

Supplemental Table. All known patients with mutations affecting *ZIC2*.

Patient*	HPE type	Gender	Case Status	Inheritance	DNA Alteration	Predicted Protein Alteration in ZIC2	Functional activity	Reference
1	U	F	P	<i>de novo</i>	c.21delG	p.Q8SfsX33	Predicted null	23
2	S	M	P	<i>de novo</i>	c.81_86delGG CGGCinsTCG GT	p.A28RfsX13	Predicted null	17
3a	S	F	P	Maternal	c.107A>C (assumed)	p.Q36P (assumed)	170%	28, 30
3b	Mic	F	Mother	Unknown	c.107A>C	p.Q36P	170%	28, 30
4a	L	F	P	Paternal	c.109G>A	p.D37N	Unknown	17
4b	N	M	Father	Unknown	c.109G>A	p.D37N	Unknown	17
5	S	F	P	<i>de novo</i>	c.129_184dup 56	p.L62Rfs175	Predicted null	17
6	S	F	P	<i>de novo</i>	c.136C>T	p.Q46X	Predicted null	30
7	A	F	P	<i>de novo</i>	c.172G>T	p.G58X	Predicted null	30
8	S	F	P	<i>de novo</i>	c.177ins56	p.F60QfsX176	Predicted null	16
9a	S	F	P	Maternal	c.191dupC	p.A66RfsX301	Predicted null	17
9b	L	M	Brother	Maternal	c.191dupC	p.A66RfsX301	Predicted null	17
9c	Mic	F	Mother	Unknown	c.191dupC	p.A66RfsX301	Predicted null	17
10	L	M	P	<i>de novo</i>	c.217C>T	p.Q73X	Predicted null	17
11	A	F	P	Unknown	c.217delC	p.Q73Rfs145	Predicted null	17
12	A	M	P	<i>de novo</i>	c.367delA	p.S123AfsX95	Predicted null	17
13	A	M	P	<i>de novo</i>	c.382G>A	p.D128N	Unknown	17
14a	A	M	P	Paternal	c.386_392del CGGCGCC	p.S129WfsX87	Predicted null	17
14b	S	M	Brother	Paternal	c.386_392del CGGCGCC (assumed)	p.S129WfsX87 (assumed)	Predicted null	17
14c	Mic	M	Father	Unknown	c.386_392del CGGCGCC (assumed)	p.S129WfsX87 (assumed)	Predicted null	17
15	U	U	P	Unknown	C.392_398del 7	p.G133SfsX83	Predicted null	17
16a	L	F	P	Maternal	c.454_455deli nsTT	p.D152F	60%	23, 30
16b	N	F	Mother	Unknown	c.454_455deli nsTT	p.D152F	60%	23, 30
17	L	U	P	Germline	c.479delC	p.P160RfsX58	Predicted null	17
18	A	M	P	<i>de novo</i>	c.490G>T	p.E164X	Predicted null	17
19	U	U	P	Unknown	c.557_572dup 16	p.E192GfsX180	Predicted null	17
20a	U	F	P (triplet)	Unknown	c.577delC	p.Q193NfsX25	Predicted null	17
20b	U	F	Sister (triplet)	Unknown	c.577delC	p.Q193NfsX25	Predicted null	17
21	A	M	P	<i>de novo</i>	c.582C>A	p.Y194X	Predicted null	17
22	S	F	P	<i>de novo</i>	c.612delC	p.Y205TfsX13	Predicted null	17
23	S	M	P	Unknown	c.622GC>TT	p.A208L	Unknown	This report
24	A	M	P	Unknown	c.659delA	p.N220TfsX4	Predicted null	17

