High Resolution QTL Maps Of 31 Traits in Contemporary U.S. Holstein Cows

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August 2010
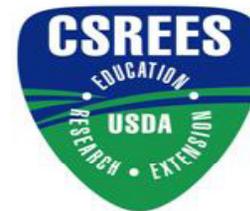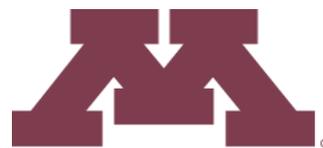
Objectives

- Identify SNP effects and gene regions associated with 31 dairy traits in contemporary U.S. Holstein cows

- 9 net merit traits:

  MY, FY, PY, FPC, PPC, SCS, DPR, PL, NM

- 4 calving traits: SCE, DCE, SSB, DSB

- 18 body conformation traits

  – Body size: STA, STR, BD, RW (4)

  – Body shape: DF, RA (2)

  – Udder and teats: FUA, RUH, UD, UC, FTP, RTP, TL (7)

  – Feet-legs: FA, RLS, RLR, FL (4)

  – Final score: FS (1)

Material and methods

- 1654 Contemporary Holstein cows

- 45,878 SNPs from Illumina Bovine SNP50^{TM} chip

- SNP locations by UMD 3.1

- Gene locations by UMD 3.1 and BTAU_4.0

- PTA values as phenotypic values

- Statistical tests by EPISNPmpi program

  – Testing 3 effects per SNP: genotypic, additive and dominance effects

  – Results were partially checked by PLINK

 – (All reported effects were additive effects)

Results

- Top 100 effects of each trait are reported
  - Too many effects exceeding genome-wide significance
- 3100 effects involved 1586 SNP markers
  - 1300 NM and calving traits involved 725 SNPs with 258 SNPs (36%) inside 217 genes
  - 1800 type traits involved 1005 SNPs with 366 SNPs (36%) inside 297 genes
- Different traits had a tendency to be affected by different chromosomes
- X chromosome had highest frequencies of significant effects
- SNP effects of most traits had strong correlations

Distribution of top 100 most significant results for each of the 13 net merit and calving traits by chromosome (10 or more effects are in bold face).

| Chr	MY	FY	PY	FPC	PPC	SCS	DPR	PL	NM	SCE	DCE	SSB	DSB	SUM
1	2	4	4	4	5	4	17	15	15	7	6	7	3	93
2	3	0	0	0	1	11	2	1	0	0	0	0	2	20
3	10	4	1	4	1	7	17	9	1	4	0	4	6	68
4	3	2	2	0	0	0	0	4	0	2	0	3	0	16
5	2	2	2	7	13	4	0	0	2	7	3	10	0	52
6	2	2	5	1	6	9	0	2	5	0	6	0	1	39
7	0	6	1	1	2	13	15	11	4	4	11	0	6	74
8	2	1	0	0	0	1	3	4	1	0	0	0	3	15
9	7	6	1	1	2	0	0	0	4	4	3	1	6	35
10	5	0	0	0	3	2	6	0	0	1	0	4	0	21
11	3	3	3	1	3	1	0	0	0	1	0	0	5	20
12	2	1	1	2	3	6	0	0	1	8	2	6	1	33
13	13	12	8	4	1	1	2	0	4	1	0	0	7	53
14	2	1	1	24	2	0	2	0	0	0	0	6	4	42
15	1	2	1	2	0	0	0	1	1	1	1	4	5	19
16	1	0	0	0	0	11	1	2	0	0	0	3	3	21
17	4	7	6	11	14	1	5	9	14	20	21	7	2	121
18	8	4	6	5	4	2	5	8	10	9	12	6	4	83
19	2	3	2	0	0	0	0	0	0	0	0	0	3	10
20	0	2	11	0	2	2	0	0	0	1	1	1	5	25
21	4	1	5	0	5	0	0	0	1	2	1	6	5	30
22	1	0	0	0	0	2	3	3	1	0	1	0	2	13
23	5	5	9	2	3	1	0	0	3	2	1	1	16	48
24	2	1	2	2	2	1	0	1	2	1	1	3	0	18
25	0	2	0	3	0	5	1	0	0	0	0	1	0	12
26	0	7	6	6	10	3	4	9	11	6	10	9	1	82
27	5	6	7	0	1	1	0	1	3	3	1	0	1	29
28	0	0	5	0	1	0	3	2	3	3	1	1	1	20
29	0	0	0	0	0	2	1	1	1	0	2	1	3	11
X	11	16	11	19	16	9	12	15	12	12	16	15	3	167
U	0	0	0	1	0	1	1	2	1	1	0	1	2	10
P[a]	10^{-12}	10^{-24}	10^{-22}	10^{-17}	10^{-23}	10^{-29}	10^{-34}	10^{-25}	10^{-23}	10^{-38}	10^{-23}	10^{-24}	10^{-21}	
R^2	0.42	0.43	0.42	0.45	0.40	0.54	0.53	0.54	0.49	0.52	0.42	0.56	0.55	

