

MicroRNA-guided prioritization of genome-wide association signals reveals the importance of microRNA-target gene networks for complex traits in cattle

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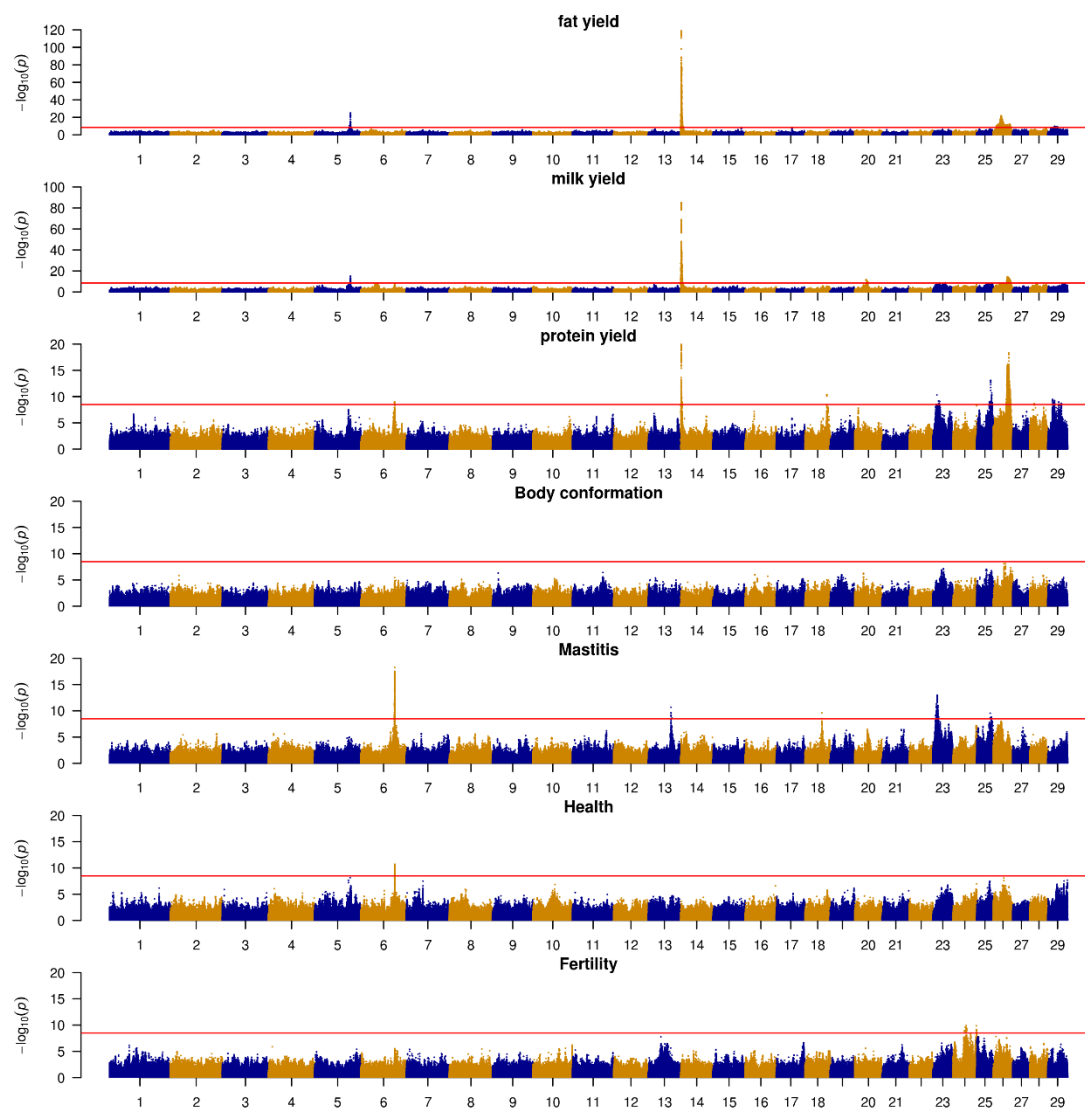
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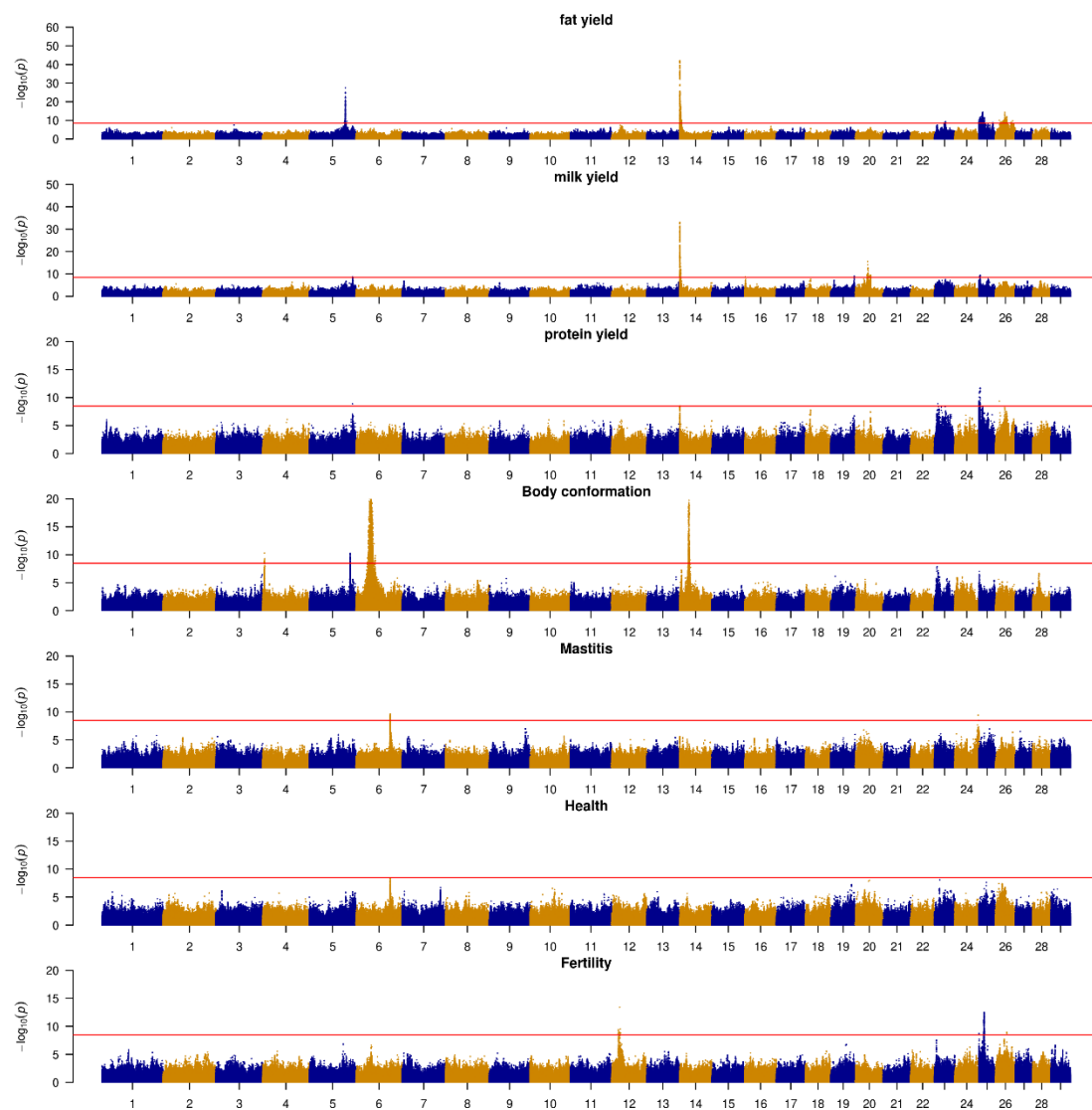
