

Identification of genetic variants regulating the abundance of clinically relevant plasma proteins using the Diversity Outbred mouse model

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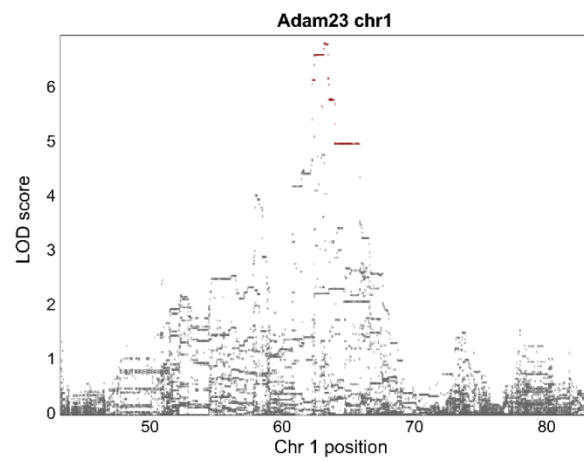
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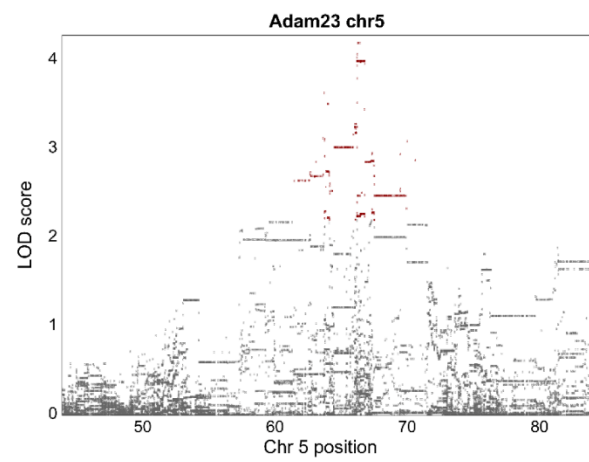
¶These authors contributed equally to this work

