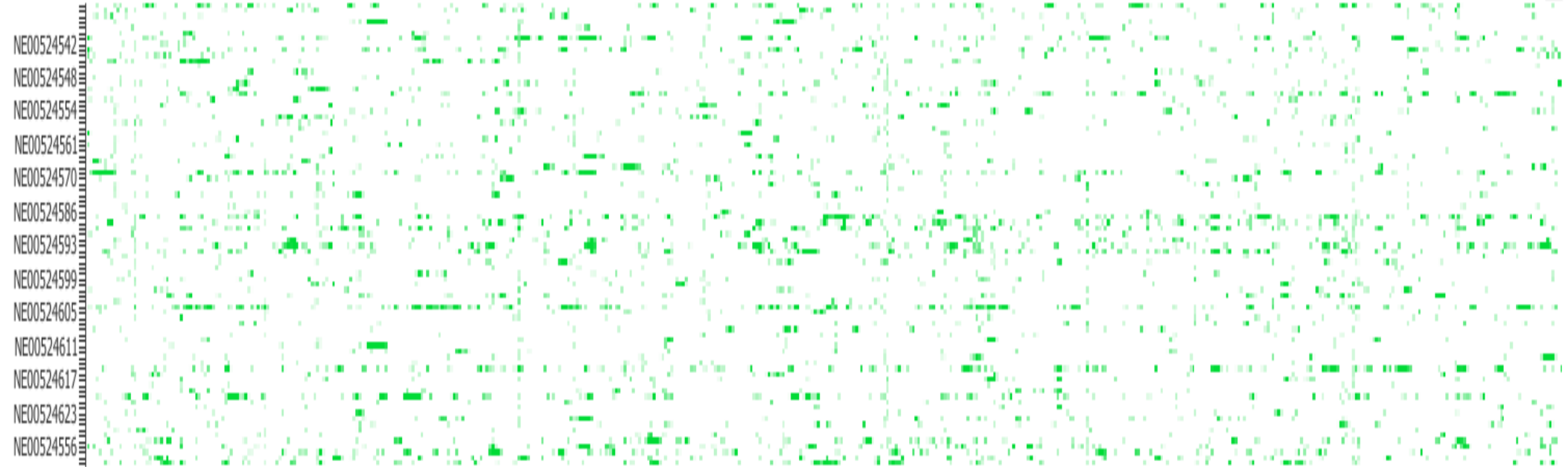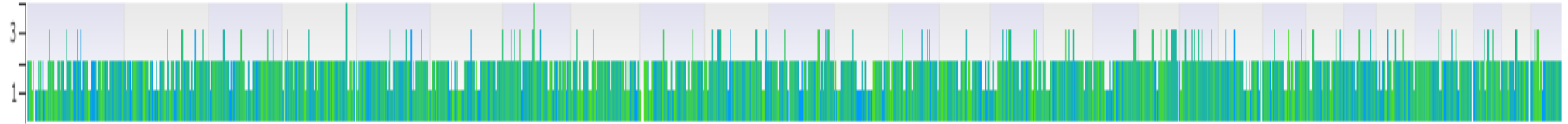
Conclusion

- **1964 Control Holstein cows still exist and may provide interesting results for gene discovery of dairy cattle health**

- **Gene discovery will continue for calf health traits in grazing dairy herds**

- **Genome wide association studies for grazing dairy cattle**
  - **Identify markers and regulation of traits that affect health of cattle**

Future work

- **PBAT Family analysis**

- **Candidate gene analysis**

- **G x E analysis with crossbreds and Holstein and comparing studies**

- **Jersey calf health in automatic feeder**

- **Genomic selection and genomic evaluation to improve economic weights for grazing merit.**

- **More sensor analysis – Phenotype is king**

  - **USDA animal blueprint**

  - **Body temperature, activity, rumination time, feed & water intake**

- **Graduate student course**

Acknowledgments

- **Collaborators**
  - **Chad Dechow – Penn State**
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  - **Glenda Pereira – University of Minnesota**
  - **Kirsten Sharpe – University of Minnesota**
  - **Les Hansen – University of Minnesota**

USDA United States Department of Agriculture   National Institute of Food and Agriculture

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**https://wcroc.cfans.umn.edu/research-
programs/dairy**

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