Fig. S1

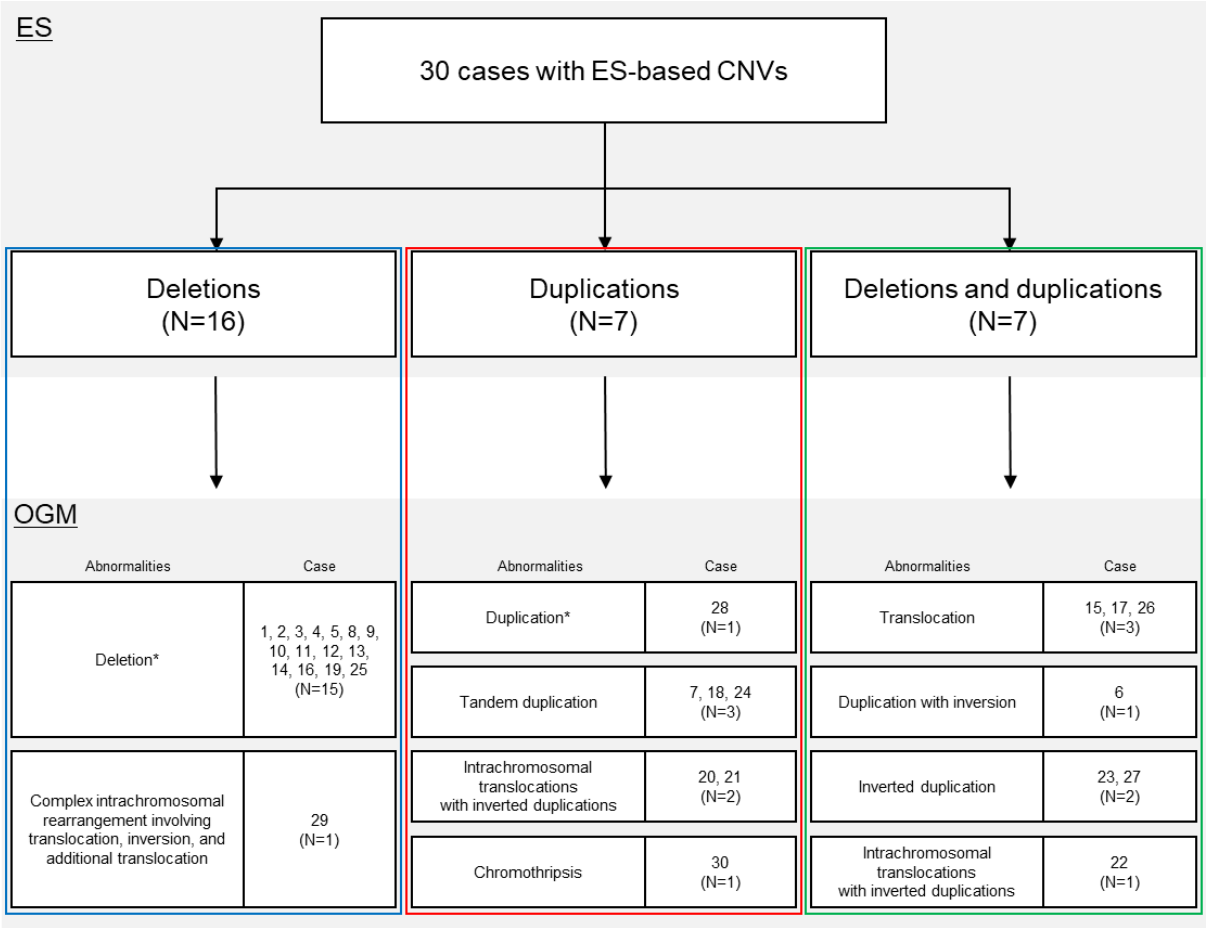
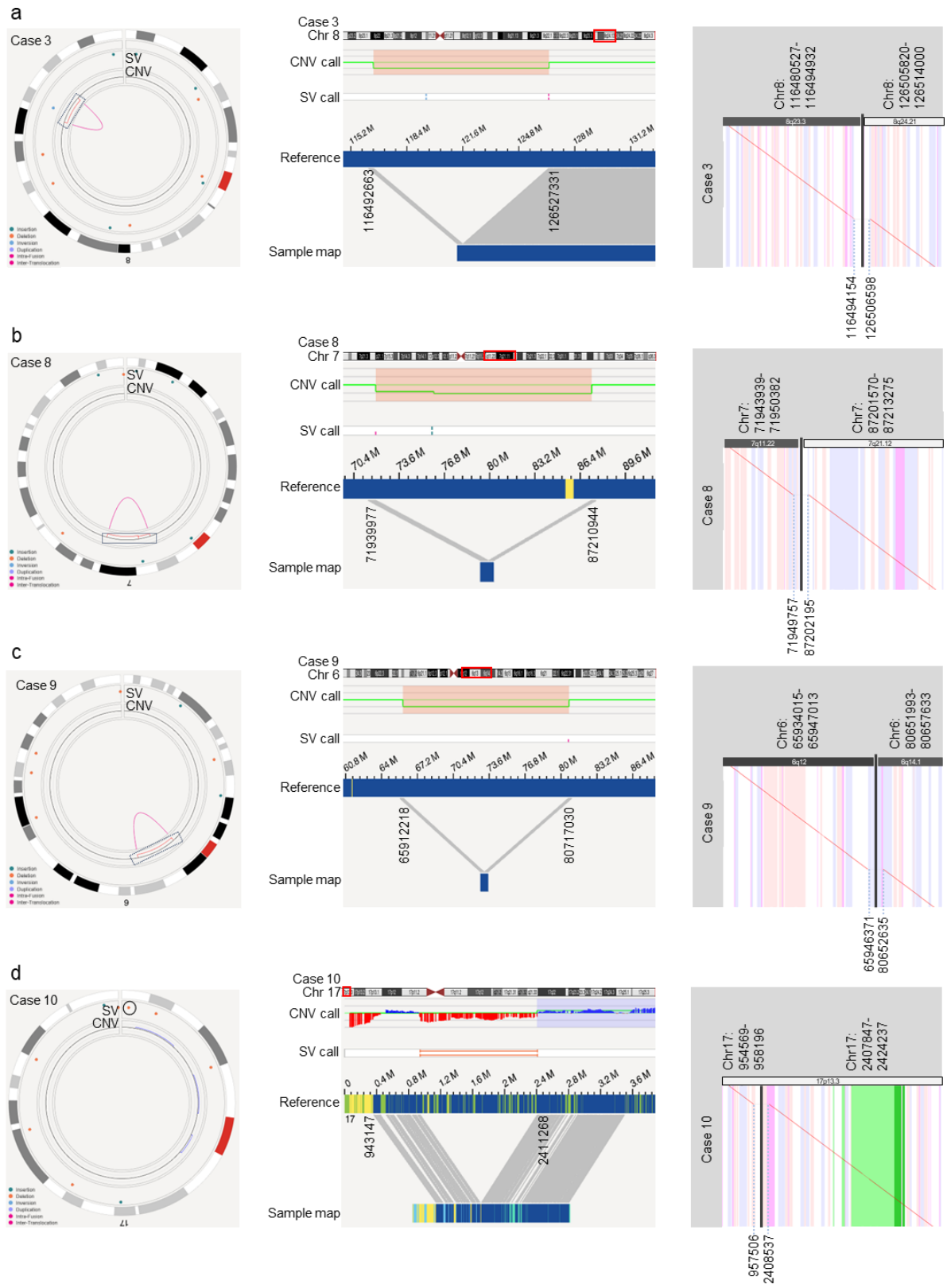
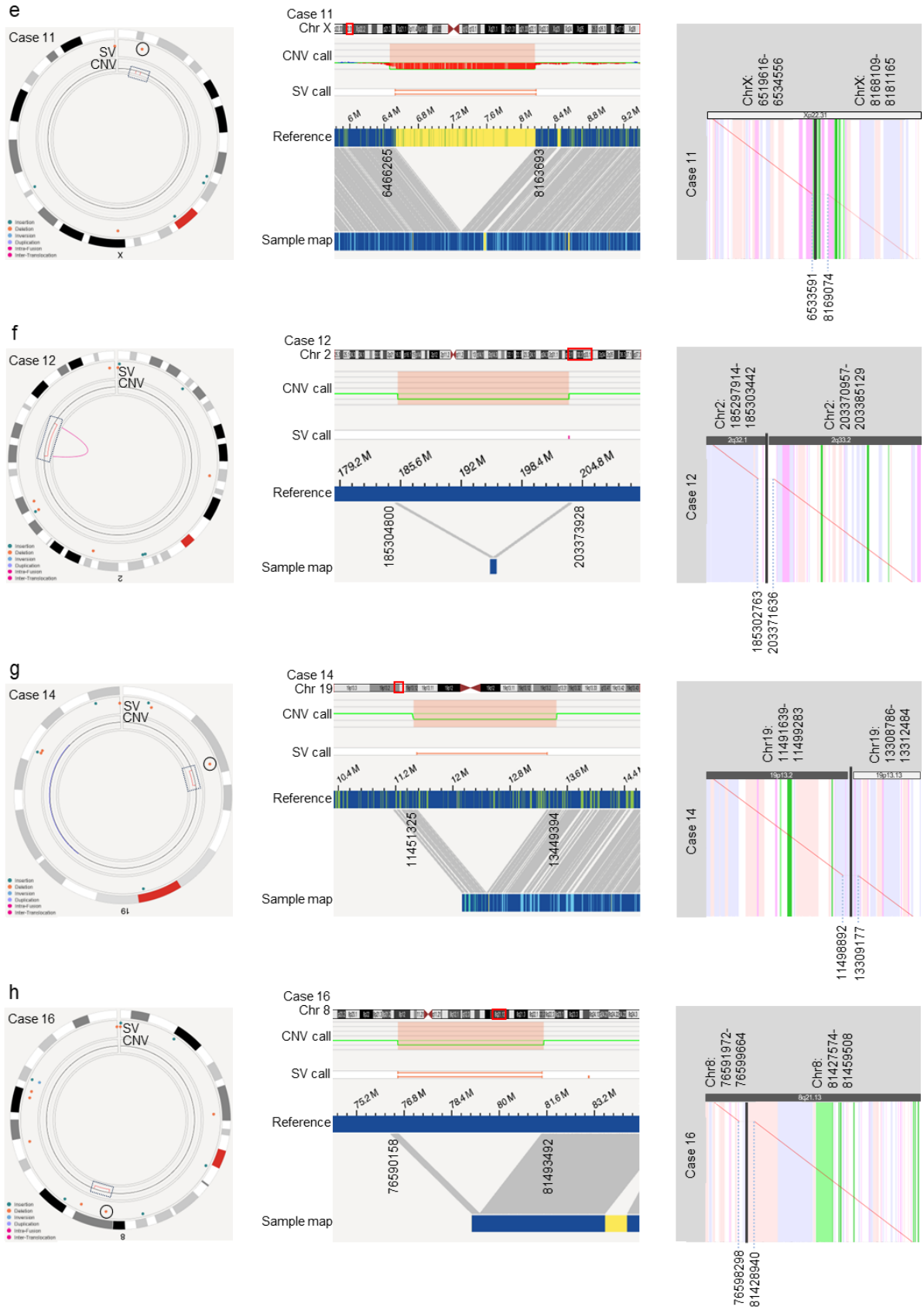


Fig. S1. Overview of the 30 cases verified by OGM with adaptive sampling. *Indicates expected structural variants that were previously detected using exome sequencing. CNV, copy number variant; ES, exome screening; OGM, optical genome mapping.

