Association Studies and Direct DNA Sequencing Implicate Genetic Susceptibility Loci in the Etiology of Nonsyndromic Orofacial Clefts in Sub-Saharan African Populations

L.J.J. Gowans, W.L. Adeyemo, M. Eshete, P.A. Mossey, T. Busch, B. Aregbesola, P. Donkor, F.K.N. Arthur, S.A. Bello, A. Martinez, M. Li, E.A. Augustine-Akpan, W. Deressa, P. Twumasi, J. Olutayo, M. Deribew, P. Agbenorku, A.A. Oti, R. Braimah, G. Plange-Rhule, M. Gesses, S. Obiri-Yeboah, G.O. Oseni, P.B. Olaitan, L. Abdur-Rahman, F. Abate, T. Hailu, P. Gravem, M.O. Ogunlewe, C.J. Buxó, M.L. Marazita, A.A. Adeyemo, J.C. Murray, A. Butali

Appendix Table 4: Case-control analyses for Nigeria

Part A: Case-control analyses for NSCL/P and NSCPO for Nigeria							
	Probable	NSCL/P			NSCPO		
SNP	gene/loci	*p*	OR	95% CI	*p*	OR	95% CI
rs1801131	*MTHFR*	0.42	1.17	0.80 - 1.70	0.28	0.62	0.26 - 1.47
rs1801133	*MTHFR*	0.07	1.53	0.96 - 2.45	0.73	0.83	0.29 - 2.37
rs766325	*PAX7*	0.56	0.90	0.64 - 1.27	0.07	0.50	0.27 - 1.07
rs742071	*PAX7*	0.05	1.30	1.00 - 1.67	0.93	1.02	0.65 - 1.62
rs560426	*ABCA4*	0.77	0.96	0.75 - 1.24	0.94	0.98	0.63 - 1.55
rs481931	*ABCA4*	0.12	1.40	0.92 - 2.12	0.89	0.94	0.39 - 2.25
rs4147811	*ABCA4*	**7.48E-03**[a]	**1.72**	**1.15 - 2.56**	0.44	1.34	0.64 - 2.80
rs138751793	*ARHGAP29*	0.12	1.69	0.86 - 3.32	0.57	1.43	0.41 - 4.93
rs6677101	*SLC25A24*	0.66	0.94	0.72 - 1.23	0.08	0.63	0.38 - 1.06
rs861020	*IRF6*	0.90	1.02	0.70 - 1.49	0.78	0.91	0.47 - 1.77
rs34743335	*IRF6*	0.28	2.16	0.51 - 9.08	0.06	9.33	0.58 - 150.60
rs642961	*IRF6*	0.60	0.89	0.57 - 1.38	0.67	0.85	0.39 - 1.82
rs7590268	*THADA*	0.89	0.98	0.71 - 1.35	0.66	0.87	0.48 - 1.60
rs4332945	*DYSF*	0.51	1.13	0.79 - 1.60	0.55	1.21	0.66 - 2.22
rs2303596	*DYSF*	0.14	1.28	0.92 - 1.77	0.21	0.63	0.31 - 1.30
rs227782	*DYSF*	0.79	0.97	0.74 - 1.25	0.29	0.77	0.48 - 1.24
rs115200552	*MSX1*	0.23	0.59	0.24 - 1.41	0.15	1.93	0.78 - 4.79
rs12532	*MSX1*	0.49	0.91	0.71 - 1.18	0.15	0.72	0.45 - 1.13
rs2674394	Gene Desert	0.81	1.04	0.74 - 1.47	0.97	1.01	0.54 - 1.89
rs651333	*TULP4*	0.51	0.91	0.68 - 1.21	0.12	1.45	0.91 - 2.32
rs6558002	*EPHX2*	0.92	0.98	0.71 - 1.36	0.80	1.08	0.62 - 1.86
rs987525	8q24	0.74	0.96	0.73 - 1.25	0.31	0.78	0.49 - 1.26
rs894673	*FOXE1*	0.49	1.10	0.84 - 1.46	0.73	1.09	0.67 - 1.79
rs3758249	*FOXE1*	0.40	1.13	0.85 - 1.18	0.74	1.09	0.66 - 1.78
rs7078160	*VAX1*	0.63	1.07	0.80 - 1.44	1.00	1.00	0.59 - 1.70
rs4752028	*VAX1*	0.68	1.06	0.82 - 1.36	0.98	0.99	0.63 - 1.57

