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# Damaging mutations in Afadin contribute to risk of nonsyndromic cleft lip with or without cleft palate

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Chr:Pos	Ref/Alt	Gene Names	Effect (Combined)	HGVS c. (Clinically Relevant)	HGVS p. (Clinically Relevant)	PLI score	Missense metrics (Z)
1:11762306	G/C	<i>C1orf167</i>	LoF	c.-71+1G>C		0	0.88
1:11769006	C/T	<i>C1orf167</i>	LoF	c.1576C>T	p.Gln526Ter	0	0.88
1:12827690	C/T	<i>PRAMEF11</i>	Missense	c.434G>A	p.Gly145Glu	-	-2.59
3:57377068	G/C	<i>DNAH12</i>	Missense	c.8378C>G	p.Ala2793Gly	0	0.62
3:57384914	T/C	<i>DNAH12</i>	Missense	c.7775A>G	p.Gln2592Arg	0	0.62
3:57385388	T/G	<i>DNAH12</i>	Missense	c.7644A>C	p.Lys2548Asn	0	0.62
3:57386475	T/C	<i>DNAH12</i>	Missense	c.7568A>G	p.Asn2523Ser	0	0.62
4:2535505	C/A	<i>FAM193A</i>	Missense	c.58C>A	p.His20Asn	1	0.91
5:139980	C/A	<i>PLEKHG4B</i>	Missense	c.741C>A	p.Asp247Glu	0	-0.27
8:2101041	G/A	<i>MYOM2</i>	Missense	c.2606G>A	p.Ser869Asn	0	-5.3
9:130319603	G/A	<i>HMCN2</i>	Missense	c.2459G>A	p.Arg820His	0	1.07
9:130320790	G/A	<i>HMCN2</i>	Missense	c.2662G>A	p.Ala888Thr	0	1.07
9:130320863	G/A	<i>HMCN2</i>	Missense	c.2735G>A	p.Arg912Gln	0	1.07
9:130325648	G/C	<i>HMCN2</i>	Missense	c.2974G>C	p.Ala992Pro	0	1.07
9:130341237	T/G	<i>HMCN2</i>	Missense	c.3614T>G	p.Leu1205Trp	0	1.07
9:130341296	G/A	<i>HMCN2</i>	Missense	c.3673G>A	p.Gly1225Arg	0	1.07
9:130342433	A/G	<i>HMCN2</i>	Missense	c.3826A>G	p.Arg1276Gly	0	1.07
10:125026513	T/C	<i>CTBP2</i>	Missense	c.1247A>G	p.Glu416Gly	0	1.06
10:7563138	G/A	<i>ITIH5</i>	Missense	c.2774C>T	p.Ser925Phe	0	0.14
11:1174954	G/A	<i>MUC5AC</i>	Missense	c.2165G>A	p.Arg722His	0	1.26
11:1176608	T/G	<i>MUC5AC</i>	Missense	c.2597T>G	p.Val866Gly	0	1.26
11:1176631	G/A	<i>MUC5AC</i>	Missense	c.2620G>A	p.Ala874Thr	0	1.26
11:1176647	G/A	<i>MUC5AC</i>	Missense	c.2636G>A	p.Arg879Gln	0	1.26
11:1177500	C/T	<i>MUC5AC</i>	Missense	c.2954C>T	p.Thr985Met	0	1.26
11:1177632	A/G	<i>MUC5AC</i>	Missense	c.3086A>G	p.Lys1029Arg	0	1.26