Fig. S2


a
Case 3
SV
CNV
Case 3
Chr 8
CNV call
SV call
Reference
Sample map
116492663
126527331
Chr8:
116480527-
116494932
Chr8:
126505820-
126514000
Case 3
116494154
126506598
b
Case 8
SV
CNV
Case 8
Chr 7
CNV call
SV call
Reference
Sample map
71939977
87210944
Chr7:
71943939-
71950382
Chr7:
87201570-
87213275
Case 8
71949757
87202195
c
Case 9
SV
CNV
Case 9
Chr 6
CNV call
SV call
Reference
Sample map
65912218
80717030
Chr6:
65934015-
65947013
Chr6:
80651993-
80657633
Case 9
65946371
80652635
d
Case 10
SV
CNV
Case 10
Chr 17
CNV call
SV call
Reference
Sample map
943147
2411268
Chr17:
954569-
958196
Chr17:
2407847-
2424237
Case 10
957506
2408537


e
Case 11
SV
CNV
Case 11
Chr X
CNV call
SV call
Reference
Sample map
6466265
8163693
ChrX:
6519616-
6534556
ChrX:
8168109-
8181165
Case 11
6533591
8169074
f
Case 12
SV
CNV
Case 12
Chr 2
CNV call
SV call
Reference
Sample map
185304800
203373928
Chr2:
185297914-
185303442
Chr2:
203370957-
203385129
Case 12
185302763
203371636
g
Case 14
SV
CNV
Case 14
Chr 19
CNV call
SV call
Reference
Sample map
11451325
13449394
Chr19:
11491639-
11499283
Chr19:
13308786-
13312484
Case 14
11498892
13309177
h
Case 16
SV
CNV
Case 16
Chr 8
CNV call
SV call
Reference
Sample map
76590158
81493492
Chr8:
76591972-
76599664
Chr8:
81427574-
81459508
Case 16
76598298
81428940

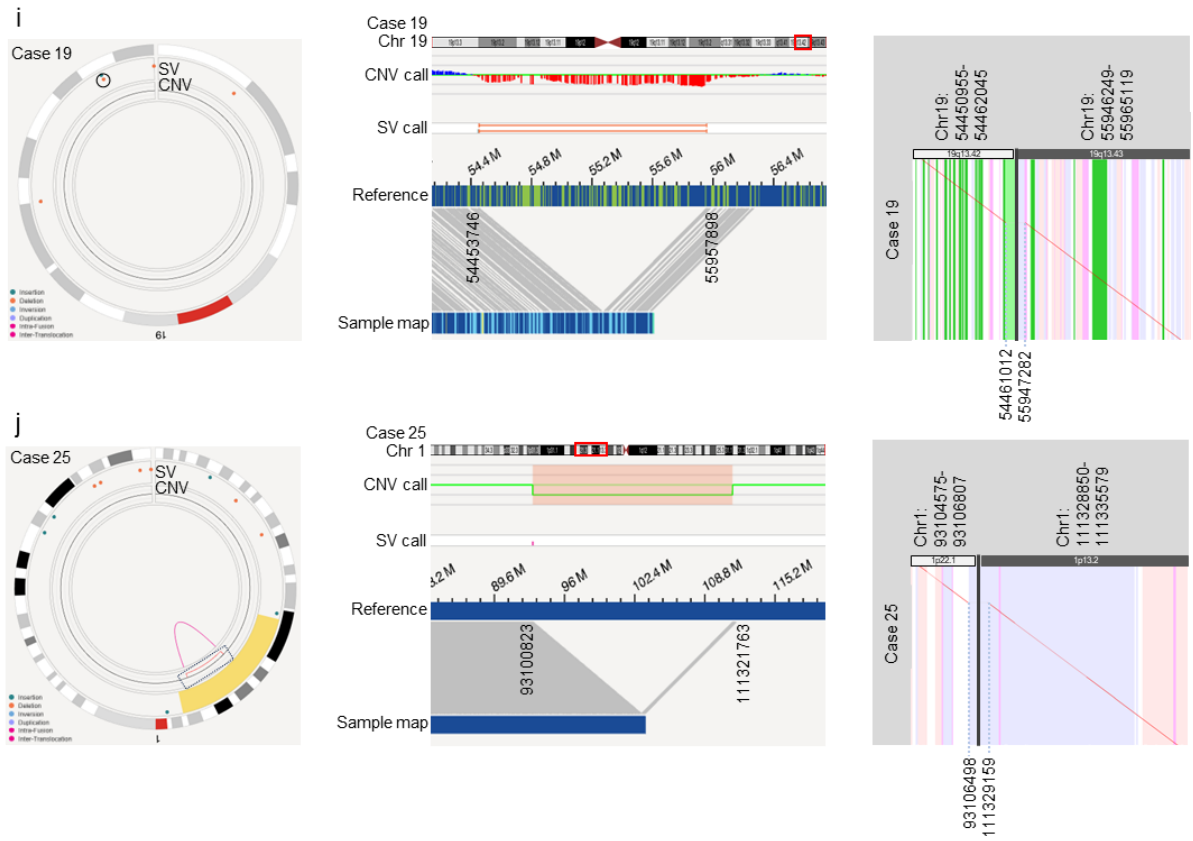


Fig. S2. Results of OGM and long-read sequencing in Cases 3 (a), 8 (b), 9 (c), 10 (d), 11 (e), 12 (f), 14 (g), 16 (h), 19 (i), and 25 (j). (a–j) Left diagrams are Circos plots of OGM, and large deletions are visualized as red bars in the CNV call track or red dots in the SV call track of each chromosome. Middle diagrams are the genome browser, and large deletions are visualized as red bars in the CNV or SV call tracks. Right diagrams are dot-plots of the consensus sequence from long-read sequencing data. (j) A yellow region in the Circos plot demonstrates absence of heterozygosity. Molecular karyotypes in all cases are described in Table S4. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

Fig. S3

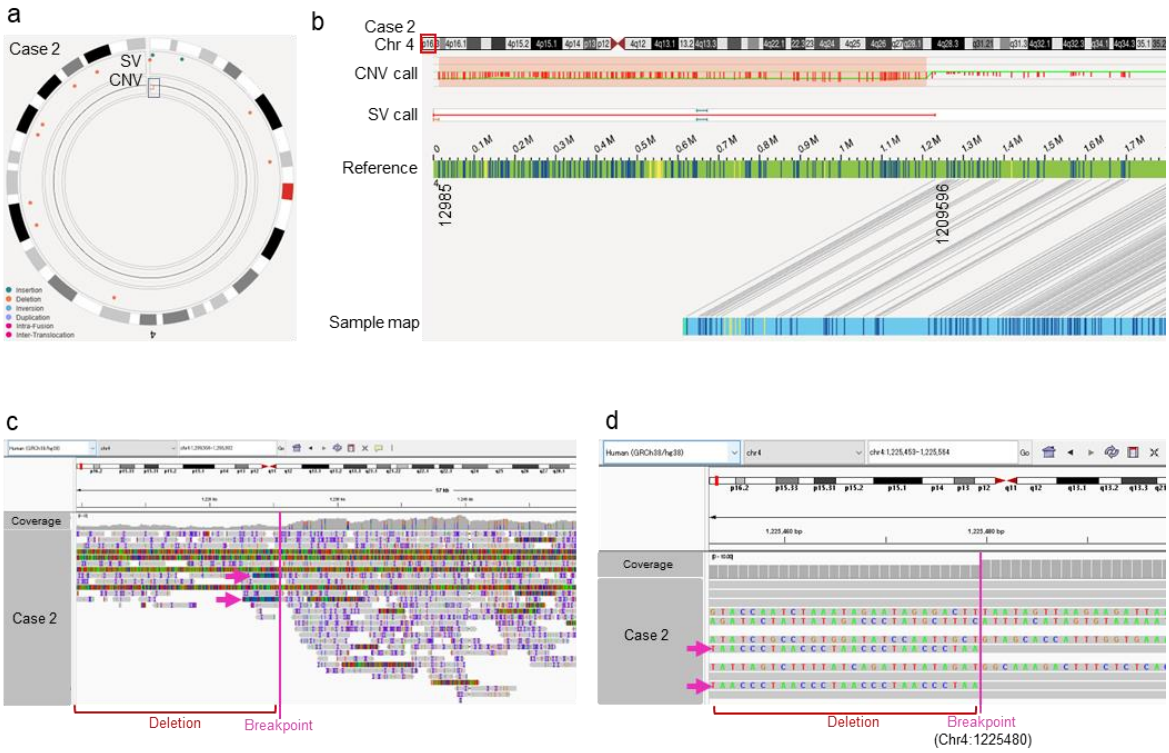


Fig. S3. Results of OGM and long-read sequencing in Case 2. (a) Circos plot of OGM shows a deletion as a red line in the CNV track of Chr 4. (b) OGM results in the genome browser. A large deletion in Chr 4 is visualized as a red bar in the CNV and SV call tracks. (c) IGV of long-read sequencing data in Chr 4. The breakpoint of a deletion downstream is shown as a pink line. Two soft-clipped reads from a deletion upstream are shown by pink arrows. A deletion in Chr 4 is illustrated as lower coverage upstream of the breakpoint. (d) Enlarged view of the breakpoint at Chr 4 in IGV. Two soft-clipped reads (pink arrows) show repetitive telomeric sequences (CCCTAA), indicating that this deletion is located at the terminal of the short arm of Chr 4. Molecular karyotype is described in Table S4. Chr, chromosome; CNV, copy number variant; IGV, Integrative Genomics Viewer; OGM, optical genome mapping; SV, structural variant.

