

**Table S2. Amino acid substitution impact predictions for 71 functional SNVs in CDH proband**

CHROMO SOME	POSITION	Novel	1k				RE F	Type	Substitu ALT tion	Gene Symbol	Gene ID	PhastCo		
			e Freq (%)	EvsEur Freq (%)	EvsAfr Freq (%)	EvsF req (%)						ns	GERP	
<b>8</b>	<b>11606565</b>	<b>TRUE</b>	.	.	.	.	<b>missense</b>	<b>C T</b>	<b>R252W</b>	<b>GATA4</b>	<b>2626</b>	<b>1</b>	<b>4.71</b>	
3	53133472	rs143232904	.	0.09	0.06	0	0.04	missense	T C	Y339C	RFT1	91869	0.822	5.34
16	10631899	TRUE	.	.	.	.	.	missense	T C	M68V	EMP2	2013	0.999	5.26
7	107626530	TRUE	.	.	.	.	.	missense	C T	V205M	LAMB1	3912	1	5.2
17	36498966	TRUE	.	.	.	.	.	missense	C T	C236Y	GPR179	440435	1	5.09
17	45916053	TRUE	.	.	.	.	.	missense	G A	T261M	SCRN2	90507	0.836	5.08
6	158454575	TRUE	.	.	0.03	0	0.02	missense	C T	R192C	SYNJ2	8871	1	4.83
4	86491702	rs150698221	.	.	0.09	0	0.06	missense	A G	E148G	ARHGAP24	83478	0.999	5.46
20	18471068	rs140409239	.	0.05	0.07	0.03	0.06	missense	T G	D102A	RBBP9	10741	1	4.83
18	70417487	TRUE	.	.	.	.	.	missense	C T	D451N	NETO1	81832	1	5.2
6	7583947	TRUE	.	.	0.01	0	0.01	missense	G A	R2151Q	DSP	1834	0.969	5.2
1	34102110	TRUE	.	.	0.03	0	0.02	missense	C T	G1567S	CSMD2	114784	0.919	4.36
1	94027838	TRUE	.	.	.	.	.	missense	C T	R722H	BCAR3	8412	0.936	5.2
14	94100957	rs149171722	.	.	0.04	0	0.03	missense	C T	P1936L	UNC79	57578	1	5.45
3	121354608	TRUE	.	.	.	.	.	missense	T A	Y222F	HCLS1	3059	1	4.71
22	40807902	TRUE	.	0.05	.	.	.	missense	G A	A763V	MKL1	57591	1	4.45
13	26128056	TRUE	.	.	.	.	.	missense	T G	W355G	ATP8A2	51761	1	3.73
1	8930519	rs146619828	.	.	0.03	0	0.02	missense	C A	V78F	ENO1	2023	1	3.28
16	72832031	rs144091993	.	.	0.03	0.03	0.03	missense	G A	S1517L	ZFHX3	463	0.982	5.73
7	44153427	TRUE	.	.	0.07	0	0.05	missense	A T	Q1015L	AEBP1	165	0.997	4.98
7	150761676	TRUE	.	.	.	.	.	missense	G A	R94H	SLC4A2	6522	0.993	3.8
15	26107955	TRUE	.	.	.	.	.	missense	G A	L97F	ATP10A	57194	1	2.56
5	1463817	TRUE	.	.	.	.	.	missense	G C	S518R	LPCAT1	79888	0.996	3.88
1	155891258	TRUE	.	.	0.01	0	0.01	missense	G A	P392S	KIAA0907	22889	1	5.12
14	39650922	TRUE	.	.	.	.	.	missense	G A	G670D	PNN	5411	1	4.69
16	85688002	TRUE	.	.	.	.	.	missense	C T	P182L	KIAA0182	23199	1	4.62
17	7749463	rs145085233	.	.	0.01	0	0.01	missense	C T	R102W	KDM6B	23135	1	3.69
19	45556432	TRUE	.	.	0.01	0	0.01	missense	G A	G64S	CLASRP	11129	0.951	3.95
20	13850792	TRUE	.	.	.	.	.	missense	G A	P388S	SEL1L2	80343	1	2.84