Supplementary Figures

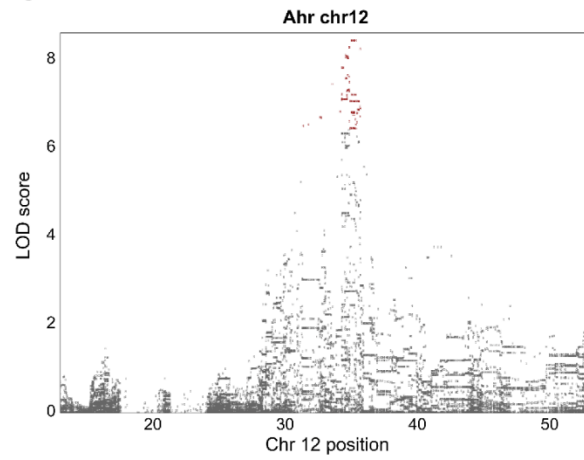
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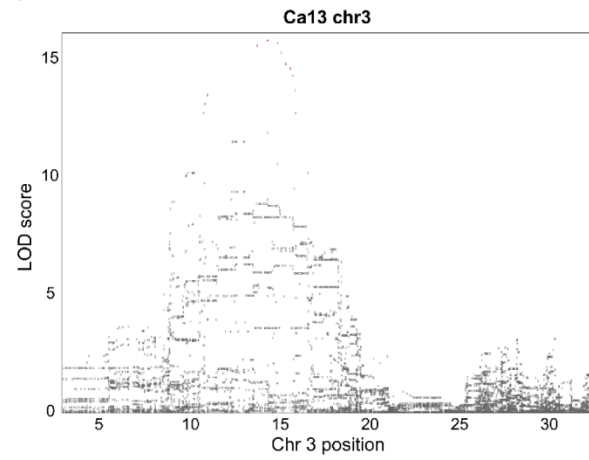
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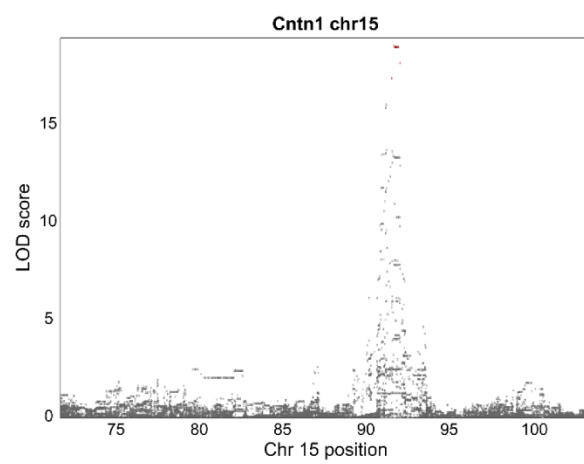
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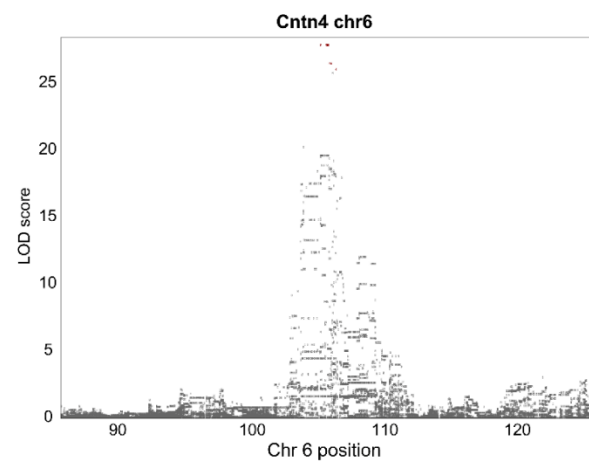