Fig. S4

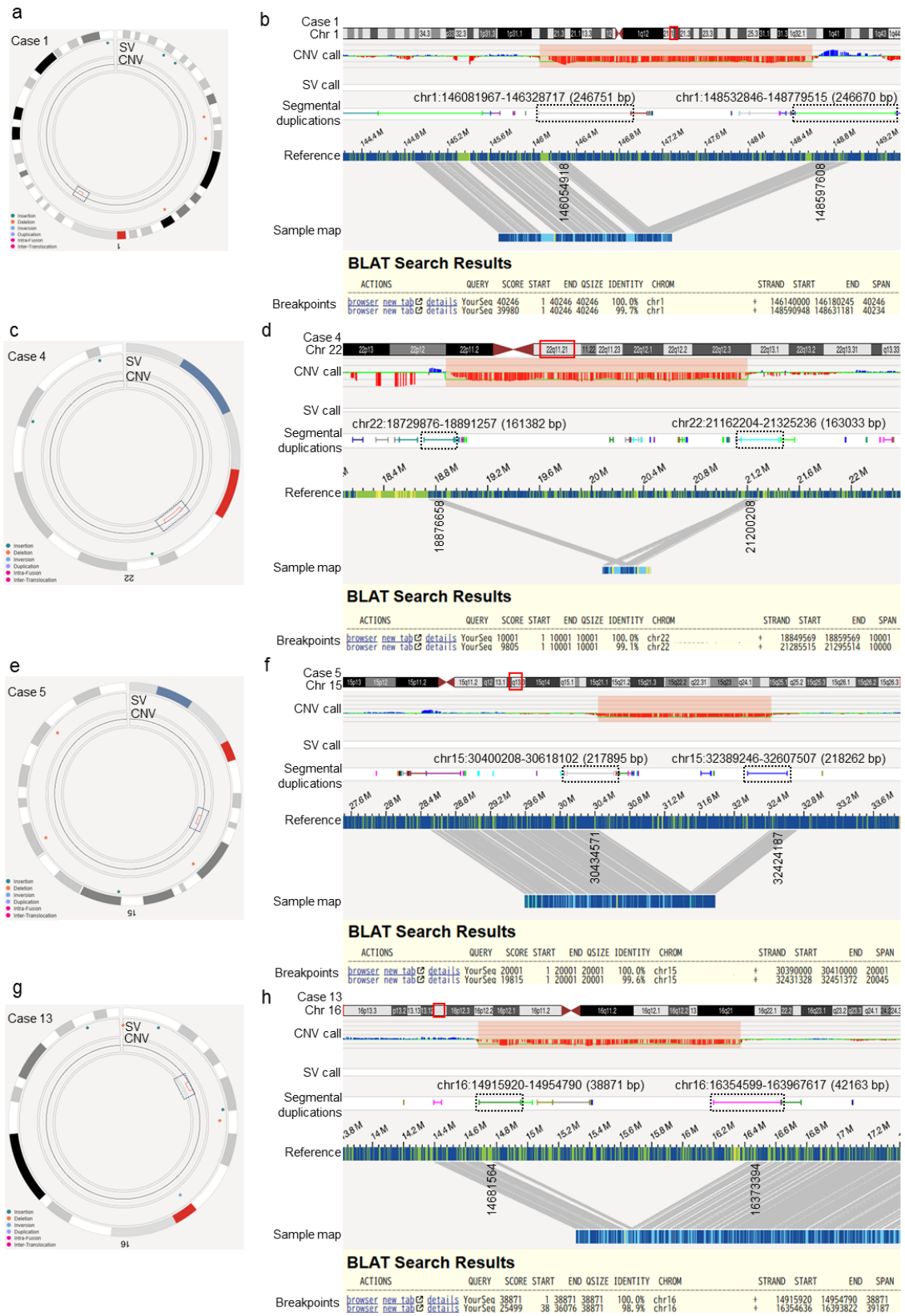

a
Case 1
SV
CNV
b
Case 1
Chr 1
CNV call
SV call
Segmental duplications
chr1:146081967-146328717 (246751 bp)
chr1:148532846-148779515 (246670 bp)
Reference
146054918
148597608
Sample map
BLAT Search Results
Breakpoints
c
Case 4
SV
CNV
d
Case 4
Chr 22
chr22:18729876-18891257 (161382 bp)
chr22:21162204-21325236 (163033 bp)
18876658
21200208
e
Case 5
SV
CNV
f
Case 5
Chr 15
chr15:30400208-30618102 (217895 bp)
chr15:32389246-32607507 (218262 bp)
30434571
32424187
g
Case 13
SV
CNV
h
Case 13
Chr 16
chr16:14915920-14954790 (38871 bp)
chr16:16354599-16396761 (42163 bp)
14681564
16373394

Fig. S4. Results of OGM in Cases 1 (a, b), 4 (c, d), 5 (e, f), and 13 (g, h). (a, c, e, g) Circos plot of OGM shows deletions as red lines in the CNV track of each chromosome. (b, d, f, h) Upper diagrams show OGM results in the genome browser. Large deletions are visualized as red bars in the CNV call track. Both ends of each deletion overlap with segmental duplications shown in the segmental duplications call track. The regions and sizes of segmental duplications are shown in the segmental duplications call track, and segmental duplications in each case are directly oriented within the same chromosomes. Lower diagrams show BLAT search results in the UCSC Genome Browser. Each result shows high sequence identity between two segmental duplications in each case. IDENTITY indicates the sequence identity, STRAND indicates the direction of sequences, START and END indicates the position of sequences, and SPAN indicates the size of sequences. Molecular karyotypes in the four cases are described in Table S4. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

Fig. S5

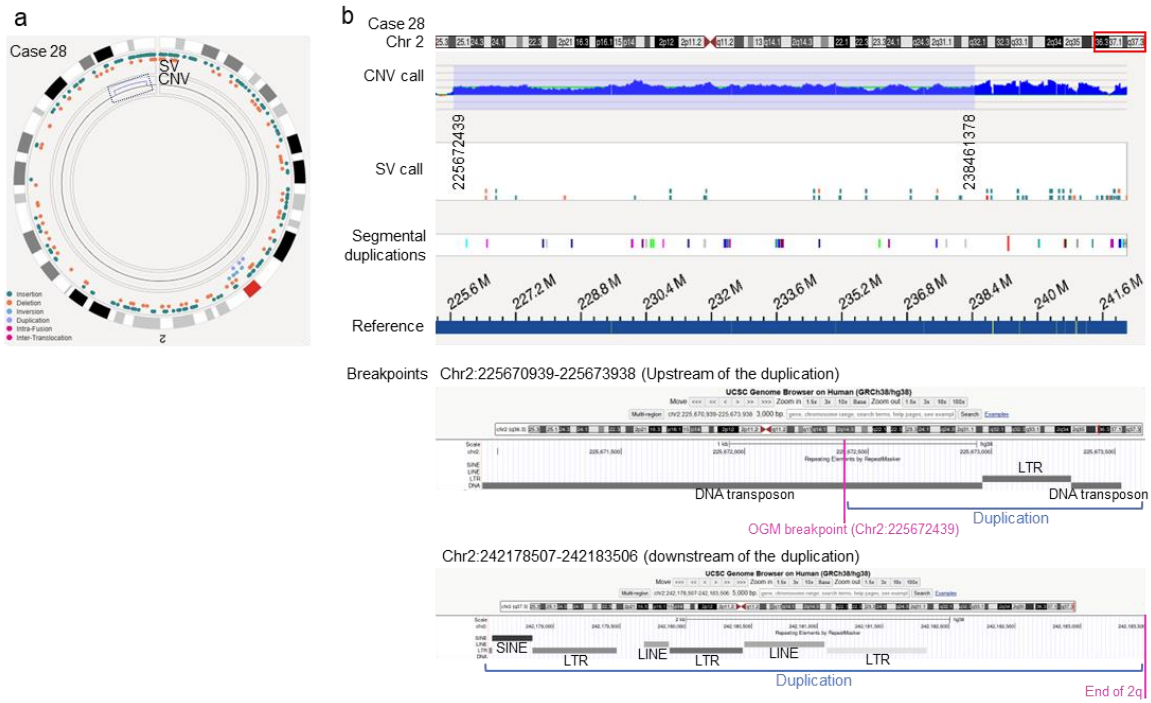
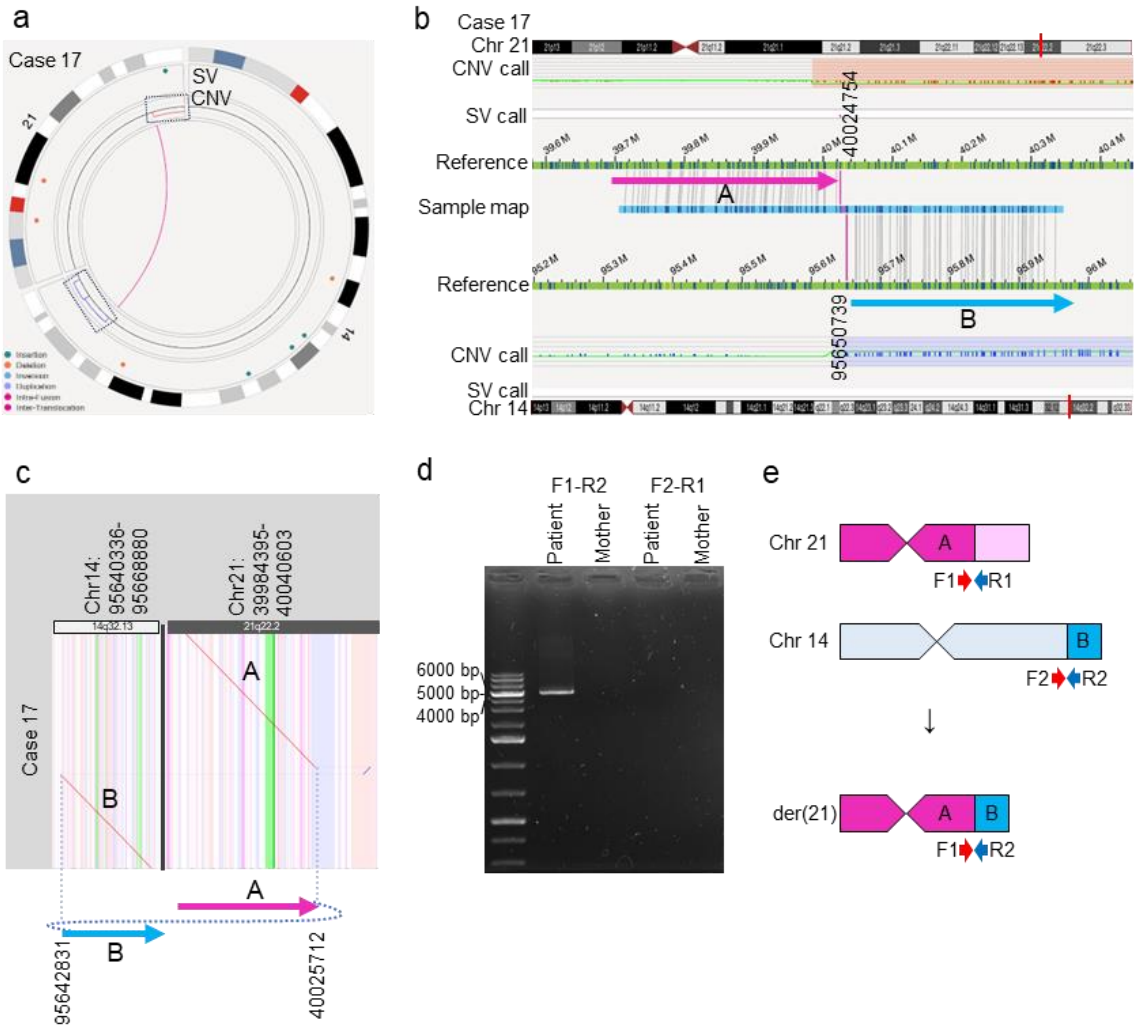