rs10785430	*ADAMTS20*	0.77	1.04	0.79 - 1.36	0.67	0.90	0.55 - 1.47
rs9574565	*SPRY2*	0.57	0.92	0.70 - 1.21	0.77	0.93	0.58 - 1.49
rs8001641	*SPRY2*	0.80	0.94	0.58 - 1.52	0.75	1.13	0.52 - 2.45
rs17563	*BMP4*	0.29	1.21	0.85 - 1.72	0.38	1.31	0.72 - 2.37
rs1258763	*GREM1*	0.46	1.10	0.85 - 1.42	0.84	0.95	0.61 - 1.50
rs8049367	*ADCY9*	0.09	1.26	0.97 - 1.64	0.11	0.66	0.39 - 1.11
rs16260	*CDH1*	0.78	1.06	0.71 - 1.58	0.53	0.78	0.37 - 1.68
rs11642413	*CDH1*	0.62	0.93	0.69 - 1.25	0.33	0.75	0.42 - 1.34
rs1546124	*CRISPLD2*	0.62	0.93	0.68 - 1.26	0.51	0.83	0.48 - 1.44
rs4783099	*CRISPLD2*	0.98	1.00	0.77 - 1.31	**0.04**[a]	**0.58**	**0.34 - 0.98**
rs8069536	*NTN1*	0.06	1.28	0.99 - 1.66	0.62	1.12	0.71 - 1.78
rs8081823	*NTN1*	0.30	0.85	0.63 - 1.15	0.67	0.89	0.53 - 1.51
rs17760296	*NOG1*	0.29	1.45	0.73 - 2.88	0.11	2.21	0.81 - 6.02
rs227731	*NOG1*	0.83	0.97	0.70 - 1.34	0.56	1.17	0.68 - 2.02
rs7224837	*AXIN2*	0.71	0.92	0.60 - 1.42	0.67	1.16	0.58 - 2.35
rs3923086	*AXIN2*	0.35	0.00	0.00 - NA	0.56	0.00	0.00 - NA
rs17820943	*MAFB*	0.81	1.04	0.76 - 1.42	0.21	1.38	0.83 - 2.30
rs13041247	*MAFB*	0.81	1.04	0.76 - 1.42	0.22	1.38	0.83 - 2.30
rs11696257	*MAFB*	0.78	1.05	0.77 - 1.43	0.21	1.38	0.83 - 2.31
Part B: Case-control analyses for NSCL/P subphenotypes for Nigeria							
SNP	Probable gene/loci	NSCL			NSCLP		
		p	OR	95% CI	*p*	OR	95% CI
rs1801131	*MTHFR*	0.61	1.14	0.68 - 1.91	0.36	1.27	0.76 - 2.10
rs1801133	*MTHFR*	0.17	1.56	0.82 - 2.95	0.15	1.59	0.84 - 3.00
rs766325	*PAX7*	0.87	0.96	0.61 - 1.52	0.38	0.80	0.49 - 1.31
rs742071	*PAX7*	**0.02**[a]	**1.48**	**1.05 - 2.08**	0.27	1.22	0.86 - 1.74
rs560426	*ABCA4*	0.98	1.01	0.71 - 1.41	0.63	1.09	0.77 - 1.56
rs481931	*ABCA4*	0.66	0.86	0.43 - 1.71	**2.87E-03**[a]	**2.10**	**1.28 - 3.46**
rs4147811	*ABCA4*	**0.02**[a]	**1.88**	**1.11 - 3.18**	0.05	1.72	1.00 - 2.95
rs138751793	*ARHGAP29*	**0.04**[a]	**2.30**	**1.04 - 5.09**	0.80	1.15	0.39 - 3.39
rs6677101	*SLC25A24*	0.88	1.03	0.72 - 1.47	0.35	0.83	0.57 - 1.22
rs861020	*IRF6*	0.59	0.87	0.52 - 1.46	0.87	1.04	0.63 - 1.74
rs34743335	*IRF6*	0.38	2.79	0.25 - 30.91	0.16	3.20	0.58 - 17.63
rs642961	*IRF6*	0.20	0.66	0.34 - 1.26	0.97	1.01	0.57 - 1.80
rs7590268	*THADA*	0.94	1.02	0.67 - 1.55	0.87	0.96	0.61 - 1.52
rs4332945	*DYSF*	0.63	1.13	0.70 - 1.81	0.62	1.13	0.70 - 1.84
rs2303596	*DYSF*	0.89	0.97	0.60 - 1.57	0.05	1.51	0.99 - 2.31
rs227782	*DYSF*	0.88	1.03	0.73 - 1.45	0.76	0.95	0.66 - 2.56
rs115200552	*MSX1*	0.16	0.37	0.09 - 1.56	0.68	0.80	0.28 - 2.30
rs12532	*MSX1*	0.25	0.82	0.58 - 1.15	0.82	0.96	0.67 - 1.37
rs2674394	Gene Desert	0.57	1.14	0.73 - 1.80	0.97	0.99	0.62 - 1.59

