

Supplemental Information

Zygotes segregate entire parental genomes in distinct blastomere lineages causing cleavage stage chimaerism and mixolpoidy.

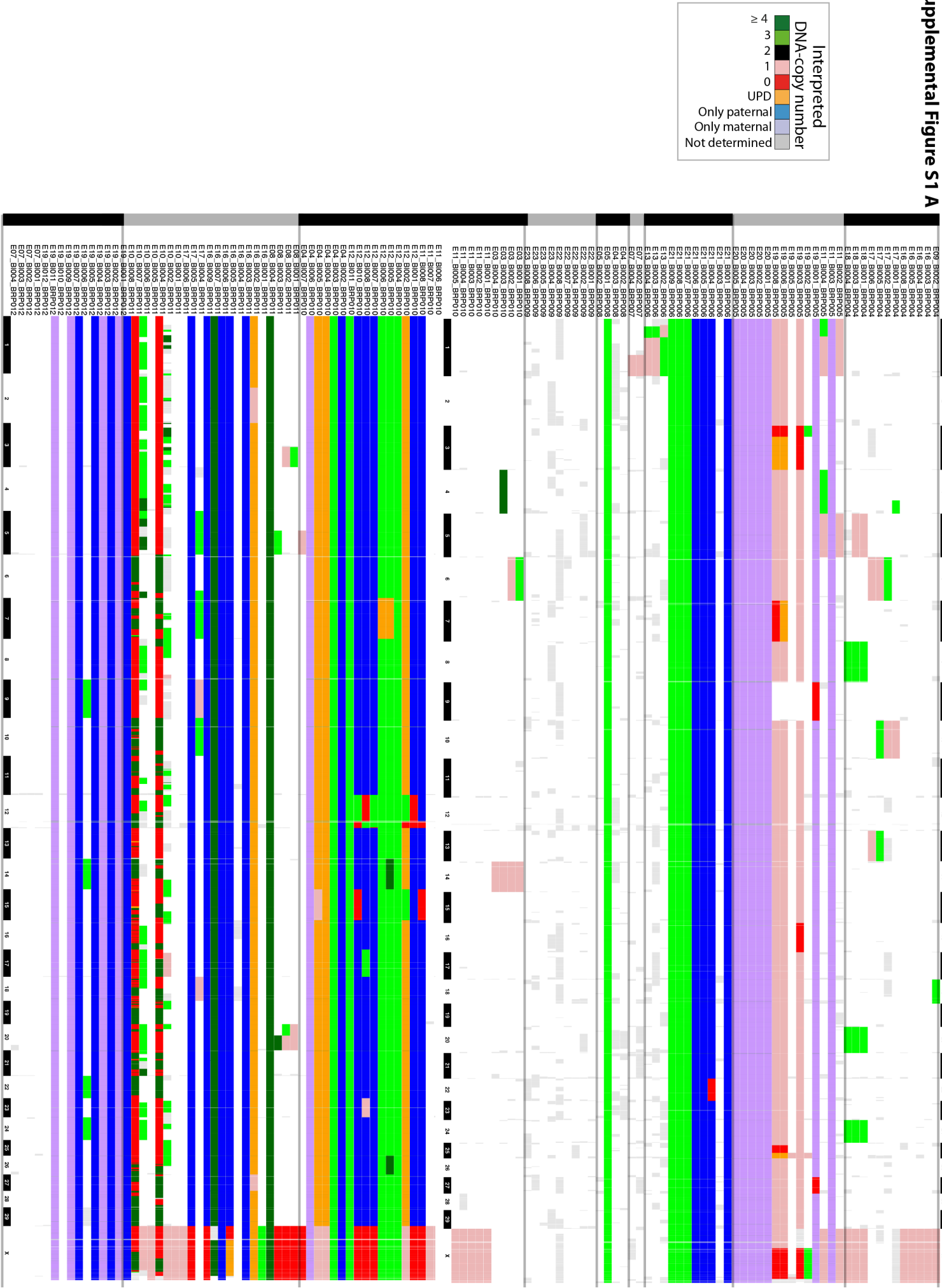
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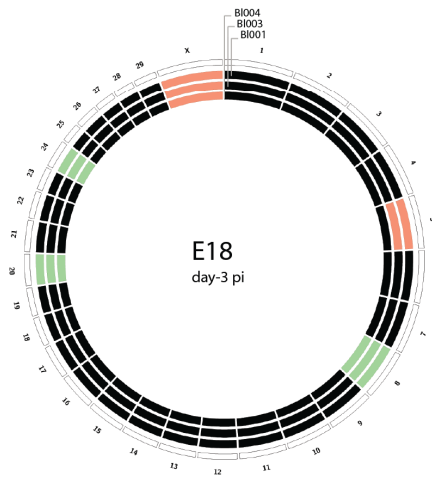