Fig. S5. Results of OGM in Case 28. (a) Circos plot of OGM shows a duplication as a blue line in the CNV track of Chr 2. (b) Upper diagram shows the OGM result in the genome browser. A large duplication is visualized as a blue bar in the CNV call track; the CNV call of the telomere region at the long arm of Chr 2 is not shown despite copy number gains of 2.47–4.04. The types and sizes of repeat sequences at the breakpoint and its surrounding regions are shown in the UCSC Genome Browser of the lower diagram. Both end regions of a duplication contain repetitive sequences. Molecular karyotype is described in Table S4. Chr, chromosome; CNV, copy number variant; LINE, long interspersed nuclear elements; LTR, long terminal repeat; OGM, optical genome mapping; SINE, short interspersed nuclear elements; SV, structural variant.

Fig. S6


a
Case 17
SV
CNV
b
Case 17
Chr 21
CNV call
SV call
40024754
Reference
Sample map
A
Reference
95650739
B
CNV call
SV call
Chr 14
c
Chr14: 95640336-95668880
Chr21: 39984395-40040603
Case 17
A
B
A
B
95642831
40025712
d
F1-R2
F2-R1
Patient
Mother
Patient
Mother
6000 bp
5000 bp
4000 bp
e
Chr 21
A
F1
R1
Chr 14
B
F2
R2
der(21)
A
B
F1
R2

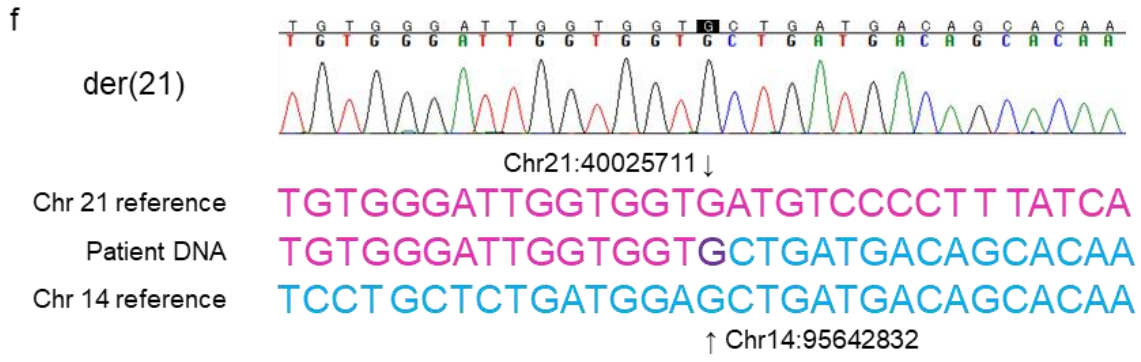

f
der(21)
Chr21:40025711
Chr 21 reference
TGTGGGATTGGTGGTGATGTCCCCTTTATCA
Patient DNA
TGTGGGATTGGTGGTGCTGATGACAGCACAA
Chr 14 reference
TCCTGCTCTGATGGAGCTGATGACAGCACAA
Chr14:95642832

Fig. S6. Results of OGM and long-read sequencing in Case 17. (a) Circos plot of OGM shows unbalanced reciprocal translocation between Chr 21 and 14. (b) OGM results in the genome browser. A large deletion in Chr 21 is visualized as a red bar and a large duplication in Chr 14 is visualized as a blue bar in the CNV call track. Translocation breakpoints are shown in purple on the sample map between two matching chromosomes. (c) Dot-plot of the consensus sequence from long-read sequencing data. (d) Electrophoresis image of PCR products. (e) Schematic presentation of translocation and PCR primers. (f) Sanger sequencing electropherograms of breakpoints. Translocation breakpoint sequence (middle line) and matching reference sequences (top and bottom lines) are shown in pink (Chr 21) and sky blue (Chr 14). A common single nucleotide G between Chr 14 and 21 at breakpoint is shown in purple. Molecular karyotype is described in Table S4. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; PCR, polymerase chain reaction; SV, structural variant.

Fig. S7

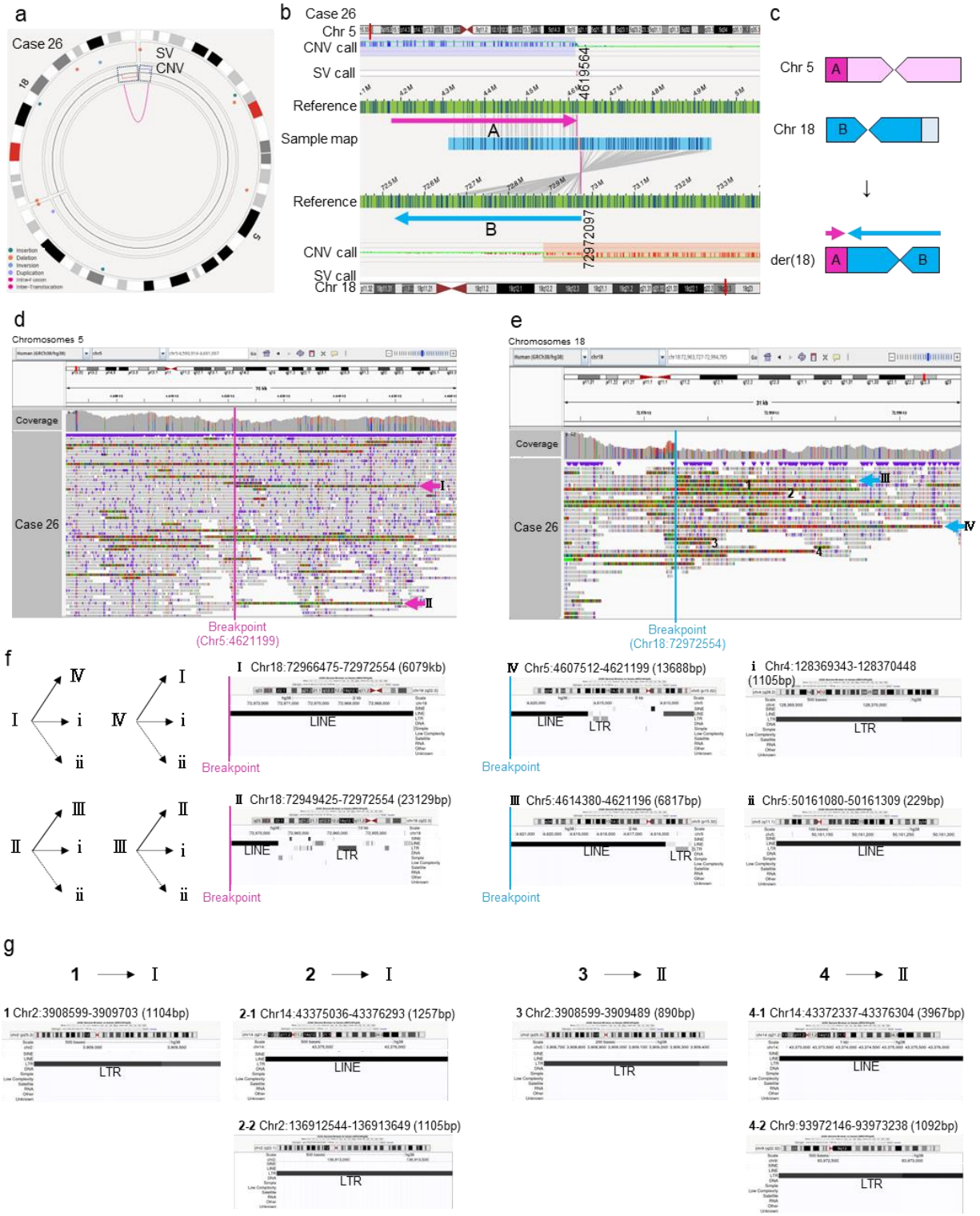

a
Case 26
SV
CNV
b
Case 26
Chr 5
CNV call
SV call
Reference
Sample map
Reference
CNV call
SV call
Chr 18
46195564
72972097
A
B
c
Chr 5
Chr 18
der(18)
d
Chromosomes 5
Coverage
Case 26
Breakpoint
(Chr5:4621199)
e
Chromosomes 18
Coverage
Case 26
Breakpoint
(Chr18:72972554)
f
I Chr18:72966475-72972554 (6079kb)
Breakpoint
Ⅳ Chr5:4607512-4621199 (13688bp)
Breakpoint
i Chr4:128369343-128370448
(1105bp)
Ⅱ Chr18:72949425-72972554 (23129bp)
Breakpoint
Ⅲ Chr5:4614380-4621196 (6817bp)
Breakpoint
ii Chr5:50161080-50161309 (229bp)
g
1 → I
2 → I
3 → Ⅱ
4 → Ⅱ
1 Chr2:3908599-3909703 (1104bp)
2-1 Chr14:43375036-43376293 (1257bp)
2-2 Chr2:136912544-136913649 (1105bp)
3 Chr2:3908599-3909489 (890bp)
4-1 Chr14:43372337-43376304 (3967bp)
4-2 Chr9:93972146-93973238 (1092bp)