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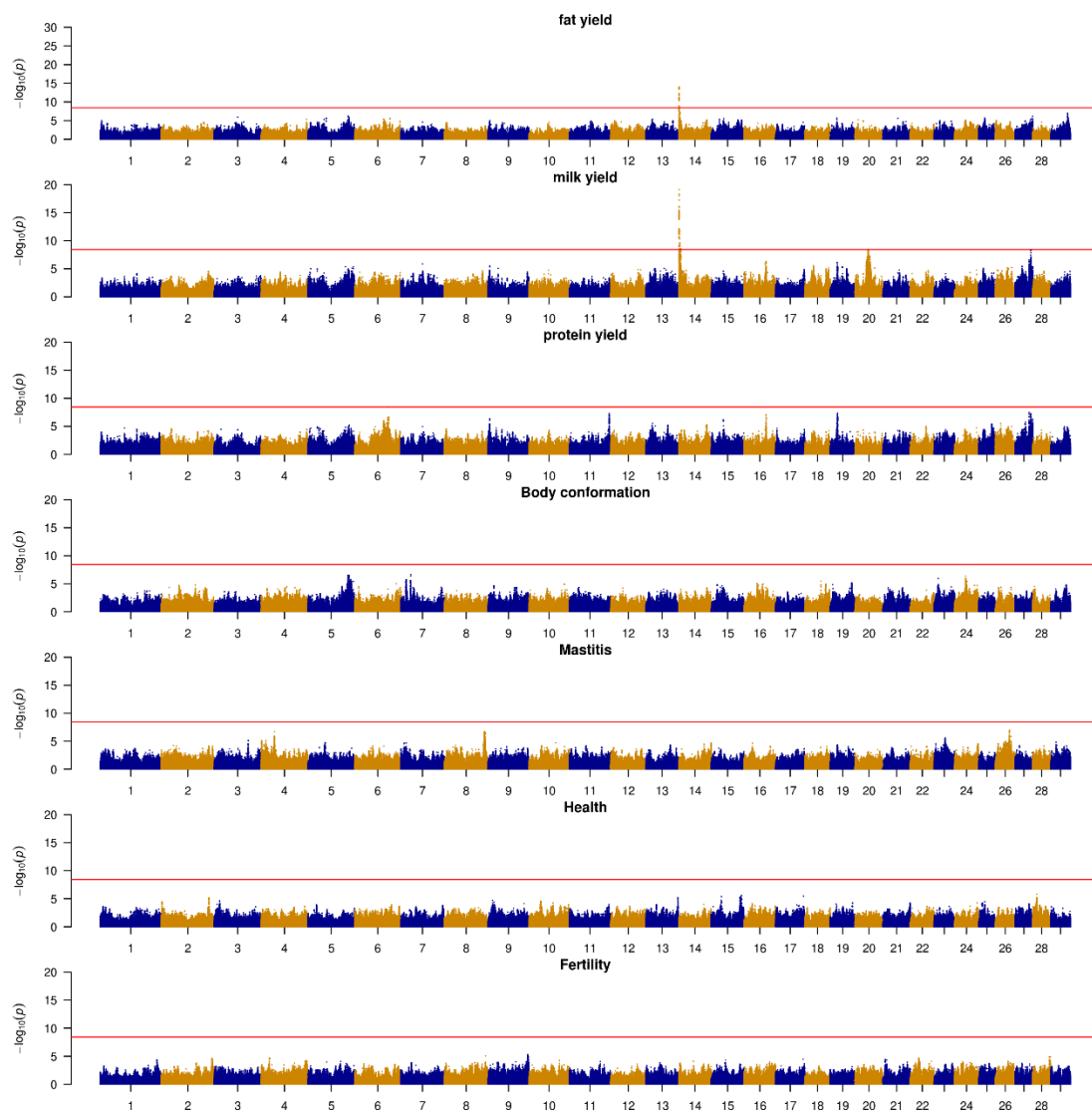
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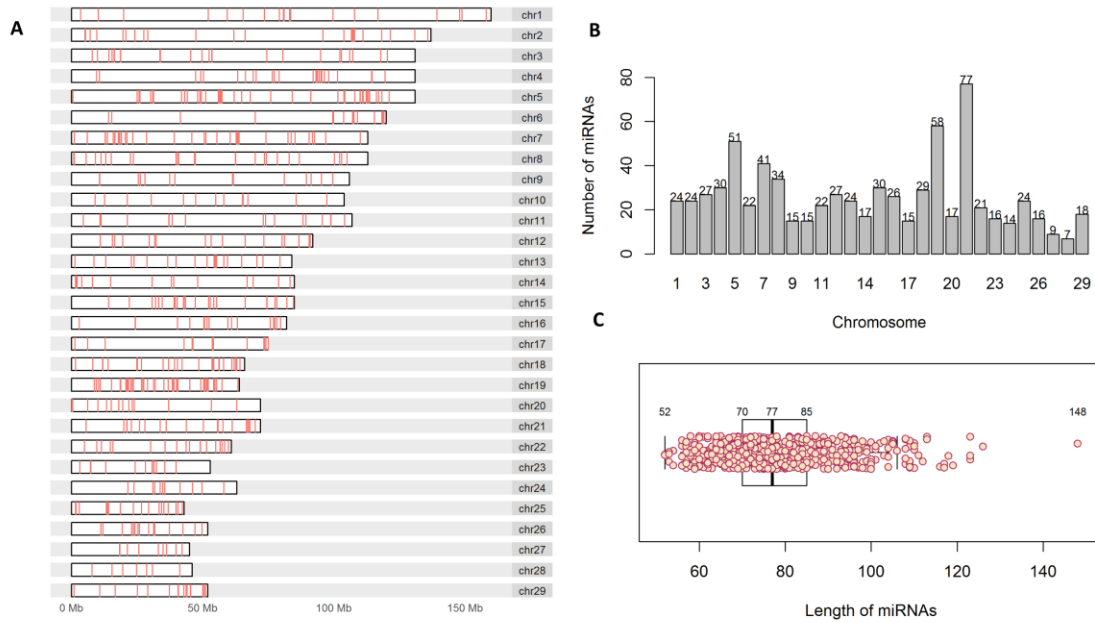
Supplementary Fig. S1. Manhattan plot for sequence-based genome-wide association study (GWAS) of seven traits in Holstein (HOL)