2	149247339	rs142293829	.	.	0	0.05	0.02	missense	C T	R1147W	MBD5	55777	0.997	2.71
19	59022697	rs148336155	.	.	0.07	0.03	0.06	missense	C T	R209Q	SLC27A5	10998	0.003	2.31
14	31358935	rs149072811	.	.	0.04	0	0.03	missense	G C	E531Q	COCH	1690	1	4.74
1	32674932	TRUE	.	.	.	.	.	missense	G A	A80T	DCDC2B	149069	1	5.02
1	161029482	TRUE	.	.	.	.	.	missense	G A	A41V	ARHGAP30	257106	0.997	4.96

17	80136979	TRUE	.	0.07	0.03	0.06	missense	C	T	R433H	CCDC57	284001	1	5.17
5	64875331	rs142815878	.	0.01	0	0.01	missense	G	A	R384H	PPWD1	23398	1	3.24
8	132052136	TRUE	.	.	.	.	missense	G	C	S148R	ADCY8	114	1	2.57
16	3340477	TRUE	.	.	.	.	missense	A	C	R657S	ZNF263	10127	1	1.97
11	17617669	TRUE	.	.	.	.	missense	C	T	L192F	OTOG	340990	1	4.98
1	6605111	TRUE	.	.	.	.	missense	A	G	S292P	NOL9	79707	0.025	3.62
11	63141435	rs139591412	.	0.03	0	0.02	missense	C	T	A244V	SLC22A9	114571	0.008	2.9
19	10970611	TRUE	.	0.04	0	0.03	missense	C	T	A161V	C19orf38	255809	1	3.73
17	27030715	TRUE	.	.	.	.	missense	C	T	S291N	PROCA1	147011	0.993	2.83
5	140516502	rs143201420	.	0.01	0.03	0.02	missense	C	T	H496Y	PCDHB5	26167	0.034	0.656
3	130381153	TRUE	.	0.08	0	0.05	splice-5	G	A		COL6A6	131873	1	5.61
4	165961726	TRUE	.	.	.	.	missense	A	G	K168E	TRIM60	166655	0.002	2.06
6	33169111	TRUE	.	.	.	.	missense	G	C	G30A	SLC39A7	7922	1	1.39
14	21215891	TRUE	.	.	.	.	missense	A	G	D51G	EDDM3A	10876	0.11	2.19
3	14693365	TRUE	.	.	.	.	missense	T	A	L8M	C3orf19	51244	0.997	0.337
4	185578475	TRUE	.	.	.	.	splice-5	G	T		CCDC111	201973	1	5.56
17	18054449	TRUE	.	.	.	.	missense	C	T	P2500L	MYO15A	51168	0.086	0.494
10	51769408	TRUE	.	.	.	.	missense	G	C	S508T	AGAP6	414189	0.039	0.046
11	1088711	TRUE	.	0.03	0.03	0.03	missense	C	T	R1166W	MUC2	4583	0.821	-1.61
2	71036207	rs189899717	0.05	.	.	.	utr-3	A	C		CLEC4F	165530	0.996	3.56
14	38064189	TRUE	.	0.01	0	0.01	utr-5	C	G		FOXA1	3169	0.952	3.03
19	7505268	TRUE	.	.	.	.	missense	G	T	D148Y	ARHGEF18	23370	0.516	0.532
1	156563879	TRUE	.	.	.	.	utr-3	G	T		APOA1BP	128240	0.867	2.17
17	45507298	TRUE	.	.	.	.	missense	C	T	T870I	C17orf57	124989	0.001	-0.925
6	150390181	TRUE	.	.	.	.	missense	C	T	A8T	ULBP3	79465	0	-0.889
17	26988896	TRUE	.	0.01	0	0.01	utr-5	C	T		SDF2	6388	0.831	1.71
1	11167534	TRUE	.	.	.	.	utr-3	G	T		MTOR	2475	0.011	2.03
6	55638913	TRUE	.	.	.	.	nonsense	G	A	R321*	BMP5	653	0.967	-2.11
4	10076973	TRUE	.	.	.	.	utr-3	G	A		WDR1	9948	0.001	0.896
11	73078831	TRUE	.	.	.	.	utr-3	T	G		ARHGEF17	9828	0.72	N/A
