

Supplementary Table 1. Genotype and allele frequency of four main ethnic groups and relative risk estimation for homozygous variant and heterozygous genotype

Gene polymorphism	Population	Genotype Frequency			High Risk Homozygous variant Population/All	Moderate Risk Heterozygous Population/All	Allele frequency	
		Homozygous wild type	Homozygous variant	Heterozygous			Major allele	Minor allele
NRF2 rs6721961 C617A (in the promoter)		GG	TT	GT	TT	GT	G	T
	African	0.887	0.002	0.112	0.069	0.483	0.943	0.057
	East Asian	0.577	0.063	0.359	2.172	1.547	0.757	0.243
Oxidative Stress	South Asian	0.726	0.031	0.243	1.069	1.047	0.848	0.152
	European	0.763	0.014	0.223	0.483	0.961	0.875	0.125
	All	0.739	0.029	0.232			0.855	0.145
NRF2 rs35652124 A653G (in the promoter)		TT	CC	CT	CC	CT	T	C
	African	0.720	0.015	0.265	0.091	0.626	0.852	0.148
	East Asian	0.208	0.312	0.480	1.902	1.135	0.448	0.552
Oxidative Stress	South Asian	0.207	0.286	0.507	1.744	1.199	0.460	0.540
	European	0.479	0.091	0.429	0.555	1.014	0.694	0.306
	All	0.413	0.164	0.423			0.624	0.376
NQO1 rs1800566 C609T or C559T (base transition in exon 6) (Pro ¹⁸⁷ Ser)		GG	AA	AG	AA	AG	G	A
	African	0.675	0.026	0.300	0.295	0.748	0.825	0.175
	East Asian	0.319	0.157	0.524	1.784	1.307	0.581	0.419
Oxidative Stress	South Asian	0.411	0.127	0.462	1.443	1.152	0.642	0.358
	European	0.626	0.048	0.326	0.545	0.813	0.789	0.211
	All	0.510	0.088	0.401			0.711	0.289
NQO1 rs1131341 C465T(Arg ¹³⁹ Trp)		GG	AA	AG	AA	AG	G	A
	African	0.994	0	0.006	0	0	0.997	0.003
	East Asian	0.960	0	0.040	0	1	0.980	0.020
Oxidative Stress	South Asian	0.910	0.010	0.080	5	2.051	0.950	0.050
	European	0.950	0	0.050	0	1.282	0.975	0.025
	All	0.959	0.002	0.039			0.979	0.021

HO-1 rs2071746							
-413A>T		AA	TT	AT	TT	AT	T
Oxidative Stress	African	0.098	0.474	0.428	1.596	0.926	0.688
	East Asian	0.242	0.288	0.470	0.970	1.017	0.523
	South Asian	0.190	0.309	0.501	1.040	1.084	0.559
	European	0.306	0.187	0.507	0.630	1.097	0.440
	All	0.241	0.297	0.462			0.528
							0.472
SOD2 rs4880G/A (exon 2) (Ala ¹⁶ Val)							
Oxidative Stress	AA	GG	AG	GG	AG	A	G
	African	0.333	0.180	0.487	0.923	1.127	0.576
	East Asian	0.764	0.014	0.222	0.072	0.514	0.875
	South Asian	0.245	0.262	0.493	1.344	1.141	0.492
	European	0.294	0.227	0.479	1.164	1.109	0.534
	All	0.373	0.195	0.432			0.589
GST-A1 rs3957357							
Detoxification	C69T (non coding)	GG	AA	AG	AA	AG	G
	African	0.470	0.103	0.427	0.972	1.062	0.684
	East Asian	0.740	0.018	0.242	0.170	0.601	0.861
	South Asian	0.440	0.131	0.429	1.236	1.067	0.654
	European	0.318	0.177	0.505	1.670	1.256	0.571
	All	0.492	0.106	0.402			0.693
GST-M1 rs366631							
Detoxification	African					Positive	Null
	East Asian					0.684	0.316
	South Asian					0.479	0.521
	European					0.597	0.403
	All					0.488	0.512
						0.520	0.480* (no Americans were included)
GST-T1 rs17856199							
Detoxification	African					Positive	Null
	East Asian					0.629	0.371
	South					0.524	0.476