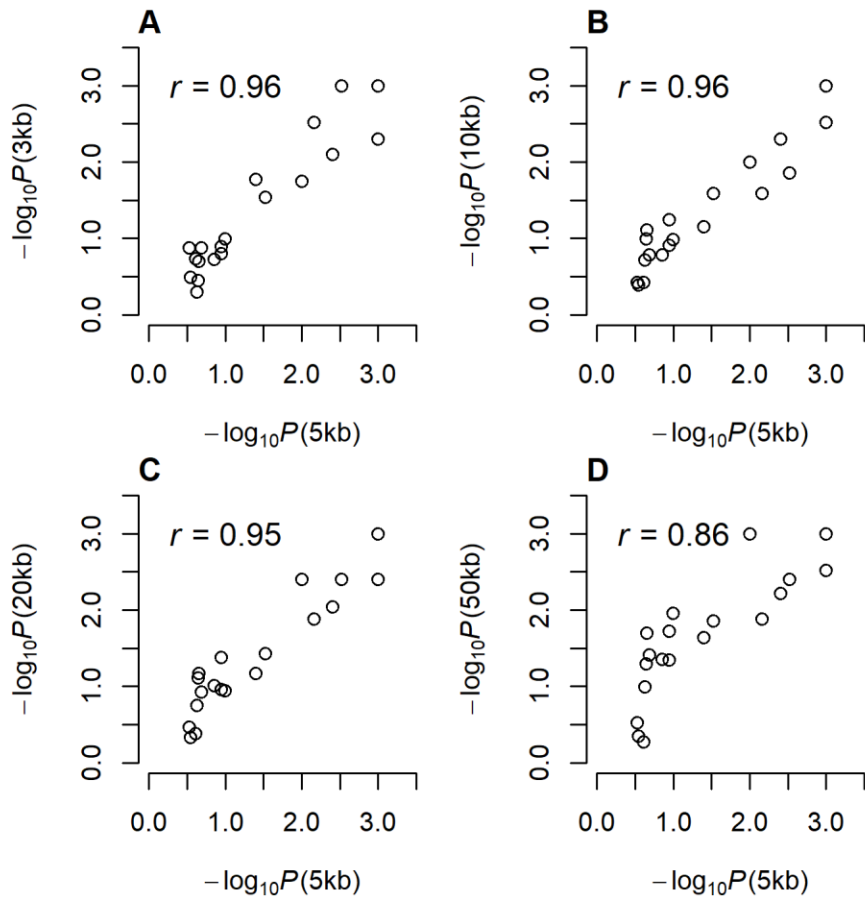
Supplementary Fig. S2. Manhattan plot for sequence-based genome-wide association study (GWAS) of seven traits in Nordic Red cattle (RDC)