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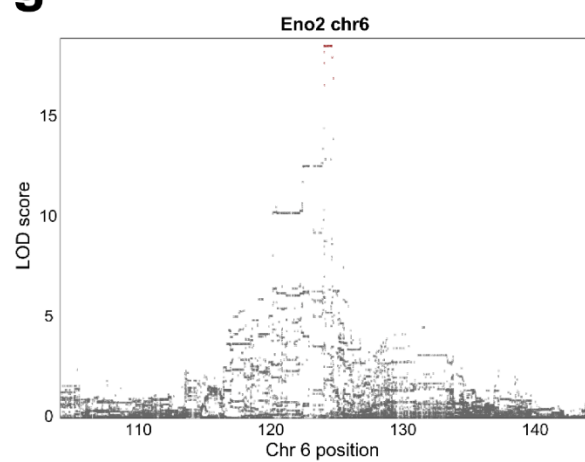
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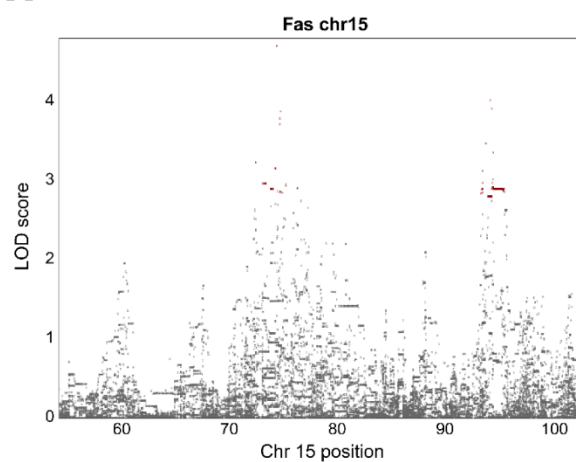
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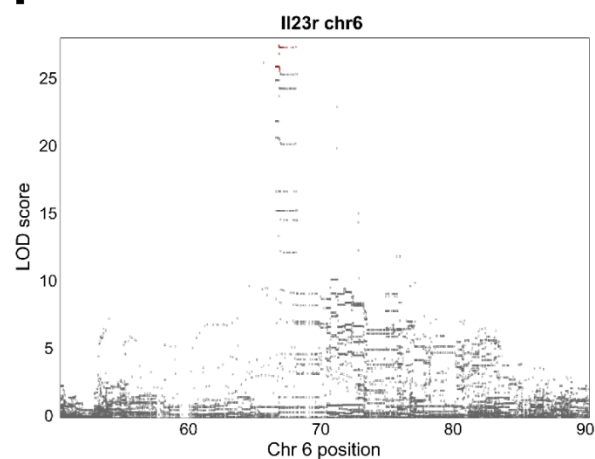
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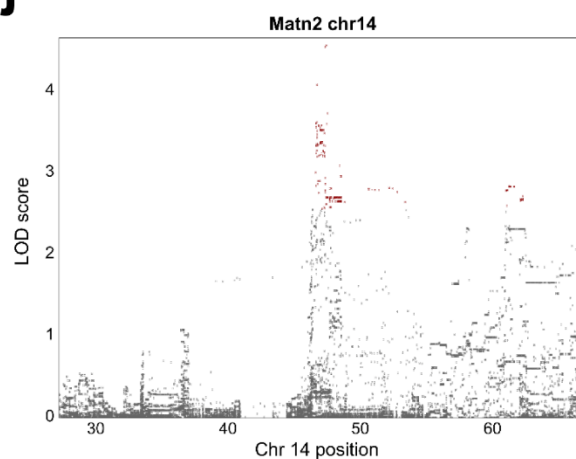
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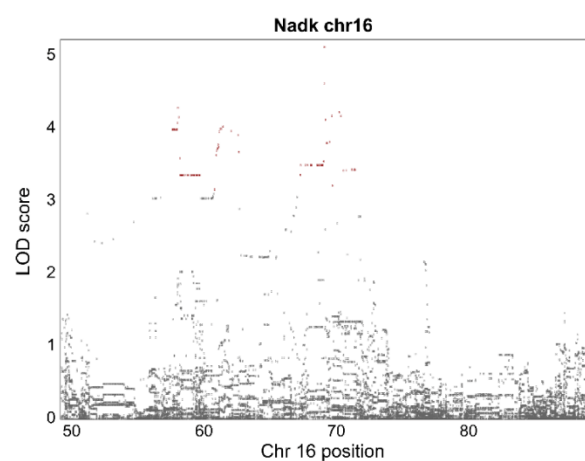
