

## SUPPLEMENTARY MATERIAL.

**Supplementary Table 1.** Lead SNPs at suggestive loci (p-values between  $5 \times 10^{-8}$  and  $5 \times 10^{-6}$ ) for Cu, Se and Zn.

**Supplementary Table 2.** Allelic effects of low-MAF SNPs near *EPHA6* on Cu and Zn.

**Supplementary Table 3.** Association with erythrocyte Zn concentration for SNPs at the chromosome 8 locus showing significant effects on expression of *CA2* (carbonic anhydrase 2).

**Supplementary Table 4.** SNPs affecting *KLF8* expression near the Zn locus on chromosome X.

**Supplementary Figure 1.** Comparison of QIMR and ALSPAC results for Se, chromosome 5.

**Supplementary Figure 2.** Meta-analysis results for Se, showing two independent associations.

**Supplementary Figure 3.** Regional plots for Cu and Zn, which both show suggestive associations with SNPs around *EPHN6*.

**Supplementary Figure 4.** Metabolism of sulphur-containing aminoacids.

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**Additional data files can be downloaded from the QIMR Genetic Epidemiology website at <http://genepi.qimr.edu.au/>. These files contain effect sizes and p-values for approximately 2.5M SNPs for each element.**

**Supplementary Table 1.** Suggestive SNPs ( $5.0E-08 < p < 5.0E-06$ ). Results for Cu and Zn are from QIMR data only, while results for Se are from the combined QIMR and ALSPAC meta-analysis.

Element	SNP	Chr.	HapMap III R3	Beta	SE	P	Nearest Gene
Cu	rs1458303	3	98,651,430	2.978	0.581	2.91E-07	<i>EPHA6</i>
Cu	rs10014072	4	114,168,239	0.164	0.034	1.13E-06	<i>ANK2</i>
Cu	rs12153606	5	84,619,525	0.159	0.034	2.49E-06	Between <i>EDIL3</i> and <i>COX7C</i>
Cu	rs3857536	6	66,985,769	0.129	0.028	4.08E-06	<i>EGFL11</i>
Cu	rs12582659	12	74,350,795	1.262	0.270	2.86E-06	Between <i>KRR1</i> and <i>PHLDA1</i>
Se	rs3770549	2	216,568,795	0.161	0.035	3.11E-06	<i>MREG</i>
Se	rs679582	6	139,872,873	0.095	0.020	3.37E-06	<i>CITED2</i>
Se	rs10812641	9	2,767,384	0.091	0.019	2.73E-06	<i>KCNV2-KIAA0020</i>
Se	rs7226229	17	20,864,669	0.117	0.024	1.38E-06	<i>MGC87631-DHRS7B</i>
Se	rs8081523	17	73,816,105	0.130	0.028	4.64E-06	<i>BIRC5-SOCS3</i>
Se	rs2017698	19	55,030,048	0.492	0.093	1.15E-07	<i>MED25</i>
Se	rs11084337	19	59,607,916	0.134	0.027	8.69E-07	<i>TTYH1</i>
Se	rs6586282	21	43,351,566	0.117	0.025	4.58E-06	<i>CBS</i> ; CYSTATHIONINE BETA-SYNTASE
Zn	rs10931753	2	154,277,003	0.129	0.028	4.94E-06	<i>RPRM-GALNT13</i>
Zn	rs6793516	3	97,883,289	2.372	0.518	4.75E-06	<i>EPHA6</i>
Zn	rs4333127	4	5,980,934	0.218	0.047	3.00E-06	<i>CRMP1-FLJ46481</i>
Zn	rs11763353	7	15,597,396	0.192	0.039	6.90E-07	<i>MEOX2</i>
Zn	rs11232535	11	80,606,457	0.325	0.065	6.73E-07	
Zn	rs7148590	14	64,542,949	0.140	0.026	1.37E-07	<i>FNTB, MAX</i>
Zn	rs10484100	14	85,886,849	0.209	0.045	3.30E-06	<i>FLRT2</i>
Zn	rs9958032	18	37,482,308	1.467	0.313	2.76E-06	<i>PIK3C3</i>