rs651333	*TULP4*	0.40	0.85	0.58 - 1.25	0.93	0.98	0.67 - 1.45
rs6558002	*EPHX2*	0.53	0.87	0.55 - 1.36	0.86	1.04	0.67 - 1.63
rs987525	8q24	0.44	0.87	0.61 - 1.24	0.81	0.96	0.66 - 1.38
rs894673	*FOXE1*	0.15	1.30	0.91 - 1.87	0.78	0.94	0.63 - 1.41
rs3758249	*FOXE1*	0.14	1.31	0.91 - 1.87	0.89	0.97	0.65 - 1.44
rs7078160	*VAX1*	0.17	1.30	0.89 - 1.89	0.37	0.82	0.53 - 1.27
rs4752028	*VAX1*	0.42	1.15	0.82 - 1.62	0.96	1.01	0.71 - 1.44
rs10785430	*ADAMTS20*	0.53	0.89	0.61 - 1.29	0.27	1.23	0.85 - 1.77
rs9574565	*SPRY2*	0.90	0.98	0.68 - 1.40	0.34	0.83	0.57 - 1.22
rs8001641	*SPRY2*	0.71	0.88	0.47 - 1.67	0.85	0.94	0.48 - 1.82
rs17563	*BMP4*	0.17	1.38	0.87 - 2.18	0.64	1.12	0.69 - 1.82
rs1258763	*GREM1*	0.64	1.09	0.77 - 1.53	0.31	1.20	0.84 - 1.71
rs8049367	*ADCY9*	0.09	1.36	0.96 - 1.93	0.45	1.15	0.80 - 1.66
rs16260	*CDH1*	0.75	1.09	0.65 - 1.82	0.85	0.94	0.53 - 1.68
rs11642413	*CDH1*	0.31	0.81	0.53 - 1.23	0.50	1.15	0.77 - 1.71
rs1546124	*CRISPLD2*	0.49	0.87	0.57 - 1.31	0.82	0.95	0.62 - 1.45
rs4783099	*CRISPLD2*	0.73	1.07	0.75 - 1.52	0.83	0.96	0.66 - 1.39
rs8069536	*NTN1*	0.19	1.26	0.89 - 1.78	0.12	1.33	0.93 - 1.92
rs8081823	*NTN1*	0.85	0.96	0.65 - 1.42	0.10	0.70	0.45 - 1.08
rs17760296	*NOG1*	0.19	1.71	0.76 - 3.86	0.80	1.15	0.39 - 3.40
rs227731	*NOG1*	0.31	0.79	0.50 - 1.25	0.44	1.18	0.77 - 1.82
rs7224837	*AXIN2*	0.97	1.01	0.58 - 1.78	0.61	0.85	0.46 - 1.57
rs3923086	*AXIN2*	0.46	0.00	0.00 - NA	0.48	0.00	0.00 - NA
rs17820943	*MAFB*	0.91	1.02	0.67 - 1.56	0.62	1.11	0.73 - 1.70
rs13041247	*MAFB*	0.94	1.02	0.67 - 1.54	0.61	1.12	0.73 - 1.70
rs11696257	*MAFB*	0.91	1.02	0.67 - 1.56	0.59	1.12	0.74 - 1.71

[a]Loci that reached nominal significance