

Supplementary Materials for  
Evidence for SNP-SNP interaction identified through targeted sequencing of cleft  
case-parent trios

by

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**Supplementary Table I Most significant results from the 4 df Likelihood Ratio Test for GxG interaction in 375 European case-parent trios**

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
8q24	ARHGAP29	rs1356762	rs61782236	20.037	0.000491	0.79
8q24	BMP4	rs4236742	rs2224835	13.676	0.008404	0.97
8q24	FGFR2	rs1464154	rs10886946	19.885	0.000526	0.61
8q24	FOXE1	rs72730212	rs16923269	25.354	4.27E-05	0.1
8q24	IRF6	rs4602853	rs28630860	17.694	0.001416	0.9
8q24	MAFB	rs6470670	rs3092775	28.050	1.22E-05	0.05
8q24	MSX1	rs12676542	rs2220746	20.167	0.000463	0.62
8q24	NOG	rs1372992	rs12450049	19.833	0.000539	0.74
8q24	NTN1	rs13265167	rs7207143	21.154	0.000295	0.81
8q24	PAX7	rs13251901	rs4075768	20.067	0.000485	0.9
8q24	PTCH1	rs13249571	rs62558314	24.087	7.67E-05	0.14
8q24	VAX1	rs10090304	rs1681736	22.295	0.000175	0.39
ARHGAP29	BMP4	rs12121974	rs12883570	16.541	0.002373	0.7
ARHGAP29	FGFR2	rs17394161	rs10466213	21.451	0.000258	0.41
ARHGAP29	FOXE1	rs472908	rs2120263	21.102	0.000302	0.46
ARHGAP29	IRF6	rs11165073	rs74487756	20.673	0.000368	0.5
ARHGAP29	MAFB	rs2022395	rs6065286	22.125	0.000189	0.51
ARHGAP29	MSX1	rs4147848	rs730575	29.005	7.80E-06	0.03
ARHGAP29	NOG	rs1761375	rs227688	21.818	0.000218	0.47

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
ARHGAP29	NTN1	rs1765622	rs7222455	20.511	0.000396	0.88
ARHGAP29	PAX7	rs1320502	rs4920501	22.646	0.000149	0.58
ARHGAP29	PTCH1	rs12088309	rs357542	19.429	0.000647	0.66
ARHGAP29	VAX1	rs762485	rs2921962	23.745	8.98E-05	0.28
BMP4	FGFR2	rs4243595	rs12256320	14.272	0.006476	0.88
BMP4	FOXE1	rs8014363	rs7033765	18.611	0.000937	0.31
BMP4	IRF6	rs2761884	rs1983614	20.174	0.000461	0.16
BMP4	MAFB	rs11157993	rs3092011	19.550	0.000612	0.34
BMP4	MSX1	rs72680512	rs4689186	18.760	0.000876	0.34
BMP4	NOG	rs12587398	rs12951993	17.365	0.001641	0.53
BMP4	NTN1	rs8014363	rs7208881	17.710	0.001406	0.71
BMP4	PAX7	rs8014363	rs1537843	15.167	0.004367	0.96
BMP4	PTCH1	rs11157993	rs11793640	19.277	0.000693	0.23
BMP4	VAX1	rs8014071	rs1638673	18.615	0.000935	0.41
FGFR2	FOXE1	rs1696835	rs10739476	19.905	0.000521	0.44
FGFR2	IRF6	rs2420941	rs845451	20.600	0.00038	0.33
FGFR2	MAFB	rs10886928	rs6016377	20.190	0.000458	0.61
FGFR2	MSX1	rs4752571	rs4435686	19.468	0.000636	0.53
FGFR2	NOG	rs4752571	rs11654202	20.942	0.000325	0.4
FGFR2	NTN1	rs10466213	rs61409745	20.079	0.000482	0.74
FGFR2	PAX7	rs10510099	rs626600	21.580	0.000243	0.53