11	77589989	TRUE	.	.	.	.	utr-3	T	G		INTS4	92105	0.004	N/A
14	70177718	TRUE	.	.	.	.	utr-3	C	G		KIAA0247	9766	0	-1.35
19	48806950	TRUE	.	.	.	.	missense	C	A	M278I	CCDC114	93233	0.883	-4.87
19	622835	TRUE	.	0.03	0	0.02	missense	G	A	R481W	POLRMT	5442	0	-8.13
19	37382373	TRUE	.	.	.	.	utr-3	A	G		ZNF829	374899	0.012	-5.89
14	23845092	TRUE	0.05	0.07	0.08	0.07	utr-3	G	A		IL25	64806	0	-7.37
10	7604991	TRUE	.	.	.	.	utr-3	C	T		ITIH5	80760	0	-8.64

Gene Symbol	SIFT Prediction	SIFT score	1-SIFT score	polyphen n2 predictio	polyphen 2 score	PhyloP	LRT	Mutation taster score	Pmut	Pmut Score
<b>GATA4</b>	<b>DAMAGING</b>	<b>0</b>	<b>1</b>	<b>probably c</b>	<b>1</b>	<b>0.98469</b>	<b>0.999999</b>	<b>1</b>	<b>PATHOLO</b>	<b>0.9807</b>
RFT1	DAMAGING	0.01	0.99	probably c	0.996	0.998059	1	0.999979	PATHOLO	0.7301
EMP2	DAMAGING	0.05	0.95	probably c	0.983	0.998727	1	0.995712	NEUTRAL	0.4309
LAMB1	DAMAGING	0	1	probably c	0.996	0.99882	1	0.997055	NEUTRAL	0.2023
GPR179	DAMAGING	0	1	probably c	0.992	0.999245	1	0.996803	PATHOLO	0.5528
SCRN2	DAMAGING	0	1	probably c	0.988	0.999531	1	0.999859	PATHOLO	0.7146
SYNJ2	DAMAGING	0.04	0.96	probably c	0.93	0.999002	0.999996	0.907342	PATHOLO	0.9003
ARHGAP24	DAMAGING	0	1	possibly d	0.753	0.99896	0.999802	0.860085	PATHOLO	0.7013
RBBP9	TOLERATED	0.45	0.55	probably c	0.982	0.998099	0.999987	0.933046	PATHOLO	0.7947
NETO1	DAMAGING *Warning! Low	0.05	0.95	possibly d	0.857	0.998803	0.999858	0.574597	NEUTRAL	0.1411
DSP	TOLERATED	0.34	0.66	probably c	0.924	0.999601	0.999991	0.619088	PATHOLO	0.8291
CSMD2	DAMAGING	0.05	0.95	probably c	0.999	0.984655	1	0.999998	NEUTRAL	0.4574
BCAR3	TOLERATED	0.64	0.36	probably c	0.993	0.998828	1	0.999962	PATHOLO	0.8586
UNC79	DAMAGING	0.01	0.99	possibly d	0.896	0.999094	1	0.264198	PATHOLO	0.8656
HCLS1	TOLERATED	0.63	0.37	probably c	0.938	0.997867	1	0.987971	NEUTRAL	0.1445
MKL1	TOLERATED	0.47	0.53	probably c	0.917	0.998906	0.99531	0.610796	PATHOLO	0.6737
ATP8A2	TOLERATED	0.33	0.67	probably c	0.995	0.972837	1	0.997509	NEUTRAL	0.1449
ENO1	DAMAGING *Warning! Low	0	1	benign	0.008	0.922022	0.991881	0.984522	PATHOLO	0.6942
ZFHX3	TOLERATED	0.81	0.19	possibly d	0.667	0.9998	0.999652	0.900437	NEUTRAL	0.4605
AEBP1	DAMAGING	0.01	0.99	benign	0.037	0.99829	0.993539	0.631769	PATHOLO	0.9357
SLC4A2	DAMAGING	0.02	0.98	possibly d	0.52	0.999376	0.999883	0.21017	PATHOLO	0.523
ATP10A	DAMAGING	0.02	0.98	probably c	0.998	0.998317	0.99993	0.959022	NEUTRAL	0.1093
