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

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Appendix Table 5: Other rare and/or potentially aetiologic variants observed in seven sequenced genes

HGVS	HGVp	α	¶	b	Polyphen-2	SIFT	§	¥	Reference
ARHGAP29									
c.560-199T>C	N/A	1	NSCLP	N/A	N/A	N/A	β	N/A	dbSNP
c.1144-18T>C	N/A	2	1 NSCLP and I NSCL	N/A	N/A	N/A	β,μ	N/A	dbSNP
c.2738C>T	p.Ser913Leu	4	2 NSCLP, 1 NSCL and 1 CPO	4 d	Benign	Deleterious	N/A	N/A	dbSNP
c.2957T>C	p.Ile986Thr	1	NSCLP	N/A	Benign	Tolerated	N/A	N/A	dbSNP
c.2962G>T	p.Asp988Tyr	2	NSCLP	1 d, 1 g	Probably Damaging	Deleterious	N/A	N/A	dbSNP
c.3023G>A	p.Arg1008Lys	2	1 NSCLP and 1 CPO	N/A	Benign	Tolerated	N/A	N/A	dbSNP
VAX1									
c.390G>A	p.Arg130Arg	1	NSCPO	N/A	Benign	Tolerated	ε	N/A	Novel
c.429+37G>C	N/A	1	NSCLP	N/A	N/A	N/A	β	N/A	1000Genome
c.429+50C>A	N/A	4	1 NSCLP, 1 NSCL and 2 CPO	N/A	N/A	N/A	μ	λ	1000Genome
c.693C>A	p.Ala231Ala	4	1 NSCLP and 3 NSCPO	N/A	Benign	Tolerated	γ, ε	λ	Novel
c.754G>T	p.Gly252Cys	1	NSCL	e	Probably	Deleterious	N/A	N/A	Novel

					Damaging				
PAX7									
c.703G>A	p.Ala235Thr	2	NSCLP	1 c, 1 d	Probably Damaging	Deleterious	N/A	N/A	dbSNP and ExAC
c.1223C>T	p.Pro408Leu	1	CPO	d	Probably Damaging	Deleterious	N/A	N/A	dbSNP and ExAC
MSX1									
c.95C>T	p.Ala32Val	4	2 NSCL and 2 CPO	N/A	Benign	Tolerated	η,ε	N/A	ExAc
c.218C>T	p.Pro73Leu	3	NSCL	2 d, 1 f	Possibly Damaging	Deleterious	N/A	N/A	dbSNP
c.522G>A	p.Lys174Lys	1	NSCL	N/A	Benign	Tolerated	N/A	N/A	Novel
BMP4									
c.860G>A	p.Arg287His	1	NSCL	N/A	Benign	Tolerated	N/A	N/A	dbSNP
c.371-164G>A	N/A	2	1 NSCLP and 1 NSCL	N/A	N/A	N/A	β, μ	N/A	Novel
c.280G>A	p.Glu94Lys	1	NSCL	N/A	Benign	Tolerated	N/A	N/A	Novel
c.228T>A	p.Ser76Arg	3	2 NSCLP and 1 NSCL	1 d, 2 f	Possibly Damaging	Damaging to two isoforms	N/A	N/A	dbSNP
FOXE1									

c.107C>T	p.Thr36Met	1	NSCLP	d	Possibly Damaging	Deleterious	N/A	N/A	ExAc
c.569C>G	p.Pro190Arg	6	3 NSCLP, 2 NSCL and 1 CPO	1 c, 2 d, 1 e, 2 f	Possibly Damaging	Deleterious	N/A	N/A	dbSNP
MAFB									
c.-1G>A	N/A	2	1 NSCL and 1 CPO	N/A	N/A	N/A	δ	N/A	dbSNP
c.-75C>A	N/A	1	NSCLP	N/A	N/A	N/A	N/A	λ	dbSNP
c.603G>C	p.Ala201Ala	1	NSCL	N/A	Benign	Tolerated	N/A	N/A	Novel

α: Total number of cases with variant, ¶: subphenotype of probands in which the variant was observed, **b**: segregation analyses, **c**: variant was observed in clinically unaffected father, **d**: variant was observed in clinically unaffected mother, **e**: variant was absent in the only paternal sample available, **f**: variant was absent in the only maternal sample available, **g**: no parental sample was available, **§**: Human Splice Finder, **¥:** RegulomeDB, **β:** alteration of Exonic Splicing Silencer (ESS) Site, **μ:** creation of new Exonic Splicing Enhancer (ESE) site, **δ:** Alteration of the wildtype (WT) donor site, **ε:** alteration of an ESE site, **γ**: creation of new Acceptor site with branch points, **η:** creation of new Donor site, **λ:** 2b - Likely to affect binding of *EZH2*, **N/A:** Not Applicable, **NSCLP**: nonsyndromic cleft lip and palate, **NSCL**: nonsyndromic cleft lip only, **CPO**: cleft palate only. All analyses were based on genome assembly number GRCh37/hg19, 2009 (http://genome.ucsc.edu).