Fig. S7. Results of OGM and long-read sequencing in Case 26. (a) Circos plot of OGM shows unbalanced reciprocal translocation between Chr 5 and 18. (b) OGM results in the genome browser. A large duplication in Chr 5 is shown as a blue bar and a large deletion in Chr 18 is visualized as a red bar in the CNV call track. Translocation breakpoint is shown in purple on the sample map between two matching chromosomes. (c) Scheme of translocation. (d) IGV of long-read sequencing data in Chr 5. The breakpoint of translocation is shown as a pink line. Two soft-clipped reads (pink arrows; I and II) show translocation to Chr 18. Duplication in Chr 5 is illustrated as slightly higher coverage upstream of the breakpoint. (e) IGV of long-read sequencing data in Chr 18. The breakpoint of translocation is shown as a sky blue line. Two soft-clipped reads (blue arrows; III and IV) show translocation to Chr 5 and four soft-clipped reads (1–4) are aligned to other chromosomes. A deletion in Chr 18 is illustrated as lower coverage downstream of the breakpoint. (f) Left diagrams indicate the relationship between four soft-clipped reads (I–IV) shown in (d and e) and the aligned regions (i and ii) from four soft-clipped reads. All four soft-clipped reads (I–IV) also map to i and ii, aligned to other chromosomes unrelated to the translocation. The types and sizes of repeat sequences in the regions of supplementary alignments are shown in the UCSC Genome Browser in the right diagrams. (g) Upper tree diagrams of supplementary alignment reads (1–4) of Chr 18 from the IGV in (e). Supplementary alignment reads 1 and 2 mapped to soft-clipped read I, and supplementary alignment reads 3 and 4 mapped to soft-clipped read II of Chr 5. In addition, the IGV information indicated that alignment read 2 included sequences 2-1 and 2-2 and supplementary alignment read 4 included sequences 4-1 and 4-2. Lower diagrams show the regions of supplementary alignments (1, 2-1, 2-2, 3, 4-1, and 4-2) in the UCSC Genome Browser. Molecular karyotype is described in Table S4. Chr, chromosome; CNV, copy number variant; IGV, Integrative Genomics Viewer; LINE, long interspersed nuclear elements; LTR, long terminal repeat; OGM, optical genome mapping; SV, structural variant.

Fig. S8

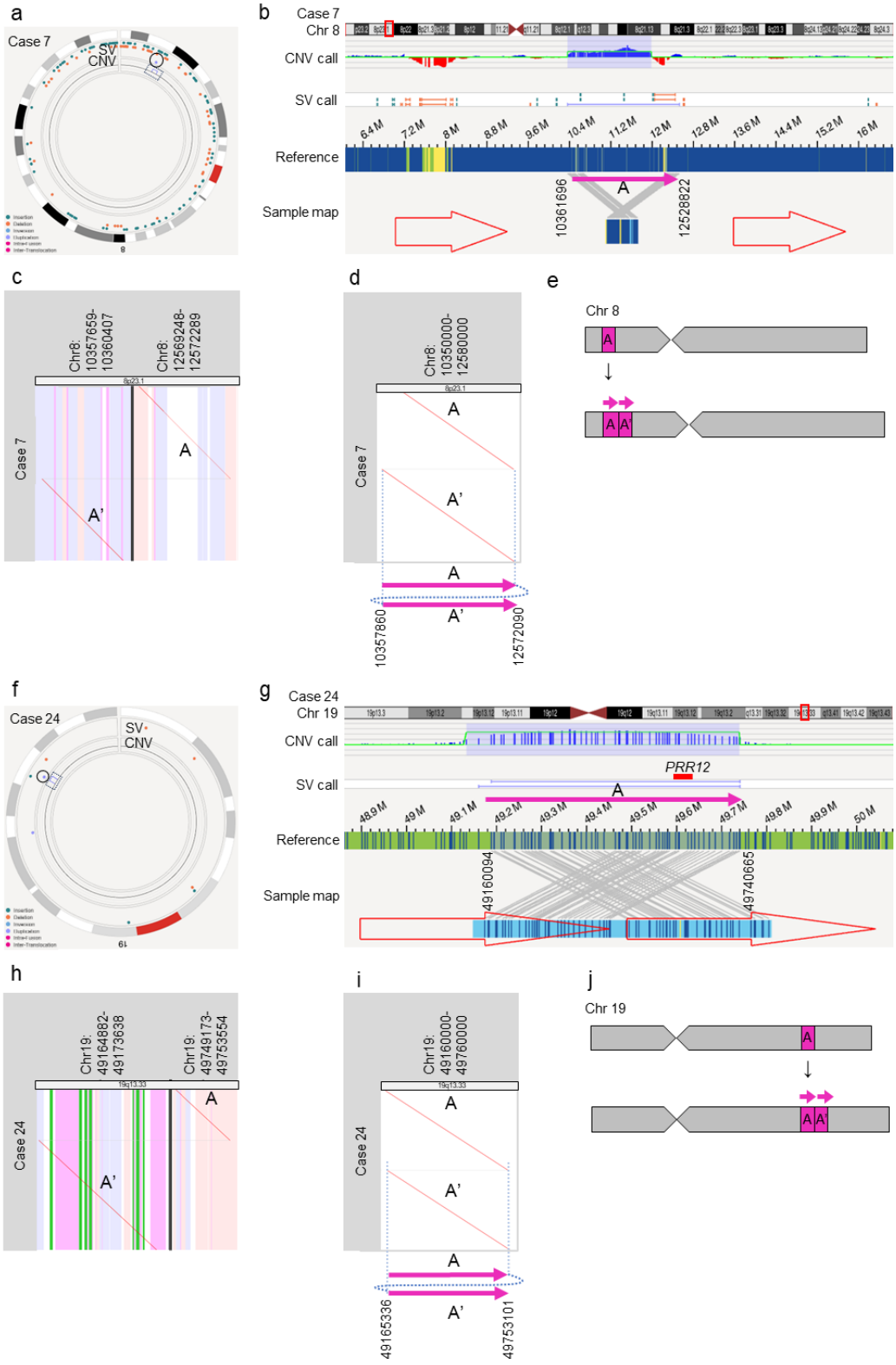

a
Case 7
SV
CNV
b
Case 7
Chr 8
CNV call
SV call
Reference
Sample map
6.4M
7.2M
8M
8.8M
9.6M
10.4M
11.2M
12M
12.8M
13.6M
14.4M
15.2M
16M
10361696
12528822
A
c
Chr8: 10357659-10360407
Chr8: 12569248-12572269
Case 7
A
A'
d
Chr8: 10350000-12580000
Case 7
A
A'
A
A'
10357860
12572090
e
Chr 8
A
A
A'
f
Case 24
SV
CNV
g
Case 24
Chr 19
CNV call
SV call
PRR12
A
Reference
Sample map
48.9M
49M
49.1M
49.2M
49.3M
49.4M
49.5M
49.6M
49.7M
49.8M
49.9M
50M
49160094
49740665
h
Chr19: 49164882-49173638
Chr19: 49749173-49753554
Case 24
A
A'
i
Chr19: 49160000-49760000
Case 24
A
A'
A
A'
49165336
49753101
j
Chr 19
A
A
A'

Fig. S8. Results of OGM and long-read sequencing in Cases 7 (a–e) and 24 (f–j) with tandem duplications. (a) Duplication is indicated as a purple dot in the SV track and a blue line in the CNV track of the Circos plot. There are more SV calls than in other cases because of duplication in the SV track that was not called unless the default filter setting was removed. (b) A large duplication is visualized as a blue bar in the CNV call track and a blue line in the SV call track in the genome browser. Arrow A indicates that the map has a forward orientation to the reference genome. Copy number loss located immediately downstream of a tandem duplication is shown by a red line in the SV call track and was confirmed to be different from the duplication allele using Bionano Access. (c) Dot-plot of the consensus sequence from long-read sequencing data. (d) Dot-plot containing a tandem duplication region created from long-read sequencing data using dnarrange. (e) Scheme of tandem duplication. (f) Duplication is indicated as a purple dot in the SV track and a blue line in the CNV track of the Circos plot. (g) A large duplication is visualized as a blue bar in the CNV call track and a blue line in the SV call track in the genome browser. *PRR12* was located in the duplication as a possible causative gene in Case 24. (h) Dot-plot of the consensus sequence from long-read sequencing data. (i) Dot-plot containing a tandem duplication region created from long-read sequencing data using dnarrange. (j) Scheme of tandem duplication. Molecular karyotypes in the two cases are described in Table S4. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