**Supplementary Table 2.** Allelic effects of low-MAF SNPs near *EPHA6* on Cu and Zn.

<b>SNP</b>	<b>A1</b>	<b>A2</b>	<b>Freq1</b>	<b>Beta</b>	<b>Cu SE</b>	<b>p</b>	<b>Beta</b>	<b>Zn SE</b>	<b>p</b>
rs6793516	A	G	0.002	-2.329	0.531	1.13E-05	-2.372	0.518	4.75E-06
rs1458303	A	T	0.996	2.978	0.581	2.91e-07	2.216	0.566	9.17E-05

**Supplementary Table 3.** Association with erythrocyte Zn concentration for SNPs at the chromosome 8 locus showing significant effects on expression of CA2 (carbonic anhydrase 2) in lymphoblastoid cell lines. Expression data are from <http://www.sph.umich.edu/csg/liang/asthma/> and the association with Zn concentration is from this study.

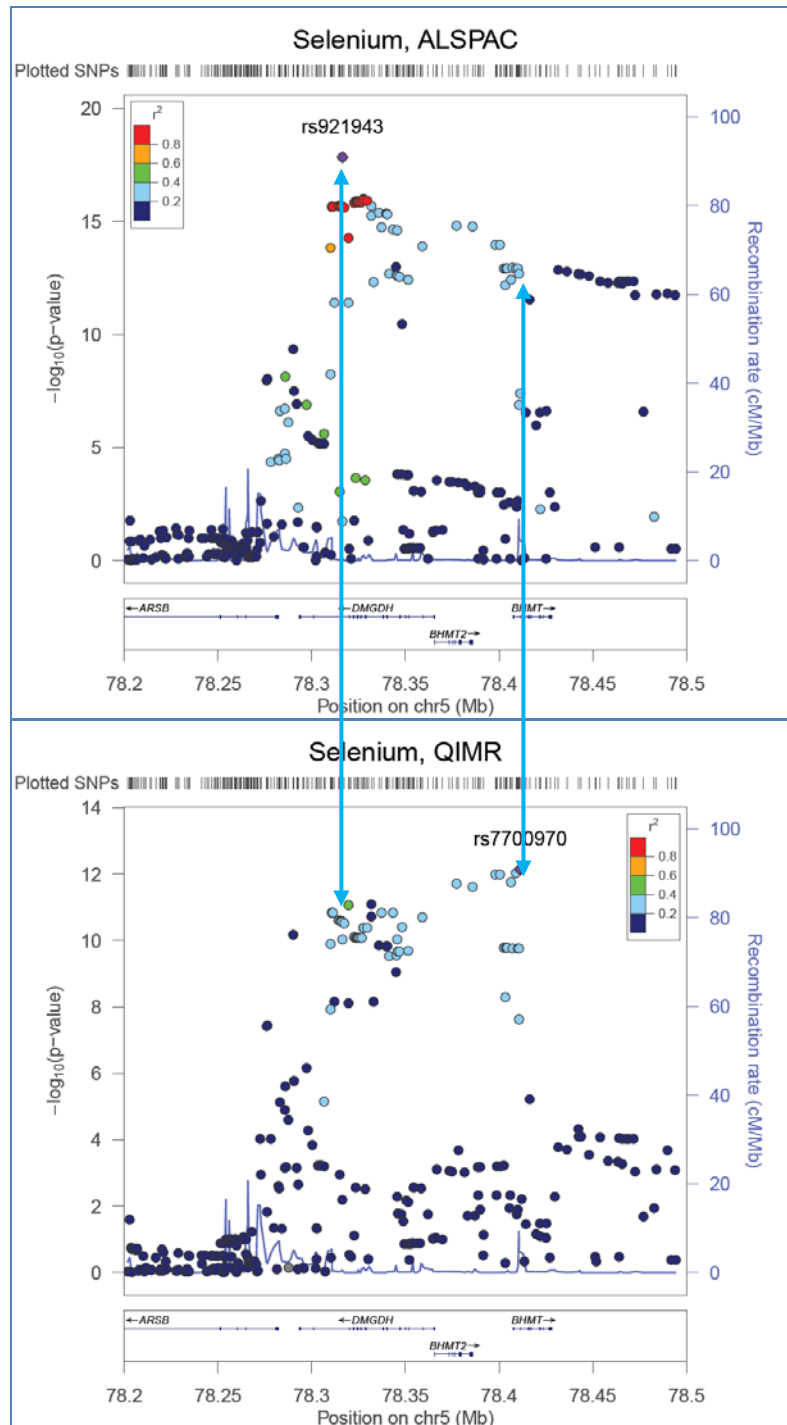
Gene	SNP	p for Zn	Position (bp)		Expression (for probe 209301_at, CA2)			
			(HapMap III r3, Feb09, on NCBI B36 assembly, dbSNP b126)		Allele	Effect	h2	p-value
CA2	rs2548281	2.88E-06	86,498,028		C	0.256	3.13	0.00068
CA2	rs20571	1.84E-07	86,539,249		A	0.284	3.94	5.10E-05
CA2	rs1389245	4.45E-06	86,539,640		C	0.273	3.54	0.00012
CA2	rs1543852	1.84E-07	86,540,010		G	0.296	4.26	2.60E-05
CA2	rs10095352	1.84E-07	86,559,684		C	0.293	4.19	3.30E-05
CA2	rs3758078	2.96E-06	86,561,916		C	0.275	3.58	0.0001
CA2	rs2307075	1.86E-07	86,575,480		G	0.294	4.26	3.00E-05
CA2	rs9329911	4.06E-05	86,594,772		T	0.287	4.09	0.00012
CA2	rs359535	0.012	86,603,211		C	0.298	3.94	0.00019
CA2	rs1369938	0.097	86,627,957		G	0.358	3.96	0.00019
CA2	rs434496	0.499	86,685,205		T	0.312	3.25	0.00077