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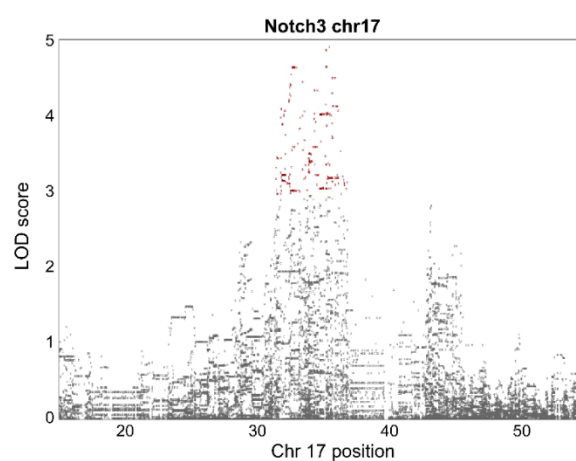
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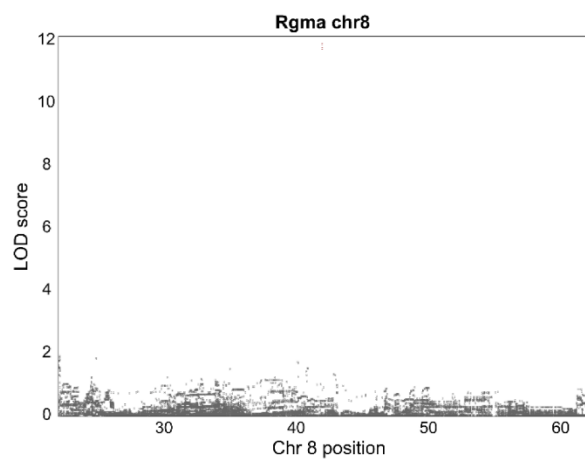
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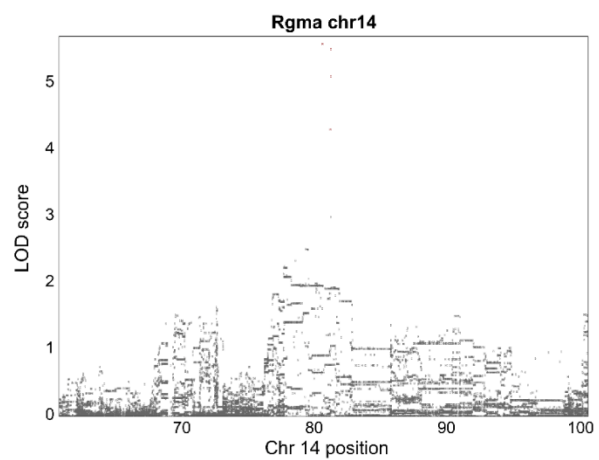
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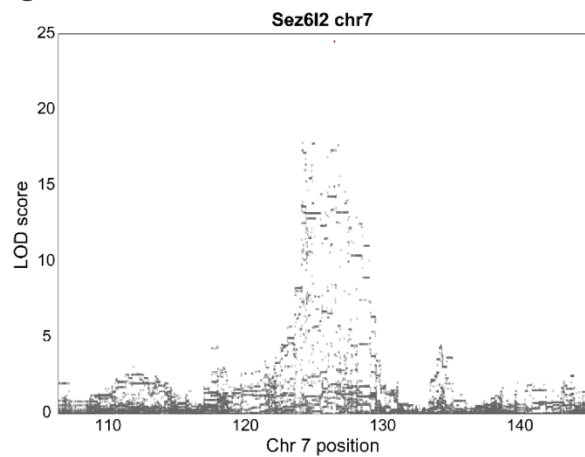
