

Supplementary table 1a. FISH probes used in this study

Chromosome	Probe	Company	Case #
22p	Acro-P	CYTOCELL	1
22	HIRA / NA85A3	CYTOCELL	4, 7, 9
22	BCR	Vysis	13

Supplementary table 1b. qPCR primers for verification of genomic abnormalities on chromosome 22					
Primers	Primers sequences	Amplified region	Amplicon size (bp)	Target genes	Patients
Target primers	Forward: gctgcccgacaattaacagcaat Reverse: tcctgccatctcattcgctggat	chr22:18131287-18131426	140	<i>TBX1</i>	2 to 9
Target primers	Forward: aacagcaggtcctaggttgggaa Reverse: ttctggctcactccggaaggaat	chr22:19543945-19544052	108	<i>SNAP29</i>	10,11
Target primers	Forward: tccaagaacccgctcggaatgta Reverse: tcctgctgtattcccaccaccaa	chr22:19652376-19652519	144	<i>AIFM3</i>	12
Target primers	Forward: agtggcaccatcagagcttactgt Reverse: catgatgggtgtgcctgtggtt	chr22:20650320-20650421	102	<i>TOP3B</i>	13
Target primers	Forward: tgaatgaccaggagttcaaggct Reverse: aagtggaatctgcacatctgcct	chr22:21885935-21886107	173	<i>BCR</i>	14,15
Target primers	Forward: aggagcagcgagacagagaaacat Reverse: acctcgttggcagaagtagtcaca	chr22:23624368-23624492	125	<i>SGSM1</i>	16
Target primers	Forward: tcctctgtttgacaggtgaggcaa Reverse: tgaatcagcctgctgctccatact	chr22:31578128-31578273	146	<i>TIMP3</i>	17
Target primers	Forward: accaccgatccagcagtcacatcaat Reverse: attcaatcagagctgaggcagggt	chr22:40793787-40793966	180	<i>NAGA</i>	18
Target primers	Forward: cacagaaagccttgagttgcgt Reverse: tcattggccagttggagactctgt	chr22:49249064-49249176	113	<i>SBF1</i>	19,20
Reference primers	Forward: atcaaagcttccttgccctctga Reverse: ttggaagaggtaatcgaggcact	chrX:13684972-13685109	138bp	<i>OFD</i>	2 to 20

Supplementary table 2. Total CNVs on chromosome 22

Benign CNV	Start Coordinate (kb)	Stop Coordinate (kb)	Number of Duplications	Number of Deletions	Total Number of CNVs
1	14504.02	14797.21	0	15	15
2	14504.02	14884.50	0	1	1
3	14504.02	15654.03	1	0	1
4	14884.10	15835.04	1	0	1
5	15275.40	15670.48	1	0	1
6	15438.75	15670.48	4	0	4
7	17021.56	17390.65	1	1	2
8	17041.52	17390.65	2	2	4
9	17085.80	17390.65	0	5	5
10	17270.07	17390.65	6	2	8
11	17270.07	17409.80	3	0	3
12	17274.64	17390.65	3	0	3
13	17280.25	17380.00	0	1	1
14	17280.25	17390.65	0	1	1
15	17284.91	17390.65	1	0	1
16	17303.82	17343.51	0	1	1
17	17348.69	17390.65	3	0	3
18	17348.69	17519.23	1	0	1
19	18358.24	18383.27	0	1	1
20	18412.08	18438.18	0	4	4
21	18513.41	18544.73	1	0	1
22	18513.41	18650.64	0	1	1
23	18523.88	18544.73	1	0	1
24	18589.03	18635.31	1	0	1
25	18596.93	18635.31	1	0	1
26	18691.50	19039.09	0	1	1
27	19125.59	19179.27	2	0	2
28	19153.63	19214.77	1	0	1
29	19337.10	19464.33	1	0	1
30	19709.70	19776.01	1	0	1
31	20558.49	20627.98	1	0	1
32	20637.38	20797.50	1	0	1
33	20642.93	20904.96	5	2	7
34	20642.93	20912.54	2	0	2
35	20652.91	20904.96	1	1	2
36	21328.08	21984.36	0	1	1
37	21346.55	21417.29	0	1	1
38	21362.06	21417.29	0	8	8
39	21375.99	21427.38	0	1	1
40	21409.08	21427.38	0	1	1
41	22250.23	22304.30	0	1	1
42	22255.13	22289.35	1	0	1
43	22255.13	22296.95	1	0	1
44	22443.05	22452.53	1	0	1
45	22611.90	22671.57	0	1	1
46	22611.90	22686.89	1	0	1
47	22611.90	22725.51	0	3	3
48	22611.90	22731.40	0	4	4
49	22611.90	22759.75	0	2	2
50	22644.08	22731.40	0	1	1
51	22656.63	22671.57	0	1	1
52	22656.63	22725.51	7	1	8
53	22658.34	22725.51	0	1	1