25a	A	F	P	Maternal	c.665_676dup 12	p.G222_M225dup	Unknown	17
25b	U	F	Mother	Unknown	c.665_676dup 12	p.G222_M225dup	Unknown	17
26	S	F	P	<i>de novo</i>	c.748C>T	p.Q250X	Predicted null	17
27	A	M	P	<i>de novo</i>	c.779G>A	p.W260X	Predicted null	17
28a	S	M	P	Unknown	c.793C>T	p.Q265X	Predicted null	17
28b	U	F	Sister	Unknown	c.793C>T	p.Q265X	Predicted null	This report
29	A	M	P	<i>de novo</i>	c.797_801del	p.L266QfsX99	Predicted null	This report
30a	MIHV	F	P	Maternal (assumed germline mosaicism)	c.808_809ins1 7	p.K270TfsX2	Predicted null	30
30b	A	M	Brother	Maternal (assumed germline mosaicism)	c.808_809ins1 7 (assumed)	p.K270TfsX2 (assumed)	Predicted null	30
30c	U	M	Brother	Maternal (assumed germline mosaicism)	c.808_809ins1 7 (assumed)	p.K270TfsX2 (assumed)	Predicted null	30
30d	N	F	Mother	Unknown	c.808_809ins1 7 (assumed germline mosaicism)	p.K270TfsX2 (assumed germline mosaicism)	Predicted null	30
31	A	M	P	Unknown	c.815G>A and c. 974 G>T	p.S272N p.R325L	Predicted null (for both mutations)	17
32	U	U	P	Unknown	c.825_826del AA	p.K275NfsX91	Predicted null	17
33	U	F	P	Unknown	p.829_830dup TT	p.T279AfsX7	Predicted null	17
34	A	M	P	<i>de novo</i>	c.856C>T	p.H286Y	Predicted null	17
35	U	U	P	Unknown	p.857A>T	p.H286L	Predicted null	17
36	A	F	P	Unknown	c.858C>G	p.H286Q	Predicted null	17
37	S	U	P	<i>de novo</i>	c.862_863del TC	p.S288GfsX78	Predicted null	17, 27
38a	L	M	P	Paternal	c.871C>T	p.H291Y	Predicted null	17
38b	Mic	M	Father	Unknown	c.871C>T	p.H291Y	Predicted null	17
39	S	M	P	Unknown	c.910T>A (Also SIX3: c.850G>C)	p.W304R (Also SIX3: p.A284P)	Predicted null	17
40	A	F	P	Unknown	c.912G>A	p.W304X	Predicted null	17
41	U	M	P	Unknown	c.912G>A	p.W304X	Predicted null	17
42	L	F	P	<i>de novo</i>	c.928G>T	p.E310X	Predicted null	17
43	S	F	P	<i>de novo</i>	c.932delG	p.G311AfsX102	Predicted null	23
44	A	F	P	Unknown	c.941T>G	P.F314C	Predicted null	17
45	S	F	P	<i>de novo</i>	c.973C>A	p.R325S	Predicted null	17
46	U	M	P	<i>de novo</i>	c.979C>T	p.H327Y	Predicted null	17