Fig. S9

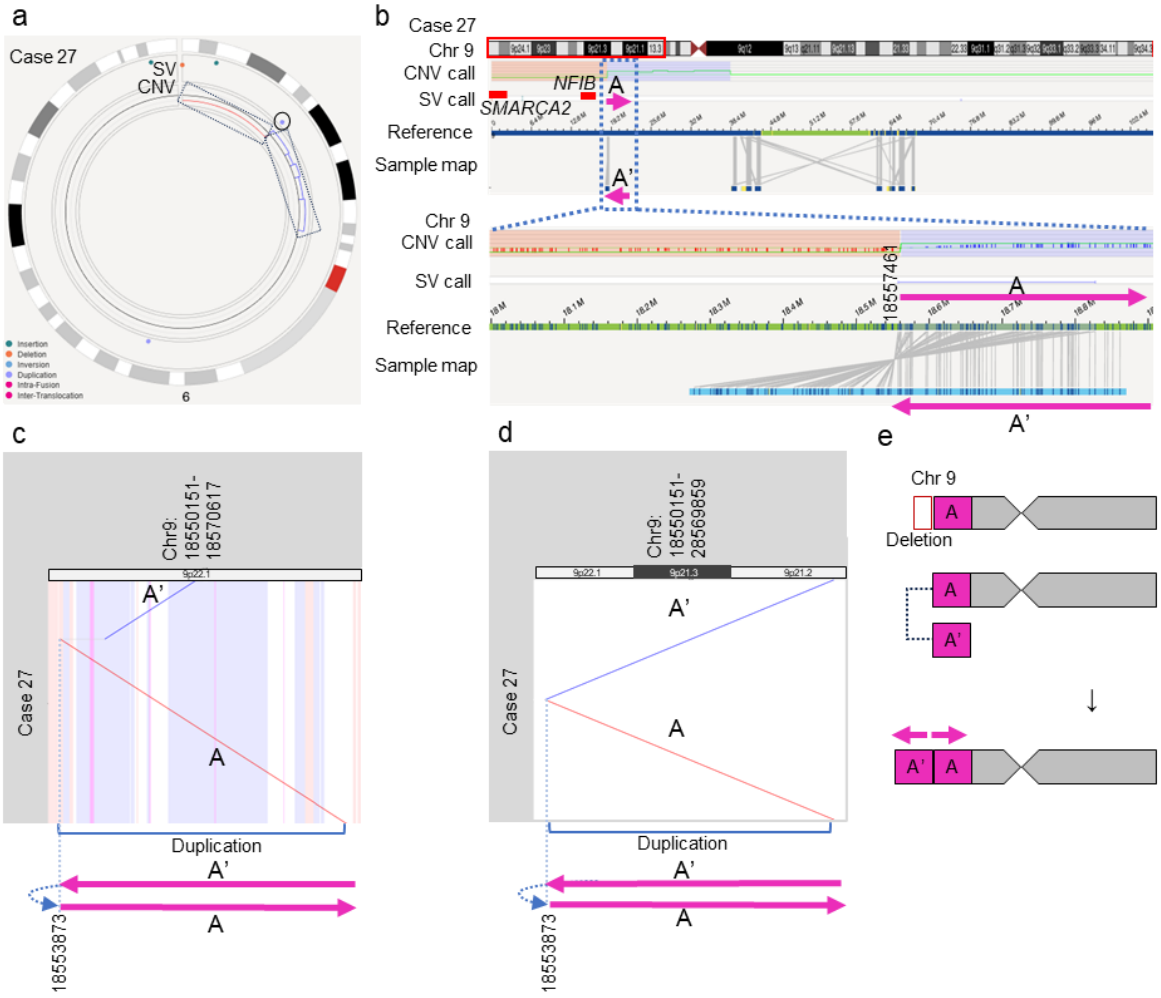


Fig. S9. Results of OGM and long-read sequencing in Case 27. (a) Circos plot of Chr 9 shows deletion and duplication as red and blue lines, respectively, in the CNV track; duplication is indicated as a purple dot in the SV track. (b) The entire Chr 9 (upper diagram) and its enlargement within the dotted square (lower diagram) in the genome browser. Large deletions and duplications are visualized as red and blue bars, respectively, in the CNV call track. An inverted duplication is indicated by a blue line in the SV call track and is shown in the sample map below. *NFIB* and *SMARCA2* were located in the deletion. (c) Dot-plot of the consensus sequence from long-read sequencing data. (d) Dot-plot containing the inverted duplication region created from long-read sequencing data using dnarrange. (e) Scheme of inverted duplication. Molecular karyotype is described in Table S4. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

Fig. S10

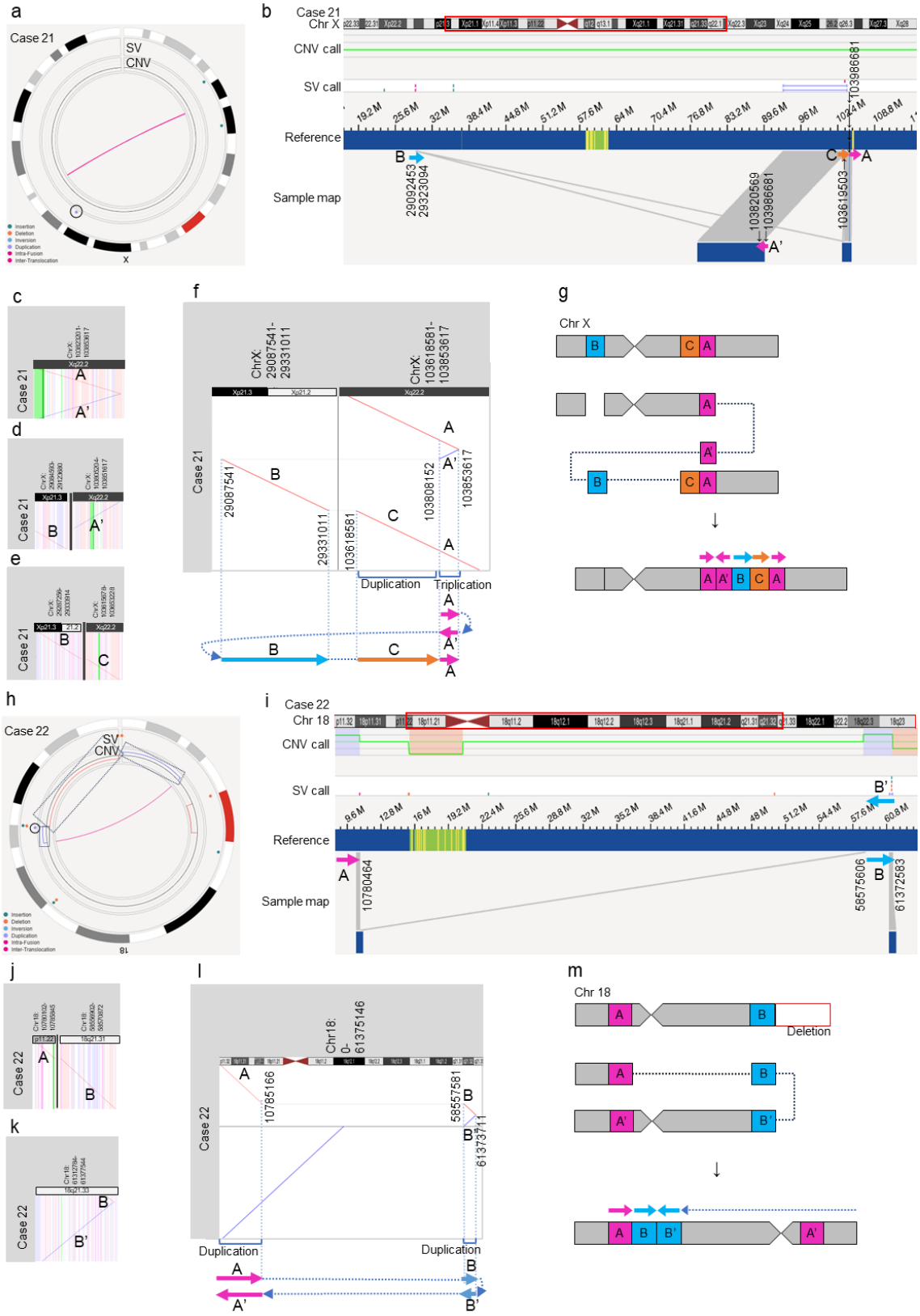
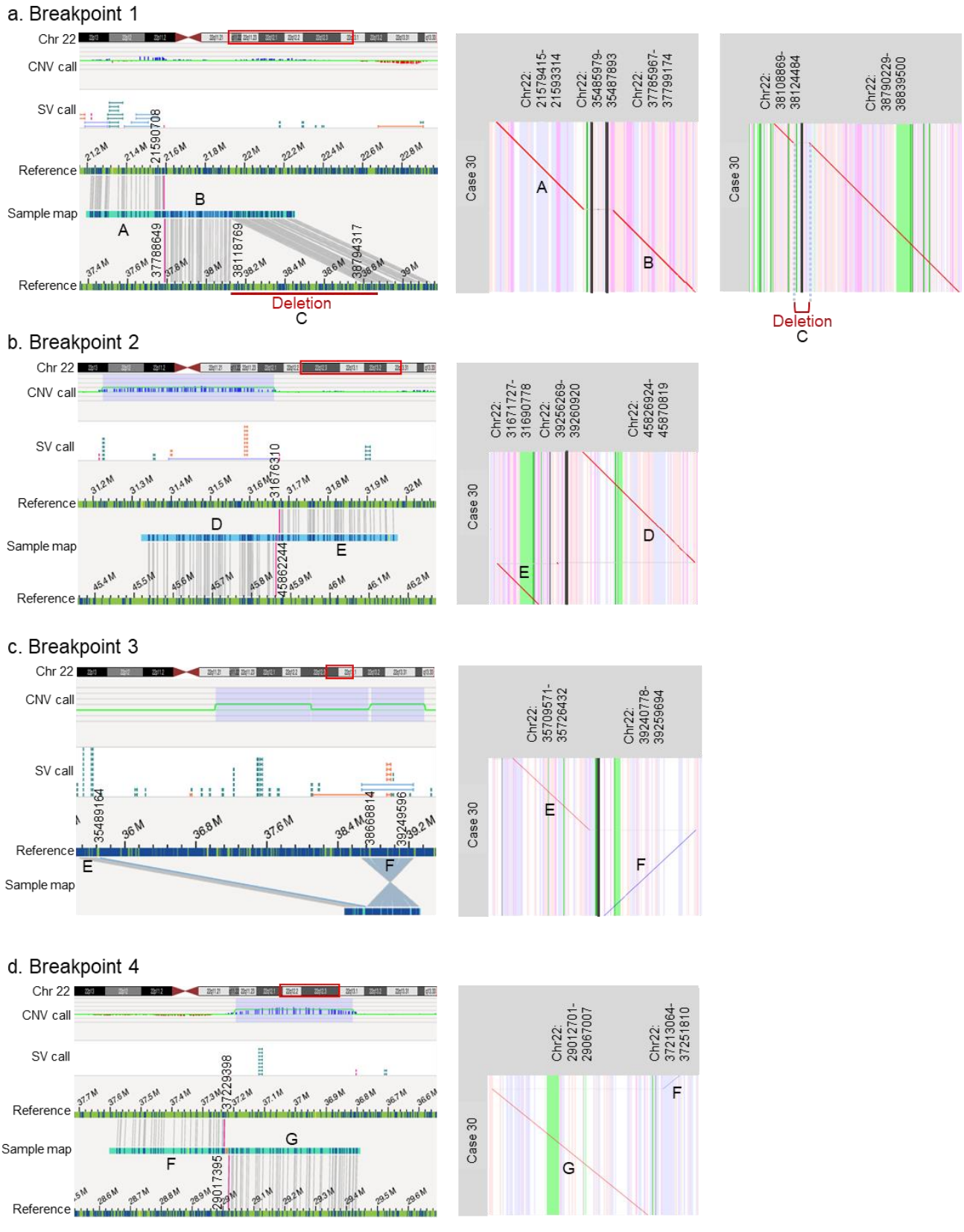
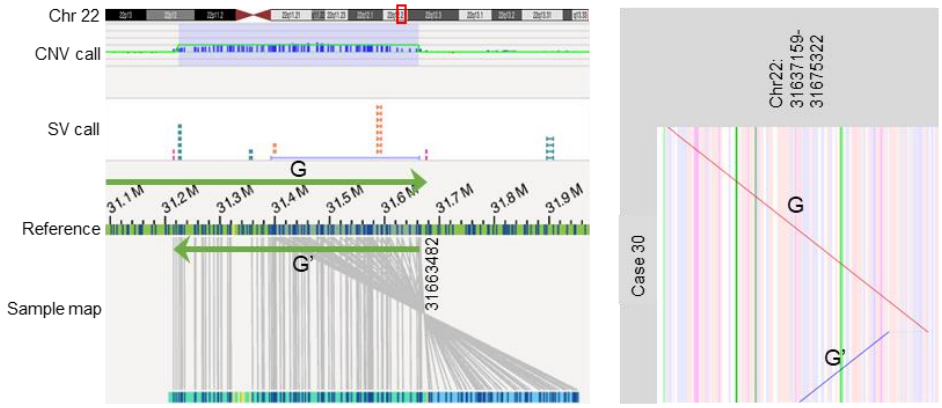

a
Case 21
SV
CNV
b
Case 21
Chr X
CNV call
SV call
Reference
Sample map
c
d
e
f
Duplication
Triplication
g
Chr X
h
Case 22
i
Case 22
Chr 18
j
k
l
Duplication
Duplication
m
Chr 18
Deletion