[a] This is the rounded cut-off p-value for the top 100 most significant SNPs of this trait.

QTL Maps of 4 Chromosomes for Net Merit and Calving Traits
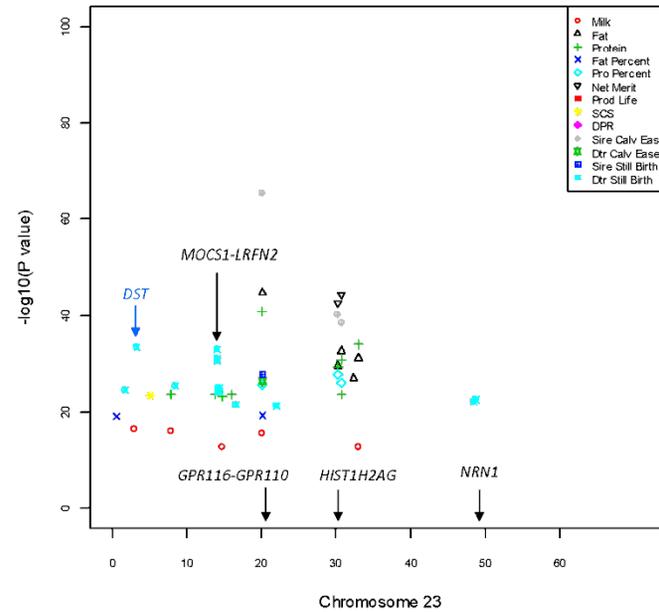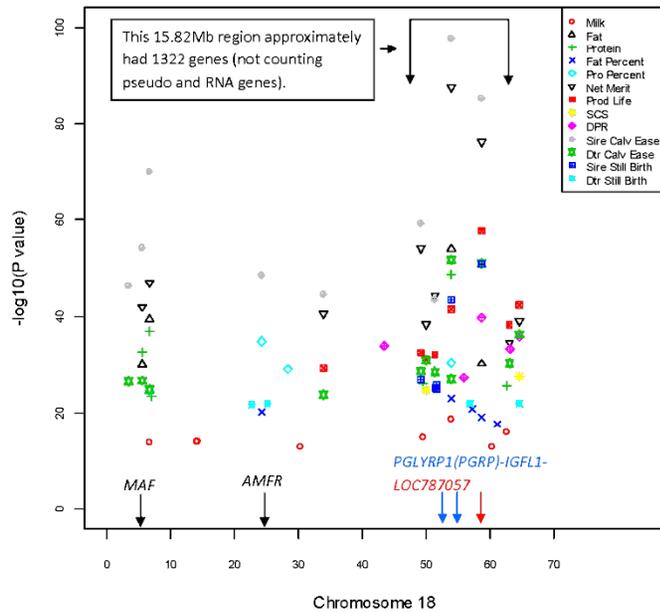