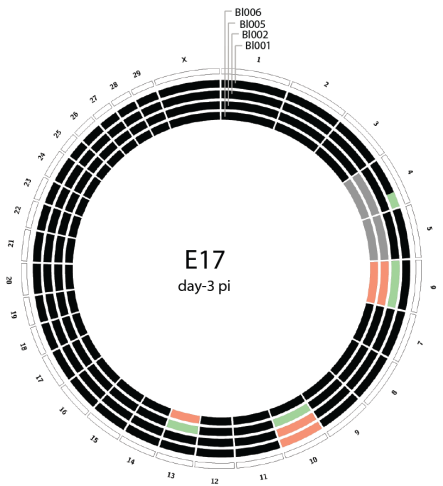
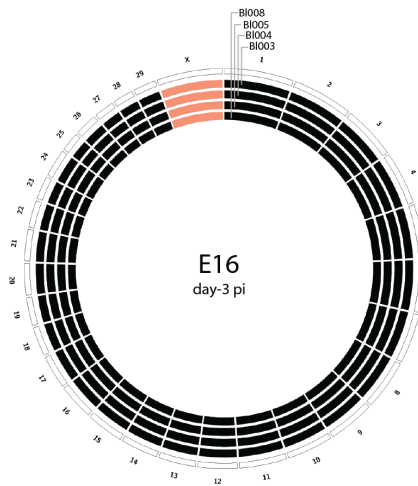
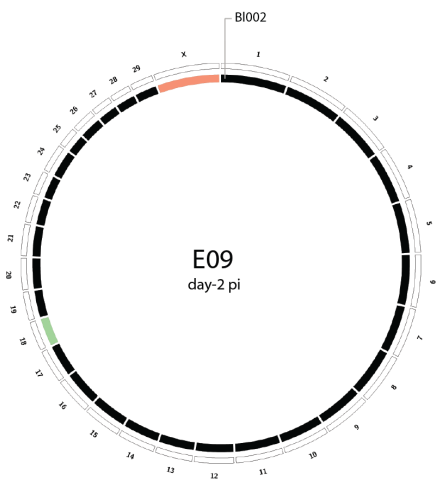
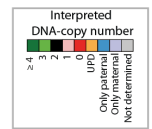
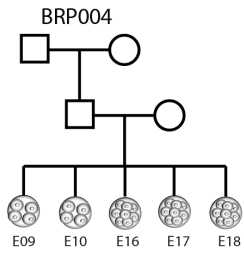
⁸ These authors are joint first-authors and contributed equally to this work.