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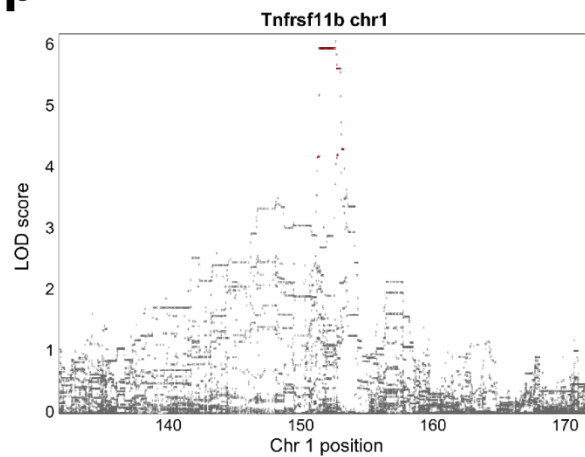
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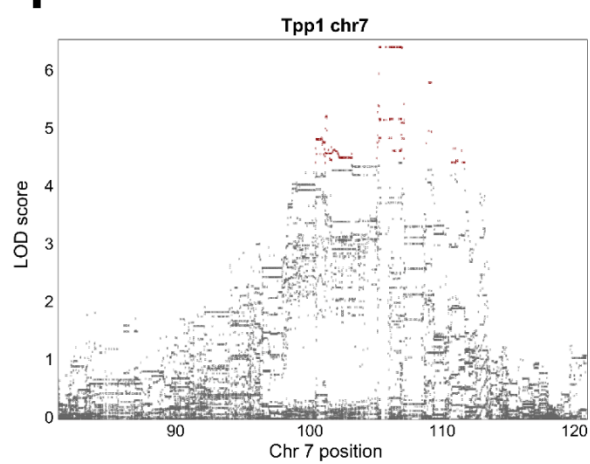
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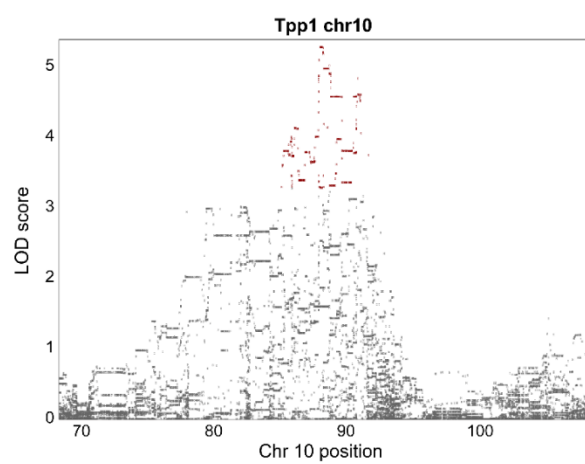
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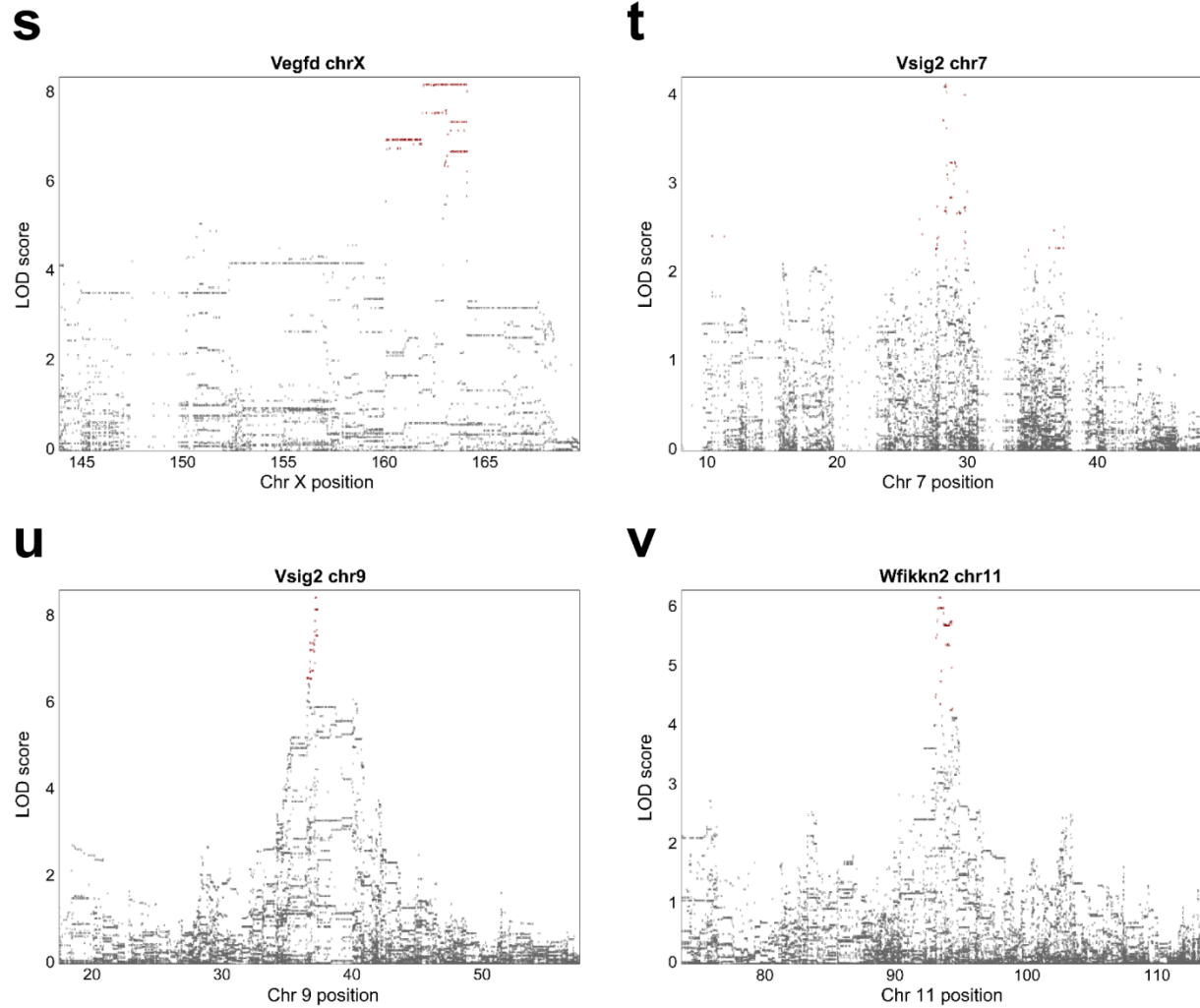


