Supplementary Information:

Mapping *cis* and *trans* regulatory effects across multiple tissues in twins

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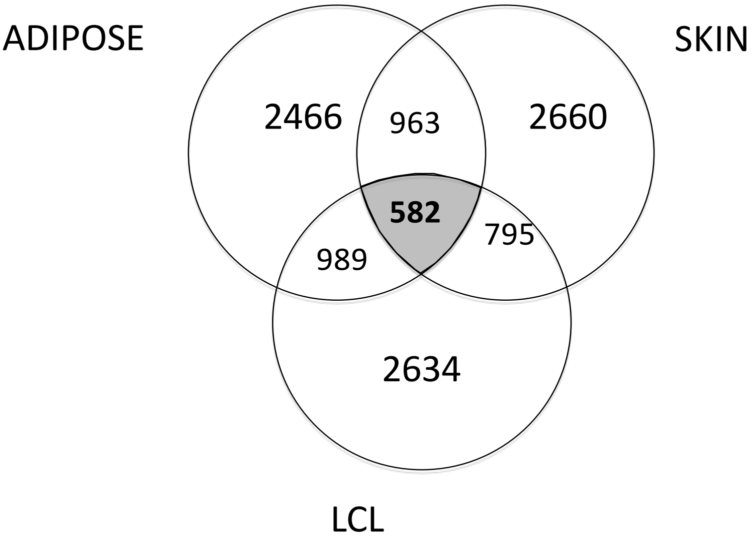
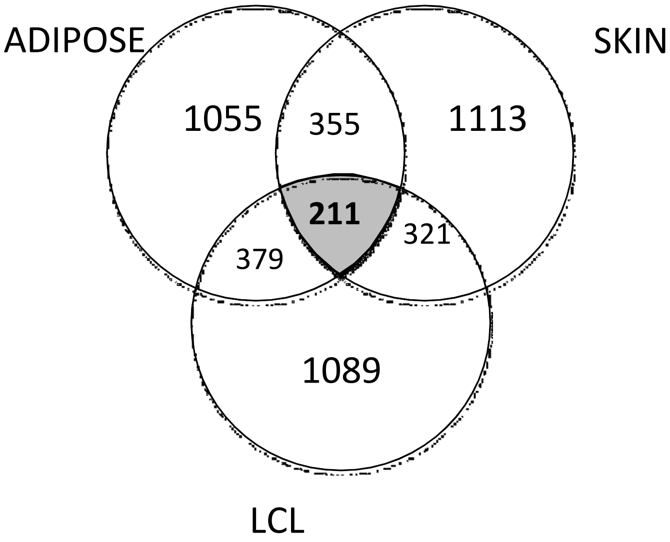
Supplementary Fig 1. Venn diagram of transcript heritability across tissues
(A) The top 5000 heritable transcripts in each tissue (of in total of ~20K transcripts) where included which corresponded to $h^2_{\text{adipose}} > 0.33$, $h^2_{\text{LCL}} > 0.27$ and $h^2_{\text{skin}} > 0.22$. **(B)** Venn diagram showing comparison of transcript heritability across tissues limited to transcripts expressed in all tissues. The top 2000 heritable expressed transcripts in each tissue (in total of 8619 transcripts expressed in all three tissues) where included corresponding to $h^2_{\text{adipose}} > 0.41$, $h^2_{\text{LCL}} > 0.33$ and $h^2_{\text{skin}} > 0.28$.

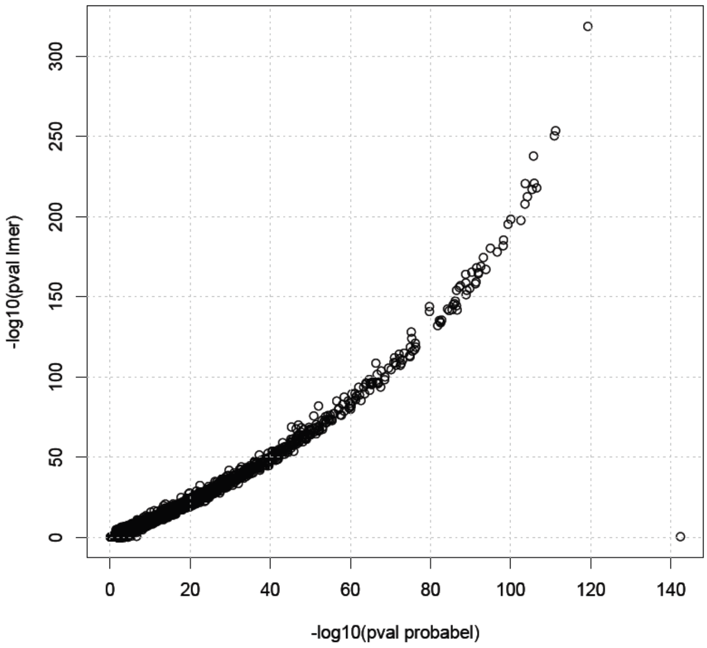
A



B

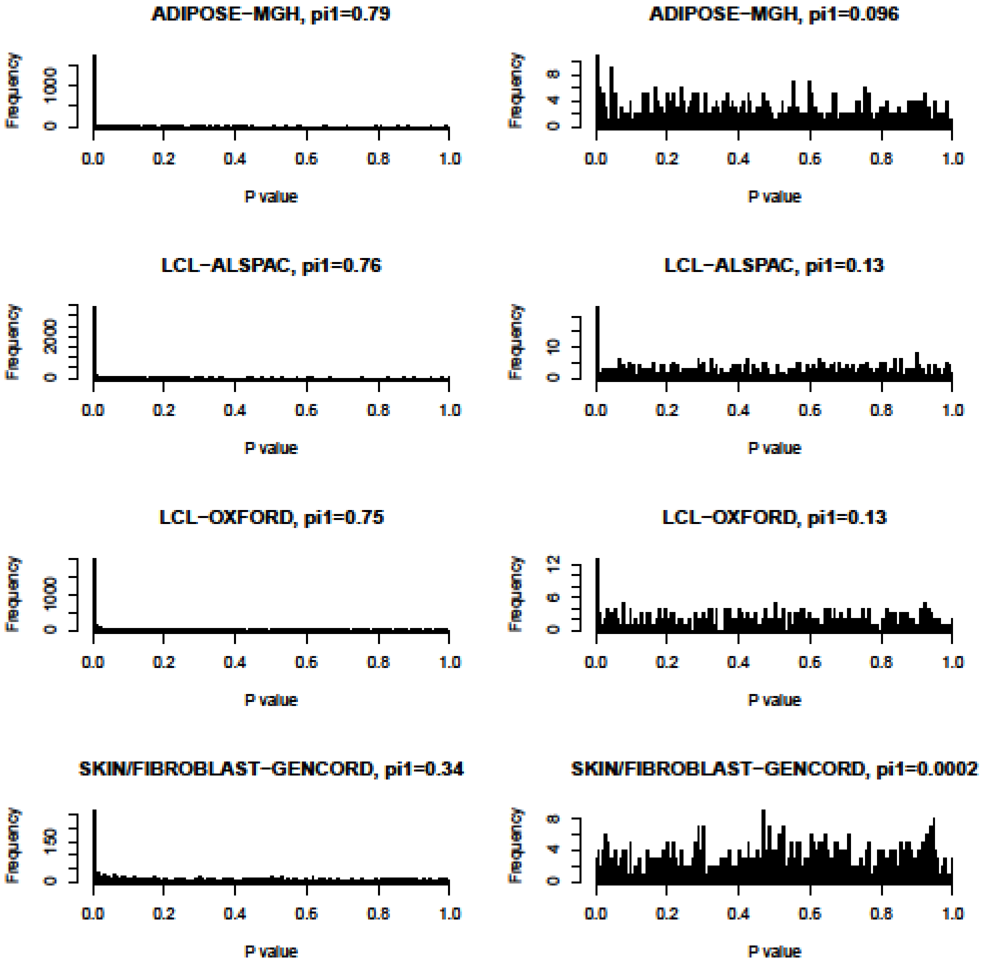


Supplementary Fig 2. Validation of cis-eQTLs
Top *cis*-eQTLs per transcript identified in the two-step statistical approach implemented in the GenABEL/ProbABEL were validated in a full linear mixed-effects model. The –log10 p value from the mixed model (*y-axis*) is graphed against the–log10 p value from ProbABEL (*x-axis*)



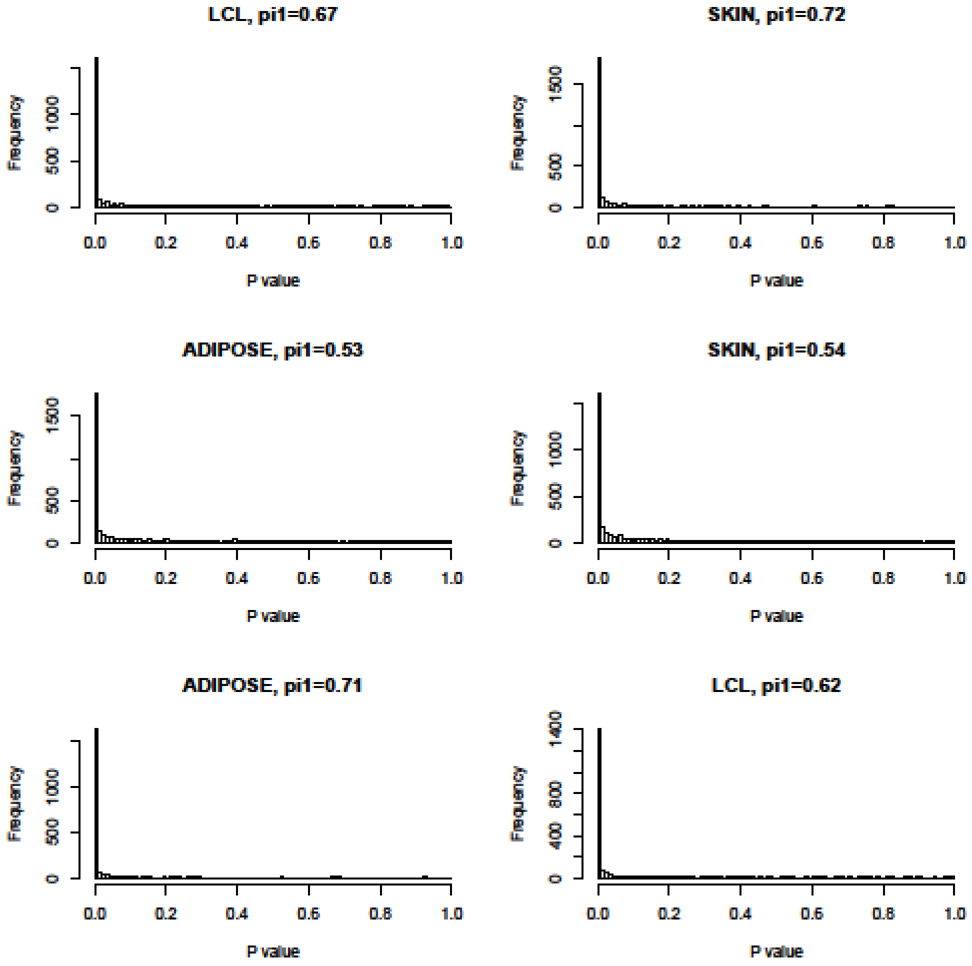
Supplementary Fig 3. Replication of cis- and trans associations in independent cohorts

P-value distributions of *cis* (*left panel*) and *trans*-associations (*right panel*) identified in the MuTHER study in four different replication cohorts: MGH (adipose), ALSPAC (LCL), OXFORD (LCL) and GenCORD (skin/fibroblasts). *Cis*-associations identified at 1% FDR and *trans*-associations at $P<5x10^{-8}$ were tested in the replication cohorts, respectively. The replication P-values from the different data sets were used to estimate $\pi0$ which is the overall proportion of true null hypotheses among all tests performed after which the proportion of significant replicated *cis* and *trans* results in each study, $\pi1$ could be calculated.