⁹ Co-senior author, * Correspondence: Joris.Vermeesch@med.kuleuven.be and Thierry.voet@med.kuleuven.be

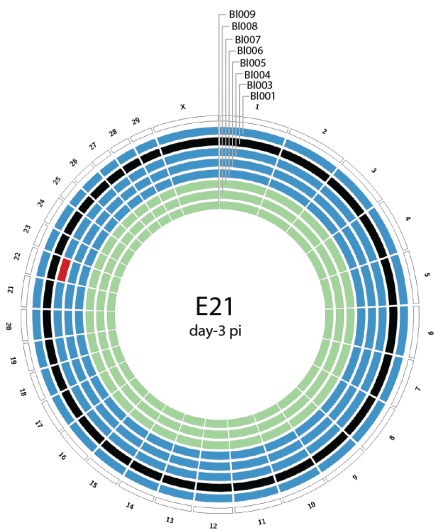
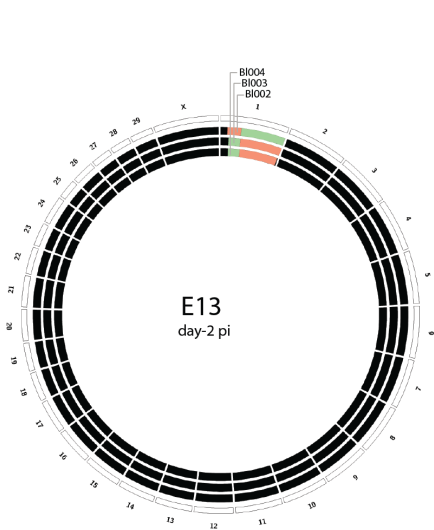