Fig. S1: Association mapping of the significant and suggestive pQTL showing the QTL support interval. Zoom in on the different chromosomes showing the QTL support intervals for (a) Adam23 chromosome 1, (b) Adam23 chromosome 5, (c) Ahr chromosome 12, (d) Ca13 chromosome 3, (e) Cntn1 chromosome 15, (f) Cntn4 chromosome 6, (g) Eno2 chromosome 6, (h) Fas chromosome 15, (i) Il23r chromosome 6, (j) Matn2 chromosome 14, (k) Nadk chromosome 16, (l) Notch3 chromosome 17, (m) Rgma chromosome 8, (n) Rgma chromosome 14, (o) Sez6l2 chromosome 7, (p) Tnfrsf11b chromosome 1, (q) Tpp1 chromosome 7, (r) Tpp1 chromosome 10, (s) Vegfd chromosome X, (t) Vsig2 chromosome 7, (u) Vsig2 chromosome 9 & (v) Wfikkn2 chromosome 11. Magenta marks SNPs with a LOD drop < 2 from the top SNP

C **RFX1** c.*935G>A

Mouse	C	C	C	T	-	T	C	C	C	A	G	T	G	C	T	C	A	A	A	G	T
Human	C	C	C	T	C	T	C	C	C	G	G	T	G	G	T	G	A	A	A	G	T

c.*1063G>A

Supplementary Tables

Table S1. Overview of proteins analyzed using the Olink Mouse Exploratory Panel

Protein name	Uniprot ID	Average $\pm$ SD	Range	Missing data freq. (%)
<i>Proteins included in pQTL analysis</i>				
ACVRL1	Q61288	4.45 $\pm$ 0.73	2.85 – 5.93	0
ADAM23	Q9R1V7	1.29 $\pm$ 0.67	-0.27 – 2.74	0
AHR	P30561	2.40 $\pm$ 0.60	1.19 – 4.10	3
APBB1IP	Q8R5A3	3.26 $\pm$ 0.62	2.15 – 5.48	0
AXIN1	O35625	3.98 $\pm$ 0.68	2.99 – 6.26	2
CA13	Q9D6N1	2.80 $\pm$ 1.04	0.87 – 5.18	8
CANT1	Q8VCF1	0.67 $\pm$ 1.01	-0.08 – 1.51	2
CASP3	P70677	8.42 $\pm$ 0.75	6.71 – 10.08	0
CCL2	P10148	9.79 $\pm$ 1.37	8.04 – 13.84	0
CCL3	P10855	2.79 $\pm$ 0.62	1.92 – 6.47	0
CCL5	P30882	0.82 $\pm$ 1.91	-0.27 – 5.20	3
CCL20	O89093	7.54 $\pm$ 1.32	6.40 – 10.35	2
CDH6	P97326	3.45 $\pm$ 0.46	2.33 – 4.45	0
CLMP	Q8R373	6.17 $\pm$ 0.34	5.48 – 7.90	0
CNTN1	P12960	7.06 $\pm$ 0.61	5.58 – 8.03	0
CNTN4	Q69Z26	4.57 $\pm$ 1.47	2.42 – 6.56	0
CPE	Q00493	6.44 $\pm$ 0.37	5.56 – 7.46	0
CRIM1	Q9JLL0	1.51 $\pm$ 1.13	0.65 – 4.62	1
CXCL1	P12850	8.17 $\pm$ 1.53	6.34 – 11.99	2
CXCL9	P18340	4.57 $\pm$ 0.95	2.77 – 7.01	0
CYR61	P18406	5.58 $\pm$ 0.56	3.54 – 6.96	0
DCTN2	Q99KJ8	2.35 $\pm$ 0.62	1.49 – 4.27	5
DLK1	Q09163	3.47 $\pm$ 1.64	1.98 – 5.84	0
DLL1	Q61483	3.39 $\pm$ 1.18	1.87 – 4.33	0
EDA2R	Q8BX35	5.41 $\pm$ 0.68	4.44 – 9.16	0
ENO2	P17183	3.31 $\pm$ 0.44	2.56 – 4.47	0
EPCAM	Q99JW5	2.36 $\pm$ 1.65	0.98 – 3.59	0
EPO	P07321	4.04 $\pm$ 1.18	2.21 – 9.07	0
ERBB4	Q61527	4.65 $\pm$ 0.70	3.86 – 5.43	0
FAS	P25446	3.27 $\pm$ 0.52	2.63 – 4.93	2
FLRT2	Q8BLU0	4.51 $\pm$ 0.38	3.61 – 5.42	0
FST	P47931	8.50 $\pm$ 0.51	7.41 – 10.98	0
FSTL3	Q9EQC7	5.70 $\pm$ 0.68	4.74 – 6.53	0
GFRA1	P97785	3.30 $\pm$ 0.80	1.65 – 4.90	0
GHRL	Q9EQX0	3.50 $\pm$ 0.96	2.16 – 4.96	0
HGF	Q08048	4.46 $\pm$ 1.01	3.51 – 9.72	1
IGSF3	Q6ZQA6	4.58 $\pm$ 0.33	3.73 – 5.82	0
IL1A	P01582	3.58 $\pm$ 1.00	1.52 – 6.84	2
IL17A	Q62386	2.14 $\pm$ 1.45	0.006 – 7.40	5
IL17F	Q7TNI7	3.09 $\pm$ 1.23	1.11 – 8.16	4
IL23R	Q8K4B4	3.59 $\pm$ 1.03	1.69 – 5.29	2