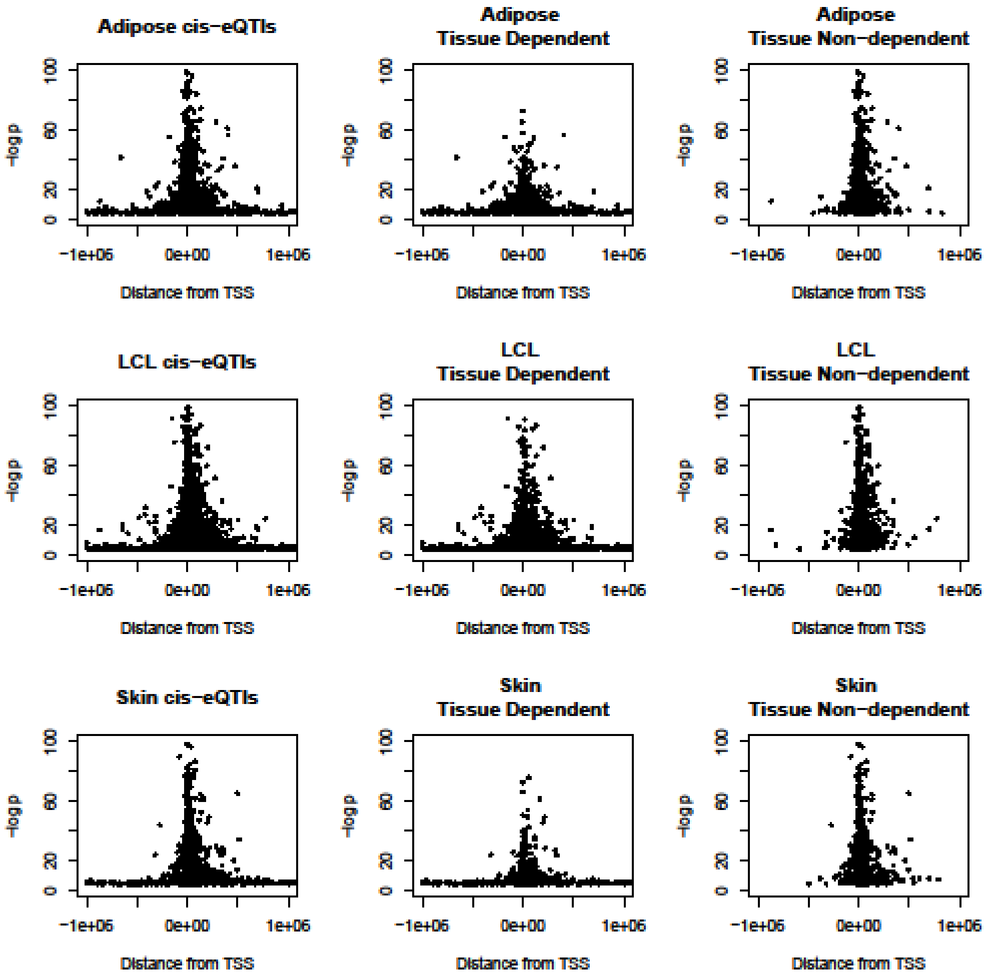
Supplementary Fig 4. Tissue-independency of cis-eQTLs

P-value distribution of *cis*-associations identified at 1% FDR in adipose (*upper panel*), LCL (*middle panel*) and skin tissue (*lower panel*) in corresponding comparing tissue.

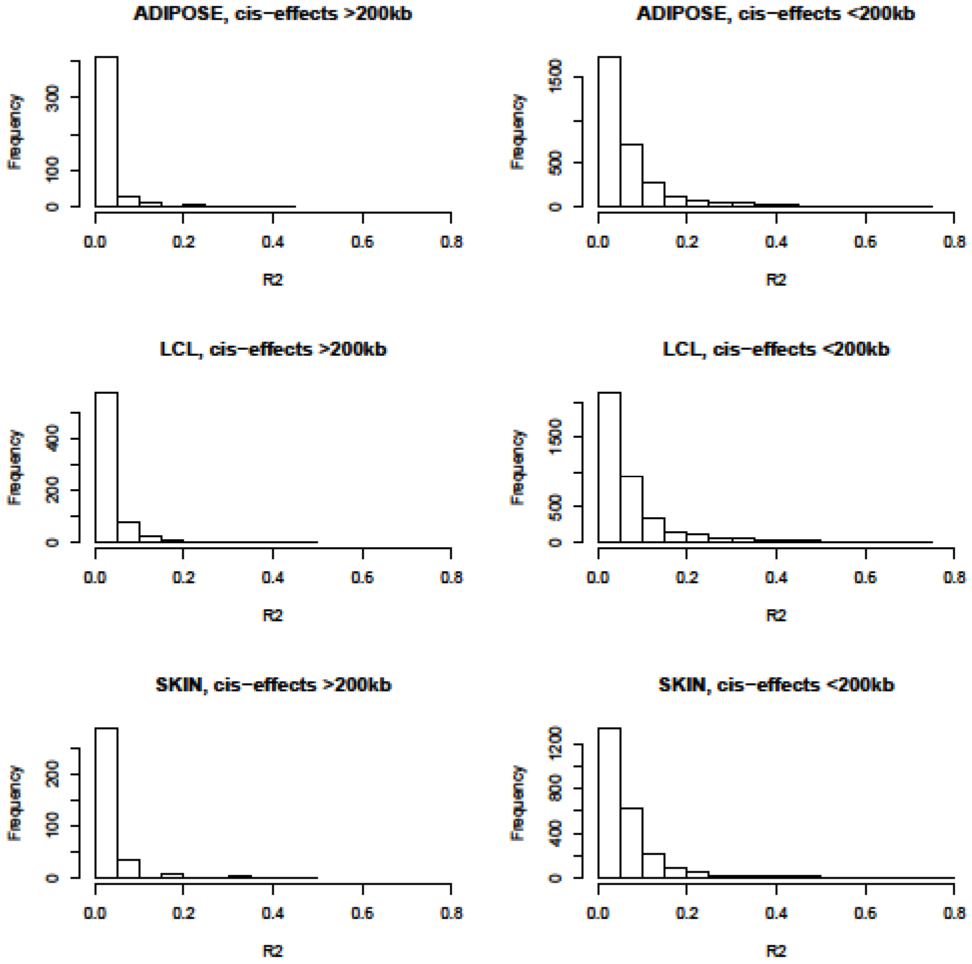


Supplementary Fig 5. Properties of cis-eQTLs

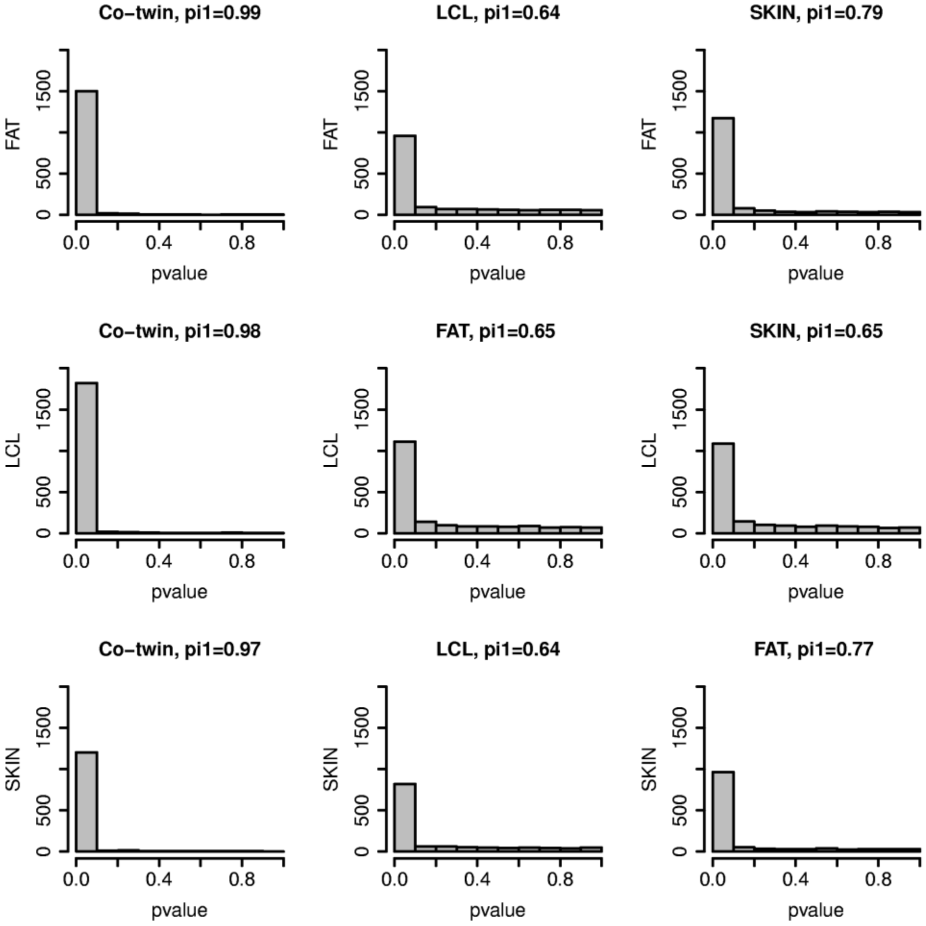
Plots show the localization of *cis*-eQTLs in adipose (*upper panel*), LCL (*middle panel*) and skin (*lower panel*) with regards to transcription start site (TSS) for all *cis*-eQTLs identified at 1% FDR (*left panel*), tissue-dependent *cis*-eQTLs identified at 1% FDR in discovery tissue not meeting the same cut off in either of the other tissues (*middle panel*) and tissue-independent *cis*-eQTLs identified at 1 % FDR in at least two tissues (*right panel*).



Supplementary Fig 6. Properties of cis-eQTLs dependent on localization
Histograms showing the coefficient of determination (R^2) of *cis*-eQTLs identified at 1% FDR with either long-range effects (>200kb from TSS) (*left panel*) or located less than 200kb from TSS (*right panel*) in adipose (*upper panel*), LCL (*middle panel*) and skin tissue (*lower panel*) respectively.