11:1178654	G/A	<i>MUC5AC</i>	Missense	c.3298G>A	p.Gly1100Ser	0	1.26
11:1180060	G/A	<i>MUC5AC</i>	Missense	c.3523G>A	p.Glu1175Lys	0	1.26
11:1180138	C/T	<i>MUC5AC</i>	Missense	c.3601C>T	p.Arg1201Trp	0	1.26
11:1181153	G/A	<i>MUC5AC</i>	Missense	c.3791G>A	p.Arg1264His	0	1.26
11:1182220	G/A	<i>MUC5AC</i>	Missense	c.4075G>A	p.Ala1359Thr	0	1.26
11:1182388	G/A	<i>MUC5AC</i>	Missense	c.4243G>A	p.Ala1415Thr	0	1.26
11:1182493	C/G	<i>MUC5AC</i>	Missense	c.4348C>G	p.Pro1450Ala	0	1.26
11:1182561	G/C	<i>MUC5AC</i>	Missense	c.4416G>C	p.Arg1472Ser	0	1.26
11:1183901	C/T	<i>MUC5AC</i>	Missense	c.5756C>T	p.Pro1919Leu	0	1.26
11:1184798	A/G	<i>MUC5AC</i>	Missense	c.6653A>G	p.Lys2218Arg	0	1.26
11:1185131	C/T	<i>MUC5AC</i>	Missense	c.6986C>T	p.Thr2329Ile	0	1.26
11:1185343	C/T	<i>MUC5AC</i>	Missense	c.7198C>T	p.Pro2400Ser	0	1.26
11:1185503	G/T	<i>MUC5AC</i>	Missense	c.7358G>T	p.Ser2453Ile	0	1.26
11:1185584	C/T	<i>MUC5AC</i>	Missense	c.7439C>T	p.Ala2480Val	0	1.26
11:1185685	A/G	<i>MUC5AC</i>	Missense	c.7540A>G	p.Thr2514Ala	0	1.26
11:1186069	G/A	<i>MUC5AC</i>	Missense	c.7924G>A	p.Ala2642Thr	0	1.26
11:1186174	A/G	<i>MUC5AC</i>	Missense	c.8029A>G	p.Thr2677Ala	0	1.26
11:1186763	C/A	<i>MUC5AC</i>	Missense	c.8618C>A	p.Thr2873Lys	0	1.26
11:1186976	C/T	<i>MUC5AC</i>	Missense	c.8831C>T	p.Pro2944Leu	0	1.26
11:1187198	C/G	<i>MUC5AC</i>	Missense	c.9053C>G	p.Thr3018Ser	0	1.26
11:1187255	C/A	<i>MUC5AC</i>	Missense	c.9110C>A	p.Thr3037Asn	0	1.26
11:1187320	A/G	<i>MUC5AC</i>	Missense	c.9175A>G	p.Ser3059Gly	0	1.26
11:1187447	C/T	<i>MUC5AC</i>	Missense	c.9302C>T	p.Thr3101Met	0	1.26
11:1187819	G/T	<i>MUC5AC</i>	Missense	c.9674G>T	p.Arg3225Leu	0	1.26
11:1188350	C/T	<i>MUC5AC</i>	Missense	c.10205C>T	p.Pro3402Leu	0	1.26
11:1188422	G/C	<i>MUC5AC</i>	Missense	c.10277G>C	p.Arg3426Pro	0	1.26
11:1188586	G/A	<i>MUC5AC</i>	Missense	c.10441G>A	p.Gly3481Ser	0	1.26
11:1188914	G/A	<i>MUC5AC</i>	Missense	c.10769G>A	p.Arg3590His	0	1.26

11:1189034	C/T	<i>MUC5AC</i>	Missense	c.10889C>T	p.Ser3630Phe	0	1.26
11:1189147	A/C	<i>MUC5AC</i>	Missense	c.11002A>C	p.Thr3668Pro	0	1.26
11:1190398	C/A	<i>MUC5AC</i>	Missense	c.12253C>A	p.Gln4085Lys	0	1.26
11:1190429	C/G	<i>MUC5AC</i>	Missense	c.12284C>G	p.Thr4095Ser	0	1.26
11:1190453	C/T	<i>MUC5AC</i>	Missense	c.12308C>T	p.Thr4103Ile	0	1.26
11:1190489	C/G	<i>MUC5AC</i>	Missense	c.12344C>G	p.Pro4115Arg	0	1.26
11:1190491	G/T	<i>MUC5AC</i>	Missense	c.12346G>T	p.Ala4116Ser	0	1.26
11:1190666	C/T	<i>MUC5AC</i>	Missense	c.12521C>T	p.Thr4174Ile	0	1.26
11:1190684	C/T	<i>MUC5AC</i>	Missense	c.12539C>T	p.Ala4180Val	0	1.26
11:1191460	A/G	<i>MUC5AC</i>	Missense	c.13315A>G	p.Thr4439Ala	0	1.26
11:124225542	A/G	<i>OR8G2P</i>	Missense	c.850A>G	p.Arg284Gly	N/A	N/A
11:125950922	G/T	<i>VSIG10L2</i>	Missense	c.998G>T	p.Gly333Val	N/A	N/A
11:125955832	C/A	<i>VSIG10L2</i>	Missense	c.2300C>A	p.Thr767Asn	N/A	N/A
11:30931839	A/T	<i>DCDC1</i>	Missense	c.2829T>A	p.Asn943Lys	0	-0.04
12:40415093	C/G	<i>MUC19</i>	Missense	c.961C>G	p.Leu321Val	0	0.49
12:40421215	A/G	<i>MUC19</i>	Missense	c.1671A>G	p.Ile557Met	0	0.49
12:40428068	C/T	<i>MUC19</i>	LoF	c.2371C>T	p.Arg791Ter	0	0.49
12:40450670	A/G	<i>MUC19</i>	LoF	c.5015-2A>G		0	0.49
12:40464185	C/T	<i>MUC19</i>	Missense	c.5329C>T	p.Pro1777Ser	0	0.49
12:40482191	C/A	<i>MUC19</i>	LoF	c.9239C>A	p.Ser3080Ter	0	0.49
12:40483066	G/A	<i>MUC19</i>	Missense	c.10114G>A	p.Gly3372Arg	0	0.49
12:40483822	G/T	<i>MUC19</i>	Missense	c.10870G>T	p.Gly3624Cys	0	0.49
12:40486317	C/A	<i>MUC19</i>	LoF	c.13364C>A	p.Ser4455Ter	0	0.49
12:40530291	C/T	<i>MUC19</i>	Missense	c.21290C>T	p.Thr7097Ile	0	0.49
12:40531056	G/A	<i>MUC19</i>	LoF	c.21374-1G>A		0	0.49
12:40531104	C/T	<i>MUC19</i>	Missense	c.21421C>T	p.His7141Tyr	0	0.49
12:40532282	G/A	<i>MUC19</i>	Missense	c.21589G>A	p.Gly7197Ser	0	0.49
12:40537695	C/T	<i>MUC19</i>	Missense	c.22154C>T	p.Ala7385Val	0	0.49