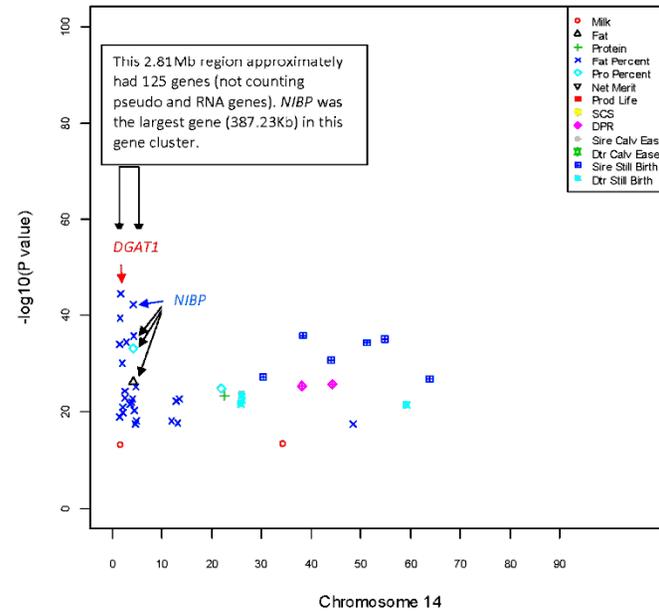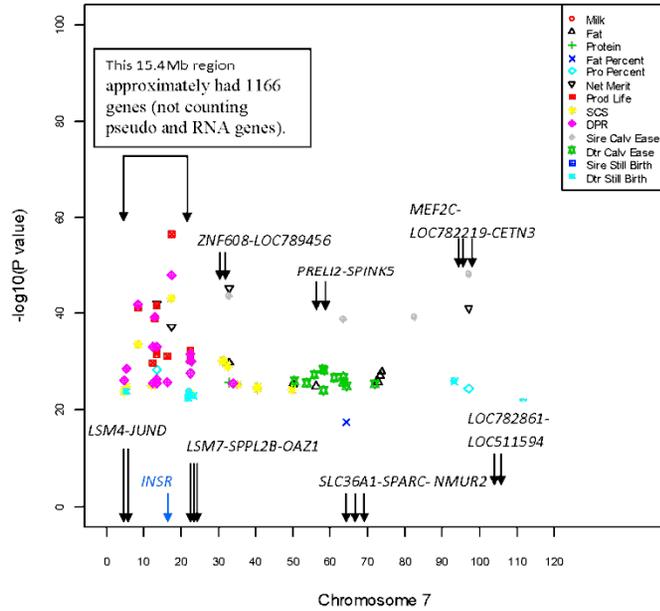
A: Significant SNP effects from data analysis
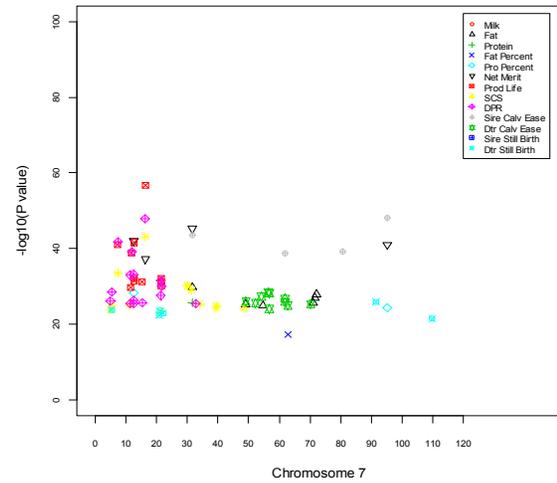
B: Bioinformatics analysis revealed a large gene cluster underneath the SNP effects