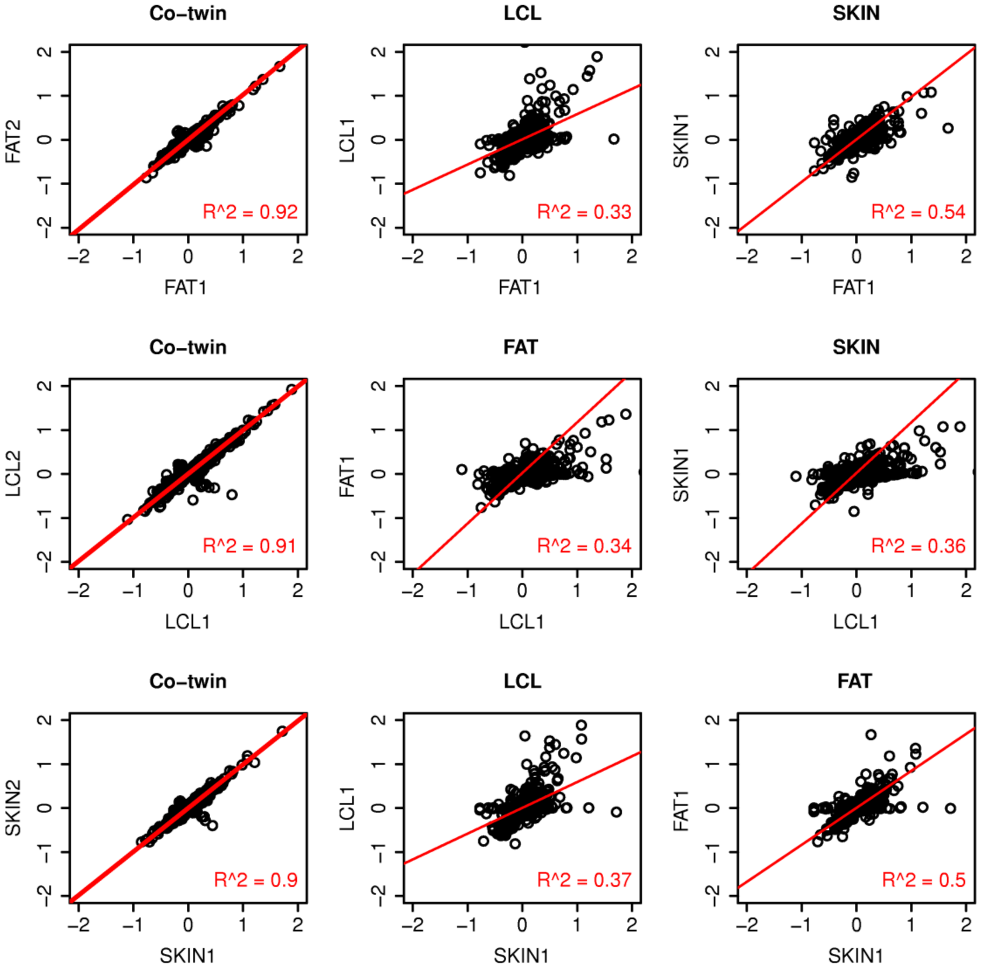


Supplementary Fig 7. cis-eQTL mapping using matched co-twin design
P-value distribution of *cis*-associations identified using a matched co-twin design at 1% FDR in adipose (*upper panel*), LCL (*middle panel*) and skin tissue (*lower panel*) in corresponding co-twin or tissue.



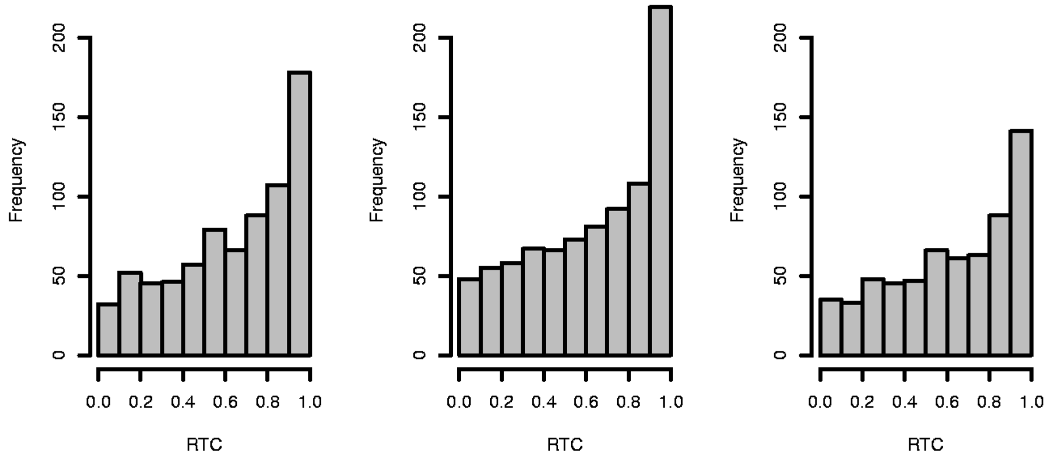
Supplementary Fig 8. Expressions fold change within twins and across tissues for cis-eQTLs

Tissue-dependency of *cis*-eQTLs was evaluated by contrasting expression fold changes between tissues and estimating the predictive value (R^2) of each tissue against the other two. The plotted fold change on the X and Y-axes was calculated as the difference in mean expression of homozygous genotypic classes. For each pair wise twin or tissue comparison, the predictive value (R^2) between fold changes is shown.



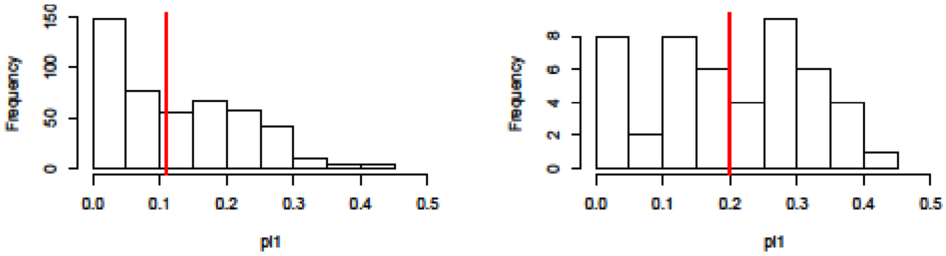
Supplementary Fig. 9*. *RTC distribution

Histogram of RTC score distribution across adipose (*left*), LCL (*middle*) and skin (*right*) tissue for all tested hotspot intervals where *cis*-eQTLs (1% FDR) and GWA SNPs co-localize ($N_{adipose} = 765$, $N_{LCL} = 887$, $N_{skin} = 639$). Under the null (regulatory polymorphisms cannot explain GWA SNPs of complex traits) we expect a uniform distribution of RTC scores. We observe an overrepresentation of high scores (RTC > 0.9) in all three tissues.



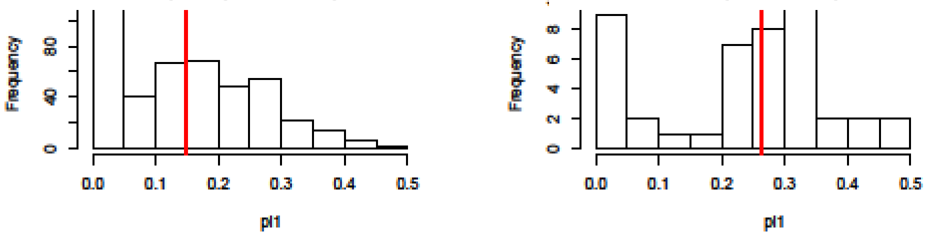
Supplementary Fig 10. Multi-gene regulators of expression

Distributions of π1 values for single-gene (*left panel*) and multi-gene regulators (*right panel*) across tissues. In each tissue, the median π1 of multi-gene regulators are greater than that for single-gene regulators, 0.20 vs. 0.11 in adipose, 0.26 vs. 0.14 in LCL and 0.23 vs. 0.12 in skin, respectively.



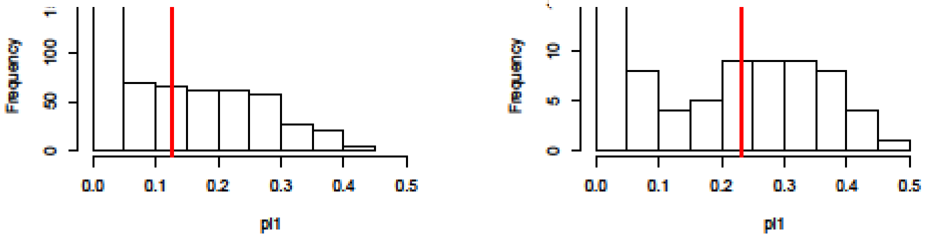
Adipose single-gene regulators

Adipose multi-gene regulators



LCL single-gene regulators

LCL multi-gene regulators



Skin single-gene regulators

Skin multi-gene regulators

Supplementary Tables

Supplementary Table 1. MuTHER cohort characteristics

	N	(MZ pairs/DZ pairs/singletons)
Study participants	856	154/232/84
Adipose biopsies	855	153/232/85
Skin biopsies	847	153/225/91
LCL	837	143/227/97
	N	**Mean±SD (range)**
Age (years)	856	59.4±9.0 (38.7-84.6)
Weight (kg)	855	69.5±13.9 (37.4-134.1)
Height (cm)	856	161.4±5.9 (143-179.9)
BMI (kg/m^2)	855	26.6±4.9 (16.2-47.1)

Supplementary Table 2. MuTHER gene expression heritability estimates across tissues

Tissue	**All transcripts**	**All transcripts $h^2>0.5$ (%)**	**Expressed transcripts***	**Expressed transcripts $h^2>0.5$ (%)**
Adipose	23423	1711 (7.3)	11394	1550 (13.6)
LCL	23428	908 (3.9)	10631	691 (6.5)
SKIN	23426	1043 (4.4)	11932	839 (7.0)
Tissue	**All transcripts**	**All transcripts $h^2>0.4$ (%)**	**Expressed transcripts***	**Expressed transcripts $h^2>0.4$ (%)**
Adipose	23423	3417 (14.6)	11394	3009 (26.4)
LCL	23428	2155 (9.2)	10631	1544 (14.5)
SKIN	23426	2073 (8.8)	11932	1611 (13.5)
Tissue	**All transcripts**	**All transcripts $h^2>0.3$ (%)**	**Expressed transcripts***	**Expressed transcripts $h^2>0.3$ (%)**
Adipose	23423	5714 (24.4)	11394	4864 (42.7)
LCL	23428	4184 (17.8)	10631	2987 (28.1)
SKIN	23426	3617 (15.4)	11932	2690 (22.5)
Tissue	**All transcripts**	**All transcripts $h^2>0.2$ (%)**	**Expressed transcripts***	**Expressed transcripts $h^2>0.2$ (%)**
Adipose	23423	7972 (34.0)	11394	6695 (58.7)
LCL	23428	7054 (30.1)	10631	5068 (47.7)
SKIN	23426	5461 (23.3)	11932	4088 (34.3)
Tissue	**All transcripts**	**All transcripts $h^2>0.1$ (%)**	**Expressed transcripts***	**Expressed transcripts $h^2>0.1$ (%)**
Adipose	23423	10027 (42.8)	11394	8128 (71.3)
LCL	23428	10219 (43.6)	10631	7200 (67.7)
SKIN	23426	7511 (32.1)	11932	5574 (46.7)