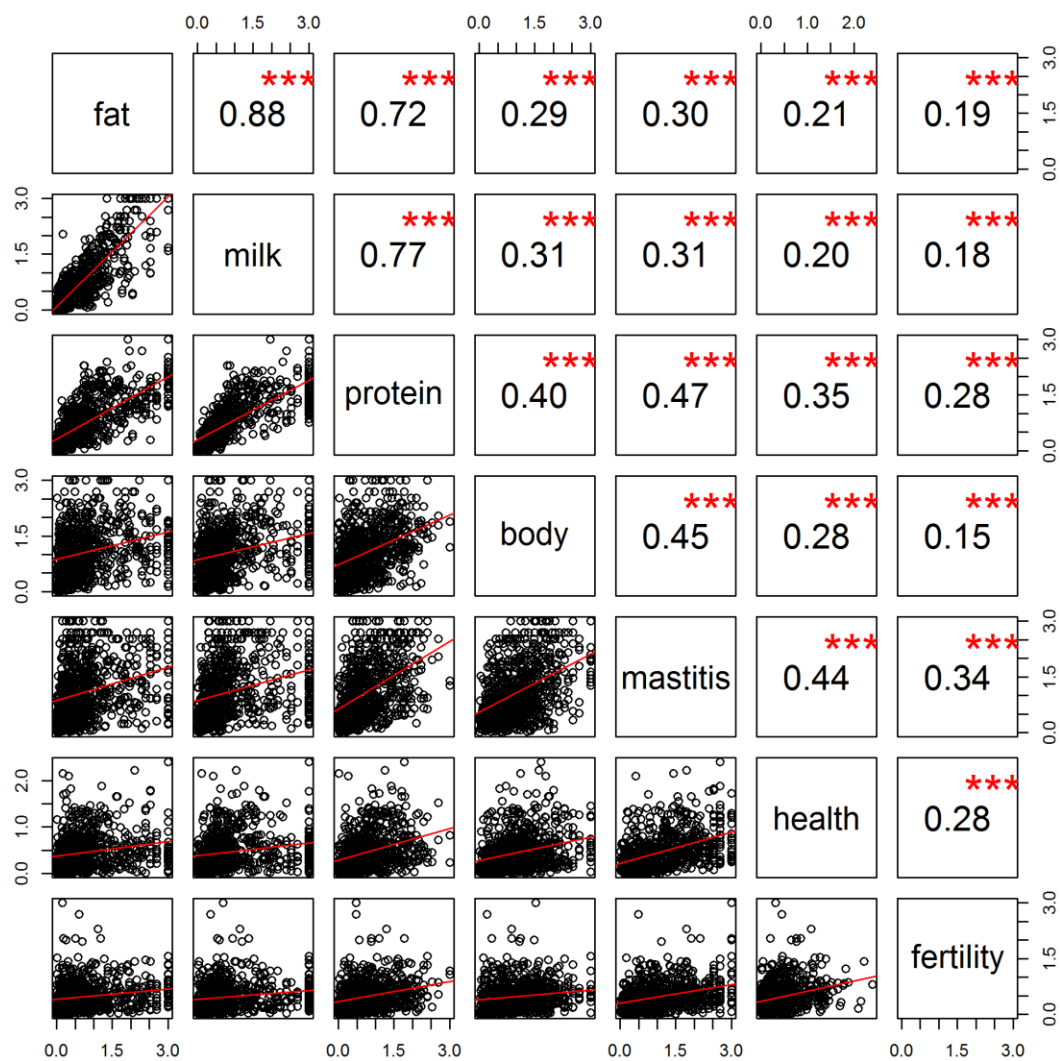
Supplementary Fig. S3. Manhattan plot for sequence-based genome-wide association study (GWAS) of seven traits in Jersey (JER)