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
FGFR2	PTCH1	rs35462105	rs357521	15.749	0.003375	0.95
FGFR2	VAX1	rs34143724	rs11593912	20.616	0.000377	0.46
FOXE1	IRF6	rs12001675	rs633352	17.450	0.00158	0.78
FOXE1	MAFB	rs3780419	rs3092011	20.629	0.000375	0.56
FOXE1	MSX1	rs1475695	rs13117093	20.500	0.000398	0.41
FOXE1	NOG	rs13049	rs8074637	16.678	0.002232	0.94
FOXE1	NTN1	rs10984601	rs7215971	20.930	0.000327	0.66
FOXE1	PAX7	rs12349452	rs61761365	21.464	0.000256	0.56
FOXE1	PTCH1	rs6478391	rs1889617	14.934	0.004839	0.98
FOXE1	VAX1	rs10984977	rs181512	16.489	0.002428	0.96
<b>IRF6</b>	<b>MAFB</b>	<b>rs6681355</b>	<b>rs6029315</b>	<b>40.255</b>	<b>3.83E-08</b>	<b>&lt;0.001</b>
IRF6	MSX1	rs1983614	rs6851263	17.965	0.001254	0.73
IRF6	NOG	rs590152	rs2159226	25.014	5.00E-05	0.09
IRF6	NTN1	rs599021	rs181533	22.893	0.000133	0.37
IRF6	PAX7	rs2484030	rs10907314	25.723	3.60E-05	0.1
IRF6	PTCH1	rs590152	rs357565	18.197	0.001129	0.63
IRF6	VAX1	rs4421592	rs3010467	19.968	0.000507	0.56
MAFB	MSX1	rs6029145	rs6851263	26.748	2.23E-05	0.06
MAFB	NOG	rs4812455	rs10852990	19.657	0.000584	0.77
MAFB	NTN1	rs6029421	rs8081873	32.174	1.76E-06	0.02
MAFB	PAX7	rs6029182	rs11584404	31.253	2.72E-06	0.02
MAFB	PTCH1	rs6102167	rs10990303	21.285	0.000278	0.42

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
MAFB	VAX1	rs6072087	rs11197835	17.749	0.001381	0.97
MSX1	NOG	rs2933586	rs4605230	18.376	0.001042	0.8
MSX1	NTN1	rs2968669	rs9892906	27.966	1.27E-05	0.05
MSX1	PAX7	rs3815544	rs61760688	18.531	0.000971	0.94
MSX1	PTCH1	rs60726571	rs1932075	17.959	0.001257	0.71
MSX1	VAX1	rs2968702	rs2420309	17.204	0.001764	0.92
NOG	NTN1	rs8074637	rs2315286	29.622	5.84E-06	0.04
NOG	PAX7	rs8073455	rs9439729	25.310	4.36E-05	0.21
NOG	PTCH1	rs3867600	rs357551	15.649	0.003529	0.98
NOG	VAX1	rs8069500	rs10886011	17.493	0.00155	0.94
NTN1	PAX7	rs7219272	rs4075768	20.593	0.000381	0.95
NTN1	PTCH1	rs62069969	rs574688	18.484	0.000992	0.93
NTN1	VAX1	rs7214739	rs2619106	21.651	0.000235	0.67
PAX7	PTCH1	rs28441017	rs28716262	18.794	0.000863	0.89
PAX7	VAX1	rs2236799	rs11197835	25.224	4.54E-05	0.21
PTCH1	VAX1	rs4742697	rs77204400	23.847	8.57E-05	0.14

**Supplementary Table II Most significant results from the 4df Likelihood Ratio Test for GxG interaction in 1,034 Asian case-parent trios**

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
8q24	ARHGAP29	rs873232	rs3789398	25.819	3.44E-05	0.1
8q24	BMP4	rs7845615	rs3742556	17.763	0.001373	0.75
8q24	FGFR2	rs1464154	rs11200102	21.989	0.000201	0.54
8q24	FOXE1	rs72609875	rs12352658	20.460	0.000405	0.47
8q24	IRF6	rs10111530	rs6540559	24.945	5.16E-05	0.14
8q24	MAFB	rs1516960	rs7509091	18.577	0.000951	0.94
8q24	MSX1	rs1835851	rs56398386	23.657	9.36E-05	0.12
8q24	NOG	rs9643244	rs4794668	17.262	0.001719	0.96
8q24	NTN1	rs10956419	rs2429370	24.393	6.66E-05	0.26
8q24	PAX7	rs55830016	rs2841087	23.506	0.0001	0.4
8q24	PTCH1	rs9643244	rs28716262	19.820	0.000542	0.7
8q24	VAX1	rs6984251	rs181505	23.873	8.47E-05	0.26
ARHGAP29	BMP4	rs581244	rs67475977	21.206	0.000288	0.26
ARHGAP29	FGFR2	rs3789692	rs2981451	21.681	0.000232	0.58
ARHGAP29	FOXE1	rs582798	rs12347079	20.079	0.000482	0.49
ARHGAP29	IRF6	rs1324214	rs650854	21.460	0.000257	0.45
ARHGAP29	MAFB	rs950283	rs6072160	23.221	0.000114	0.33
ARHGAP29	MSX1	rs4147830	rs3821949	19.450	0.000641	0.5
ARHGAP29	NOG	rs6674226	rs8069500	19.992	0.000501	0.65