54	22671.17	22725.51	0	2	2
55	22677.76	22686.89	0	3	3
56	22677.76	22696.36	0	13	13
57	22677.76	22706.37	0	1	1
58	22677.76	22716.12	1	0	1
59	22677.76	22725.51	322	189	511
60	22677.76	22731.40	3	0	3
61	22677.76	22737.19	1	0	1
62	22681.80	22696.36	0	15	15
63	22686.49	22716.12	1	0	1
64	22686.49	22720.40	6	0	6
65	22686.49	22725.51	7	1	8
66	22686.49	22731.40	0	1	1
67	22695.96	22706.37	1	0	1
68	22695.96	22720.40	12	17	29
69	22695.96	22725.51	10	13	23
70	22701.01	22712.41	0	1	1
71	22701.01	22720.40	8	63	71
72	22701.01	22725.51	0	7	7
73	22705.97	22720.40	0	48	48
74	22705.97	22725.51	0	1	1
75	22712.01	22720.40	0	13	13
76	22712.01	22725.51	0	1	1
77	23951.72	24254.23	1	0	1
78	23972.84	24233.68	4	0	4
79	23972.84	24254.23	1	0	1
80	23983.87	24233.68	17	0	17
81	23983.87	24254.23	1	0	1
82	23983.87	24268.76	1	0	1
83	23983.87	24331.64	1	0	1
84	23994.42	24233.68	16	18	34
85	23994.42	24254.23	6	2	8
86	23994.42	24268.76	0	1	1
87	24017.49	24233.68	1	1	2
88	24031.93	24331.64	1	0	1
89	24087.52	24098.65	0	1	1
90	24716.72	24738.26	0	1	1
91	25347.91	25359.07	0	1	1
92	28472.98	28481.88	0	2	2
93	28835.48	28877.98	1	0	1
94	29973.26	30181.38	1	0	1
95	29997.18	30106.91	1	0	1
96	30608.73	30638.87	0	2	2
97	30868.16	31015.99	1	0	1
98	31345.09	31428.70	1	0	1
99	31375.79	31509.06	1	0	1
100	31695.77	31716.88	0	1	1
101	32340.14	32373.88	0	1	1
102	32494.43	32518.80	0	1	1
103	34950.07	35039.31	1	0	1
104	36663.48	36673.17	0	1	1
105	37677.01	37715.59	0	2	2
106	37683.32	37715.59	0	11	11
107	37688.86	37702.49	0	2	2
108	37688.86	37707.20	2	2	4
109	37688.86	37715.59	1	170	171
110	37688.86	37718.87	0	2	2