Fig. S10. Results of OGM and long-read sequencing in Cases 21 (a–g) and 22 (h–m). (a) Circos plot in Chr X shows two intrachromosomal translocations, indicated by two magenta lines, and a small duplication, visualized as a purple dot, in the SV track. (b) Inverted duplication is visualized as a blue line in the SV call track of the genome browser. Arrows A and A' indicate inverted duplication, and arrows A', B, and C indicate two intrachromosomal translocations. (c–e) Dot-plots of the consensus sequence from long-read sequencing data. (f) Dot-plot containing inverted duplication and intrachromosomal translocation regions created from long-read sequencing data using dnarrange. (g) Scheme of SVs. **(**h) Circos plot in Chr 18 shows an intrachromosomal translocation indicated by a magenta line, large duplications and deletions visualized as blue and red lines, respectively, in the CNV track, and a small duplication shown as a purple dot in the SV track at the edge of the large duplication. (i) Large duplications and deletions are visualized as blue and red squares, respectively, in the CNV call track, and an inverted duplication is visualized as a blue line in the SV call track of the genome browser. Arrows A and B indicate intrachromosomal translocation, and arrows B and B' indicate inverted duplication. (j and k) Dot-plots of the consensus sequence from long-read sequencing data. (l) Dot-plot containing the inverted duplication and intrachromosomal translocation regions created from long-read sequencing data using dnarrange. (m) Scheme of SVs. Molecular karyotypes in the two cases are described in Table S4. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

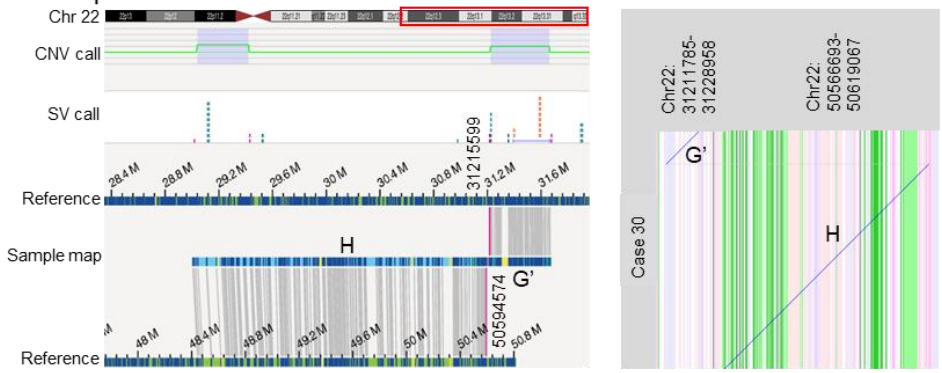
Fig. S11


a. Breakpoint 1
Chr 22
CNV call
SV call
Reference
Sample map
Reference
Deletion
C
Chr22: 21579415-21593314
Chr22: 35485979-35487893
Chr22: 37785967-37799174
Chr22: 38108869-38124484
Chr22: 38790229-38839500
Case 30
A
B
b. Breakpoint 2
D
E
c. Breakpoint 3
F
d. Breakpoint 4
G

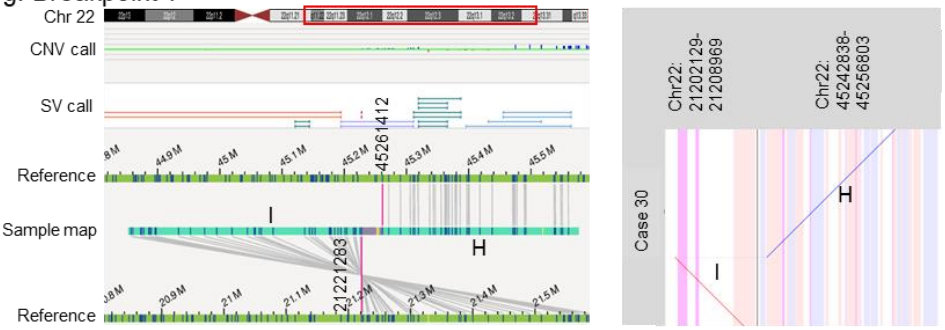
e. Breakpoint 5



f. Breakpoint 6



g. Breakpoint 7



h. Breakpoint 8

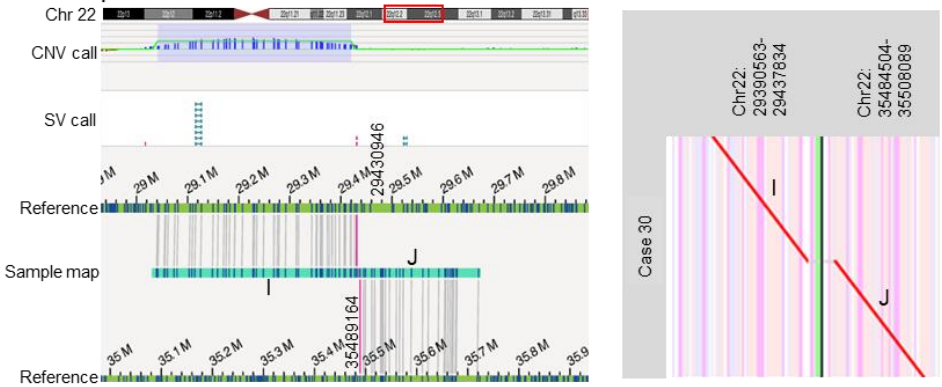


Fig. S11. Results of OGM and long-read sequencing in Case 30. Left diagrams are the genome browser in Chr 22; large duplications are visualized as blue bars in the CNV call track. Right diagrams are dot-plots of the consensus sequence from long-read sequencing data. The numbers and letters in each figure correspond to those in Fig. 5b and 5c. (a, b, d, f, g, and h) At breakpoints 1, 2, 4, 6, 7, and 8 in the genome browsers, intrachromosomal translocation breakpoints are shown in the region on the sample map between two matching references of Chr 22. (a) This region includes the deletion shown in C. (c) Inversion is visualized as blue lines in the SV call track. (e) Inverted duplication is indicated by a blue line in the SV call track and is shown below in the sample map. Chr, chromosome; CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

Table S1. DNA molecule quality of OGM.

Case	Saphyr	Molecule N50 (kbp) [value: >230]	Label density (/100kb) [value: 14–17]	Effective coverage of reference (×) [value: >80]
1	109	267.422	16.391	105.918
2	110	286.442	16.04	112.024
3	111	278.008	16.216	110.273
4	112	273.603	16.008	96.439
5	115	369.813	15.645	106.249
6	116	390.251	16.213	117.724
7	117	448.098	16.878	121.303
8	118	440.497	16.983	121.454
9	119	418.941	16.953	121.765
10	120	452.298	16.901	123.217
11	121	396.177	15.502	109.128
12	122	403.824	15.866	109.483
13	123	404.708	16.597	113.798
14	124	402.528	16.19	117.646
15	125	469.351	16.51	117.494
16	133	452.828	16.256	112.756
17	134	436.898	16.426	130.299
18	135	410.239	16.594	119.932
19	136	301.874	15.993	103.262
20	137	267.422	16.391	105.918
21	138	286.442	16.04	112.024
22	139	278.008	16.216	110.273
23	140	273.603	16.008	96.439
24	141	369.813	15.645	106.249
25	142	390.251	16.213	117.724
26	143	448.098	16.878	121.303
27	144	440.497	16.983	121.454
28	145	418.941	16.953	121.765
29	147	396.177	15.502	109.128
30	14	403.824	15.866	109.483

OGM, optical genome mapping.

Table S2. Read coverage of targeted long-read sequencing using adaptive sampling with GridION.

Case	Saphyr	Target region of adaptive sampling (GRCh38/hg38)				Mean depth
		Chr	Start position	End position	Target region size (bp)	
1	109	1	144179918 146722608	147929918 150472608	7500000	12.62×
2	110	4	1	7500000	7500000	15.87×
3	111	8	114617663 124652331	118367663 128402331	7500000	14.21×
4	112	22	17001658 19325208	20751658 23075208	7500000	27.51×
5	115	15	28559571 30549187	32309571 34299187	7500000	20.39×
6	116	21	38544399	46044399	7500000	23.13×
7	117	8	7695259	15195259	7500000	11.72×
8	118	7	70064977 85335944	73814977 89085944	7500000	16.31×
9	119	6	64037218 78842030	67787218 82592030	7500000	20.83×
10	120	17	1 536268	3750000 4286268	7500000	13.01×
11	121	X	4591265 6288693	8341265 10038693	7500000	6.10×
12	122	2	183429800 201498928	187179800 205248928	7500000	18.87×
13	123	16	12806564 14498394	16556564 18248394	7500000	18.13×
14	124	19	9576325 11574394	13326325 15324394	7500000	10.59×
15	125	1 17	1956717 2081287	5456717 5581287	7500000	28× 41.14×
16	133	8	74715158 79618492	78465158 83368492	7500000	15.72×
17	134	14 21	93900739 38274754	97400739 41774754	7500000	28.58× 16.65×

18	135	2	161970538	169470538	7500000	24.53×
19	136	19	52578746 54082898	56328746 57832898	7500000	7.55×
20	137	X	95604335 104251620	99104335 108035726	7284106	34.47×
21	138	X	28123094 91736405 102419503	30523094 94136405 105186681	7567178	26.07×
22	139	18	57375606 9580464	62572583 11980464	7596977	35.79×
23	140	9	10623459	18392814	7769355	30.48×
24	141	19	45560094	53340665	7780571	31.60×
25	142	1	91225823 109446763	94975823 113196763	7500000	9.14×
26	143	18	71122097	74822097	7400000	30.21×
		5	2769564	6469564		47.38×
27	144	9	14807461	22577498	7770037	33.51×
28	145	2	223797439 236586378	227547439 240336378	7500000	54.42×
29	147	12	70420270 77201558	73006564 78886157	7539944	31.83×
		14	83632163	86901214		34.14×
30	14	22	21161283	50654574	29493291	26.97×

Chr, chromosome.

Table S3. Gene list in SVs detected by OGM.