This 15.4Mb region approximately had 1166 genes (not counting pseudo and RNA genes).

LSM4-JUND
LSM7-SPPL2B-OAZ1
INSR
SLC6A7
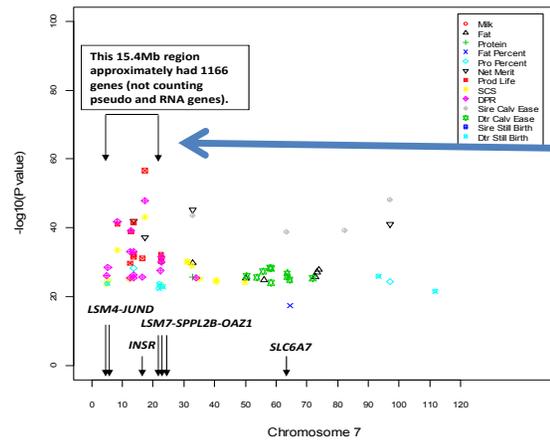
C: The large gene cluster of 1166 genes underneath the SNP effects

DGAT1-*NIBP* regions associated with fat percent (FPC)

This 2.81 Mb region approximately had 125 genes (not counting pseudo and RNA genes). *NIBP* was the largest gene (387.23Kb) in this gene cluster.

Gene regions associated with daughter stillbirth (DSB)

MOCS1 is related to early infant death (molybdenum cofactor deficiency Type A)

DST 10.6 Mb upstream ←   MOCS1   3,5,7   37,39,47,36   44,34

CD82   CD82
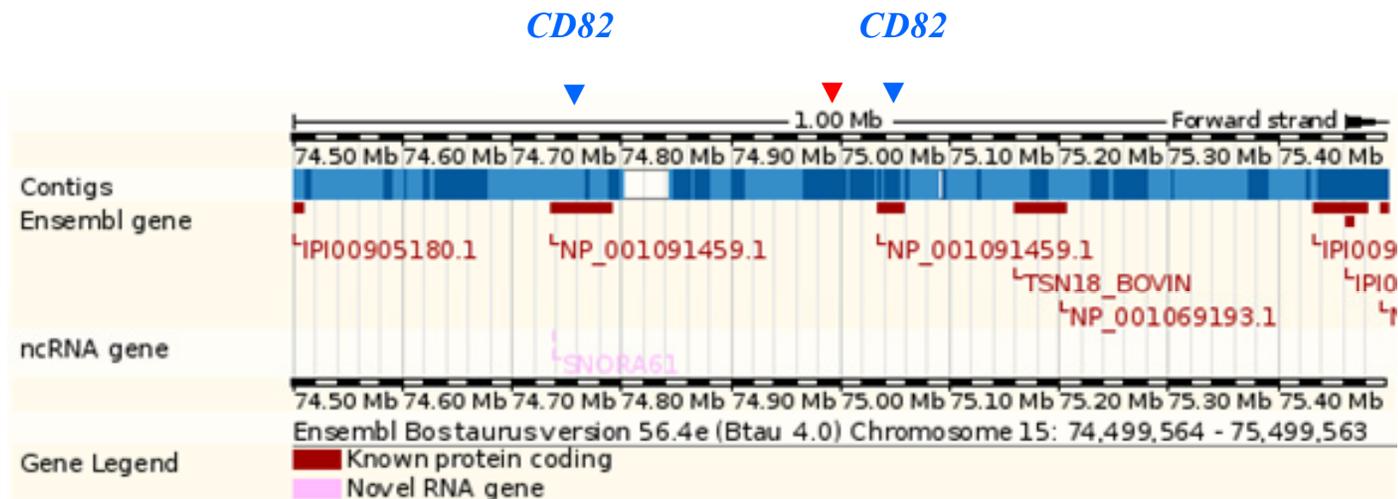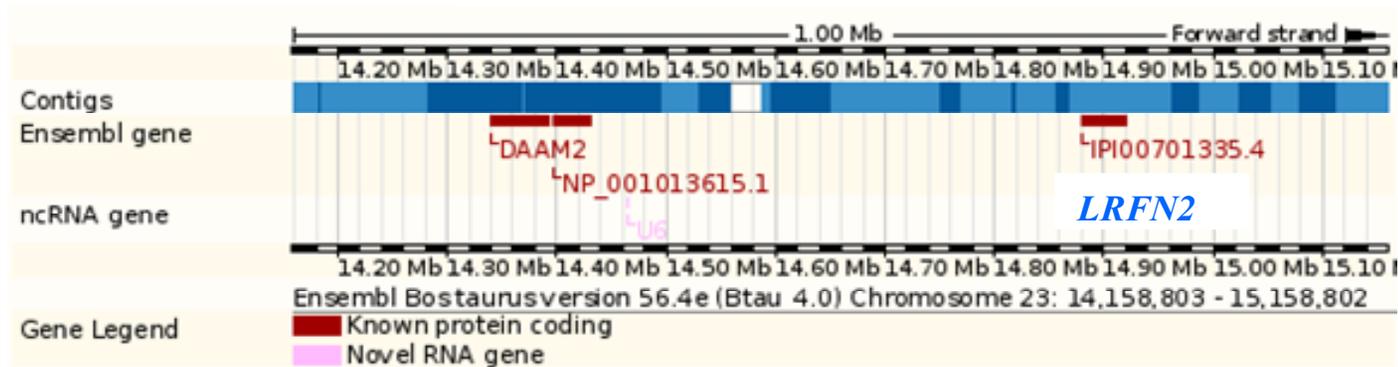
# Gene regions of top two effects of net merit and calving traits