111	37696.76	37715.59	0	3	3
112	37710.56	37738.75	1	0	1
113	37752.45	37775.17	0	1	1
114	39213.55	39224.33	1	0	1
115	39504.85	39517.10	1	0	1
116	40091.06	40135.94	0	1	1
117	40848.31	40867.53	3	0	3
118	40960.49	41312.82	0	1	1
119	41110.92	41219.60	1	0	1
120	41226.44	41275.16	0	1	1
121	41226.44	41279.69	5	15	20
122	41226.44	41287.26	0	6	6
123	41226.44	41363.43	0	1	1
124	41237.53	41248.37	2	0	2
125	41237.53	41254.71	1	0	1
126	41237.53	41275.16	4	2	6
127	41237.53	41279.69	19	10	29
128	41237.53	41287.26	0	1	1
129	41241.59	41295.87	1	0	1
130	41241.59	41299.23	1	0	1
131	41279.29	41295.87	2	1	3
132	41286.86	41295.87	0	11	11
133	41286.86	41299.23	1	0	1
134	41941.22	41989.93	1	0	1
135	43012.01	43034.91	1	0	1
136	43498.80	43571.98	0	2	2
137	43571.58	43602.91	0	1	1
138	43752.63	43772.26	0	1	1
139	44319.81	44504.16	1	0	1
140	44696.65	44735.38	0	1	1
141	44717.63	44735.38	4	3	7
142	44857.05	49566.02	0	1	1
143	44871.50	44884.63	0	1	1
144	45129.03	45152.07	0	1	1
145	45729.18	45826.12	0	1	1
146	46904.27	46912.86	1	0	1
147	47672.56	47802.40	1	0	1
148	47785.45	48381.33	1	0	1
149	48229.79	48292.08	0	2	2
150	48319.49	48429.87	1	0	1
151	48553.80	48573.55	3	0	3
152	48850.95	48865.84	1	0	1
153	48958.91	48966.27	1	2	3
154	49000.59	49059.34	0	1	1
155	49364.90	49377.30	1	0	1
156	49483.99	49499.91	1	0	1
Grand Total			550	748	1298

Supplementary table 3: Consolidated benign CNVs on chromosome 22

Benign CNV	Start Coordinate (kb)	Stop Coordinate (kb)	Number of Duplications	Number of Deletions	Total Number of CNVs
1	14504.018	14797.208 - 15654.025	1	16	17
2	14884.098	15835.035	1	0	1
3	15275.397 - 15438.746	15670.475	5	0	5
4	17021.562 - 17348.691	17390.649 - 17519.227	20	13	33
5	18358.244 - 18691.504	18383.270 - 19039.090	4	7	11
6	19125.592 - 19337.095	19179.268 - 19464.326	4	0	4
7	19709.703	19776.005	1	0	1
8	20558.485	20627.977	1	0	1
9	20637.383 - 20652.905	20797.502 - 20912.542	9	3	12
10	21328.084 - 21409.081	21417.294 - 21984.363	0	12	12
11	22250.229 - 22443.048	22289.345 - 22452.528	3	1	4
12	22611.900 - 22712.011	22671.574 - 22759.751	380	403	783
13	23951.722 - 24087.522	24098.654 - 24331.637	50	23	73
14	24716.719	24738.256	0	1	1
15	25347.913	25359.066	0	1	1
16	28472.977	28481.880	0	2	2
17	28835.482	28877.983	1	0	1
18	29973.262	30181.384	1	0	1
19	29997.180	30106.905	1	0	1
20	30608.730	30638.865	0	2	2
21	30868.157	31015.993	1	0	1
22	31345.092	31428.696	1	0	1
23	31375.790	31509.063	1	0	1
24	31695.771	31716.875	0	1	1
25	32340.138	32373.879	0	1	1
26	32494.428	32518.800	0	1	1
27	34950.070	35039.313	1	0	1
28	36663.477	36673.173	0	1	1
29	37677.010 - 37710.556	37702.489 - 37738.747	4	192	196
30	37752.446	37775.173	0	1	1
31	39213.551	39224.333	1	0	1
32	39504.850	39517.097	1	0	1
33	40091.064	40135.938	0	1	1
34	40848.310	40867.531	3	0	3
35	40960.494 - 41286.860	41219.595 - 41363.433	37	49	86
36	41941.224	41989.926	1	0	1
37	43012.006	43034.911	1	0	1
38	43498.796	43571.983	0	2	2
39	43571.583	43602.910	0	1	1
40	43752.632	43772.259	0	1	1
41	44319.810	44504.161	1	0	1
42	44696.650	44735.383	0	1	1
43	44717.631	44735.383	4	3	7
44	44857.050	49566.016	0	1	1
45	44871.498	44884.632	0	1	1
46	45129.031	45152.073	0	1	1
47	45729.181	45826.122	0	1	1
48	46904.272	46912.855	1	0	1
49	47672.563	47802.402	1	0	1
50	47785.450	48381.327	1	0	1
51	48229.788	48292.084	0	2	2
52	48319.488	48429.872	1	0	1
53	48553.800	48573.553	3	0	3