*defined according to the lumi algorithm were more than 10% of the arrays having a detected transcript ($P<0.01$)

***Supplementary Table 3**. cis-eQTL mapping across multiple tissues*

Significance level	**No. of *cis*-eQTLs (top SNP/transcript)**			**No. of *cis*-eQTLs (top SNP/expressed transcript)**		
	ADIPOSE	**LCL**	**SKIN**	**ADIPOSE**	**LCL**	**SKIN**
$P<5x10^{-8}$	1738 (7.5%)	2377 (10.3%)	1341 (5.8%)	1511 (13.4%)	1987 (18.9%)	1185 (10.0%)
0.1% FDR	2469 (10.6%)	3332 (14.4%)	1932 (8.4%)	2195 (19.4%)	2710 (28.8%)	1668 (14.1%)
1% FDR	3523 (15.2%)	4625 (20.0%)	2796 (12.2%)	3006 (26.6%)	3544 (33.7%)	2314 (19.6%)

Supplementary Table 4. Characteristics of study cohorts for replication of cis and trans-associations

Tissue	**Cohort**	**N**	**Gender (Female%: Male%)**	**Age (mean±SD)**	**Study population**	**Microarray platform**	**Replication**
Adipose (subcutaneous)	Decode	585	60:40	47.0±14.0	Healthy donors	Agilent Custom array	*trans* only
Adipose (subcutaneous)	MGH	701	75:25	44.7±11.5	Gastric bypass patients	Agilent Custom array	*cis* and *trans*
LCL	ALSPAC	931	52:48	7.0±0	Healthy donors	IlluminaHT12-V BeadChips	*cis* and *trans*
LCL	Oxford (TwinsUK)	331	80:20	53.8.0±13.1	Healthy donors	IlluminaWG6-V2BeadChips	*cis* and *trans*
Skin (fibroblasts)	GenCORD	68	56:44	Umbilical cord (38-41weeks)	Healthy donors	IlluminaWG6-V3BeadChips	*cis* and *trans*

Supplementary Table 5. Highly heritable transcripts across tissues and the relative contribution of common cis-effects

Probe	Chr	Gene	h^2_{Adipose}	*cis*-SNP$_{\text{Adipose}}$	% h^2	h^2_{LCL}	*cis*-SNP$_{\text{LCL}}$	% h^2	h^2_{Skin}	*cis*-SNP$_{\text{Skin}}$	% h^2
ILMN_1659411	16	POLR2C	0.79	rs17323082	0.23	0.75	rs17323082	0.26	0.62	rs17375948	0.20
ILMN_1663866	5	TGFBI	0.78	rs17168967	0.02	0.78	rs11740868	0.04	0.70	rs2237066	0.03
ILMN_1664641	13	MED4	0.73	rs2025864	0.69	0.93	rs1886977	0.50	0.77	rs2094190	0.45
ILMN_1665107	2	ITGB1BP1	0.89	rs2715860	0.03	0.86	rs11887079	0.03	0.63	rs7589401	0.07
ILMN_1683279	6	PEX6	0.74	rs2296804	0.53	0.91	rs2296804	0.67	0.81	rs2296804	0.55
ILMN_1719064	12	KCTD10	0.88	rs4766601	0.77	0.73	rs4766601	0.93	0.93	rs4766601	0.80
ILMN_1723116	16	AMFR	0.69	rs2432540	0.74	0.78	rs7205545	0.47	0.79	rs2432540	0.49
ILMN_1730054	22	GSTT1	1.00	rs5760147	0.47	1.00	rs5760147	0.44	1.00	rs5760147	0.55
ILMN_1743145	5	ERAP2	0.77	rs2910686	0.91	0.83	rs2910686	0.88	0.64	rs2910686	1.00
ILMN_1762255	1	GSTM1	0.91	rs11101992	0.17	1.00	rs11101992	0.14	0.98	rs11101992	0.16
ILMN_1765332	11	TIMM10	1.00	rs2511983	0.58	0.72	rs2511983	0.57	1.00	rs2729371	0.57
ILMN_1773313	10	USMG5	1.00	rs7911488	0.71	0.88	rs7911488	0.82	0.77	rs12220267	0.85
ILMN_1778488	5	WDR41	0.78	rs335628	0.68	1.00	rs441102	0.55	0.78	rs335628	0.74
ILMN_1784608	12	CLEC2B	0.80	rs33872	0.67	0.68	rs33872	0.50	1.00	rs33872	0.39
ILMN_1798177	14	CHURC1	0.89	rs7143432	0.74	1.00	rs4902345	0.73	0.86	rs4902345	0.70
ILMN_1807206	14	DHRS1	0.65	rs2295307	0.44	0.67	rs4568	0.18	0.61	rs10136508	0.06
ILMN_1809147	22	FAM118A	0.97	rs104664	0.61	0.76	rs104664	0.94	0.84	rs104664	0.88
ILMN_1810191	19	PLA2G4C	0.97	rs1653554	0.14	0.87	rs274861	0.26	1.00	rs156645	0.12
ILMN_2112049	9	DNLZ	0.64	rs8413	0.08	0.87	rs8413	0.10	0.66	rs11145922	0.13
ILMN_2115862	2	ESPNL	0.72	rs12479385	0.57	0.64	rs2278742	0.26	0.83	rs12479385	0.44
ILMN_2134224	19	ATP13A1	0.98	rs2304130	0.55	1.00	rs2304130	0.57	0.67	rs2304130	0.71
ILMN_2151579	21	HMGN1	0.72	rs2776311	0.81	0.78	rs2776311	0.72	0.76	rs2776311	0.66
ILMN_2173294	2	FLJ10916	0.84	rs6547752	0.62	0.80	rs7581571	0.26	0.63	rs10865489	0.87

Supplementary Table 6. Integration of cis-eQTL (FDR 1%) with disease loci

	Tissue	**#Interval-Disease (RTC ≥ 0.9)**	**% Total**
3 tissues	Adipose-LCL-Skin	52	14.5
2 tissues only	Adipose-LCL	36	10.1
	Adipose-Skin	27	7.5
	LCL-Skin	26	7.3
1 tissue only	Adipose only	66	18.4
	LCL only	111	31
	Skin only	40	11.2
Total RTC≥ 0.9	Adipose	181	
	LCL	225	
	Skin	145	
Union of total RTC ≥ 0.9		358	

Supplementary Table 7. Candidate GWAS signals mediated through cis regulatory variants (RTC ≥0.9) in adipose, LCL and skin

GWAS SNP	Trait	eQTL	Adipose p	LCL p	SKIN p	Gene	RTC
rs11170631	Height	rs11170631	2.49E-40	6.68E-13	1.47E-27	ATP5G2	1.00
rs1172822	Menarche and menopause (age at onset)	rs1172822	3.55E-08	2.68E-05	0.1543	BRSK1	1.00
rs1878047	Body mass index	rs12975233	2.54E-06	0.5897	0.0729	ETFB	1.00
rs2074518	QT interval	rs1003918	1.92E-15	9.63E-28	2.61E-18	LIG3	1.00
rs2280401	Hematological and biochemical traits	rs2280401	2.92E-06	0.0074	0.9488	FCGRT	1.00
rs2304130	Cholesterol, total;LDL cholesterol;Triglycerides	rs2304130	4.07E-86	3.38E-95	5.65E-71	ATP13A1	1.00
rs247616	Cardiovascular disease risk factors	rs3764261	4.50E-06	1.09E-07	0.1348	CETP	1.00
rs3018362	Bone mineral density (hip);Pagets disease	rs3018362	1.24E-10	2.17E-11	8.90E-09	PIGN	1.00
rs3129900	Lumiracoxib-related liver injury	rs3129934	5.84E-09	0.0034	0.0053	HSPA1B	1.00
rs314370	Resting heart rate	rs314370	2.59E-05	0.2867	0.0066	ACHE	1.00
rs3772130	Cognitive performance	rs3772130	3.90E-12	4.42E-05	0.0004889	IQCB1	1.00
rs402710	Lung cancer	rs402710	2.19E-06	0.8848	0.0453	CLPTM1L	1.00
rs4077515	Ulcerative colitis	rs10781496	2.68E-05	0.5494	0.0007273	GPSM1	1.00
rs439401	Triglycerides	rs439401	2.38E-09	0.2153	1.27E-10	APOE	1.00
rs4925386	Colorectal cancer	rs4925386	1.94E-05	3.04E-11	1.14E-09	OSBPL2	1.00
rs531676	Metabolic syndrome	rs531676	2.81E-13	0.8666	0.018	CRTAC1	1.00
rs619865	Freckling	rs619865	1.27E-05	0.0018	0.9087	TP53INP2	1.00
rs744166	Crohns disease;Multiple sclerosis	rs744166	9.07E-06	0.0008314	0.0037	STAT3	1.00

rs7993214	Psoriasis	rs7993214	1.98E-05	0.3435	0.2107	COG6	1.00
rs8396	Serum metabolites	rs8396	4.06E-20	0.000381	4.42E-09	ETFDH	1.00
rs867186	Plasma coagulation factors;Plasma levels of Protein C	rs867186	3.24E-15	0.0909	1.01E-11	PROCR	1.00
rs886427	Metabolic syndrome	rs886427	3.38E-07	0.0002198	0.0277	FLYWCH1	1.00
rs900400	Birth weight	rs900400	6.75E-58	0.3332	0.0154	TIPARP	1.00
rs9469578	Serum phosphorus concentrations	rs9469578	9.26E-06	0.8254	0.826	ITPR3	1.00
rs3134792	Psoriasis	rs2523567	5.53E-08	0.0075	4.42E-07	HCP5	1.00
rs1805007	Blond vs. brown hair color;Freckles;Red vs non-red hair color;Skin sensitivity to sun	rs8049897	9.88E-12	0.0232	0.0023	DBNDD1	1.00
rs3806156	Vitiligo	rs3806156	3.43E-05	0.0009382	0.0035	ATP6V1G2	1.00
rs3761847	Rheumatoid arthritis	rs10818488	2.47E-10	0.0424	0.0088	MEGF9	1.00
rs910873	Melanoma	rs910873	3.57E-06	1.42E-05	0.0822	EIF2S2	1.00
rs2188962	Crohns disease	rs11242110	3.69E-05	5.82E-05	0.0413	P4HA2	1.00
rs2187668	Celiac disease;Immunoglobulin A;Systemic lupus erythematosus	rs1794282	1.57E-08	3.81E-10	5.54E-09	HLA-DPB1	0.99
rs9630182	Bone mineral density	rs7125774	4.50E-06	0.5625	0.5663	FAR1	0.99
rs2338104	HDL cholesterol	rs918106	3.14E-06	6.68E-12	7.95E-05	MMAB	0.99
rs710865	Brain structure	rs709683	2.09E-05	2.52E-07	0.0011	KIAA0090	0.99
rs6495122	Diastolic blood pressure	rs6495122	3.13E-05	0.9338	0.0166	RPP25	0.99
rs1003719	Eye color traits	rs1003721	9.77E-16	2.43E-06	1.45E-06	TTC3	0.99
rs3135388	Multiple sclerosis	rs7197	1.45E-07	0.0376	0.0105	HSPA1B	0.99