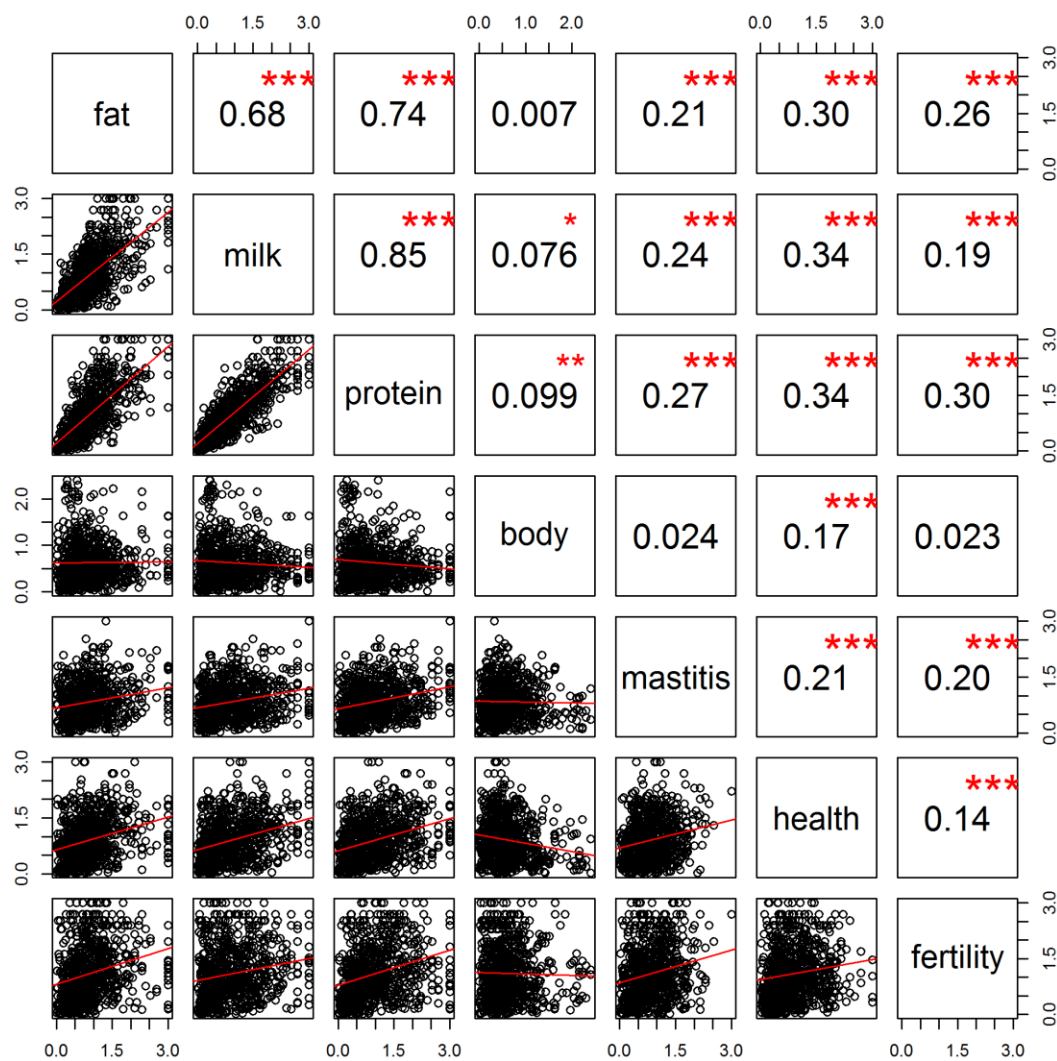
Supplementary Fig. S4. General characteristics of 750 bovine autosome miRNA genes. **A** is the distribution of miRNA genes along the bovine genome, and each red bar is a miRNA gene. **B** is the number of miRNA genes on each chromosome. **C** is the length (base-pair, bp) of miRNA genes, and each dot is a miRNA gene.



