

Supplemental Data

Mutations in the Epithelial Cadherin-p120-Catenin

Complex Cause Mendelian Non-Syndromic

Cleft Lip with or without Cleft Palate

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Table S1: Additional Class 3 Variants

Gene	Variant	Domain	Splice Prediction	Family	Origin	Family Structure	Cohort	gnomAD	ACMG	Interpretation/ Comments
<i>CTNND1</i>	chr11:g.57572251A>G p.Lys574Arg	ARM5, abolishes salt bridge AA577/855	Reduced at following base	2328	Philippines	Singleton	Replication	Nil	PM1, PM2, PP3	Class 3C VOUS Interacts with <i>CDH1</i> Glu757
	chr11:g.57572217C>G p.Gln563Glu	ARM5	-	2328	Philippines	Singleton	Replication	Nil	PM1, PM2, PP3	Class 3C VOUS
<i>PLEKHA5</i>	chr12:g.19427853A>G p.Met411Val	-	-	20020088	Philippines	Singleton	Replication	1 NFE, 1 EA	PM2, PP3	Class 3C VOUS
	chr12:g.19506842T>G p.Val849Gly	-	Possible Upstream Acceptor	6049	USA	Singleton	Replication	2 A, 3 SA, 2 O	PM2, PP3	Class 3C VOUS
	chr12:g.19506917A>T p.Lys874Met	-	-	20002102	Philippines	Multi-affected AD	Replication	4 EA, 3 O, 1 A	PM2, PP3	Class 3C VOUS
	chr12:g.19506917A>T p.Lys874Met	-	-	20010335	Philippines	Multi-affected AD	Replication	4 EA, 3 O, 1 A	PM2, PP3	Class 3C VOUS
	chr12:g.19436560G>A p.Gly548Arg	CTNND1 interaction domain	New Acceptor Site	20020446	Philippines	Multi-affected AD	Replication	2 L, 1 EA, 1 NFE	PM1, PP2, PP3, BS4	Class 3B VOUS
<i>PLEKHA7</i>	chr11:g.17035896C>A p.Gly18Val	WW domain	-	20013646	Philippines	Singleton	Replication	Nil	PM1, PM2, PP3	Class 3B VOUS
	chr11:g.16872791C>T p.Val215Met	PH Domain	-	20000506	Philippines	Multi-affected AD non- penetrant	Replication	1 NFE	PM1, PM2	Class 3B VOUS
	chr11:g.16848096T>A p.Asn305Ile	-	-	20040014	USA	Singleton	Replication	3 Asj, 1 NFE	PM2, PP3	Class 3B VOUS
<i>ESRP2</i>	chr16:g.68266552C>T p.Arg250Gln	1 st RNA recognition motif	-	CSc167	USA	Singleton	Replication	3 EA, 1 A	PM1, PM2, PP3	Class 3C VOUS, Residue conserved in all ESRP1/2 proteins to <i>C. elegans</i>
	chr16:g.68265269G>A p.Ser508Leu	3 rd RNA recognition motif / H-bond disruption	-	20040446	Philippines	Multi-affected AD	Replication	2 NFE, 1 SA	PM1, PM2, PP3	Class 3C VOUS
	chr16:g.68265151_68265153del p.Glu547del	Third RNA recognition motif	-	20021591	Philippines	Singleton	Replication	2 A, 2 NFE, 1 L	PM1, PM2, BP5	Class 3C VOUS

Abbreviations: Asj – Ashkenazi Jewish, NFE – Non-Finnish European, L – Latino, O – Other, SA – South Asian, FE- Finnish European, AD – Autosomal Dominant

Table S2: CLP gene expression in mouse epithelial tissues. A) Heat maps (gradient of orange to yellow) represents high to low expression. Examples of previously known CLP gene (grey). CLP genes reported in this paper (olive). Analysis in B) emphasizes the prominent expression of CLP genes in the maxillary epithelium.

Gene symbol	E10.5. Central Neural Epithelium	E10.5. Flanking Neural Epithelium	E10.5. Lateral Eminence Neural Epithelium	E10.5. Mandibular Columnar Epithelium	E10.5. Medial Eminence Neural Epithelium	E10.5. Maxillary Columnar Epithelium	E10.5. Medial Neuro-Epithelium
A) Heatmap of all genes compared with respect to each other in all listed tissues							
Arhgap29	38.07	38.72	39.74	58.04	38.11	48.65	38.87
Irf6	46.56	47.59	57.22	83.55	47.66	96.10	62.16
Pvr11	69.68	93.92	80.22	96.87	66.37	139.63	87.09
Fgfr2	32.08	43.36	38.56	70.38	32.43	52.46	36.59
Tfap2a	33.02	30.00	35.53	95.65	34.40	58.88	35.88
Cdh1	52.43	56.02	54.55	75.06	50.35	92.12	59.11
Esrp2	52.13	41.97	58.53	63.08	42.04	144.44	72.78
Plekha5	36.67	44.64	27.38	25.40	46.30	36.12	26.80
Ctnnd1	73.67	71.99	70.46	53.61	73.09	69.07	59.86
Plekha7	67.05	61.61	59.87	59.87	55.38	66.16	56.51
B) Gene-specific (row-wise) heatmap expression in all listed tissues							
Arhgap29	38.07	38.72	39.74	58.04	38.11	48.65	38.87
Irf6	46.56	47.59	57.22	83.55	47.66	96.10	62.16
Pvr11	69.68	93.92	80.22	96.87	66.37	139.63	87.09
Fgfr2	32.08	43.36	38.56	70.38	32.43	52.46	36.59
Tfap2a	33.02	30.00	35.53	95.65	34.40	58.88	35.88
Cdh1	52.43	56.02	54.55	75.06	50.35	92.12	59.11
Esrp2	52.13	41.97	58.53	63.08	42.04	144.44	72.78
Plekha5	36.67	44.64	27.38	25.40	46.30	36.12	26.80
Ctnnd1	73.67	71.99	70.46	53.61	73.09	69.07	59.86
Plekha7	67.05	61.61	59.87	59.87	55.38	66.16	56.51