Trait	Chr	UMD position	A	FA	FAF	Gene Region
MY	13	58070117	AG	G	0.291	19.7Kb D *GNAS*
MY	3	47165828	AG	G	0.362	114Kb U *LOC781902*
FY, PY, PL, NM, SCE, DCE	18	53948569	AG	G	0.091	409 bases D *PGLYRP1*, 16Kb D *IGFL1*
FY	X	146244046	AG	A	0.096	113.2Kb D *LOC616260*
PY, NM, SCE	1	28362687	AG	G	0.067	220.9Kb U *LOC521010*
FPC	14	1801116	AG	G	0.183	*DGAT1*
FPC	14	4336714	AG	G	0.322	*NIBP*
PPC	X	12604306	AG	A	0.074	1 Mb Blank
PPC	26	49137602	AG	G	0.089	29.9Kb U *MGMT*
SCS, DPR	7	17403976	AC	A	0.323	1.5Kb D *INSR*
SCS	2	27814925	AG	A	0.253	*LASS6-STK39*
DPR	X	3167117	AG	A	0.245	80Kb U *ATP1B4*
PL	X	106241123	CG	C	0.131	30.1Kb U *LOC520057*
SSB, DCE	18	58696066	AG	A	0.114	*LOC787057***zinc finger protein 415-like** (NCBI)
DSB	15	75749702	AG	G	0.848	23.9Kb U 2nd *CD82*
DSB	23	3320932	AG	A	0.476	*DST*

Distribution of top 100 most significant results of each of the 18 body conformation traits by chromosome

Chr	STA	STR	BD	RW	DF	RA	FUA	RUH	UD	UC	FTP	RTP	TL	FA	RLS	RLR	FL	FS	SUM
1	3	3	3	1	5	2	3	5	5	4	2	7	8	3	12	1	2	3	72
2	1	1	1	1	4	5	3	11	1	5	6	10	2	0	6	7	5	3	72
3	1	4	0	1	10	2	1	1	3	3	1	2	2	0	7	0	0	0	38
4	3	3	0	1	0	1	1	1	1	0	8	1	7	1	0	4	2	2	36
5	8	6	14	5	0	12	7	4	7	0	4	1	6	7	4	3	11	9	108
6	0	6	3	10	0	7	9	5	2	8	14	5	4	5	2	3	5	8	96
7	2	2	0	0	11	0	5	5	5	13	7	7	2	0	3	0	0	5	67
8	1	1	1	1	6	16	0	0	0	4	1	1	1	1	1	0	1	0	36
9	1	0	1	0	0	14	2	0	1	1	7	5	0	3	0	0	0	0	35
10	7	1	10	14	19	4	12	21	4	3	2	4	0	0	1	0	0	16	118
11	30	13	23	2	6	2	4	15	2	5	0	4	13	4	1	32	11	16	183
12	3	0	0	0	1	3	0	0	3	3	1	3	5	0	4	0	1	3	30
13	3	13	9	5	2	1	4	1	3	1	4	3	1	8	1	4	9	1	73
14	0	0	1	0	5	0	0	1	0	3	1	0	0	1	2	1	2	0	17
15	1	2	1	2	0	2	1	0	3	6	0	5	0	2	0	0	1	0	26
16	1	3	4	8	5	2	7	2	4	1	8	7	3	2	10	2	1	3	73
17	1	1	0	0	3	0	2	0	6	1	2	1	15	15	6	1	5	0	59
18	0	0	0	0	0	3	0	0	1	1	0	2	3	7	8	1	2	0	28
19	3	2	2	10	1	1	7	3	4	8	4	5	0	0	0	1	0	5	56
20	7	5	4	1	0	0	7	3	7	1	4	3	0	10	1	9	3	2	67
21	1	0	0	2	0	0	2	1	9	4	5	1	9	2	3	1	2	1	43
22	1	2	2	2	2	5	2	1	3	1	3	1	2	1	4	2	4	3	41
23	2	1	1	1	1	1	2	2	2	2	4	1	0	0	1	0	0	2	23
24	0	0	0	0	2	0	0	0	2	1	1	2	3	1	4	0	0	0	16
25	0	2	2	0	2	0	1	0	3	1	1	1	0	2	0	1	1	1	18
26	3	7	2	4	2	2	8	4	11	1	1	1	4	13	5	9	16	5	98
27	0	0	0	0	1	0	1	0	2	10	0	6	0	0	3	0	1	0	24
28	1	0	0	0	0	0	1	2	0	0	4	1	0	0	0	0	1	1	11
29	0	0	0	1	0	4	0	0	0	1	1	1	0	2	1	0	1	0	12
X	14	22	15	27	12	9	8	10	6	7	2	9	10	10	7	18	12	10	208
U	2	0	1	1	0	2	0	2	0	1	2	0	0	0	3	0	1	1	16
P^a	10^{-21}	10^{-20}	10^{-18}	10^{-18}	10^{-20}	10^{-11}	10^{-18}	10^{-16}	10^{-19}	10^{-18}	10^{-12}	10^{-12}	10^{-13}	10^{-20}	10^{-15}	10^{-17}	10^{-17}	10^{-19}	
R^2	0.56	0.49	0.48	0.53	0.45	0.40	0.56	0.50	0.55	0.52	0.48	0.46	0.39	0.52	0.38	0.47	0.49	0.56	

[a] This is the rounded cut-off p-value for the top 100 most significant SNPs of this trait.