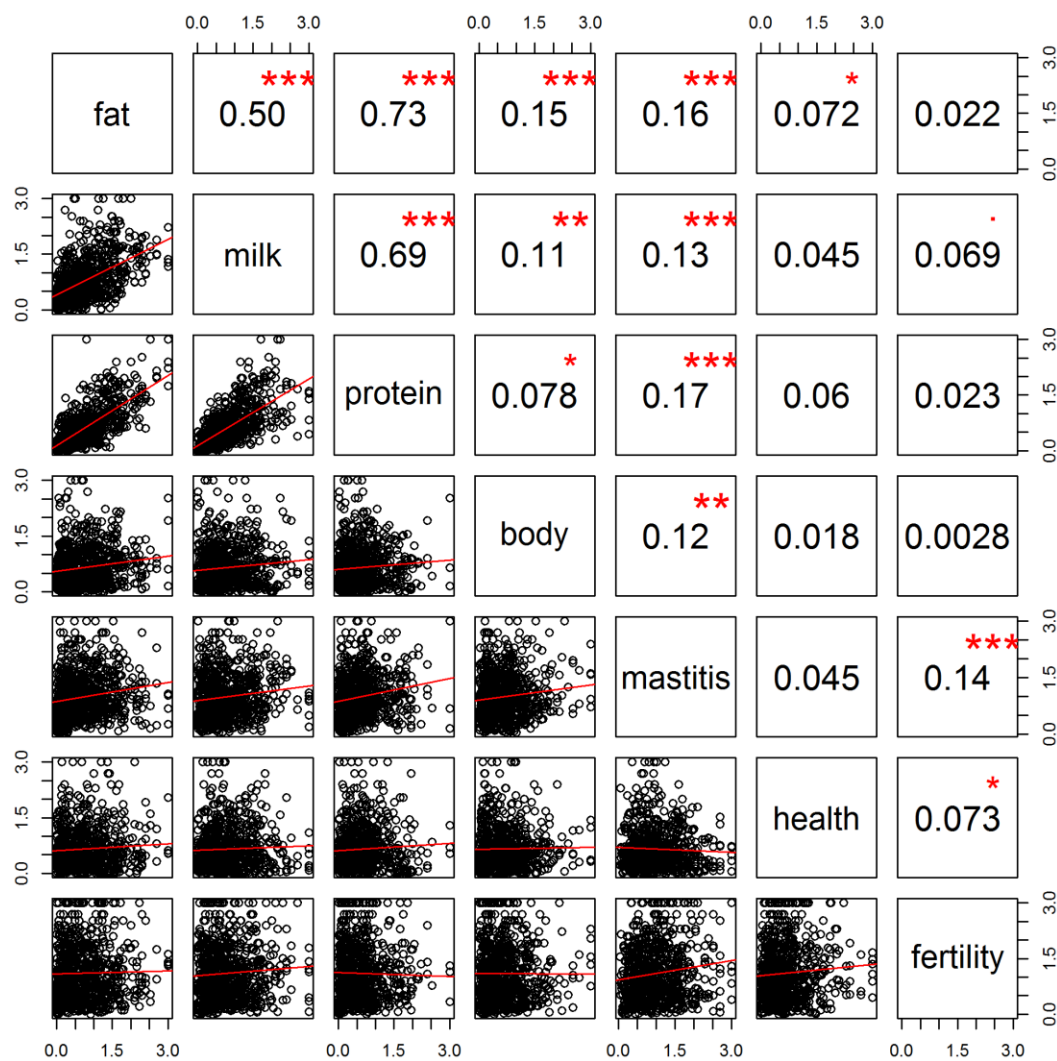
Supplementary Fig. S5. Correlations of $-\log_{10} P$ values (marker-set test) between different extensions in seven traits among three breeds