**Supplementary Table 4.** Reported effects of SNPs at the locus with significant effects for Zn on chromosome X, on *KLF8* gene expression (probe ID 230986\_at) in lymphoblastoid cell lines. From 'mRNA by SNP browser', <http://www.sph.umich.edu/csg/liang/asthma/> (accessed 2013-04-09). Data from Dixon et al., A genome-wide association study of global gene expression. *Nature Genetics* 2007;39:1202-7.

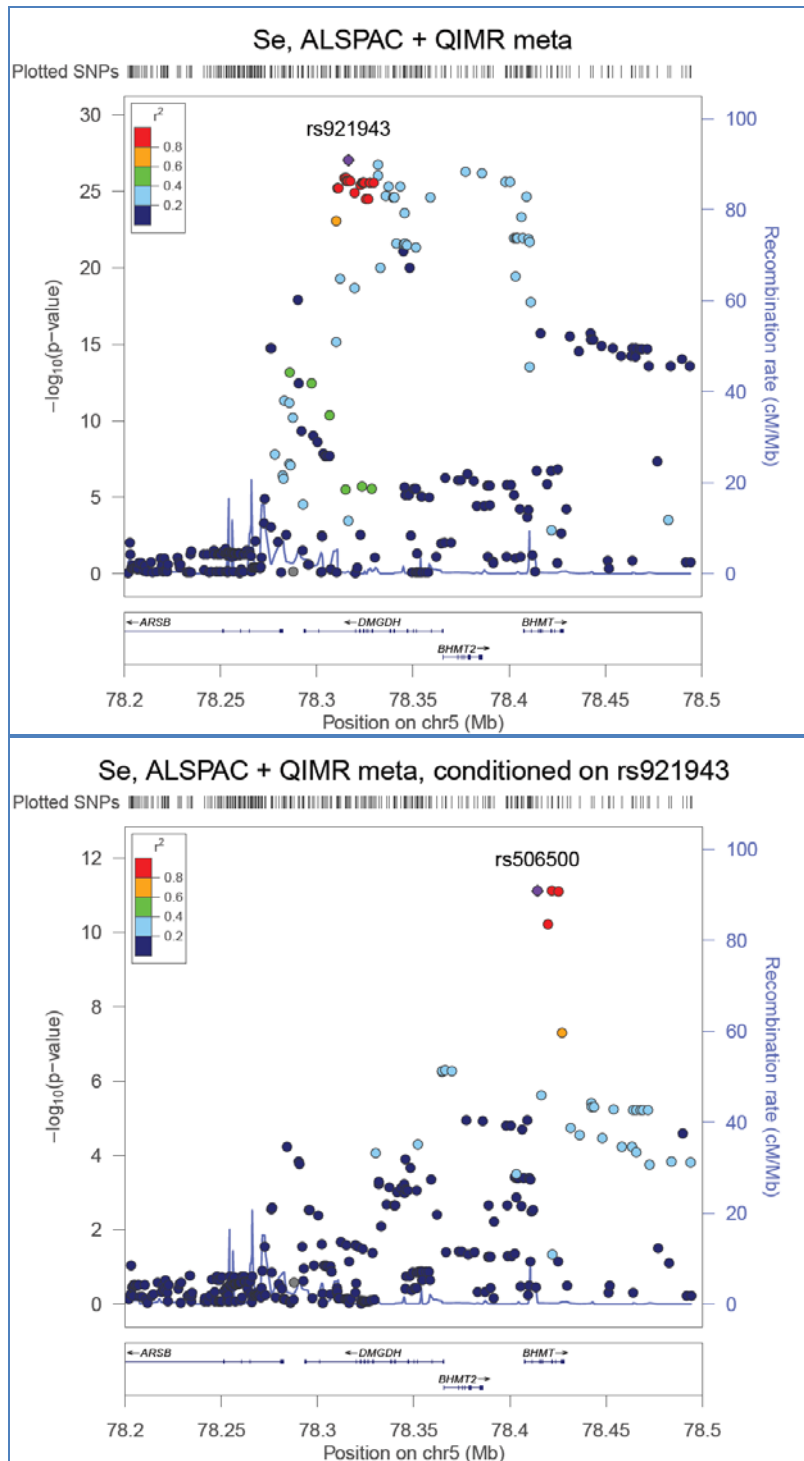
Marker	Position (B36)	Allele	Effect	p-value, 230986_at expression	p-value, Zn concentration
rs12690009	53,888,348	A	0.460	0.00094	0.350
rs5960307	53,924,723	C	0.231	0.00014	0.340
rs5960060	55,099,743	C	0.239	7.90E-05	0.0053
rs954958	55,146,707	C	0.200	0.00057	-
rs1874110	55,200,825	G	0.275	7.00E-06	0.045
rs937280	55,208,137	C	0.218	0.00016	0.930
rs6611396	55,215,683	G	0.259	2.30E-05	0.037