QTL Maps of 4 Chromosomes for Type Traits
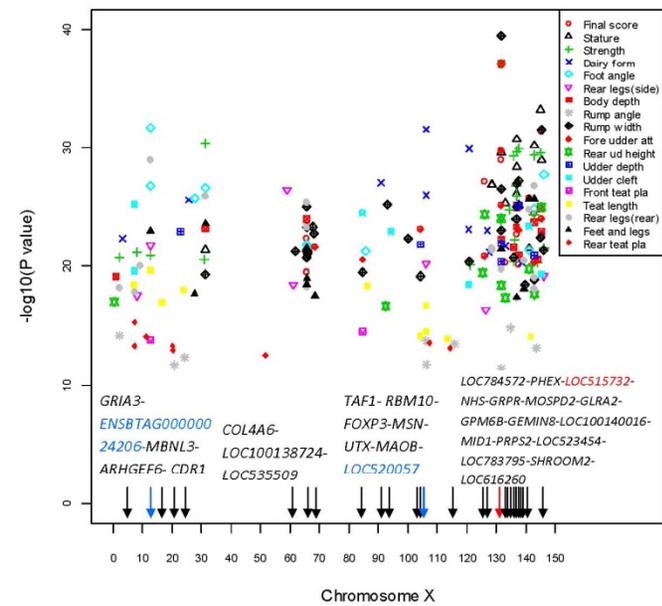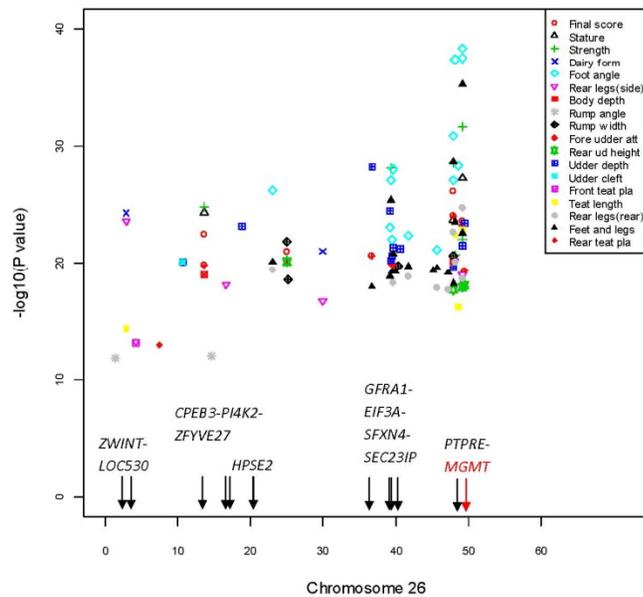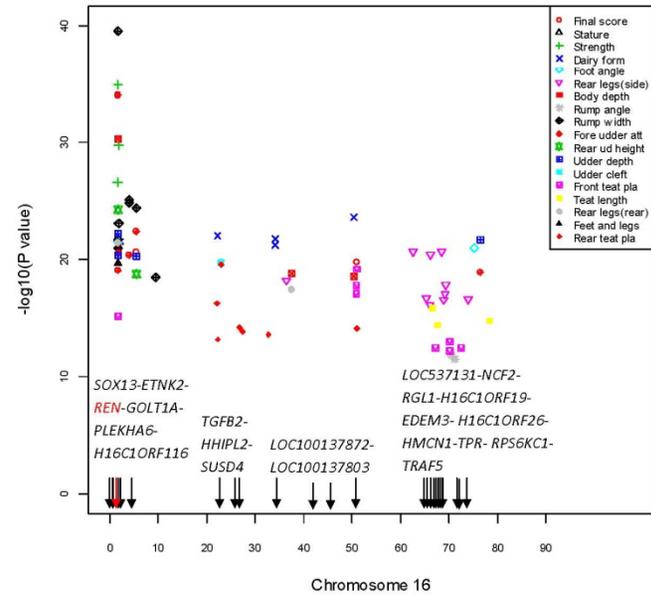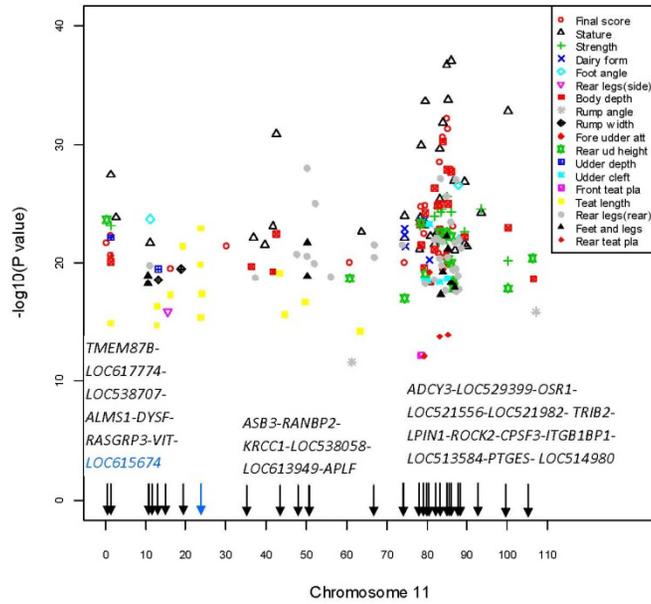
Gene regions of top two effects of each body conformation trait