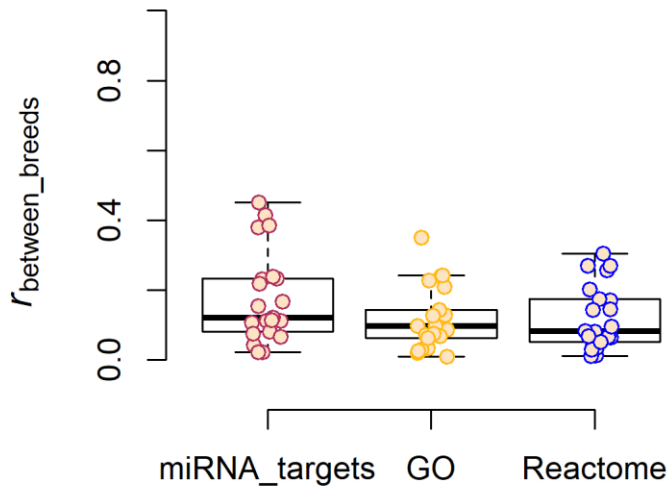
Supplementary Fig. S6. The correlations between traits based on marker-set test analyses of miRNA-target networks in Holstein (HOL)



Supplementary Fig. S7. The correlations between traits based on marker-set test analyses of miRNA-target networks in Nordic red cattle (RDC)



Supplementary Fig. S8. The correlations between traits based on marker-set test analyses of miRNA-target networks in Jersey (JER)



Supplementary Fig. S9. The difference in between-breeds correlations of enrichments among miRNA-target networks, Gene Ontology (GO) and Reactome terms

Supplementary Table S1. General characteristics of quantitative trait loci (QTL) detected in seven complex traits in three dairy cattle breeds using single-marker genome-wide association

Trait	Breed	BT A	QTL regions	# of SNPs	Position (top SNP)	rsID (top SNP)	P-value (top SNP)	H^2_{snp} (%)	H^2_{total} (%)
MY	HOL	5	93944849-93948804	76	93944849	rs109422971	8.79e-16	2.2	24.1
		14	1569809-1892784	880	1825125	rs208113678	6.16e-86	13.9	
		20	29996719-34170153	26353	29996727	rs43116342	1.79e-12	2.3	
		23	17821120	1	17821120	rs472216679	1.55e-09	4.3	
		23	32417317-32417355	10	32417347	rs443822447	1.75e-09	0.2	
		26	36022272-44280829	66341	37869380	rs456998485	3.80e-15	1.2	

	RDC	5	11234320 4- 11245086 0	700	11234320 4	rs383553819	2.00e-09	1.1	13.0
		14	1722033- 1892559	441	1743939	rs133033480	9.75e-34	7.2	
		16	1322611	1	1322611	rs108979795	2.63e-09	0.1	
		19	61447138- 61449096	10	61449096	rs210324693	1.19e-09	0.6	
		20	31909478- 32647105	3904	31909478	rs385640152	2.78e-16	3.2	
		25	1627283- 3516671	1701 7	3498960	rs110749311	4.83e-10	0.8	
	JER	14	1799066- 1950961	366	1828456	rs135431494	1.21e-21	2.8	3.9
		20	33922713	1	33922713	rs440493451	3.38e-09	1.1	
FY	HOL	5	93945738- 93954751	153	93945991	rs208248675	8.95e-26	1.8	22.3
		14	1706207- 1823757	314	1810124	rs133931291	3.64e- 132	18.3	
		26	20488043- 21746946	6830	20547445	rs136702635	2.06e-22	1.5	
		29	17503000- 25606561	8081 9	17696734	rs208845484	1.82e-10	0.7	
	RDC	5	93945694- 93948804	59	93945694	rs209818856	3.23e-28	2.6	13.3
		14	1722033- 1892559	441	1807140	rs136783505	9.80e-43	6.3	
		23	24986204- 25169530	5172	24986204	rs516784604	2.46e-09	0.7	
		23	28567796- 28591530	1093	28567796	rs381390819	4.35e-10	0.8	
		25	8663907- 9997825	1232 5	9870005	rs379546164	3.98e-15	1.3	
		26	23948021- 29821952	5681 5	24379571	rs438420348	5.20e-15	1.6	
	JER	14	1756075- 1892559	59	1802667	NA	9.36e-15	3.1	3.1
PY	HOL	6	88477501- 88481616	48	88478678	rs380681629	9.79e-10	1.5	19.3
		14	1448510- 2080840	2133	1892784	rs207633422	6.93e-22	2.9	
		18	57015407- 57038020	129	57015407	rs378839347	4.23e-11	1.2	
		23	10504197	1	10504197	rs379304770	4.80e-11	5.0	
		23	14536448- 16488114	1433 0	14536448	rs382497921	6.89e-10	0.7	
		25	36371535- 39391747	2626 9	36403719	rs135912796	8.36e-14	0.9	
		26	37695494- 41579300	2840 1	41231611	rs136027702	4.72e-19	1.4	
		28	10749791	1	10749791	rs797640658	1.91e-09	1.9	
		29	12122106- 14947666	3033 6	12741604	rs453104040	3.38e-10	2.6	