14:21670341	T/G	<i>OR4E1</i>	Missense	c.595A>C	p.Ile199Leu	N/A	N/A
17:17164564	G/T	<i>MPRIIP</i>	Missense	c.3069G>T	p.Gln1023His	0.98	1.81
17:17165529	G/C	<i>MPRIIP</i>	Missense	c.4034G>C	p.Gly1345Ala	0.98	1.81
17:36450176	G/T	<i>TBC1D3J</i>	Missense	c.1347C>A	p.Asp449Glu	N/A	N/A
17:36450189	T/C	<i>TBC1D3J</i>	Missense	c.1334A>G	p.Asn445Ser	N/A	N/A
17:36450192	T/A	<i>TBC1D3J</i>	Missense	c.1331A>T	p.His444Leu	N/A	N/A
17:36493981	T/G	<i>ZNHIT3</i>	Missense	c.261T>G	p.Val87=	0	-0.6
17:42040266	C/T	<i>C17orf113</i>	LoF	c.1467G>A	p.Trp489Ter	N/A	N/A
17:64350416	T/C	<i>PECAM1</i>	Missense	c.2008A>G	p.Arg670Gly	N/A	N/A
17:64356203	C/T	<i>PECAM1</i>	Missense	c.1688G>A	p.Ser563Asn	N/A	N/A
17:64360355	G/T	<i>PECAM1</i>	Missense	c.1277C>A	p.Thr426Asn	N/A	N/A
17:64363380	C/T	<i>PECAM1</i>	Missense	c.985G>A	p.Glu329Lys	N/A	N/A
17:64377836	C/G	<i>PECAM1</i>	Missense	c.373G>C	p.Val125Leu	N/A	N/A
17:64378094	T/C	<i>PECAM1</i>	Missense	c.115A>G	p.Met39Val	N/A	N/A
17:75588382	C/G	<i>MYO15B</i>	Missense	c.325C>G	p.Arg109Gly	0	0.52
17:75591185	A/G	<i>MYO15B</i>	Missense	c.2374A>G	p.Ile792Val	0	0.52
17:75592759	G/C	<i>MYO15B</i>	Missense	c.2796G>C	p.Leu932Phe	0	0.52
17:75601478	A/T	<i>MYO15B</i>	Missense	c.3452A>T	p.His1151Leu	0	0.52
17:75613448	C/T	<i>MYO15B</i>	Missense	c.5009C>T	p.Ala1670Val	0	0.52
19:41761981	T/G	<i>CEACAM6</i>	Missense	c.716T>G	p.Val239Gly	0	-0.19
19:52780724	C/A	<i>ZNF600</i>	Missense	c.-163G>T	p.Met1ext-54	-	-1.73
19:54220765	T/C	<i>LILRB3</i>	Missense	c.1021A>G	p.Met341Val	0	-1.01
19:56228252	C/A	<i>ZSCAN5A</i>	Missense	c.157G>T	p.Asp53Tyr	0.01	-0.25
22:17569936	C/G	<i>SLC25A18</i>	Missense	c.-251C>G	p.Met1ext-84	0	0.62

**Supplementary Table:** Genetic variants with minor allele frequency < 0.01. These variants are in genes with copy number variation data with craniofacial phenotype in Humans but no craniofacial evidence reported in mouse knockout data.

 Highlighted variants are within genes that have evidence showing their high mutability.

PLI: probability that the gene will be intolerant to loss of function variants

Missense metrics (Z) score: Indicates the degree of single nucleotide variants observed compared to that expected. It measures the mutability of the gene.