Trait	Chr	UMD position	A	PA	FPA	Gene Region
STA, STR, BD, RW, FUA, FS	X	131766182	AG	G	0.422	LOC515732 **PHKA2 phosphorylase kinase, alpha 2**
STA	11	86048363	AG	G	0.329	2.7Kb U LPIN1
STR, RW, FUA, FS	16	1756016	AG	A	0.586	REN
BD	23	18197600	AG	G	0.899	25.6Kb U SUPT3H
DF	X	106241123	CG	G	0.869	30.9Kb U LOC520057
DF	X	120691496	AC	A	0.688	6.5Kb U ATP1B4
RA	5	43736571	AG	A	0.459	9.9Kb U MGC139000
RA	9	2284075	AG	G	0.689	1 Mb Blank
RUH	2	35004695	AG	G	0.307	58.3Kb U TBR1
RUH	10	64905140	AG	A	0.511	APC
UD	25	5836611	AG	A	0.364	135.1Kb U A2BP1
UD	22	34385123	AG	G	0.514	132.7Kb D SUCLG2
UC	7	91946384	CG	C	0.380	347.4Kb U CETN3
UC	19	57655339	AG	A	0.176	GPRC5C
FTP	6	109719477	AG	G	0.421	LETM1
FTP	6	101414694	AG	A	0.669	WDFY3
RTP	7	91946384	CG	C	0.380	347.4Kb U CETN3
RTP	X	84566018	AG	A	0.446	TAF1
TL	11	23741433	AC	A	0.708	98.5Kb D LOC615674
TL, FA	26	49137602	AG	A	0.911	80.8Kb U MGMT
FA, FL	26	49185154	CG	G	0.149	MGMT
RLS	1	28362687	AG	A	0.933	220.9Kb U LOC521010
RLS	18	49167271	AG	A	0.831	1 Mb Blank
RLR	X	12754120	AT	T	0.386	142.868Kb U ENSBTAG00000024206
RLR	11	50264058	AG	A	0.621	LOC538058
FL	13	18783020	AC	A	0.678	PARD3

Correlations between SNP effects (upper triangle) of the 725 SNPs and between PTA values (lower triangle) of net merit and calving traits.