		29	17617875-17696775	471	17692377	rs137254498	6.09e-10	0.6	
		29	28915962-28966625	300	28915962	rs798193137	1.12e-09	0.7	
		29	35446115-35699001	2176	35699001	rs110014432	1.94e-09	0.6	
	RDC	5	112450860	1	112450860	rs109041054	1.32e-09	1.1	9.3
		14	1802667	1	1802667	NA	3.02e-09	1.1	
		23	8581891	1	8581891	NA	1.22e-09	0.8	
		25	294674-300548	53	298901	rs132704315	4.34e-10	0.9	
		25	3306363-3516671	2168	3498960	rs110749311	1.98e-12	1.0	
		26	10268885-10268923	5	10268885	rs449946672	4.48e-10	4.4	
BC	RDC	4	4495782-5368115	9752	4495782	rs208985165	5.01e-11	2.6	33.3
		5	105821790-106292827	2934	106252827	rs137527436	5.50e-11	1.9	
		6	38614055-39518299	6470	38651270	rs799919722	9.82e-71	22.4	
		14	24973953-24991209	75	24974811	rs137303549	7.86e-33	6.4	
Mastitis	HOL	6	88683517-89081567	5275	88840407	rs381295092	5.55e-19	4.1	9.7
		13	59258639-620175067	1905	59260175	rs42927066	2.09e-11	2.0	
		18	43909571-43924396	109	43909571	rs464881101	2.44e-10	1.9	
		23	9156030-13608649	3419	11477969	rs110729743	1.10e-13	1.3	
		25	35353527-37918904	2346	35353527	rs43722749	2.89e-10	0.4	
	RDC	6	88683517-89070689	5058	88723742	rs436532576	2.31e-10	2.3	6.8
		24	60,959,835	1	60959835	rs380418573	3.72e-10	4.5	
Health	HOL	6	88770377-89147179	5241	89118971	rs384330814	2.00e-11	8.2	8.2
Fertility	HOL	24	29556826-36261453	49258	34729148	rs451469340	1.19e-10	1.3	5.3
		24	61446132-61954906	3944	61552100	rs211207269	1.32e-10	4.0	
	RDC	12	20893092	1	20893092	rs384315836	3.62e-14	3.6	8.1
		25	325322	1	325322	rs109501400	1.90e-09	1.3	
		25	13063588-14584307	16170	13430119	rs380980565	3.00e-13	1.7	
		26	29797179-29821952	398	29797179	rs379654767	1.21e-09	1.5	

Supplementary Table S2. Number of miRNA genes (number of SNPs within miRNA genes) included in marker-set test based on different up- and down-stream extensions of miRNA genes (*i.e.*, 0kb, ± 3 kb, ± 5 kb, ± 10 kb, ± 20 kb, ± 50 kb)

Breed	0kb	± 3 kb	± 5 kb	± 10 kb	± 20 kb	± 50 kb
HOL	126(178)	657(17,320)	661(28,314)	665(55,122)	671(108,706)	680(272,061)
RDC	127(173)	658(18,051)	664(29,526)	666(57,614)	673(113,233)	682(282,179)
JER	106(160)	652(14,697)	658(24,013)	661(46,633)	667(91,895)	679(233,658)

Supplementary Table S3. Enrichments (*P* values, marker-set test) of miRNA genes including or excluding (in brackets) miRNAs close to *DGAT1* for three milk production traits

	Fat yield	Milk yield	Protein yield
HOL	0.001(0.106)	0.001(0.099)	0.040(0.082)
RDC	0.001(0.031)	0.030(0.024)	0.004(0.011)
JER	0.001(0.017)	0.003(0.001)	0.007(0.003)