47	S	M	P	<i>de novo</i>	c.994_1005dup	p.C335_P338dup	Predicted loss-of-function	This report
48	A	F	P	<i>de novo</i>	c.1004G>T	p.C335F	Predicted null	17
49	S	F	P	<i>de novo</i>	c.1025_1026delAA	p.K342SfsX24	Predicted null	30
50	S	U	P	<i>de novo</i>	c.1031_1032delITC	p.F344CfsX22	Predicted null	23
51	A	F	P	<i>de novo</i>	c.1040_1046del	p.E348SfsX63	Predicted null	16, 23
52	S	M	P	Unknown	c.1051A>T	p.K351X	Predicted null	17
53	S	F	P	<i>de novo</i>	c.1052_1053insAAAGGTT CACACAGA ACCTCAA	p.K351_I352Ins7	Predicted null	17
54	A	M	P	<i>de novo</i>	c.1075+2T>A (IVS+1T>A)	p.G359fsX62	Predicted null	17
55	U	F	P	Unknown	c.1076-1G>A (IVS1-1G>A)	Alternative splicing	Predicted null	17
56	A	M	P	<i>de novo</i>	c.1076-1G>A (IVS1-1G>A)	Alternative splicing	Predicted null	17
57	S	M	P	Unknown	c.1076-1G>A (IVS1-1G>A)	Alternative splicing	Predicted null	17
58	S	U	P	<i>de novo</i>	c.1090C>T	p.Q364X	Predicted null	17
59a	S	M	P (Twin)	<i>de novo</i>	c.1091_1092delAG	p.Q364LfsX2	Predicted null	23, 30
59b	U	M	P	<i>de novo</i>	c.1091_1092delAG	p.Q364LfsX2	Predicted null	This report
60	U	U	P	Unknown	c.1095_1096delTTG	p.C365X	Predicted null	17
61a	S	F	P	Maternal	c.1095_1096delTTG	p.C365X	Predicted null	17
61b	U	M	Half-sibling	Maternal (assumed)	c.1095_1096delTTG (assumed)	p.C365X (assumed)	Predicted null	This report
61c	U	F	Mother	Unknown	c.1095_1096delTTG	p.C365X	Predicted null	This report
62	S	M	P	<i>de novo</i>	c.1097_1098delAG	p.E366Vfs2	Predicted null	23
63	U	U	P	Unknown	c.1118G>C	p.R373P	Predicted null	17
64	S	M	P	Unknown	c.1119_1120delCT	p.F374RfsX17	Predicted null	17
65	U	U	P	Unknown	c.1204T>A	p.Y402N	Predicted null	17
66a	S	F	P	Maternal	c.1206C>G	p.Y402X	Predicted null	17
66b	U	M	Brother	Maternal	c.1206C>G	p.Y402X*	Predicted null	This report
66c	Mic	F	Mother	Unknown	c.1206C>G	p.Y402X	Predicted null	This report
67a	S	F	P	Maternal	c.1208C>A	p.T403K	Predicted null	17
67b	U	F	½ sister	Maternal (assumed)	c.1208C>A (assumed)	p.T403K (assumed)	Predicted null	This report
67c	U	F	½ sister	Maternal (assumed)	c.1208C>A (assumed)	p.T403K (assumed)	Predicted null	This report
67d	U	F	Mother	Unknown (assumed)	c.1208C>A (assumed)	p.T403K (assumed)	Predicted null	This report
68	S	M	P	Unknown	c.1211A>G	p.H404R	Predicted null	17
69	S	F	P	Unknown	c.1225C>T	p.R409W	Predicted null	17
70	U	U	P	Unknown	c.1239+1G>C (IVS1-1G>A)	Possible inclusion of intron 2 codons	Predicted null	17

						or alternative splicing		
71	U	U	P	Unknown	c.1240-2A>G (IVS2-2A>G)	Alternative splicing	Predicted null	17
72	L	M	P	Unknown	c.1245T>G	p.H415Q	Predicted null	17
73	S	F	P	Unknown	c.1277delC	p.P426RfsX129	Predicted null	17
74	A	M	P	<i>de novo</i>	c.1313dupC	p.L440AfsX90	Predicted null	16
75	L	F	P	<i>de novo</i>	c.1323dupG	p.S442Vfs88	2%	23, 28
76	A	M	P	Unknown	c.1329delC	p.S444AfsX111	Predicted null	This report
77	MIHV	M	P	<i>de novo</i>	c.1330_1365del	p.444_455del	60%	23, 28
78	S	M	P	Unknown	c.1366_1395dup30	p.A456_465dup	Unknown	This report
79	MIHV	M	P	Unknown	c.1366_1395dup30	p.A456_465dup	Unknown	This report
80a	A	M	P	Paternal (assumed germline mosaicism)	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	16, 17, 23
80b	A	F	Sister	Paternal (assumed germline mosaicism)	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	This report
80c	U	M	Paternal ½ sib	Paternal (assumed germline mosaicism)	c.1377_1406dup30 (assumed)	p.A461_470dup (assumed)	5% with reduced DNA binding	This report
80d	U	F	Paternal ½ sib	Paternal (assumed germline mosaicism)	c.1377_1406dup30 (assumed)	p.A461_470dup (assumed)	5% with reduced DNA binding	This report
80e	Mic	M	Brother	Paternal (assumed germline mosaicism)	c.1377_1406dup30 (assumed)	p.A461_470dup (assumed)	5% with reduced DNA binding	This report
80f	S	F	Sister	Paternal (assumed germline mosaicism)	c.1377_1406dup30 (assumed)	p.A461_470dup (assumed)	5% with reduced DNA binding	This report
80g	N	M	Father	<i>de novo</i>	c.1377_1406dup30 (assumed germline mosaicism)	p.A461_470dup (assumed germline mosaicism)	5% with reduced DNA binding	16, 17, 23
81	U	F	P	Unknown	c.1377_1406dup30 (also SHH: c.869G>A)	p.A461_470dup (also SHH: p.G290D)	5% with reduced DNA binding	17, 25
82	S	F	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	This report
83a	S	U	P	Maternal	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17
83b	U	F	Mother	Unknown	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17