Table S1 Continued. Overview of proteins analyzed using the Olink Mouse Exploratory Panel

Protein name	Uniprot ID	Average $\pm$ SD	Range	Missing data freq. (%)
<i>Proteins included in pQTL analysis</i>				
ITGB1BP2	Q9R000	0.79 $\pm$ 0.97	-0.73 – 4.35	2
LGMN	O89017	5.30 $\pm$ 1.00	4.13 – 6.13	0
LPL	P11152	3.70 $\pm$ 0.79	2.48 – 5.30	0
MAP2K6	P70236	6.04 $\pm$ 0.95	4.76 – 8.15	0
MATN2	O08746	4.93 $\pm$ 1.11	3.73 – 6.44	0
MIA	Q61865	4.29 $\pm$ 0.95	3.21 – 5.05	0
NADK	P58058	7.05 $\pm$ 1.05	4.88 – 10.21	0
NOTCH3	Q61982	5.12 $\pm$ 1.03	4.21 – 5.66	0
NTF3	P20181	1.71 $\pm$ 0.28	1.05 – 2.41	0
PARP1	P11103	4.80 $\pm$ 1.33	2.46 – 10.13	0
PDGFB	P31240	6.67 $\pm$ 1.74	3.59 – 11.70	0
PLA2G4A	P47713	6.39 $\pm$ 0.72	5.16 – 8.73	0
PLXNA4	Q80UG2	2.86 $\pm$ 0.73	1.34 – 5.95	0
PPP1R2	Q9DCL8	2.98 $\pm$ 0.67	1.46 – 4.96	0
PRDX5	P99029	2.57 $\pm$ 0.81	0.97 – 5.21	0
QDPR	Q8BVI4	5.31 $\pm$ 0.63	3.85 – 7.14	0
RGMA	Q6PCX7	2.16 $\pm$ 1.54	1.13 – 3.95	0
RIOX2	Q8CD15	2.84 $\pm$ 1.35	0.62 – 7.36	6
S100A4	P07091	5.49 $\pm$ 0.81	4.11 – 6.85	0
SEZ6L2	Q4V9Z5	5.45 $\pm$ 1.13	4.06 – 7.38	0
SNAP29	Q9ERB0	6.72 $\pm$ 0.77	5.43 – 8.96	0
TGFA	P48030	5.31 $\pm$ 0.80	4.19 – 10.36	0
TGFB1	P04202	3.63 $\pm$ 0.79	2.49 – 6.75	0
TGFBR3	O88393	3.94 $\pm$ 1.43	2.27 – 6.40	0
TNFRSF11B	O08712	5.70 $\pm$ 0.94	4.20 – 6.93	0
TNFRSF12A	Q9CR75	3.81 $\pm$ 0.69	2.82 – 6.91	0
TNFSF12	O54907	3.94 $\pm$ 1.02	2.70 – 5.30	0
TNNI3	P48787	10.91 $\pm$ 1.89	5.11 – 14.78	0
TNR	Q8BYI9	3.83 $\pm$ 0.44	2.42 – 4.71	0
TPP1	O89023	6.29 $\pm$ 0.87	5.00 – 7.61	0
VEGFD	P97946	3.50 $\pm$ 0.88	2.35 – 4.53	0
VSIG2	Q9Z109	3.36 $\pm$ 0.79	1.27 – 5.32	0
WFIKK2	Q7TQN3	4.66 $\pm$ 1.16	3.65 – 5.67	0
WISP1	O54775	4.44 $\pm$ 0.48	3.57 – 6.01	0
YES1	Q04736	2.11 $\pm$ 0.54	1.03 – 4.00	0