LPCAT1	DAMAGING	0	1	possibly d	0.716	0.997683	1	0.996644	PATHOLO	0.5004
KIAA0907	TOLERATED	0.17	0.83	possibly d	0.714	0.99956	0.999996	0.000017	NEUTRAL	0.4696
PNN	DAMAGING	0.03	0.97	unknown	N/A	0.999814	1	0.973905	PATHOLO	0.9037
KIAA0182	DAMAGING	0.02	0.98	unknown	N/A	0.997782	0.999869	0.657402	NEUTRAL	0.4401
KDM6B	DAMAGING	0	1	benign	0.215	0.998112	0.991663	0.745727	PATHOLO	0.8039
CLASRP	TOLERATED	0.22	0.78	possibly d	0.828	0.998965	0.998833	0.970601	NEUTRAL	0.1463
SEL1L2	TOLERATED	0.19	0.81	probably c	0.996	0.899545	0.995137	0.914864	NEUTRAL	0.0973
MBD5	DAMAGING *Warning! Low	0	1	possibly d	0.827	0.985843	0.999974	0.038666	PATHOLO	0.9945
SLC27A5	DAMAGING	0	1	probably c	0.994	0.968813	0.999484	0.994634	NEUTRAL	0.4599
COCH	TOLERATED	0.63	0.37	possibly d	0.635	0.999277	0.998829	0.953052	NEUTRAL	0.0893
DCDC2B	TOLERATED	0.07	0.93	probably c	0.992	N/A	N/A	N/A	NEUTRAL	0.2479
ARHGAP30	TOLERATED	0.12	0.88	possibly d	0.651	0.99945	0.999764	0.199658	NEUTRAL	0.2388



Gene Symbol	Mutation accessor Functiona l impact	Mutation accessor score	Global Score	Endeavou r Rank	ToppGen e Rank	Total Rank
<b>GATA4</b>	<b>high</b>	<b>3.85</b>	<b>1.6525389</b>	3	1	<b>4</b>
RFT1	high	3.595	1.6464138	60	100	<b>160</b>
EMP2	medium	3.105	1.5688839	76	27	<b>103</b>
LAMB1	medium	2.96	1.5352175	1	2	<b>3</b>
GPR179	medium	2.72	1.5346848	84	11	<b>95</b>
SCRN2	medium	2.69	1.538209	71	44	<b>115</b>
SYNJ2	medium	2.395	1.486664	42	66	<b>108</b>
ARHGAP24	medium	1.935	1.4583647	50	51	<b>101</b>
RBBP9	medium	2.695	1.4548832	87	68	<b>155</b>
NETO1	medium	2.125	1.3749858	40	54	<b>94</b>
DSP	low	1.685	1.367778	28	39	<b>67</b>
CSMD2	medium	1.985	1.3629553	25	47	<b>72</b>
BCAR3	low	1.585	1.360789	66	106	<b>172</b>
UNC79	low	0.975	1.3382892	59	55	<b>114</b>
HCLS1	medium	2.275	1.3077338	12	18	<b>30</b>
MKL1	medium	2.095	1.2994212	49	73	<b>122</b>
ATP8A2	medium	2.49	1.2832746	74	74	<b>148</b>
ENO1	medium	3.375	1.2759625	16	13	<b>29</b>
ZFHX3	low	1.15	1.2507889	8	14	<b>22</b>
AEBP1	low	1.265	1.2341798	11	7	<b>18</b>
SLC4A2	medium	2.36	1.2135429	22	76	<b>98</b>
ATP10A	medium	2.51	1.2103569	101	17	<b>118</b>
LPCAT1	low	1.1	1.2044727	52	31	<b>83</b>
KIAA0907	low	1.1	1.2005173	21	61	<b>82</b>
PNN	low	0.895	1.1917419	20	42	<b>62</b>
KIAA0182	low	1.67	1.1855153	61	84	<b>145</b>
KDM6B	low	1.7	1.1751902	19	26	<b>45</b>
CLASRP	low	1.18	1.1607699	7	85	<b>92</b>