rs5960401	55,223,778	C	0.224	9.00E-05	-
rs1494365	55,230,237	C	0.256	1.90E-05	0.030
rs4826274	55,264,815	A	0.259	0.00014	-
rs7061206	55,351,768	A	0.324	5.00E-07	0.025
rs1927307	55,354,019	C	0.324	4.80E-07	0.024
rs5960434	55,372,436	C	0.317	4.40E-07	0.0088
rs7058622	55,450,925	T	0.370	1.40E-08	0.0039
rs4240024	55,457,545	T	0.321	1.20E-07	-
rs2473057	55,527,231	C	0.342	5.40E-08	-
rs3126258	55,571,535	A	0.328	6.30E-08	-
rs3126260	55,591,903	T	0.375	1.00E-08	0.0015
rs5913857	55,764,676	A	0.356	1.30E-08	-
rs5914432	55,775,133	T	0.330	5.80E-08	-
rs4826287	55,793,505	G	0.375	3.40E-09	3.9E-05
rs1007153	55,794,864	G	0.330	5.80E-08	-
rs6612384	55,869,791	C	0.328	1.10E-07	-
rs11091458	55,900,629	C	0.345	1.40E-08	-
rs6612400	55,910,716	G	0.377	2.30E-09	1.4E-05
rs723895	55,921,110	T	0.345	1.40E-08	-
rs2182191	55,937,175	G	0.344	1.40E-08	-