54	48850.948	48865.840	1	0	1
55	48958.906	48966.272	1	2	3
56	49000.586	49059.341	0	1	1
57	49364.901	49377.297	1	0	1
58	49483.992	49499.911	1	0	1
Grand Total			550	748	1298

Supplementary table 4. start coordinates in all benign CNVs

	Start Coordinate (kb)	Duplication	Deletion	Grand Total
1	14504.018	1	16	17
2	14884.098	1	0	1
3	15275.397	1	0	1
4	15438.746	4	0	4
5	17021.562	1	1	2
6	17041.524	2	2	4
7	17085.801	0	5	5
8	17270.071	9	2	11
9	17274.635	3	0	3
10	17280.246	0	2	2
11	17284.91	1	0	1
12	17303.815	0	1	1
13	17348.691	4	0	4
14	18358.244	0	1	1
15	18412.08	0	4	4
16	18513.409	1	1	2
17	18523.876	1	0	1
18	18589.033	1	0	1
19	18596.932	1	0	1
20	18691.504	0	1	1
21	19125.592	2	0	2
22	19153.629	1	0	1
23	19337.095	1	0	1
24	19709.703	1	0	1
25	20558.485	1	0	1
26	20637.383	1	0	1
27	20642.928	7	2	9
28	20652.905	1	1	2
29	21328.084	0	1	1
30	21346.55	0	1	1
31	21362.055	0	8	8
32	21375.986	0	1	1
33	21409.081	0	1	1
34	22250.229	0	1	1
35	22255.129	2	0	2
36	22443.048	1	0	1
37	22611.9	1	10	11
38	22644.079	0	1	1
39	22656.631	7	2	9
40	22658.343	0	1	1
41	22671.174	0	2	2
42	22677.759	327	206	533
43	22681.795	0	15	15
44	22686.49	14	2	16
45	22695.962	23	30	53
46	22701.005	8	71	79
47	22705.966	0	49	49

48	22712.011	0	14	14
49	23951.722	1	0	1
50	23972.84	5	0	5
51	23983.869	20	0	20
52	23994.418	22	21	43
53	24017.489	1	1	2
54	24031.933	1	0	1
55	24087.522	0	1	1
56	24716.719	0	1	1
57	25347.913	0	1	1
58	28472.977	0	2	2
59	28835.482	1	0	1
60	29973.262	1	0	1
61	29997.18	1	0	1
62	30608.73	0	2	2
63	30868.157	1	0	1
64	31345.092	1	0	1
65	31375.79	1	0	1
66	31695.771	0	1	1
67	32340.138	0	1	1
68	32494.428	0	1	1
69	34950.07	1	0	1
70	36663.477	0	1	1
71	37677.01	0	2	2
72	37683.316	0	11	11
73	37688.858	3	176	179
74	37696.764	0	3	3
75	37710.556	1	0	1
76	37752.446	0	1	1
77	39213.551	1	0	1
78	39504.85	1	0	1
79	40091.064	0	1	1
80	40848.31	1	0	1
81	40854.254	2	0	2
82	40960.494	0	1	1
83	41110.915	1	0	1
84	41226.436	5	23	28
85	41237.531	26	13	39
86	41241.586	2	0	2
87	41279.285	2	1	3
88	41286.86	1	11	12
89	41941.224	1	0	1
90	43012.006	1	0	1
91	43498.796	0	2	2
92	43571.583	0	1	1
93	43752.632	0	1	1
94	44319.81	1	0	1
95	44696.65	0	1	1
96	44717.631	4	3	7
97	44857.05	0	1	1

98	44871.498	0	1	1
99	45129.031	0	1	1
100	45729.181	0	1	1
101	46904.272	1	0	1
102	47672.563	1	0	1
103	47785.45	1	0	1
104	48229.788	0	2	2
105	48319.488	1	0	1
106	48553.8	3	0	3
107	48850.948	1	0	1
108	48958.906	1	2	3
109	49000.586	0	1	1
110	49364.901	1	0	1
111	49483.992	1	0	1
Grand Total		550	748	1298