Table S3 is shown separately in an Excel file. pHaplo scores ≥ 0.86 or pTriplo scores ≥ 0.94 denote an odds ratio ≥ 2.7, which indicates that the average effect sizes of the deletion or duplication are equivalent in strength to the loss-of-function of genes constrained by protein-truncating variants (Karczewski et al., 2020). Genes with copy number aberrations identified by OGM associated with clinical features in respective cases are colored in red, and ones previously identified by ES are underlined. CNV, copy number variant; OGM, optical genome mapping; SV, structural variant.

Table S4. Karyotype list identified using OGM with long-read sequencing.

Case	**Karyotype**
1	46,XY.ogm[GRCh38]del(1)(q21.1q21.2)(146,054,918_148,597,608)
2	46,XY.ogm[GRCh38]del(4)(pterp16.3)(pter_1,225,480), seq[GRCh38]del(4)(pterp16.3) NC_000004.12:g.1_1,225,480del
3	46,XY.ogm[GRCh38]del(8)(q23.3q24.21)(116,494,154_126,506,598), seq[GRCh38]del(8)(q23.3q24.21) NC_000008.11:g.116,494,154_126,506,598del
4	46,XX.ogm[GRCh38]del(22)(q11.21q11.21)(18,876,658_21,200,208)
5	46,XX.ogm[GRCh38]del(15)(q13.2q13.3)(30,434,571_32,424,187)
6	46,XY.ogm[GRCh38]der(21)(pter_q22.3::q22.3_q22.3::q22.3_q22.2)(pter_39,279,216::45,493,272_41,467,830::41,467,830_39,279,216), seq[GRCh38]der(21) NC_000021.9:g.1_39,279,216delins[39,279,216_41,467,830inv]
7	46,XY.ogm[GRCh38]dup(8)(p23.1)(10,357,860_12,572,090), seq[GRCh38] dup(8)(p23.1) NC_000008.11:g.10,357,860_12,572,090dup
8	46,XY.ogm[GRCh38]del(7)(q11.22q21.12)(71,949,757_87,202,195), seq[GRCh38]del(7)(q11.22q21.12) NC_000007.14:g.71,949,757_87,202,195del
9	46,XY.ogm[GRCh38]del(6)(q12q14.1)(65,946,371_80,652,635), seq[GRCh38]del(6)(q12q14.1) NC_000006.12:g.65,946,371_80,652,635del
10	46,XX.ogm[GRCh38]del(17)(p13.3p13.3)(957,506_2,408,537), seq[GRCh38]del(17)(p13.3p13.3) NC_000017.11:g.957,506_2,408,537del
11	46,XY.ogm[GRCh38]del(X)(p22.31p22.31)(6,533,591_8,169,074), seq[GRCh38]del(X)(p22.31p22.31) NC_000023.11:g.6,533,591_8,169,074del
12	46,XX.ogm[GRCh38]del(2)(q32.1q33.2)(185,302,763_203,371,636), seq[GRCh38]del(2)(q32.1q33.2) NC_000002.12:g.185,302,763_203,371,636del
13	46,XY.ogm[GRCh38]del(16)(p13.12p13.11)(14,681,564_16,373,394)

14	46,XY.ogm[GRCh38]del(19)(p13.2p13.13)(11,498,892_13,309,177), seq[GRCh38]del(19)(p13.2p13.13) NC_000019.10:g.11,498,892_13,309,177del
15	46,XX.ogm[GRCh38]der(1)(17pter_p13.2::1p36.32_1qter)(17pter_3,847,652:: 3,699,571_1qter), seq[GRCh38] NC_000001.11:g.3,699,571_qterdelins[NC_000017.11:g.pter_3,847,652]
16	46,XY.ogm[GRCh38]del(8)(q21.13q21.13)(76,598,298_81,428,940), seq[GRCh38]del(8)(q21.13q21.13) NC_000008.11:g.76,598,298_81,428,940del
17	46,XY.ogm[GRCh38]der(21)(21pter_21q22.2::14q32.13_14qter)(21pter_40,025,712::95,642,831_14qter), seq[GRCh38]der(21)t(21;14)(q22.2;q32.13) NC_000021.9:g.pter_40,025,712delins[NC_000014.9:g.95,642,831_qter]
18	46,XX.ogm[GRCh38]dup(2)(q24.3)(164,975,946_166,466,854), seq[GRCh38]dup(2)(q24.3) NC_000002.12:g.164,975,946_166,466,854dup
19	46,XY.ogm[GRCh38]del(19)(q13.42q13.43)(54,461,012_55,947,282), seq[GRCh38]del(19)(q13.42q13.43) NC_000019.10:g.54,461,012_55,947,282del
20	46,XX.ogm[GRCh38]der(X)(pter_q22.3::q22.3_q21.33::q22.3_qter)(pter_105,883,789::105,883,789_97,351,663::106,277,461_qter), seq[GRCh38]der(X) NC_000023.11:g. pter_105,883,789delins97,351,663_105,883,789inv105,883,790_106,277,460del106,277,461_qter
21	46,XY.ogm[GRCh38]der(X)(pter_p21.3::p21.2_q22.2::q22.2_q22.2::p21.3_p21.2::q22.2_pter)(pter_29,087,541::29,331,011_103,853,617 ::103,853,617_103,808,152::29,087,541_29,331,011::103,618,581_pter), seq[GRCh38]der(X) NC_000023.11:g.29,087,541_29,331,011del NC_000023.11:g.1_103,853,617inv
22	46,XY.ogm[GRCh38]der(18)(pter_p11.22::q21.31_q21.33::q21.33_pter)(pter_10,785,166::58,557,581_61,373,711::61,373,711_pter), seq[GRCh38]NC_000018.10:g.10,785,166_10,785,167ins[58,557,581_61,373,711;61,373,711_pterinv]
23	46,XX.ogm[GRCh38]inv dup del(9)(:p22.3_p22.3::p22.3_qter)(14,373,459_14,369,157:: 14,369,157_qter), seq[GRCh38] inv dup del(9)(p22.3) NC_000009.12:g. 14,369,157_14,373,459delins[14,369,158_qterinvdup]
24	46,XX.ogm[GRCh38]dup(19)(q13.33)(49,165,336_49,753,101), seq[GRCh38]dup(19)(q13.33) NC_000019.10:g.49,165,336_49,753,101dup

25	46,XX.ogm[GRCh38]del(1)(p22.1p13.2)(93,106,498_111,329,159), seq[GRCh38]del(1)(p22.1p13.2) NC_000001.11:g.93,106,498_111,329,159del
26	46,XY.ogm[GRCh38]der(18)(5pter_5p15.32::18q22.3_18pter)(5pter_4,621,199::72,972,554_18pter), seq[GRCh38]der(18)t(5;18)(p15.32;q22.3) NC_000018.10:g.pter_72,972,554delins[NC_000005.10:g.pter_4,621,199inv] NC_000005.10:g.4,621,199_qterdelins[NC_000018.10:g.pter_72,972,554inv]
27	46,XX.ogm[GRCh38]inv dup del(9)(:p21.2_p22.1::p22.1_qter)(18,557,461_18,553,873::18,553,873_qter), seq[GRCh38]inv dup del(9)(p21.2p22.1) NC_000009.12:g.18,553,873_18,557,461delins[18,553,874_qterinvdup]
28	46,XY.ogm[GRCh38]del(2)(q36.3qter)(225,672,439_qter)
29	46,XX.ogm[GRCh38]der(12)(12pter_12q15::12q21.1_12q15::12q21.2_12q21.2::14q31.3_14q31.2inv::14q31.3_14qter)(12pter_70,917,324::72,511,491_70,917,440::78,304,150_78,382,960::86,404,434_84,172,309::86,404,426_14qter),der(14)(14pter_14q31.2::12q21.2_12q21.2inv::12q21.2_12qter)(14pter_84,135,076::78,382,967_78,304,148::77,696,122_12qter), seq[GRCh38]der(12) NC_000012.12:g.pter_70,917,324;72,511,491_70,917,440inv;78,304,150_78,382,960delins[NC_000014.9:g.86,404,434_84,172,309inv;86,404,426_qter],der(14) NC_000014.9:g.pter_84,135,076delins[NC_000012.12:g.78,382,967_78,304,148inv;77,696,122_qter]
30	46,XY.ogm[GRCh38]der(22)(pter_q11.21)(pter_21,592,378)::(q13.1_q13.1)(37,786,951_38,122,247)::(q13.1_q13.31)(38,792,466_45,868,639)::(q12.2_q12.3)(31,673,907_35,725,198)::(q13.1_q12.3inv)(39,258,460_37,216,272inv)::(q12.1_q12.2)(29,015,909_31,673,909)::(q12.2_q12.2invdup)(31,673,909_31,214,183invdup)::(q13.33_q13.31inv)(50,616,489_45,243,553inv)::(q11.21_q12.1)(21,202,844_29,435,389)::(q12.3_qter)(35,486,947_qter), seq[GRCh38] NC_000022.11:g.[pter_21,592,378;37,786,951_38,122,247;38,792,466_45,868,639;31,673,907_35,725,198;39,258,460_37,216,272inv;29,015,909_31,673,909;31,673,909_31,214,183invdup;50,616,489_15,243,553inv;21,202,844_29,435,389;35,486,947_qter]

OGM, optical genome mapping.

Table S5. Primer sequences used in Case 15.

Primer name	Location		Primer sequence (forward)	Primer name	Location		Primer sequence (reverse)	Product size (bp)
	Start	End			Start	End		
F1	Chr17: 3846937	Chr17: 3846946	AGTTTCCGGCGGATATTTCT	R1	Chr17: 3848331	Chr17: 3848350	TTCTGGATGGCACTGAACTG	1414
F2	Chr1: 3698911	Chr1: 3698930	CAGTCCTGCAGACACACGTC	R2	Chr1: 3700269	Chr1: 3700288	AGAGAAACCTGCCAGCAAAA	1378

Chr, chromosome.

Table S6. Primer sequences used in Case 17.

Primer name	Location		Primer sequence (forward)	Primer name	Location		Primer sequence (reverse)	Product size (bp)
	Start	End			Start	End		
F1	Chr21: 40022468	Chr21: 40022495	AACCAGGATAAGCAGTTGTACCCCTCAG	R1	Chr21: 40028934	Chr21: 40028961	ACAGCTAGATAATGCTGCCTGCTTTGTG	6494
F2	Chr14: 95641353	Chr14: 95641379	CCTTGTAAACCTGTTGTCTGGGCTTGT	R2	Chr14: 95644289	Chr14: 95644315	CTCTTGGGGTTCCCCACTTCTATTGAG	2963

Chr, chromosome.