Marker	Position (B36)	Allele	Effect	p-value, 230986_at expression	p-value, Zn concentration
rs6612428	55,993,800	A	0.331	2.20E-07	7.5E-05
rs944611	56,049,548	C	0.347	2.30E-07	4.6E-06
rs1332008	56,131,121	T	-0.263	0.00084	0.27
rs6521354	56,161,678	A	0.331	4.30E-07	1.0E-06
rs5913902	56,162,395	A	0.301	2.40E-06	1.1E-07
rs6612472	56,169,710	A	0.301	2.60E-06	1.6E-07
rs4826456	56,210,094	A	0.324	8.30E-07	-
rs2375631	56,293,621	T	0.284	1.40E-05	-
rs1033565	56,308,241	C	0.298	4.00E-06	8.3E-09
rs5960155	56,309,087	T	0.266	2.10E-05	-
rs5960679	56,378,611	T	0.282	1.70E-05	5.6E-09
rs6521447	56,521,685	A	0.257	3.40E-05	0.023
rs5914700	56,577,077	T	0.291	6.70E-06	4.0E-07
rs4826478	56,594,703	T	0.291	6.70E-06	2.0E-05
rs5913960	56,612,359	G	0.275	2.40E-05	-
rs5960186	56,612,516	T	0.257	3.40E-05	-
rs5914710	56,616,214	A	0.287	8.40E-06	7.1E-08
rs5914778	56,774,956	G	0.303	9.40E-06	5.0E-08
rs1974070	56,791,551	G	0.272	2.90E-05	-
rs1974070	56,828,187	G	0.259	8.30E-05	-
rs5960235	57,026,431	A	0.238	0.00031	1.5E-09
rs5914036	57,033,444	G	0.238	0.00031	1.2E-09
rs10521485	57,036,587	G	0.224	0.00086	-
rs6612746	57,036,616	G	0.246	0.00018	1.1E-09
rs697664	57,159,599	A	0.238	0.0003	1.7E-09
rs4030473	57,335,632	A	0.217	0.00064	-
rs1560514	57,403,373	C	0.209	0.00077	7.4E-05
rs5914994	57,407,365	C	0.241	0.00026	4.9E-09
rs7392363	57,576,307	G	0.225	0.00086	-
rs2982249	57,645,173	G	0.228	0.00069	6.4E-05
rs5947379	57,945,459	G	0.239	0.00032	7.2E-08

**Supplementary Figure 1.** Comparison of QIMR and ALSPAC results for Se, chromosome 5. Note that in each case the associated SNPs are in the region including *DMGDH*, *BHMT2* and *BHMT*. Although the two data-sets give consistent results, the location of the most significant SNP differs between them.