Supplementary table 5. stop coordinates in all benign CNVs

	Stop Coordinate (kb)	Duplication	Deletion	Grand Total
1	14797.208	0	15	15
2	14884.498	0	1	1
3	15654.025	1	0	1
4	15670.475	5	0	5
5	15835.035	1	0	1
6	17343.506	0	1	1
7	17380.003	0	1	1
8	17390.649	16	11	27
9	17409.802	3	0	3
10	17519.227	1	0	1
11	18383.27	0	1	1
12	18438.18	0	4	4
13	18544.726	2	0	2
14	18635.31	2	0	2
15	18650.642	0	1	1
16	19039.09	0	1	1
17	19179.268	2	0	2
18	19214.768	1	0	1
19	19464.326	1	0	1
20	19776.005	1	0	1
21	20627.977	1	0	1
22	20797.502	1	0	1
23	20904.961	6	3	9
24	20912.542	2	0	2
25	21417.294	0	9	9
26	21427.378	0	2	2
27	21984.363	0	1	1
28	22289.345	1	0	1
29	22296.947	1	0	1
30	22304.297	0	1	1
31	22452.528	1	0	1
32	22671.574	0	2	2
33	22686.89	1	3	4
34	22696.362	0	28	28
35	22706.366	1	1	2
36	22712.411	0	1	1
37	22716.119	2	0	2
38	22720.395	45	161	206
39	22725.505	327	199	526
40	22731.396	3	6	9
41	22737.19	1	0	1
42	22759.751	0	2	2
43	24098.654	0	1	1
44	24233.684	38	19	57
45	24254.226	9	2	11
46	24268.762	0	1	1
47	24268.762	1	0	1
48	24331.637	2	0	2
49	24738.256	0	1	1
50	25359.066	0	1	1
51	28481.88	0	2	2
52	28877.983	1	0	1
53	30106.905	1	0	1

54	30181.384	1	0	1
55	30638.865	0	2	2
56	31015.993	1	0	1
57	31428.696	1	0	1
58	31509.063	1	0	1
59	31716.875	0	1	1
60	32373.879	0	1	1
61	32518.8	0	1	1
62	35039.313	1	0	1
63	36673.173	0	1	1
64	37702.489	0	2	2
65	37707.198	2	2	4
66	37715.585	1	186	187
67	37718.869	0	2	2
68	37738.747	1	0	1
69	37775.173	0	1	1
70	39224.333	1	0	1
71	39517.097	1	0	1
72	40135.938	0	1	1
73	40867.531	3	0	3
74	41219.595	1	0	1
75	41248.373	2	0	2
76	41254.713	1	0	1
77	41275.158	4	3	7
78	41279.685	24	25	49
79	41287.26	0	7	7
80	41295.873	3	12	15
81	41299.225	2	0	2
82	41312.82	0	1	1
83	41363.433	0	1	1
84	41989.926	1	0	1
85	43034.911	1	0	1
86	43571.983	0	2	2
87	43602.91	0	1	1
88	43772.259	0	1	1
89	44504.161	1	0	1
90	44735.383	4	4	8
91	44884.632	0	1	1
92	45152.073	0	1	1
93	45826.122	0	1	1
94	46912.855	1	0	1
95	47802.402	1	0	1
96	48292.084	0	2	2
97	48381.327	1	0	1
98	48429.872	1	0	1
99	48573.553	3	0	3
100	48865.84	1	0	1
101	48966.272	1	2	3
102	49059.341	0	1	1
103	49377.297	1	0	1
104	49499.911	1	0	1
105	49566.016	0	1	1
Grand Total		550	748	1298

Supplementary Table 6. Major clinical features in patients with a ~ 0.5 Mb deletion between LCR22-3b and LCR22-4

Kurahashi 1996	D'Angelo 2007	Fernández 2009	Patient 10	Patient 11
Facial dysmorphism, conotruncal anomaly face syndrome	Mild facial features	Atypical facial dysmorphism		Facial dysmorphism
	Neurodevelopmental, behavioural and psychiatric spectrum disorder		Developmental delay	Speech delay
Tetralogy of Fallot, Pulmonary atresia		Atypical congenital heart defect		Microcephaly, hearing loss