Asian							
European						0.867	0.183
All						0,736	0.264* (no Americans were included)

GST-P1(319A>G) rs1695 Ile ¹⁰⁵ Val (missense mutation)	AA	GG	AG	GG	AG	A	G
African	0.265	0.225	0.510	1.619	1.194	0.520	0.480
East Asian	0.673	0.030	0.298	0.216	0.698	0.821	0.179
Detoxification	South Asian	0.513	0.102	0.384	0.734	0.899	0.706
European	0.445	0.107	0.447	0.770	1.047	0.669	0.331
All	0.434	0.139	0.427			0.647	0.353

EPHX1 Ex_3 rs1051740 Tyr ¹¹³ His (slow allele)	TT	CC	TC	CC	TC	T	C
African	0.744	0.026	0.230	0.222	0.585	0.859	0.141
East Asian	0.272	0.236	0.492	2.017	1.252	0.518	0.482
Detoxification	South Asian	0.384	0.139	0.476	1.188	1.211	0.623
European	0.487	0.095	0.417	0.812	1.061	0.696	0.304
All	0.490	0.117	0.393			0.687	0.313

EPHX1 Ex_4 rs2234922 His ¹³⁹ Arg (fast allele)	AA	GG	AG	AA	AG	A	G
African	0.421	0.127	0.452	0.673	1.426	0.647	0.353
East Asian	0.780	0.016	0.204	1,246	0.644	0.882	0.118
Detoxification	South Asian	0.605	0.074	0.321	0.966	1.013	0.766
European	0.686	0.014	0.300	1,096	0.946	0.836	0.164
All	0.626	0.057	0.317			0.785	0.215

CYP1A1_2A rs4646903 (T> C mutation at 3' UTR)	AA	GG	AG	GG	AG	A	G
African	0.589	0.057	0.354	0.523	0.959	0.766	0.234
East Asian	0.329	0.188	0.482	1.725	1.306	0.570	0.430
Detoxification	South Asian	0.446	0.125	0.429	1.147	1.163	0.661
European	0.793	0.008	0.199	0.073	0.539	0.893	0.107
All	0.522	0.109	0.369			0.707	0.293

CYP1A1_2C rs1048943 Ile ⁴⁶² Val		TT	CC	TC	CC	TC	T	C
African	0.986	0	0.014	0	0.07	0.993	0.007	
East Asian	0.562	0.065	0.373	1.625	1.995	0.748	0.252	
Detoxification	South Asian	0.765	0.018	0.217	0.45	1.16	0.873	0.127
European	0.930	0	0.070	0	0.374	0.965	0.035	
All	0.773	0.040	0.187			0.867	0.133	
CYP2E1*6 rs6413432 (7632 T>A)(intron mutation)		TT	AA	AT	TT	AT	T	A
African	0.855	0.009	0.136	1.199	0.538	0.923	0.077	
East Asian	0.536	0.079	0.385	0.752	1.522	0.728	0.272	
Detoxification	South Asian	0.628	0.043	0.329	0.881	1.300	0.792	0.208
European	0.805	0.016	0.179	1.129	0.708	0.895	0.105	
All	0.713	0.034	0.253			0.839	0.161	
CYP2E1*5B rs3813867 (in the 5' UTR)		GG	CC	CG	GG	CG	G	C
African	0.871	0.005	0.124	1.032	0.873	0.933	0.067	
East Asian	0.651	0.056	0.294	1	2	0.798	0.202	
Detoxification	South Asian	0.982	0	0.018	1	0	0.991	0.009
European	0.920	0.002	0.078	1.090	0.549	0.959	0.041	
All	0.844	0.014	0.142			0.915	0.085	
MPO rs2333227 G463A (in the promoter region)		CC	TT	CT	CC	CT	C	T
African	0.415	0.145	0.440	0.675	1.375	0.635	0.365	
East Asian	0.734	0.02	0.246	1.193	0.769	0.857	0.143	
Detoxification	South Asian	0.763	0.016	0.221	1.241	0.691	0.873	0.127
European	0.588	0.064	0.348	0.956	1.088	0.762	0.238	
All	0.615	0.065	0.320			0.775	0.225	
XRCC3 rs1799782 Arg ¹⁹⁴ Trp		GG	AA	AG	AA	AG	G	A