Table S1 Continued. Overview of proteins analyzed using the Olink Mouse Exploratory Panel

Protein name	Uniprot ID	Average $\pm$ SD	Range	Missing data freq. (%)
<i>Proteins excluded from pQTL analysis</i>				
CLSTN2	Q9ER65	1.91 $\pm$ 0.88	1.20 – 2.81	11
CSF2	P01587	1.07 $\pm$ 0.10	1.06 – 2.20	98
DDAH1	Q9CWS0	1.00 $\pm$ 0.76	0.27 – 3.27	26
FLI1	P26323	1.69 $\pm$ 0.84	1.25 – 6.14	56
FOXO1	Q9R1E0	1.86 $\pm$ 0.32	1.61 – 3.82	25
GCG	P55095	1.18 $\pm$ 0.66	0.77 – 5.91	40
GDNF	P48540	0.85 $\pm$ 0.21	0.77 – 1.99	78
IL1B	P10749	2.03 $\pm$ 0.58	1.66 – 4.60	44
IL5	P04401	1.33 $\pm$ 0.11	1.31 – 2.45	95
IL6	P08505	1.84 $\pm$ 0.66	1.47 – 5.95	58
IL10	P18893	0.44 $\pm$ 0.31	0.22 – 1.80	46
ITGB6	Q9Z0T9	2.49 $\pm$ 0.53	2.38 – 3.71	92
KITLG	P20826	1.23 $\pm$ 1.58	0.91 – 2.35	79
PAK4	Q8BTW9	0.73 $\pm$ 0.35	0.60 – 3.68	72
PLIN1	Q8CGN5	2.43 $\pm$ 0.88	1.63 – 6.23	23
TNF	P06804	-0.55 $\pm$ 0.03	-0.55 – -0.28	96

Table S2. List of identified variants

Chromosome	cDNA¹	Protein²	SNP name³
<i>Ahr</i>			
12	c.-100G>A	-	UNCHS033204
12	c.1295A>G	K432R	JAX00330261
<i>Rfx1</i>			
8	c.1835T>C	F612S	UNC15100031
8	c.2172A>G	A724	UNCHS023499
8	c.*935G>A	-	UNCHS023500

¹Relative to the translation initiation codon in NM_013464.4 for *Ahr* and NM_009055.4 for *Rfx1*;

²According to NP_038492.1 for AHR and NP_033081.3 for RFX1; ³SNP identifier as used by GigaMUGA (GeneSeek, Neogen).