rs9461688	Protein quantitative trait loci	rs9263871	4.74E-27	0.0071	3.23E-14	HCG27	0.99
rs9491696	Waist-hip ratio	rs7766106	9.90E-13	0.2352	0.6477	RSPO3	0.99
rs2517713	Nasopharyngeal carcinoma	rs2735096	2.10E-16	1.49E-20	8.73E-08	HCG4	0.99
rs3117582	Lung adenocarcinoma;Lung cancer	rs3117582	3.19E-05	0.4935	4.87E-06	HCP5	0.99
rs2856683	Primary biliary cirrhosis	rs9275293	4.22E-05	0.0026	0.0011	DOM3Z	0.99
rs10786284	Attention deficit hyperactivity disorder	rs11188739	8.91E-07	0.2829	0.5401	SORBS1	0.99
rs757978	Chronic lymphocytic leukemia	rs7601738	1.72E-21	1.46E-06	1.93E-14	2-Sep	0.99
rs4810485	Rheumatoid arthritis	rs4810485	1.11E-07	0.5036	7.52E-05	CD40	0.99
rs2647044	Type 1 diabetes	rs1794282	1.57E-08	3.81E-10	5.54E-09	HLA-DPB1	0.99
rs29232	Nasopharyngeal carcinoma	rs909728	4.78E-06	4.73E-12	4.00E-05	NA	0.99
rs2858884	Narcolepsy	rs9276401	4.69E-05	0.0915	0.1098	NOTCH4	0.99
rs9268480	Ulcerative colitis	rs3806156	3.43E-05	0.0009382	0.0035	ATP6V1G2	0.99
rs2251746	Serum IgE levels	rs7540542	4.19E-05	0.0269	0.0003813	FCER1A	0.99
rs4771122	Body mass index	rs7334690	8.49E-06	9.06E-06	2.41E-07	POLR1D	0.99
rs13146355	Serum magnesium levels	rs17253722	7.32E-06	0.1277	0.0423	SHRM	0.98
rs2647044	Type 1 diabetes	rs3129843	3.41E-06	0.3835	3.14E-05	HCP5	0.98
rs2070600	Pulmonary function	rs805284	4.51E-06	0.0007175	0.0002779	VARS2	0.98
rs429608	Age-related macular degeneration	rs8192585	7.60E-06	0.0782	0.0005009	HLA-DOB	0.98
rs9253	Hemostatic factors and hematological phenotypes	rs12119795	1.34E-06	6.73E-14	0.0019	C1orf149	0.98
rs2524054	CD4:CD8 lymphocyte ratio	rs9264594	2.49E-05	0.7253	0.6545	CLIC1	0.98

rs2151145	Menopause (age at onset)	rs4387054	8.65E-07	0.0015	0.0038	TLE4	0.98
rs433598	Schizophrenia	rs163269	1.14E-05	0.8378	0.3364	ACSM5	0.98
rs3134792	Psoriasis	rs2905710	2.71E-06	0.1878	2.20E-15	MICB	0.98
rs12198173	HIV-1 control	rs12153855	4.68E-05	0.0189	0.0396	LSM2	0.98
rs6435862	Neuroblastoma (high-risk)	rs6715570	2.73E-21	1.03E-13	8.14E-16	BARD1	0.98
rs2187668	Celiac disease;Immunoglobulin A;Systemic lupus erythematosus	rs3129843	3.41E-06	0.3835	3.14E-05	HCP5	0.98
rs798544	Height	rs798565	1.33E-08	1.15E-54	6.68E-06	GNA12	0.98
rs1158867	Plasma levels of Protein C	rs7599210	5.55E-12	0.1024	0.0054	ERCC3	0.98
rs3763313	HIV-1 control	rs13209234	8.11E-08	4.95E-16	1.86E-05	TAP2	0.98
rs4077515	Ulcerative colitis	rs10870077	4.05E-05	0.2212	0.074	NA	0.98
rs3099844	Neonatal lupus	rs2734583	1.23E-06	0.1989	2.86E-09	HCP5	0.98
rs4924935	Pancreatic cancer	rs966811	7.72E-06	0.4859	0.3295	PRPSAP2	0.98
rs8170	Breast cancer;Ovarian cancer	rs12982178	4.61E-07	0.9879	0.9464	OCEL1	0.98
rs3131296	Schizophrenia	rs1150752	7.09E-06	8.05E-07	1.12E-06	HLA-DPB1	0.98
rs3131379	Systemic lupus erythematosus	rs1150755	3.60E-06	0.2065	3.20E-12	MICB	0.98
rs1799810	Self-rated health	rs7599210	5.55E-12	0.1024	0.0054	ERCC3	0.98
rs17007017	Conduct disorder (case status)	rs9637655	2.20E-05	9.86E-05	7.59E-06	ZNF330	0.98
rs227584	Bone mineral density (hip)	rs2040810	1.75E-08	7.79E-09	0.3843	C17orf53	0.98
rs9271366	Immunoglobulin A;Multiple sclerosis	rs7197	1.45E-07	0.0376	0.0105	HSPA1B	0.98

rs1678542	Rheumatoid arthritis	rs1078109	5.83E-08	0.0432	0.0042	TMEM194	0.98
rs3131379	Systemic lupus erythematosus	rs1150752	7.09E-06	8.05E-07	1.12E-06	HLA-DPB1	0.98
rs1376877	Subclinical atherosclerosis traits (other)	rs3731695	8.75E-06	0.0371	5.42E-05	ALS2CR16	0.97
rs131794	Mean corpuscular volume	rs131816	1.63E-10	1.13E-18	3.38E-07	ECGF1	0.97
rs7703051	LDL cholesterol	rs17671591	4.79E-05	0.8454	0.792	C5orf37	0.97
rs10263639	Breast cancer	rs2215137	1.51E-06	0.0152	0.0361	STAG3L4	0.97
rs429608	Age-related macular degeneration	rs609061	9.68E-08	9.55E-05	0.0001315	RDBP	0.97
rs494620	Menopause (age at onset)	rs660550	6.88E-14	0.0011	1.15E-06	HSPA1B	0.97
rs3129934	Multiple sclerosis	rs3129934	5.84E-09	0.0034	0.0053	HSPA1B	0.97
rs10903129	Cholesterol, total	rs3091242	1.83E-07	6.88E-17	1.63E-07	TMEM50A	0.97
rs11622475	Bipolar disorder	rs1187448	3.64E-09	2.44E-07	0.0098	TDRD9	0.97
rs10876432	Bone mineral density (spine)	rs10082776	4.49E-05	0.7534	0.1732	TENC1	0.97
rs17319721	Chronic kidney disease;Renal function and chronic kidney disease	rs17253722	7.32E-06	0.1277	0.0423	SHRM	0.97
rs10484561	Follicular lymphoma	rs13209234	8.11E-08	4.95E-16	1.86E-05	TAP2	0.97
rs3099844	Neonatal lupus	rs9267445	9.08E-08	0.0699	0.0003818	NOTCH4	0.97
rs258322	Black vs. red hair color;Melanoma	rs8049897	9.88E-12	0.0232	0.0023	DBNDD1	0.97
rs3764261	Age-related macular degeneration;Blood lipid traits;HDL cholesterol;LDL cholesterol;Metabolic syndrome;Waist circumference and related phenotypes	rs3764261	4.50E-06	1.09E-07	0.1348	CETP	0.97
rs4911414	Burning and freckling;Freckles;Red vs. non-red hair	rs11700255	3.84E-07	0.4134	0.0729	ITCH	0.97

	color;Skin sensitivity to sun						
rs3134792	Psoriasis	rs2248902	4.06E-09	0.4869	1.57E-05	NOTCH4	0.97
rs494620	Menopause (age at onset)	rs592229	3.51E-05	0.5091	0.1914	AGPAT1	0.97
rs12696304	Telomere length	rs9822885	4.80E-05	0.2755	0.5244	ARPM1	0.97
rs13437082	Height	rs2844580	2.03E-05	0.1133	0.3427	FLOT1	0.97
rs7758512	HIV-1 control	rs9258278	1.80E-05	NA	NA	HCG18	0.97
rs10109414	Chronic kidney disease	rs17786744	4.68E-05	0.646	0.0725	SLC25A37	0.97
rs229541	Type 1 diabetes	rs229562	1.53E-07	0.1317	0.0392	C1QTNF6	0.96
rs7209435	Height	rs12325866	1.47E-10	9.14E-05	0.000266	DDX42	0.96
rs629301	Blood lipid traits	rs611917	6.57E-06	1.33E-07	0.0001637	GSTM1	0.96
rs4794822	Neutrophil count	rs3859192	9.50E-27	0.8402	1.19E-07	GSDMA	0.96
rs2244621	Longevity	rs3751120	1.90E-14	0.9732	0.5771	VEGFB	0.96
rs2524054	CD4:CD8 lymphocyte ratio	rs2243868	3.92E-05	0.0404	0.0002639	SKIV2L	0.96
rs660895	Rheumatoid arthritis	rs9275207	1.55E-13	3.17E-07	1.15E-13	HLA-DOB	0.96
rs884205	Bone mineral density (spine)	rs3018362	1.24E-10	2.17E-11	8.90E-09	PIGN	0.96
rs167769	Eosinophilic esophagitis (pediatric)	rs2122694	2.67E-06	0.1937	0.0125	RBMS2	0.96
rs9859260	Mean corpuscular volume	rs11185506	2.22E-07	0.0005284	4.16E-05	MUC20	0.96
rs17145713	Plasma levels of Protein C	rs11974409	4.59E-16	0.9503	4.51E-23	MLXIPL	0.96
rs2571445	Pulmonary function	rs1035673	3.59E-10	0.6935	0.0959	TNS1	0.96
rs7932354	Bone mineral density (hip)	rs10769205	6.16E-13	0.6249	4.45E-05	ARHGAP1	0.96