	MY	FY	PY	FPC	PPC	DPR	PL	NM$	SCS	SCE	DCE	SSB	DSB
MY		0.87	0.92	0.56	0.58	0.24	0.42	0.69	-0.24	-0.66	-0.62	-0.51	0.11
FY	0.69		0.97	0.89	0.87	0.47	0.65	0.87	-0.45	-0.87	-0.81	-0.75	-0.03
PY	0.87	0.82		0.81	0.86	0.46	0.63	0.86	-0.42	-0.86	-0.79	-0.73	0.01
FPC	-0.22	0.56	0.10		0.93	0.59	0.72	0.85	-0.53	-0.86	-0.80	-0.80	-0.15
PPC	-0.17	0.32	0.33	0.62		0.63	0.74	0.87	-0.55	-0.90	-0.82	-0.83	-0.13
DPR	-0.29	-0.17	-0.19	0.10	0.17		0.96	0.83	-0.60	-0.78	-0.83	-0.82	-0.71
PL	0.05	0.20	0.15	0.22	0.20	0.75		0.93	-0.66	-0.87	-0.92	-0.88	-0.66
NM$	0.54	0.73	0.70	0.36	0.36	0.40	0.76		-0.52	-0.96	-0.97	-0.91	-0.44
SCS	0.08	-0.04	0.02	-0.15	-0.12	-0.94	-0.91	-0.80		0.73	0.80	0.78	0.70
SCE	-0.20	-0.35	-0.34	-0.23	-0.30	-0.40	-0.48	-0.57	0.30		0.95	0.96	0.30
DCE	-0.27	-0.35	-0.35	-0.17	-0.19	-0.33	-0.47	-0.60	0.27	0.68		0.91	0.51
SSB	-0.02	-0.16	-0.14	-0.19	-0.23	-0.34	-0.40	-0.39	0.27	0.70	0.41		0.39
DSB	-0.05	-0.08	-0.06	-0.05	-0.03	-0.41	-0.46	-0.42	0.29	0.24	0.62	0.24	

Correlation between SNP effects of type traits and net-merit-calving traits.

	MY	FY	PY	FPC	PPC	SCS	DPR	PL	NM	SCE	DCE	SSB	DSB
STA	0.55	0.60	0.53	0.51	0.36	-0.44	0.13	0.37	0.56	-0.41	-0.62	-0.39	-0.23
STR	0.63	0.77	0.71	0.73	0.62	-0.59	0.39	0.60	0.77	-0.65	-0.78	-0.60	-0.33
BD	0.55	0.59	0.52	0.50	0.33	-0.33	0.03	0.28	0.49	-0.34	-0.54	-0.30	-0.15
RW	0.40	0.42	0.36	0.35	0.21	-0.38	0.06	0.28	0.43	-0.24	-0.52	-0.21	-0.34
DF	0.03	-0.21	-0.24	-0.37	-0.52	0.45	-0.76	-0.61	-0.44	0.56	0.34	0.56	0.29
RA	0.58	0.64	0.63	0.55	0.52	-0.45	0.46	0.57	0.65	-0.64	-0.66	-0.53	-0.21
FUA	0.45	0.55	0.50	0.51	0.42	-0.65	0.38	0.59	0.68	-0.50	-0.74	-0.51	-0.55
RUH	0.45	0.43	0.38	0.32	0.17	-0.40	0.08	0.32	0.46	-0.25	-0.52	-0.25	-0.40
UD	0.38	0.51	0.47	0.52	0.46	-0.76	0.53	0.70	0.73	-0.55	-0.78	-0.59	-0.65
UC	0.02	-0.10	-0.14	-0.18	-0.30	-0.07	-0.31	-0.14	-0.07	0.26	-0.06	0.21	-0.23
FTP	0.38	0.45	0.43	0.40	0.38	-0.55	0.28	0.48	0.57	-0.39	-0.65	-0.39	-0.51
RTP	0.06	-0.02	-0.04	-0.09	-0.16	-0.12	-0.22	-0.05	0.03	0.16	-0.15	0.12	-0.31
TL	-0.22	-0.51	-0.52	-0.65	-0.76	0.67	-0.75	-0.75	-0.72	0.76	0.74	0.72	0.46
FA	0.67	0.83	0.80	0.79	0.75	-0.66	0.50	0.72	0.87	-0.76	-0.85	-0.72	-0.36
RLS	-0.55	-0.75	-0.76	-0.77	-0.82	0.63	-0.71	-0.80	-0.86	0.83	0.76	0.77	0.37
RLR	0.66	0.74	0.70	0.65	0.56	-0.34	0.12	0.39	0.63	-0.51	-0.65	-0.46	-0.12
FL	0.61	0.72	0.67	0.66	0.57	-0.58	0.34	0.60	0.75	-0.60	-0.77	-0.58	-0.39
FS	0.50	0.53	0.47	0.44	0.30	-0.48	0.16	0.40	0.55	-0.36	-0.62	-0.36	-0.39

Conclusions

- 1586 SNP markers were identified to have top-100 effects for 31 dairy traits in U.S. Holstein cows

- A large number of genes and gene regions associated with the 1586 SNP markers were identified

- Improving many dairy traits in desirable directions using SNP markers is possible

Acknowledgements