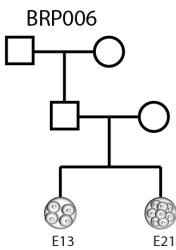
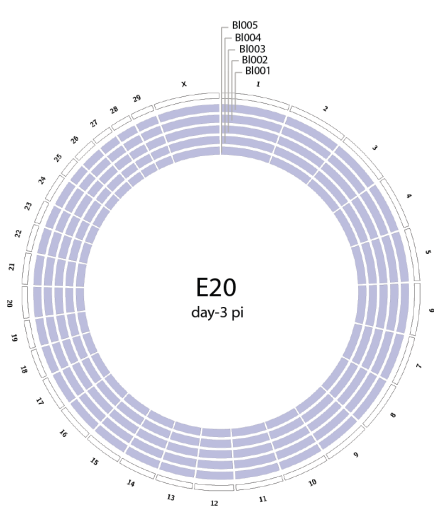
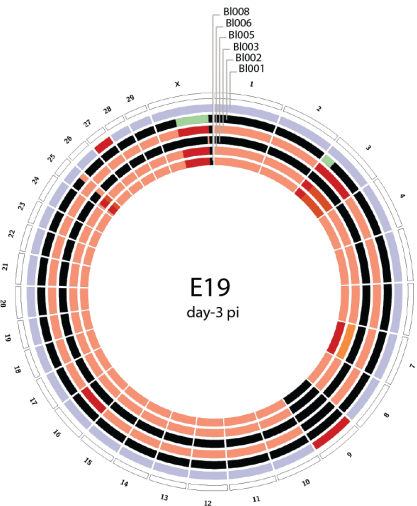
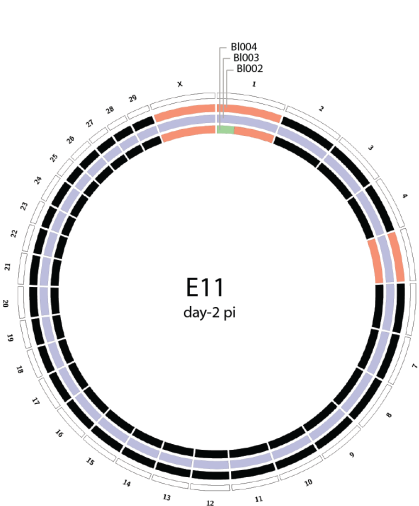
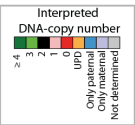