rs4785763	Melanoma	rs6500462	5.25E-06	1.41E-21	9.69E-05	CDK10	0.96
rs4130590	Bipolar disorder	rs3808839	1.61E-09	4.49E-15	0.0391	SLC2A8	0.96
rs2188962	Crohns disease	rs2248116	7.42E-07	7.75E-08	0.0002889	RAD50	0.96
rs6088792	Height	rs17421899	2.17E-05	0.0022	0.6868	TP53INP2	0.95
rs7197475	Systemic lupus erythematosus	rs9934806	2.33E-06	0.0014	0.0002222	ZNF689	0.95
rs7197475	Systemic lupus erythematosus	rs4889603	1.32E-08	0.0064	0.0082	MYST1	0.95
rs10838738	Body mass index	rs17788930	1.27E-11	1.69E-05	1.95E-07	C1QTNF4	0.95
rs11683229	Protein quantitative trait loci	rs4671052	1.01E-05	0.1984	0.2145	EHBP1	0.95
rs1678542	Rheumatoid arthritis	rs2306390	1.21E-05	0.1576	0.0258	TSPAN31	0.95
rs703842	Multiple sclerosis	rs11172343	1.21E-44	3.20E-44	3.42E-21	FAM119B	0.95
rs2523608	HIV-1 control	rs9266596	1.31E-05	0.0031	0.161	ABCF1	0.95
rs174550	Fasting glucose-related traits	rs174578	1.14E-05	0.0134	0.2072	FADS1	0.95
rs3733829	Smoking behavior	rs2305797	1.91E-35	2.82E-38	8.28E-19	RAB4B	0.95
rs2524054	CD4:CD8 lymphocyte ratio	rs9263938	1.73E-08	0.0023	4.38E-09	VARS2	0.95
rs6495122	Diastolic blood pressure	rs11630918	2.18E-06	0.0106	0.37	SNUPN	0.95
rs10507380	Electrocardiographic traits	rs9507868	1.72E-12	0.3083	3.31E-05	RASL11A	0.95
rs1980493	Anti-cyclic Citrullinated Peptide Antibody	rs1794282	1.57E-08	3.81E-10	5.54E-09	HLA-DPB1	0.95
rs2856683	Primary biliary cirrhosis	rs9275207	1.55E-13	3.17E-07	1.15E-13	HLA-DOB	0.95
rs1900004	Optic disc parameters;Vertical cup-disc ratio	rs10823171	4.41E-28	1.45E-27	3.98E-11	SLC25A16	0.95
rs9468925	Vitiligo	rs9263871	4.74E-27	0.0071	3.23E-14	HCG27	0.95

rs6861681	Waist-hip ratio	rs7736263	2.49E-26	1.76E-39	5.48E-21	CPEB4	0.95
rs6060369	Height	rs224320	2.41E-07	0.9721	7.26E-05	PROCR	0.94
rs6532197	Parkinsons disease	rs10516849	3.19E-11	0.5679	1.01E-05	MMRN1	0.94
rs9264942	HIV-1 control	rs2905710	2.71E-06	0.1878	2.20E-15	MICB	0.94
rs2072590	Ovarian cancer	rs1318778	5.01E-06	0.1405	0.002	HOXD3	0.94
rs4072037	Esophageal cancer and gastric cancer;Serum magnesium levels	rs4971088	1.46E-10	5.06E-12	0.0001261	ADAM15	0.94
rs947211	Parkinsons disease	rs708726	1.14E-05	3.88E-07	4.85E-05	RAB7L1	0.94
rs9268480	Ulcerative colitis	rs2856705	4.24E-05	0.0276	0.6376	SYNGAP1	0.94
rs6074022	Multiple sclerosis	rs4810485	1.11E-07	0.5036	7.52E-05	CD40	0.94
rs1728785	Ulcerative colitis	rs6499186	3.05E-11	1.52E-27	0.0062	ZFP90	0.94
rs216345	Bipolar disorder	rs13287325	1.19E-17	4.51E-17	1.41E-12	NUDT2	0.94
rs12928822	Celiac disease	rs7187741	5.74E-14	3.30E-36	0.0273	C16orf75	0.94
rs2277027	Pulmonary function	rs6899205	2.00E-09	2.68E-05	3.08E-09	ADAM19	0.94
rs9461688	Protein quantitative trait loci	rs2243868	3.92E-05	0.0404	0.0002639	SKIV2L	0.94
rs477515	Inflammatory bowel disease	rs3806156	3.43E-05	0.0009382	0.0035	ATP6V1G2	0.94
rs3131379	Systemic lupus erythematosus	rs3132941	1.59E-05	0.3725	1.77E-05	HCP5	0.94
rs13385191	Prostate cancer	rs12622106	5.10E-36	2.89E-49	4.44E-23	C2orf43	0.94
rs13192471	Rheumatoid arthritis	rs13209234	8.11E-08	4.95E-16	1.86E-05	TAP2	0.94
rs9271100	Systemic lupus erythematosus	rs7197	1.45E-07	0.0376	0.0105	HSPA1B	0.94

rs9469220	Crohns disease	rs9275207	1.55E-13	3.17E-07	1.15E-13	HLA-DOB	0.94
rs958672	Aging traits	rs13015501	1.11E-06	0.8395	0.0002282	GALNT13	0.94
rs470119	Hematological and biochemical traits	rs131816	1.63E-10	1.13E-18	3.38E-07	ECGF1	0.94
rs2239557	Common traits (Other)	rs4899502	1.42E-14	1.04E-17	1.26E-16	LIN52	0.94
rs2736428	Telomere length	rs660550	6.88E-14	0.0011	1.15E-06	HSPA1B	0.93
rs2839619	Biochemical measures	rs4920023	6.53E-07	0.0004251	0.0869	WDR4	0.93
rs3846663	Quantitative traits	rs17671591	4.79E-05	0.8454	0.792	C5orf37	0.93
rs429608	Age-related macular degeneration	rs4151671	1.24E-19	2.72E-31	1.23E-07	DOM3Z	0.93
rs3094212	Hematological and biochemical traits	rs3131003	4.74E-05	4.19E-05	0.0115	ATP6V1G2	0.93
rs7188697	QT interval	rs9926577	8.46E-06	3.97E-07	2.02E-06	CNOT1	0.93
rs2856683	Primary biliary cirrhosis	rs3806156	3.43E-05	0.0009382	0.0035	ATP6V1G2	0.93
rs26232	Rheumatoid arthritis	rs421946	1.86E-07	6.94E-07	0.6621	C5orf30	0.93
rs2524054	CD4:CD8 lymphocyte ratio	rs3997982	3.12E-05	0.4235	0.7358	C2	0.93
rs2301436	Crohns disease	rs9457249	4.34E-05	2.73E-07	0.0012	FGFR1OP	0.93
rs11648785	Tanning	rs7498985	6.80E-16	0.0966	0.0086	GAS8	0.93
rs12740374	LDL cholesterol	rs611917	6.57E-06	1.33E-07	0.0001637	GSTM1	0.93
rs694739	Alopecia areata	rs600377	5.01E-07	1.33E-32	2.80E-15	CCDC88B	0.93
rs185819	Height	rs592229	3.51E-05	0.5091	0.1914	AGPAT1	0.93
rs174547	HDL cholesterol;Resting heart rate;Serum metabolites;Triglycerides	rs174578	1.14E-05	0.0134	0.2072	FADS1	0.93

rs6498169	Multiple sclerosis	rs794433	4.92E-06	0.1856	0.0176	C16orf75	0.93
rs2856683	Primary biliary cirrhosis	rs2856705	4.24E-05	0.0276	0.6376	SYNGAP1	0.92
rs3807989	Electrocardiographic traits;PR interval	rs1049337	2.65E-64	6.31E-17	1.55E-53	CAV1	0.92
rs1512268	Prostate cancer	rs11774063	3.23E-07	0.0107	4.44E-13	SLC25A37	0.92
rs16889440	Radiation response	rs12523750	4.23E-09	3.16E-09	0.0002975	MRS2	0.92
rs9468925	Vitiligo	rs2243868	3.92E-05	0.0404	0.0002639	SKIV2L	0.92
rs6904029	Vitiligo	rs2735096	2.10E-16	1.49E-20	8.73E-08	HCG4	0.92
rs167769	Eosinophilic esophagitis (pediatric)	rs841718	4.55E-62	1.36E-53	5.14E-50	STAT6	0.92
rs4744712	Chronic kidney disease	rs12006032	2.93E-05	0.5268	0.1343	PRKACG	0.92
rs2040704	Serum IgE levels	rs17772583	1.19E-25	1.83E-35	3.93E-11	RAD50	0.92
rs3131296	Schizophrenia	rs3132941	1.59E-05	0.3725	1.77E-05	HCP5	0.92
rs1178979	Triglycerides	rs11974409	4.59E-16	0.9503	4.51E-23	MLXIPL	0.92
rs1805081	Obesity	rs11663558	2.56E-17	3.97E-08	4.62E-15	NPC1	0.92
rs3764021	Type 1 diabetes	rs2268146	1.88E-19	0.3119	1.49E-22	CLECL1	0.92
rs7120118	HDL cholesterol	rs4752973	1.51E-05	3.42E-05	0.1981	NR1H3	0.92
rs3806156	Vitiligo	rs2856705	4.24E-05	0.0276	0.6376	SYNGAP1	0.92
rs3761218	Bipolar disorder	rs4815603	7.86E-13	0.316	0.2766	CDC25B	0.92
rs4324798	Lung adenocarcinoma	rs7745768	4.42E-07	4.65E-05	0.0009734	HCG2P7	0.92
rs9468925	Vitiligo	rs9264594	2.49E-05	0.7253	0.6545	CLIC1	0.92
rs3131296	Schizophrenia	rs1150755	3.60E-06	0.2065	3.20E-12	MICB	0.92

rs2839619	Biochemical measures	rs11700748	1.60E-20	4.11E-40	8.20E-50	CBS	0.92
rs4925386	Colorectal cancer	rs6143035	2.87E-08	0.0058	7.57E-09	CABLES2	0.91
rs11931074	Parkinsons disease	rs3857059	1.09E-07	0.0326	1.28E-05	MMRN1	0.91
rs2075671	Other erythrocyte phenotypes	rs4727459	1.38E-05	1.13E-06	0.000244	GIGYF1	0.91
rs3129882	Parkinsons disease	rs7197	1.45E-07	0.0376	0.0105	HSPA1B	0.91
rs229527	Vitiligo	rs229562	1.53E-07	0.1317	0.0392	C1QTNF6	0.91
rs13160562	Alcohol dependence	rs17401719	4.11E-09	1.32E-26	0.0012	ERAP1	0.91
rs157580	Alzheimers disease;HDL cholesterol;LDL cholesterol	rs439401	2.38E-09	0.2153	1.27E-10	APOE	0.91
rs1390401	Height	rs6664307	1.28E-20	1.63E-14	1.52E-10	JMJD4	0.91
rs5751614	Height	rs140503	9.45E-39	1.71E-21	2.79E-38	BCR	0.91
rs646776	Cholesterol, total;Myocardial infarction (early onset);Response to statin therapy	rs611917	6.57E-06	1.33E-07	0.0001637	GSTM1	0.91
rs3129055	Nasopharyngeal carcinoma	rs441808	3.48E-14	4.27E-15	2.81E-14	HCG2P7	0.91
rs16826658	Endometriosis	rs2744721	3.53E-06	0.2057	0.0434	CDC42	0.91
rs401681	Bladder cancer;Pancreatic cancer	rs402710	2.19E-06	0.8848	0.0453	CLPTM1L	0.91
rs643531	HDL cholesterol	rs4237138	1.41E-05	0.0149	0.4615	TTC39B	0.91
rs798766	Bladder cancer;Urinary bladder cancer	rs744658	3.17E-09	0.7619	0.8843	FGFR3	0.91
rs2524054	CD4:CD8 lymphocyte ratio	rs9263871	4.74E-27	0.0071	3.23E-14	HCG27	0.91
rs1986734	Eosinophilic esophagitis (pediatric)	rs17253722	7.32E-06	0.1277	0.0423	SHRM	0.91
rs2523608	HIV-1 control	rs9266329	2.55E-05	0.1815	0.1177	DOM3Z	0.91