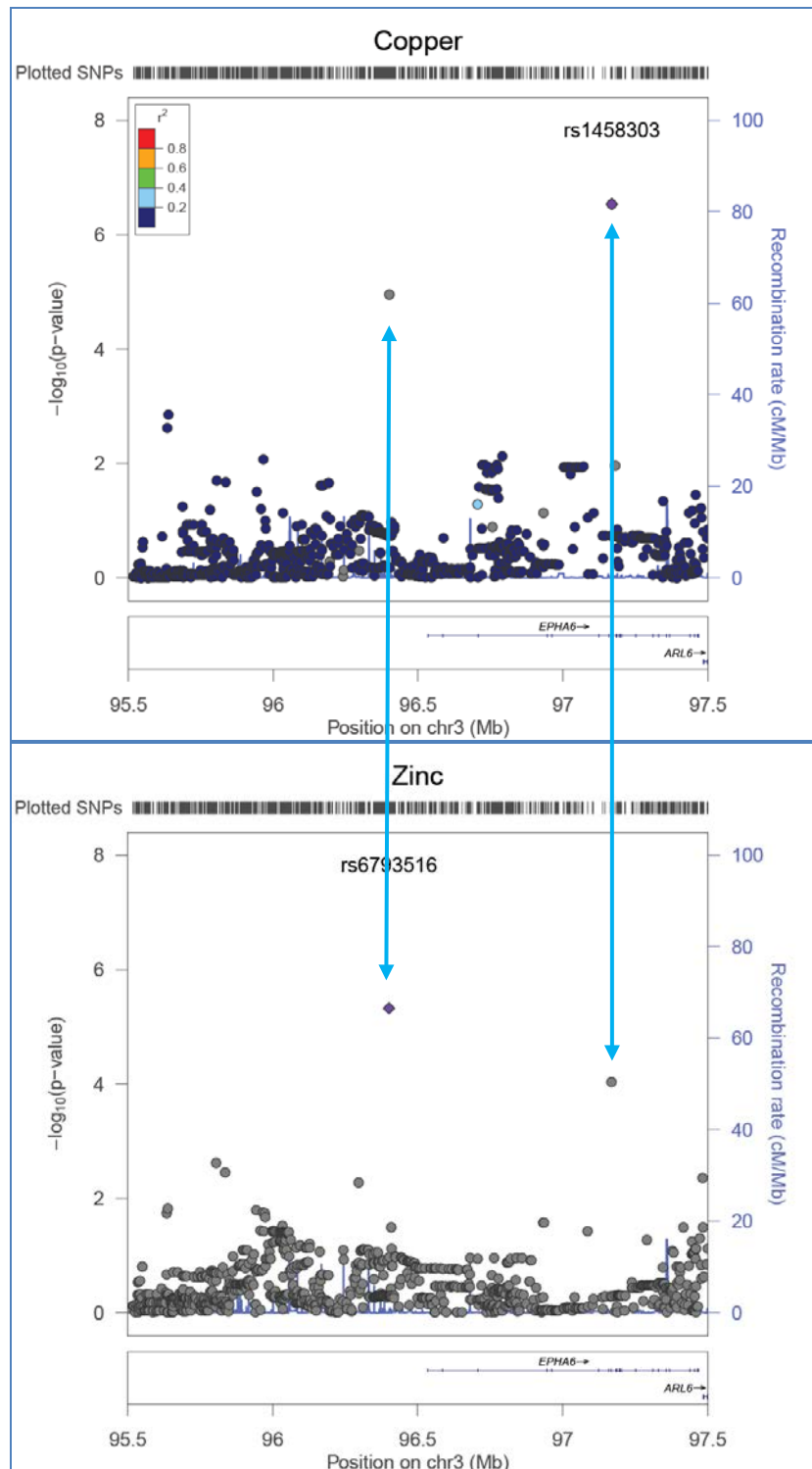


**Supplementary Figure 2.** Combined results from ALSPAC and QIMR data for Se, chromosome 5, showing the presence of two independent association effects. The upper panel shows the initial meta-analysis results and the lower panel shows results after including the most significant SNP from the initial meta-analysis (rs921943) as a covariate.





**Supplementary Figure 3.** Regional plots for chromosome 3 near *EPHA6*, showing SNPs with suggestive associations for both Cu and Zn.



**Supplementary Figure 4.** Metabolism of sulphur-containing aminoacids, showing enzymes whose genes are associated with Se status in our data.