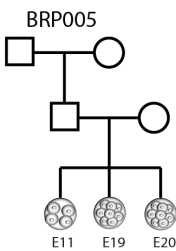
Supplemental Figure S1 A



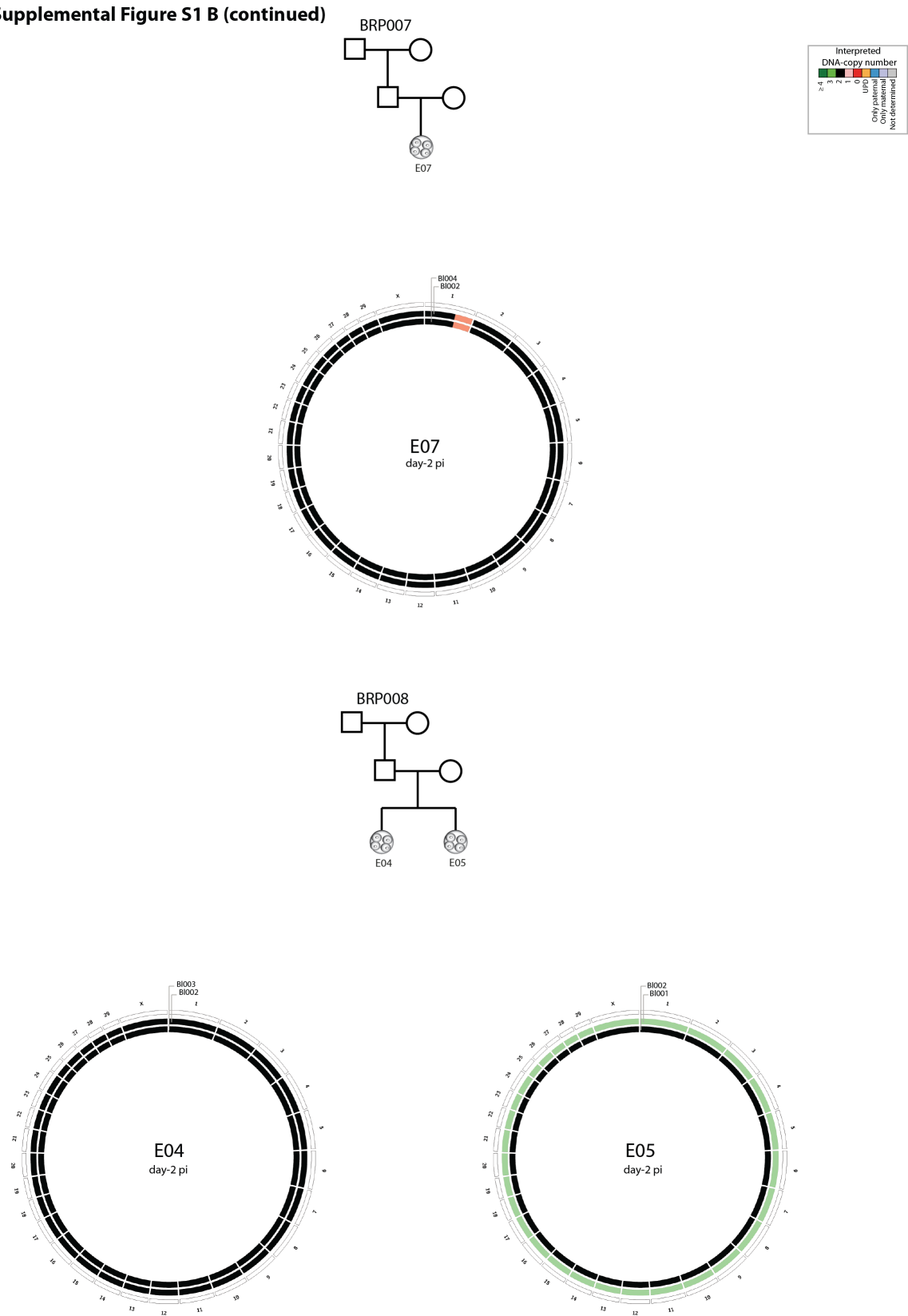
Supplemental Figure S1 B



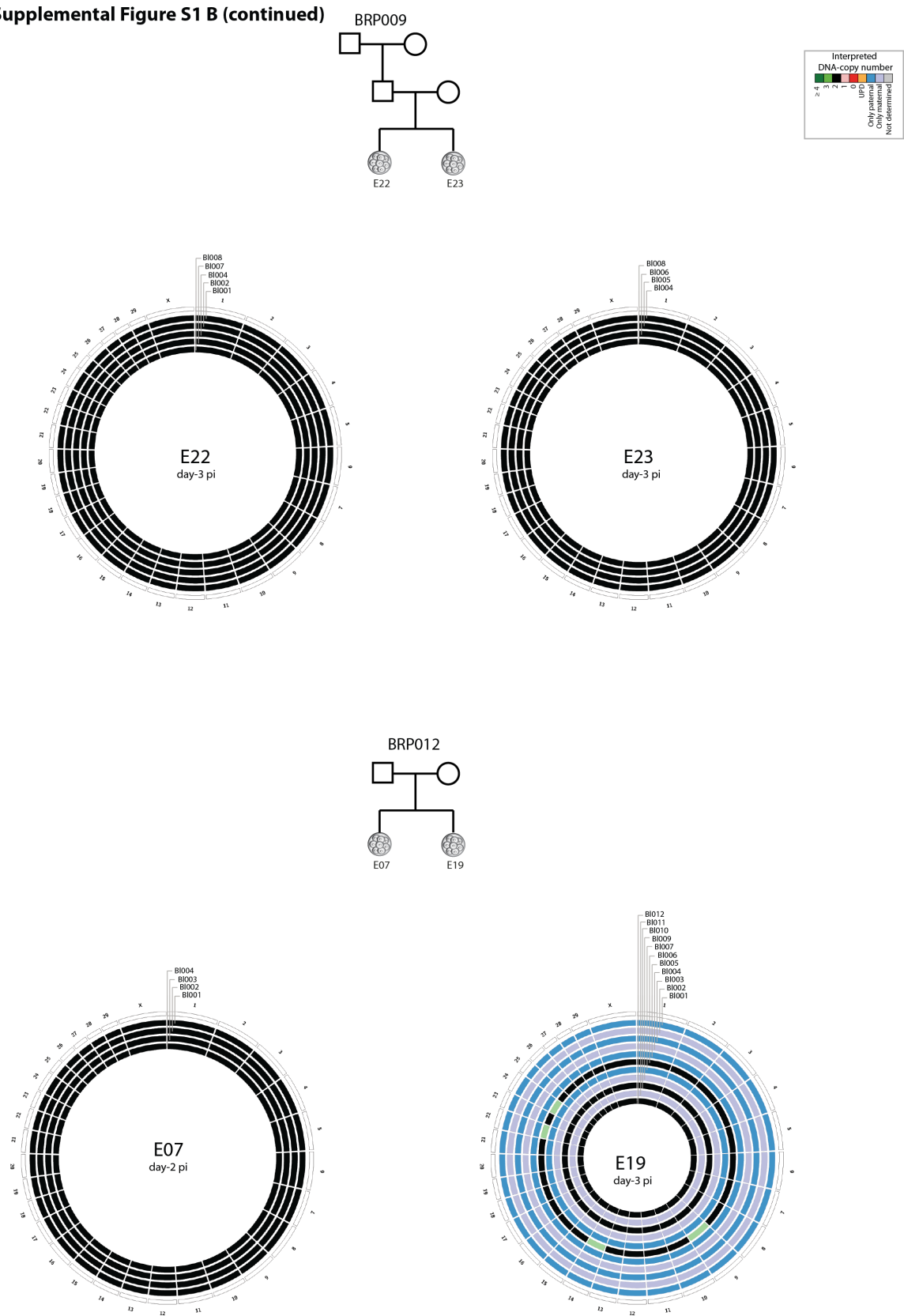