84a	MIHV	F	P	Paternal	c.1377_1406dup30n); Also sib with <i>FOXH1</i> : c.1062delT	p.A461_470dup; Also sib with <i>FOXH1</i> : FS in COOH terminus	5% with reduced DNA binding	17, 23
84b	U	M	Brother	Paternal	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17, 23
84c	N	M	Father	"Mosaic carrier"	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17, 23
85	S	U	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17, A. Paulussen et al., 2008, EJHG, abstract
86	A	F	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17
87	S	M	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17
88	L	M	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	17
89	S	F	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	This report
90	A	F	P	<i>de novo</i>	c.1377_1406dup30	p.A461_470dup	5% with reduced DNA binding	This report
91a	L	F	P	Paternal	c.1377_1406del	p.A456_465del	Predicted null	17
91b	U	M	Father	Unknown	c.1377_1406del	p.A456_465del	Predicted null	17
92a	A	M	P	Maternal	c.1392_1406del	p.A461_465del	Predicted null	17
92b	N	F	Mother	Unknown	c.1392_1406del	p.A461_465del	Predicted null	17
93a	S	M	P	Maternal	c.1401_1406dup	p.A469_470dup	Unknown	This report
93b	U	U	Sibling	Maternal	c.1401_1406dup	p.A469_470dup	Unknown	This report
93c	N	M	Mother	Unknown	c.1401_1406dup	p.A469_470dup	Unknown	This report
94	S	M	P	<i>de novo</i>	c.1420_1427dup; c.1428_1433delinsCG	p.G477CfsX54	Predicted null	17
95	S	F	P	<i>de novo</i>	c.1437_1441del	p.S480QfsX48	Predicted null	This report
96	S	F	P	<i>de novo</i>	c.1445_1461del17	p.S482RfsX42	Predicted null	17
97	A	U	P	Unknown	c.1452_1456delCGCGG	p.A485RfsX43	Predicted null	17
98	S	M	P	Unknown	c.1455_1461delinsCG	p.G487LfsX41	Predicted null	17
99	S	U	P	<i>de novo</i>	c.1508_1520delGGCGCGG	p.G503AfsX48	Predicted null	17
100a	U	U	P	Maternal	c.1559delA	p.H520PfsX35	Predicted null	17

100b	U	M	Brother	Maternal	c.1559delA	p.H520PfsX35	Predicted null	17
100c	U	F	Mother	Unknown	c.1559delA	p.H520PfsX35	Predicted null	17
101	S	F	P	Unknown	Gene deletion	N/A	Predicted null	A. Paulussen et al., 2008, EJHG, abstract
102	S	M	P	<i>de novo</i>	Gene deletion	N/A	Predicted null	This report
103	L	F	P	<i>de novo</i>	Gene deletion	N/A	Predicted null	This report
104	S	M	P	<i>de novo</i>	Gene deletion	N/A	Predicted null	This report
105	A	F	P	<i>de novo</i>	Gene deletion	N/A	Predicted null	This report
106	A	F	P	<i>de novo</i>	Gene deletion	N/A	Predicted null	This report
107	A	M	P	<i>de novo</i>	del13(q31.1-qter)	N/A	Predicted null	33
108	U	F	P	U	del13(q31.1-13qter)	N/A	Predicted null	33
109	U	M	P	U	del13(q31.3-q33.1)	N/A	Predicted null	33
110	U	M	P	U	del13(q32.3)	N/A	Predicted null	33
111	U	F	P	U	del13(q31.1-13qter)	N/A	Predicted null	33
112	A	F	P	U	del13(q32q34)	N/A	Predicted null	31
113	A	F	P	Maternal	i(13)(q10)	N/A	Predicted null	24
114	U	U	P	U	del(13)(q22qter)	N/A	Predicted null	15
115	A	M	P	U	del(13)(q22qter)	N/A	Predicted null	26
116	U	M	P	U	del(13)(q31qter)	N/A	Predicted null	29

*Each kindred is listed by a separate number; individuals within a kindred are each assigned a separate letter.

A: Alobar; F: Female; L: Lobar; M: Male; Mic: Microform; MIHV: Middle Interhemispheric Variant; N: None; P: Proband; S: Semilobar; U: Unknown