rs6465657	Prostate cancer	rs7804318	4.59E-06	0.3877	1.43E-09	TECPR1	0.91
rs2736428	Telomere length	rs805284	4.51E-06	0.0007175	0.0002779	VARS2	0.91
rs6504340	Primary tooth development (number of teeth)	rs1042815	2.05E-09	3.02E-21	9.80E-19	HOXB2	0.90
rs7931342	Prostate cancer	rs11825796	2.42E-06	0.0063	0.0087	MYEOV	0.90
rs3894194	Asthma	rs4247366	4.33E-05	0.5858	0.8229	KRT24	0.90
rs4794822	Neutrophil count	rs3213762	1.51E-05	0.1099	0.1498	PGAP3	0.90
rs7743761	Ankylosing spondylitis	rs2844580	2.03E-05	0.1133	0.3427	FLOT1	0.90
rs11648785	Tanning	rs6500462	5.25E-06	1.41E-21	9.69E-05	CDK10	0.90
rs2076529	Waist-hip ratio	rs2856705	4.24E-05	0.0276	0.6376	SYNGAP1	0.90
rs660895	Rheumatoid arthritis	rs9275293	4.22E-05	0.0026	0.0011	DOM3Z	0.90
rs29232	Nasopharyngeal carcinoma	rs9258278	1.80E-05	NA	NA	HCG18	0.90
rs11150610	Systemic lupus erythematosus	rs1106398	2.85E-06	0.0887	0.4559	MYST1	0.90
rs748404	Lung cancer	rs12912744	1.94E-05	0.3207	0.2189	SERF2	0.90
rs1678542	Rheumatoid arthritis	rs1148555	5.18E-07	0.0741	0.0447	DDIT3	0.90
rs1980493	Anti-cyclic Citrullinated Peptide Antibody	rs3129843	3.41E-06	0.3835	3.14E-05	HCP5	0.90
rs11647936	Waist circumference	rs8053334	5.08E-31	1.43E-23	2.89E-18	KLHL36	0.90

Supplementary Table 8. trans-eQTL mapping across multiple tissues

	No. of *trans*-associations at P <5×10^{-8}		
	ADIPOSE	**LCL**	**SKIN**
Trans-eQTLs	639	557	609
Transcripts	595	509	609
SNPs	518	491	493

Supplementary Table 9. Median genome-wide π_1 values for trans-SNPs in each tissue.

Tissue of Discovery	***Trans*-SNP type**	**N**	**Adipose median π_1**	**LCL median π_1**	**Skin median π_1**
Adipose	Multi-gene regulator	48	**0.2**	0.03	0.02
Adipose	Single-gene regulator	470	**0.11**	0.02	0.01
LCL	Multi-gene regulator	48	0	**0.26**	0.004
LCL	Single-gene regulator	443	0.004	**0.15**	0.02
Skin	Multi-gene regulator	44	0.002	0.01	**0.29**
Skin	Single-gene regulator	449	0	0	**0.15**

Supplementary Table 10. Replicated trans-associations in independent study cohorts

Adipose trans-replication								*MuTHER*		*DeCODE*		*MGH*	
PROBE	**Gene**	**Chr**	**SNP**	**Chr**	**Coordinate**	**Freq**	**A1**	**beta**	**p**	**beta**	**p**	**direction**	**p**
ILMN_1652166	GUCY1B2	13	rs12142688	1	49114640	0.19	T	0.05	3.0E-08	-0.009	2.6E-01	+	2.4E-02
ILMN_1722059	SAFB	19	rs7515865	1	169648370	0.65	G	0.07	2.8E-08	0.004	1.8E-01	+	3.5E-02
ILMN_1753241	SNTA1	20	rs6542665	2	3984589	0.44	T	0.07	3.2E-08	0.007	4.0E-02	+	3.3E-01
ILMN_1756417	ANKRD37	4	rs162561	2	38152381	0.21	T	-0.08	2.4E-09	-0.012	5.0E-02	-	4.3E-01
ILMN_1685574	TSC22D2	3	rs10209934	2	52116454	0.33	T	-0.13	6.3E-09	0.006	3.5E-01	-	5.4E-03
ILMN_2137464	DVL3	3	rs7595947	2	52117836	0.67	G	0.10	4.9E-08	0.000	8.5E-01	+	1.6E-02
ILMN_2363058	PAOX	10	rs9309438	2	70696282	0.33	T	0.08	2.6E-08	0.008	3.3E-02	NA	NA
ILMN_1679754	ADRA1B	5	rs6746736	2	207260638	0.06	G	0.20	3.0E-10	-0.003	5.6E-01	+	4.8E-02
ILMN_1802804	L3MBTL	20	rs12994785	2	212565670	0.46	G	-0.03	3.6E-08	-0.011	5.5E-03	+	2.6E-01
ILMN_1754660	ZCCHC24	10	rs1499258	3	1552232	0.68	T	-0.10	5.0E-09	0.000	9.5E-01	-	2.0E-02
ILMN_1723678	PRPH	12	rs4279078	3	12289846	0.88	G	-0.11	5.0E-08	0.004	3.7E-01	-	4.4E-02
ILMN_1731299	PML	15	rs4679614	3	59785907	0.82	T	0.05	2.6E-08	0.002	6.1E-01	+	4.2E-02
ILMN_1768575	SFTPD	10	rs13065597	3	157384630	0.83	T	-0.17	2.9E-08	-0.031	2.7E-02	-	6.0E-01
ILMN_1674811	OASL	12	rs3864096	3	188419970	0.92	T	-0.18	4.0E-09	-0.021	1.6E-02	+	9.0E-01
ILMN_1765299	PRIMA1	14	rs1447281	4	5274561	0.51	G	0.03	4.1E-08	0.004	2.8E-02	+	9.8E-01
ILMN_2304577	KCNK7	11	rs6822971	4	148907089	0.06	T	0.16	2.4E-10	0.018	3.9E-02	+	2.5E-01
ILMN_1761275	FUT6	19	rs2962954	5	18458951	0.13	G	-0.05	1.9E-08	0.003	5.4E-01	-	1.6E-02
ILMN_1793151	OR2T4	1	rs2548098	5	98949414	0.37	G	-0.03	4.0E-08	NA	NA	-	4.1E-02
ILMN_1760635	RAD51C	17	rs543363	6	131492805	0.20	T	-0.08	2.9E-08	-0.005	3.8E-01	-	2.2E-02
ILMN_1655924	TRNT1	3	rs783182	6	161088538	0.50	G	0.06	3.8E-09	0.007	1.3E-01	+	4.0E-02
ILMN_1740185	TPMT	6	rs13234269	7	130079726	0.52	T	0.11	2.2E-15	0.000	9.9E-01	+	7.0E-04
ILMN_1760320	GNB1	1	rs13234269	7	130079726	0.52	T	0.05	1.8E-08	0.010	8.0E-04	+	1.3E-04
ILMN_1675038	PRMT2	21	rs4731702	7	130083924	0.48	T	-0.06	6.9E-09	-0.013	8.0E-03	+	2.5E-01
ILMN_1693862	MGC70857	8	rs4731702	7	130083924	0.48	T	-0.09	4.8E-10	-0.013	3.3E-06	NA	NA
ILMN_1731745	NINJ2	12	rs11979110	7	130086999	0.48	T	-0.08	8.2E-09	-0.009	5.0E-02	-	3.6E-01
ILMN_1746948	MYL5	4	rs13233731	7	130088229	0.52	G	0.09	4.4E-08	0.013	2.0E-03	+	2.5E-04
ILMN_1681087	SLC7A10	19	rs738134	7	130118115	0.32	G	-0.32	2.0E-10	-0.047	4.0E-03	-	2.0E-09
ILMN_1784737	S1PR4	19	rs11778621	8	118434473	0.94	T	-0.11	3.9E-08	-0.024	2.6E-02	NA	NA
ILMN_2149494	NPL	1	rs12546735	8	141453121	0.29	T	0.13	4.5E-08	-0.018	1.4E-01	+	4.2E-02
ILMN_2407703	SYN1	23	rs1173106	9	92485434	0.08	T	0.06	3.5E-08	0.012	6.8E-03	NA	NA
ILMN_1773764	CECR7	22	rs10740803	10	29790196	0.35	T	0.21	4.9E-21	0.001	8.3E-01	+	4.4E-05
ILMN_2308903	WFDC3	20	rs4979805	10	79678480	0.06	G	0.10	4.8E-09	0.027	3.1E-02	+	7.7E-01
ILMN_2220735	CLEC3A	16	rs4090286	11	7601115	0.86	G	0.06	1.9E-10	0.006	2.2E-02	+	4.6E-01