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
ARHGAP29	NTN1	rs2022378	rs3785995	20.210	0.000454	0.82
ARHGAP29	PAX7	rs10874810	rs9439697	19.689	0.000575	0.89
ARHGAP29	PTCH1	rs3761910	rs2149722	29.041	7.67E-06	0.03
ARHGAP29	VAX1	rs6698203	rs1630816	20.966	0.000322	0.66
BMP4	FGFR2	rs2738265	rs2936861	27.408	1.64E-05	0.03
BMP4	FOXE1	rs56312905	rs1886002	19.531	0.000618	0.32
BMP4	IRF6	rs4898820	rs968033	17.506	0.001541	0.66
BMP4	MAFB	rs12895262	rs6102096	19.622	0.000593	0.54
BMP4	MSX1	rs12895262	rs6823800	18.178	0.001139	0.39
BMP4	NOG	rs2147105	rs8073799	18.536	0.000969	0.53
BMP4	NTN1	rs4243595	rs12602314	20.833	0.000342	0.43
BMP4	PAX7	rs6572930	rs515739	22.263	0.000178	0.28
BMP4	PTCH1	rs12895971	rs10985356	19.521	0.000621	0.4
BMP4	VAX1	rs1951866	rs877396	18.510	0.000981	0.66
FGFR2	FOXE1	rs9420327	rs58100391	19.470	0.000635	0.68
FGFR2	IRF6	rs11200101	rs12025057	22.974	0.000128	0.33
FGFR2	MAFB	rs2936861	rs6102078	20.266	0.000442	0.87
FGFR2	MSX1	rs1896422	rs2131453	19.610	0.000596	0.58
FGFR2	NOG	rs2936874	rs227725	19.411	0.000653	0.8
FGFR2	NTN1	rs2935693	rs4791823	20.709	0.000362	0.84
FGFR2	PAX7	rs12763463	rs11488726	26.233	2.84E-05	0.18

First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
FGFR2	PTCH1	rs2936864	rs55952687	19.496	0.000628	0.81
FGFR2	VAX1	rs752736	rs1665668	24.303	6.94E-05	0.27
FOXE1	IRF6	rs2417730	rs12083466	18.159	0.001149	0.73
FOXE1	MAFB	rs4743128	rs2024574	22.525	0.000158	0.24
FOXE1	MSX1	rs2417729	rs80227476	19.554	0.000611	0.34
FOXE1	NOG	rs1886002	rs28664662	22.746	0.000142	0.15
FOXE1	NTN1	rs77159549	rs2551799	22.984	0.000128	0.28
FOXE1	PAX7	rs2808685	rs34988159	19.996	0.0005	0.68
FOXE1	PTCH1	rs958346	rs1335048	19.813	0.000544	0.45
FOXE1	VAX1	rs3994138	rs363312	22.100	0.000191	0.28
IRF6	MAFB	rs72649973	rs2866114	17.137	0.001818	0.98
IRF6	MSX1	rs1473683	rs12639983	16.781	0.002132	0.83
IRF6	NOG	rs10863785	rs12450244	18.566	0.000956	0.81
IRF6	NTN1	rs7511737	rs117996464	20.482	0.000401	0.69
IRF6	PAX7	rs12029138	rs2883890	19.869	0.00053	0.84
IRF6	PTCH1	rs1040426	rs16909974	20.903	0.000331	0.45
IRF6	VAX1	rs1883308	rs17095763	22.190	0.000184	0.4
MAFB	MSX1	rs11907397	rs1907980	21.597	0.000241	0.29
MAFB	NOG	rs2425406	rs8069500	23.784	8.82E-05	0.23
MAFB	NTN1	rs13041631	rs72809908	28.161	1.16E-05	0.05
MAFB	PAX7	rs35929622	rs4075768	21.029	0.000312	0.82



First Gene	Second Gene	Marker 1	Marker 2	Test Statistic	p-value	Permutation p-value
MAFB	PTCH1	rs6016400	rs117758836	19.452	0.00064	0.81
MAFB	VAX1	rs10485671	rs10736259	19.389	0.000659	0.91
MSX1	NOG	rs9291153	rs7222986	24.345	6.81E-05	0.07
MSX1	NTN1	rs12532	rs2429370	21.060	0.000308	0.43
MSX1	PAX7	rs4395446	rs2236806	21.563	0.000245	0.4
MSX1	PTCH1	rs74485582	rs34556283	17.782	0.001362	0.72
MSX1	VAX1	rs1907980	rs758367	16.334	0.002602	0.94
NOG	NTN1	rs17821518	rs12452003	28.787	8.63E-06	0.04
NOG	PAX7	rs227723	rs2236832	24.742	5.67E-05	0.22
NOG	PTCH1	rs887088	rs10990355	20.542	0.00039	0.51
NOG	VAX1	rs1816806	rs181505	18.961	0.0008	0.87
NTN1	PAX7	rs12452951	rs6672970	21.362	0.000268	0.81
NTN1	PTCH1	rs57675223	rs10990447	24.184	7.34E-05	0.2
NTN1	VAX1	rs9901367	rs1468539	21.469	0.000256	0.69
PAX7	PTCH1	rs851123	rs28563972	23.429	0.000104	0.36
PAX7	VAX1	rs2223585	rs1638667	22.268	0.000177	0.62
PTCH1	VAX1	rs16909974	rs3125617	21.706	0.000229	0.47