	African	0.858	0.002	0.141	0.091	0.691	0.928	0.072
	East Asian	0.518	0.081	0.401	3.682	1.966	0.718	0.282
DNA repair	South Asian	0.783	0.004	0.213	0.182	1.044	0.890	0.110
	European	0.907	0.010	0.083	0.455	0.407	0.948	0.052
	All	0.774	0.022	0.204			0.876	0.124
<hr/>								
XRCC3 rs861539								
Thr ²⁴¹ Met (C/T transition at codon 241)		GG	AA	AG	AA	AG	G	A
	African	0.657	0.038	0.306	0.603	0.994	0.809	0.191
	East Asian	0.855	0.002	0.143	0.032	0.464	0.927	0.073
DNA repair	South Asian	0.630	0.049	0.321	0.778	1.042	0.790	0.210
	European	0.378	0.165	0.457	2.619	1.484	0.606	0.394
	All	0.629	0.063	0.308			0.783	0.217
<hr/>								
XPD rs1799793		CC	TT	CT	TT	CT	C	T
Asp ³¹² Asn (XPD G312A)								
	African	0.858	0.005	0.138	0.098	0.481	0.927	0.073
	East Asian	0.903	0.002	0.095	0.039	0.331	0.950	0.050
DNA repair	South Asian	0.440	0.110	0.450	2.157	1.568	0.665	0.335
	European	0.406	0.123	0.471	2.412	1.641	0.641	0.359
	All	0.662	0.051	0.287			0.806	0.194
<hr/>								
XRCC1 rs 25487 Arg ³⁹⁹ Gln		CC	TT	CT	TT	CT	C	T
	African	0.787	0.008	0.206	0.103	0.564	0.890	0.110
	East Asian	0.587	0.058	0.355	0.744	0.973	0.765	0.235
DNA repair	South Asian	0.436	0.123	0.442	1.577	1.211	0.656	0.344
	European	0.402	0.133	0.465	1.705	1.274	0.634	0.366
	All	0.557	0.078	0.365			0.740	0.260
<hr/>								
hOGG1 rs1052133		CC	GG	CG	GG	CG	C	G
Ser ³²⁶ Cys								
	African	0.726	0.036	0.238	0.313	0.638	0.845	0.155
	East Asian	0.220	0.315	0.464	2.739	1.243	0.452	0.548
DNA repair	South Asian	0.415	0.127	0.458	1.104	1.228	0.644	0.356

	European	0.624	0.030	0.346	0.261	0.928	0.797	0.203
	All	0.511	0.115	0.373			0.698	0.302
<hr/>								
XPD rs13181 Lys ⁷⁵¹ Gln (T > G)		TT	GG	GT	GG	GT	T	G
African	0.651	0.035	0.315	0.530	0.924	0.808	0.192	
East Asian	0.851	0.004	0.145	0.061	0.425	0.924	0.076	
DNA repair	South Asian	0.421	0.115	0.464	1,742	1.361	0.653	0,347
European	0.417	0.145	0.437	2.197	1.282	0.636	0.364	
All	0.593	0.066	0.341			0.763	0.237	
<hr/>								
XRCC1 rs25487 Arg ¹⁹⁴ Trp		TT	CC	CT	CC	CT	C	T
African	0.008	0.787	0.206	1.413	0.564	0.890	0.110	
East Asian	0.058	0.587	0.355	1.054	0.973	0.765	0.235	
South Asian	0.123	0.436	0.442	0.783	1.211	0.656	0.344	
European	0.133	0.402	0.465	0.722	1.274	0.634	0.366	
All	0.078	0.557	0.365			0.740	0.260	

All the genes conferring a specific (unfavourable) susceptibility are those listed in the homozygous variant genotype column.

Four genes highlighted in bold *Italics* i.e. EPHX1 rs2234922, MPO rs2333227, CYP2E1*6 rs6413432, CYP2E1*5B rs3813867 indicate polymorphisms whose homozygous wild-type genotype might confer a disadvantageous condition in the enzymatic function.