ILMN_1682227	ZNF404	19	rs509082	11	29375423	0.28	T	0.03	1.5E-08	NA	NA	+	2.3E-02
ILMN_1774334	HIGD2A	5	rs2200745	12	10065581	0.66	G	-0.08	3.1E-08	0.003	3.0E-01	-	4.2E-02
ILMN_1798612	SNX20	16	rs4763192	12	61392975	0.91	G	-0.05	3.2E-08	-0.011	1.9E-02	+	5.5E-01
ILMN_1683939	VIPR2	7	rs4942485	13	31851182	0.13	G	-0.06	4.8E-08	0.005	7.4E-01	-	5.7E-03
ILMN_2310296	C21orf58	21	rs9573847	13	75836476	0.13	G	0.10	7.3E-09	0.005	4.8E-01	+	4.5E-02
ILMN_2093343	PLAC8	4	rs7338833	13	82926073	0.13	G	0.07	1.8E-08	0.024	1.9E-02	-	5.6E-01
ILMN_1736103	ITPR2	12	rs1956368	14	59174889	0.78	T	-0.11	2.9E-09	-0.021	2.3E-02	NA	NA
ILMN_1749071	CNIH3	1	rs347932	15	30972071	0.26	G	0.04	4.0E-09	0.024	8.8E-03	-	4.7E-01
ILMN_1698996	SLC19A1	21	rs11073955	15	83471793	0.58	G	-0.06	2.2E-08	-0.018	5.1E-03	+	8.0E-01
ILMN_2340886	OTOF	2	rs4796460	17	6131231	0.36	T	0.03	1.8E-08	-0.003	1.7E-01	+	4.3E-02
ILMN_1694801	SLC39A4	8	rs6046153	20	19443671	0.28	T	0.03	1.5E-08	0.004	4.9E-02	+	2.2E-01
ILMN_1718907	TSHZ1	18	rs399355	20	31113764	0.27	T	0.09	2.0E-08	0.001	8.0E-01	+	6.7E-03
ILMN_1705813	CFTR	7	rs9977233	21	37869312	0.31	G	0.04	1.4E-08	0.002	7.3E-01	+	6.9E-03
ILMN_1735432	ISCU	12	rs3842987	21	42022606	0.43	C	0.07	4.4E-09	-0.001	7.0E-01	+	1.4E-03
ILMN_2136423	MARS2	2	rs9621258	22	30174270	0.94	G	-0.06	4.4E-08	-0.022	3.2E-02	+	4.1E-01
ILMN_2404256	PTPRT	20	rs9625970	22	42714835	0.93	T	-0.06	6.6E-09	0.013	1.1E-02	-	4.8E-04
LCL trans-replication								***MuTHER***		***ALSPAC***		***Oxford-TwinsUK***	
PROBE	**Gene**	**Chr**	**SNP**	**Chr**	**Coordinate**	**Freq**	**A1**	**beta**	**p**	**beta**	**p**	**beta**	**p**
ILMN_1751045	C20orf86	20	rs6740340	2	25550937	0.471	T	-0.04	6.0E-09	0.00	6.8E-01	-0.07	3.0E-02
ILMN_1674519	ZP2	16	rs11884490	2	152964016	0.05	G	0.11	3.2E-08	0.08	4.5E-02	NA	NA
ILMN_1716421	ADRA1D	20	rs6738805	2	230791415	0.844	T	0.12	1.9E-21	0.02	2.4E-02	-0.01	6.2E-01
ILMN_1766169	BCAT1	12	rs9989746	2	230824034	0.824	G	-0.20	5.0E-08	-0.01	6.7E-01	-0.23	6.1E-04
ILMN_1773389	PLTP	20	rs9835138	3	119371969	0.745	C	0.12	3.0E-08	0.05	2.6E-02	-0.02	7.0E-01
ILMN_1811443	AVP	20	rs1250090	4	1203697	0.133	T	0.19	2.4E-22	0.11	6.7E-09	0.17	6.9E-03
ILMN_2406439	SPTBN4	19	rs900019	4	1212836	0.867	C	-0.12	9.3E-19	-0.05	2.9E-05	NA	NA
ILMN_1654370	TESK2	1	rs1552061	4	5777297	0.148	T	-0.12	3.7E-08	0.04	4.2E-02	-0.18	2.9E-02
ILMN_1751776	CKAP2L	2	rs12500996	4	38281006	0.769	G	0.09	3.7E-09	0.02	3.2E-01	0.08	3.1E-02
ILMN_1712088	CLYBL	13	rs6820936	4	177351883	0.331	T	-0.10	2.4E-08	0.04	2.0E-02	-0.16	2.4E-02
ILMN_1796179	HIST1H2BK	6	rs7714390	5	157117358	0.202	G	0.22	8.0E-09	NA	NA	0.30	8.6E-06
ILMN_1732071	HIST2H2BE	1	rs7714390	5	157117358	0.202	G	0.07	3.2E-08	NA	NA	0.30	6.9E-05
ILMN_1724669	RUNX1T1	8	rs278016	5	166951589	0.693	G	-0.03	4.3E-08	-0.01	2.8E-02	0.05	1.6E-01
ILMN_1728810	NDUFS1	2	rs3823342	6	30021046	0.508	T	-0.17	3.8E-55	-0.09	9.9E-19	0.08	7.9E-02
ILMN_2354237	PARP2	14	rs2844511	6	31497763	0.497	G	-0.09	1.6E-13	-0.05	2.0E-05	NA	NA
ILMN_1759948	RNF5P1	8	rs3132965	6	32254975	0.216	G	-0.17	7.6E-20	-0.20	1.3E-20	NA	NA
ILMN_1768301	ERG	21	rs7194	6	32520458	0.387	G	0.15	5.4E-50	0.10	4.1E-21	0.00	9.3E-01
ILMN_1675387	LIMS1	2	rs9269491	6	32650822	0.726	C	0.15	2.8E-14	NA	NA	0.35	3.0E-13

ILMN_2099586	CCDC28B	1	rs9275141	6	32759095	0.512	T	0.13	4.8E-09	0.05	1.4E-03	NA	NA
ILMN_2307721	IL22RA2	6	rs7789197	7	40931652	0.829	G	-0.08	3.3E-08	-0.03	3.6E-02	NA	NA
ILMN_2071446	PI15	8	rs6593296	7	56085787	0.261	T	0.05	5.5E-11	0.04	1.8E-05	NA	NA
ILMN_1783709	RRAGA	9	rs2003499	7	98852920	0.896	T	0.09	1.9E-11	0.08	2.2E-04	0.05	1.1E-01
ILMN_1677877	UBE2L3	22	rs9643283	8	133185236	0.589	G	-0.08	2.5E-09	-0.04	2.3E-02	0.04	1.8E-01
ILMN_2186078	MCART2	18	rs3750551	9	71051949	0.893	G	0.04	3.4E-08	0.02	5.0E-02	NA	NA
ILMN_1700031	PRAME	22	rs7865017	9	132760043	0.066	T	0.12	9.6E-11	0.01	6.6E-01	0.16	2.7E-02
ILMN_1773764	CECR7	22	rs2182400	10	29747557	0.23	G	0.14	6.0E-20	0.09	2.3E-07	0.36	1.4E-13
ILMN_1780840	C2orf16	2	rs12280580	11	616220	0.286	G	-0.04	1.2E-08	-0.01	4.1E-01	-0.13	5.4E-03
ILMN_1794505	SHFM1	7	rs7479101	11	792115	0.674	G	-0.09	1.7E-11	-0.13	7.9E-18	-0.11	5.7E-04
ILMN_1714412	ZNF292	6	rs10902222	11	800882	0.681	T	-0.09	7.2E-10	-0.05	4.1E-08	-0.08	7.5E-02
ILMN_1758895	CTSK	1	rs10833455	11	21056463	0.567	G	-0.06	4.1E-08	-0.02	4.2E-02	0.10	1.6E-01
ILMN_1657950	RPS26P10	8	rs1873914	12	54665694	0.589	G	-0.21	8.4E-38	-0.26	9.1E-115	-0.66	1.2E-16
ILMN_1740094	BEND4	4	rs10876864	12	54687352	0.411	G	0.11	5.1E-26	0.18	1.5E-111	0.09	4.2E-02
ILMN_1749375	TNFAIP8	5	rs11110954	12	100593825	0.289	G	0.07	4.3E-08	0.01	6.4E-01	0.08	4.3E-02
ILMN_1785037	SSR2	1	rs1961056	12	126176948	0.699	T	0.08	2.7E-08	0.03	1.3E-02	0.02	4.8E-01
ILMN_1753008	REXO1	19	rs10507407	13	32960738	0.964	G	-0.15	2.2E-08	-0.15	1.4E-04	NA	NA
ILMN_1790625	CBX3	7	rs2444302	15	38565798	0.444	G	-0.07	4.4E-09	-0.05	1.6E-03	-0.02	5.9E-01
ILMN_1804945	ZNF667	19	rs220377	16	3288172	0.764	G	0.06	2.9E-08	0.04	3.3E-01	0.15	4.7E-03
ILMN_1791039	RTF1	15	rs8081803	17	2511759	0.742	T	0.07	2.4E-09	0.06	6.7E-11	NA	NA
ILMN_1674646	IRF7	11	rs17159840	19	7664194	0.239	T	-0.07	4.8E-08	-0.06	4.3E-06	-0.02	5.8E-01
ILMN_1802557	HEBP1	12	rs12462505	19	42829965	0.203	G	0.10	2.2E-08	0.05	3.0E-04	0.16	3.5E-02
ILMN_1784352	CCM2	7	rs651601	19	44618665	0.666	T	-0.14	7.6E-24	-0.15	1.2E-14	-0.17	1.1E-15
ILMN_1732467	OR2AG1	11	rs2186317	21	33515444	0.462	G	0.08	4.2E-31	0.02	1.1E-06	0.18	7.6E-07
ILMN_1666169	NBR2	17	rs2836991	21	39656593	0.914	G	0.11	1.2E-12	0.03	3.1E-02	NA	NA
ILMN_1803300	C14orf68	14	rs455941	22	21586260	0.768	T	-0.10	2.2E-21	-0.01	1.9E-01	-0.60	3.1E-14
ILMN_1721818	CLDN10	13	rs9608573	22	25794157	0.083	T	0.13	9.9E-09	0.05	1.6E-03	0.37	3.2E-03
ILMN_1685194	CLDN10	13	rs2074735	22	29865872	0.934	G	-0.12	2.3E-11	-0.01	7.1E-01	-0.31	4.6E-02
ILMN_1697710	IL1F7	2	rs4821843	22	37670583	0.805	G	0.11	1.6E-08	0.09	1.9E-11	-0.07	5.0E-01
Skin trans-replication								***MuTHER***		***GenCORD***		-	
PROBE	**Gene**	**Chr**	**SNP**	**Chr**	**Coordinate**	**Freq**	**A1**	**beta**	**p**	**rho**	**p**		
ILMN_1780236	PMM1	22	rs4652519	1	178815787	0.68	G	-0.08	2.5E-09	-0.38	1.4E-03		
ILMN_1773925	BCL2L14	12	rs1545181	2	81781849	0.79	G	-0.04	3.1E-08	-0.27	2.6E-02		
ILMN_1664543	IFIT3	10	rs1579904	3	74773407	0.95	T	-0.08	6.6E-09	-0.26	3.2E-02		
ILMN_1815951	PCYOX1L	5	rs17054719	4	170239098	0.08	G	0.06	4.1E-08	0.28	2.0E-02		
ILMN_1737164	TM9SF1	14	rs10944587	6	93102151	0.63	G	0.07	4.9E-08	0.27	2.3E-02		

ILMN_2383455	SUOX	12	rs9403102	6	140031856	0.07	T	-0.14	3.0E-08	-0.25	4.0E-02		
ILMN_1792435	STAG1	3	rs7823289	8	102669784	0.41	T	-0.06	3.9E-08	-0.27	2.7E-02		
ILMN_1811029	TLK1	2	rs10979525	9	110619957	0.10	T	0.17	1.6E-08	0.27	2.6E-02		
ILMN_2232166	CCDC90B	11	rs11012618	10	18417101	0.08	C	-0.23	1.1E-08	-0.26	3.3E-02		
ILMN_1719286	CTSA	20	rs947913	11	123028053	0.92	G	-0.15	1.1E-08	-0.33	5.6E-03		
ILMN_2375786	LECT1	13	rs1215608	12	105045459	0.54	T	-0.05	4.2E-08	-0.29	1.7E-02		
ILMN_1657955	FMNL3	12	rs872273	13	22573103	0.06	G	0.08	2.2E-09	0.26	3.1E-02		
ILMN_2103362	ARHGAP27	17	rs1539177	13	46198056	0.43	G	-0.05	3.6E-08	-0.24	4.9E-02		
ILMN_2125880	ZNF566	19	rs8022497	14	86603364	0.93	G	-0.10	1.0E-08	-0.30	1.4E-02		
ILMN_1791346	ATF3	1	rs1158689	16	13779188	0.19	G	0.04	1.1E-08	0.24	4.7E-02		

Supplementary Note

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