SEL1L2	medium	2.015	1.1470846	99	38	<b>137</b>
MBD5	medium	1.995	1.1461483	64	95	<b>159</b>
SLC27A5	medium	2.655	1.1381831	97	98	<b>195</b>
COCH	low	0.99	1.1277958	44	50	<b>94</b>
DCDC2B	low	1.83	1.09809	88	29	<b>117</b>
ARHGAP30	neutral	0.22	1.0911172	47	64	<b>111</b>

<i>CCDC57</i>	low	0.975	<b>1.06421</b>	102	35 <b>137</b>
<i>PPWD1</i>	low	1.445	<b>1.0455969</b>	35	78 <b>113</b>
<i>ADCY8</i>	medium	2.015	<b>1.0018891</b>	92	9 <b>101</b>
<i>ZNF263</i>	medium	2.515	<b>0.9850952</b>	4	87 <b>91</b>
<i>OTOG</i>	low	1.685	<b>0.9415</b>	77	33 <b>110</b>
<i>NOL9</i>	low	0.805	<b>0.9215066</b>	78	71 <b>149</b>
<i>SLC22A9</i>	low	1.79	<b>0.9052855</b>	69	56 <b>125</b>
<i>C19orf38</i>	low	0.805	<b>0.90353</b>		36 <b>36</b>
<i>PROCA1</i>	low	0.975	<b>0.8680747</b>	105	53 <b>158</b>
<i>PCDHB5</i>	medium	3.18	<b>0.8395561</b>	62	89 <b>151</b>
<i>COL6A6</i>	low	0.895	<b>0.7505</b>	81	22 <b>103</b>
<i>TRIM60</i>	low	1.025	<b>0.7410254</b>	103	49 <b>152</b>
<i>SLC39A7</i>	low	1.1	<b>0.7199409</b>	95	101 <b>196</b>
<i>EDDM3A</i>	neutral	0.695	<b>0.7085502</b>	98	59 <b>157</b>
<i>C3orf19</i>	low	1.87	<b>0.6836076</b>	70	37 <b>107</b>
<i>CCDC111</i>	N/A	N/A	<b>0.656</b>	41	45 <b>86</b>
<i>MYO15A</i>	low	0.895	<b>0.6204742</b>	37	46 <b>83</b>
<i>AGAP6</i>	medium	2.75	<b>0.52498</b>	86	32 <b>118</b>
<i>MUC2</i>	low	1.59	<b>0.4742</b>	39	97 <b>136</b>
<i>CLEC4F</i>	N/A	N/A	<b>0.4556</b>	24	58 <b>82</b>
<i>FOXA1</i>	N/A	N/A	<b>0.3982</b>	9	5 <b>14</b>
<i>ARHGEF18</i>	neutral	0.695	<b>0.39086</b>	46	93 <b>139</b>
<i>APOA1BP</i>	N/A	N/A	<b>0.3037</b>	93	69 <b>162</b>
<i>C17orf57</i>	neutral	0.55	<b>0.2792368</b>	75	40 <b>115</b>
<i>ULBP3</i>	low	1.04	<b>0.2641237</b>	94	99 <b>193</b>
<i>SDF2</i>	N/A	N/A	<b>0.2541</b>	51	83 <b>134</b>
<i>MTOR</i>	N/A	N/A	<b>0.2041</b>	15	19 <b>34</b>
<i>BMP5</i>	N/A	N/A	<b>0.1665588</b>	45	8 <b>53</b>
<i>WDR1</i>	N/A	N/A	<b>0.0897</b>	43	104 <b>147</b>
<i>ARHGEF17</i>	N/A	N/A	<b>0.072</b>	6	90 <b>96</b>
<i>INTS4</i>	N/A	N/A	<b>0.0004</b>	96	57 <b>153</b>
<i>KIAA0247</i>	N/A	N/A	<b>-0.135</b>	26	75 <b>101</b>
<i>CCDC114</i>	neutral	-0.345	<b>-0.2209571</b>	31	34 <b>65</b>
<i>POLRMT</i>	neutral	0.345	<b>-0.4384961</b>	38	91 <b>129</b>
<i>ZNF829</i>	N/A	N/A	<b>-0.5878</b>	65	41 <b>106</b>
<i>IL25</i>	N/A	N/A	<b>-0.737</b>	85	23 <b>108</b>
<i>ITIH5</i>	N/A	N/A	<b>-0.864</b>	32	10 <b>42</b>

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