Supplemental Figure S1 B (continued)



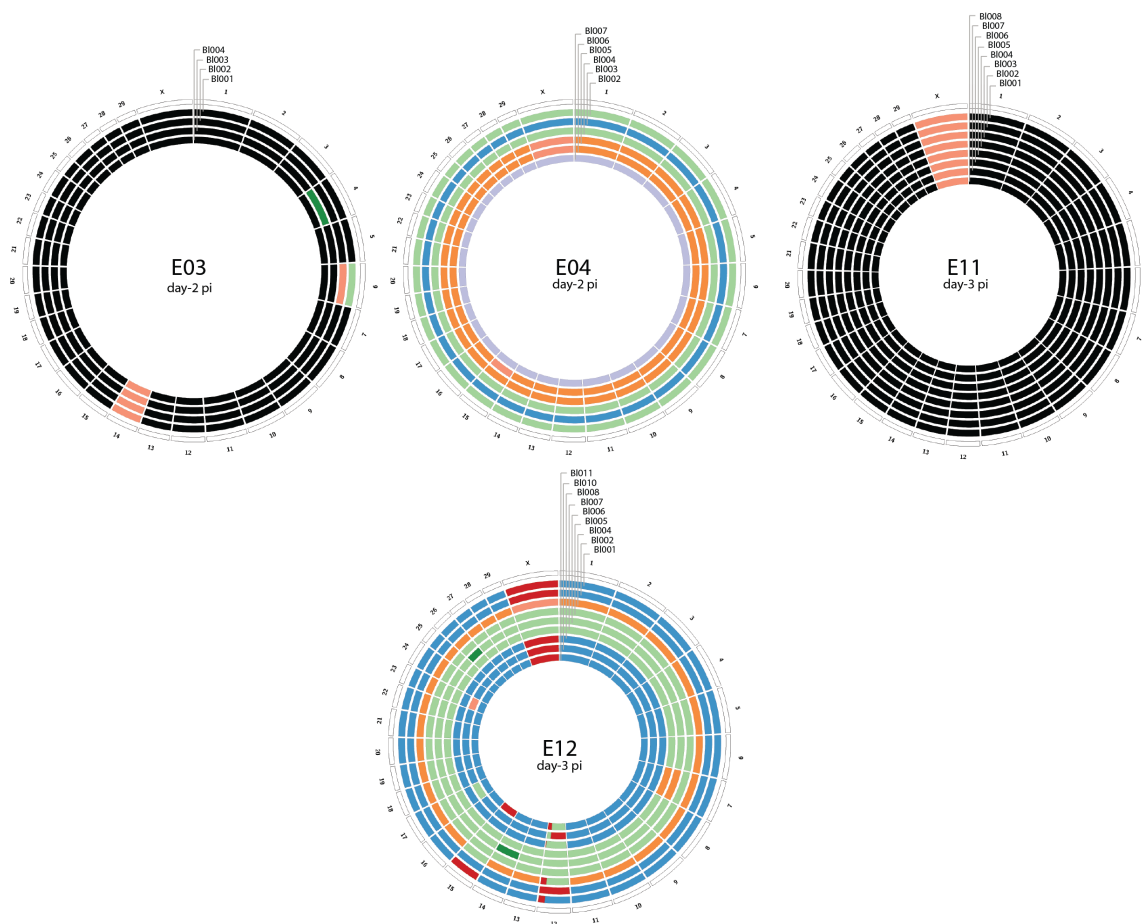
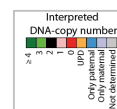
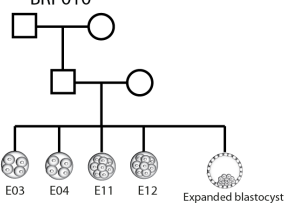
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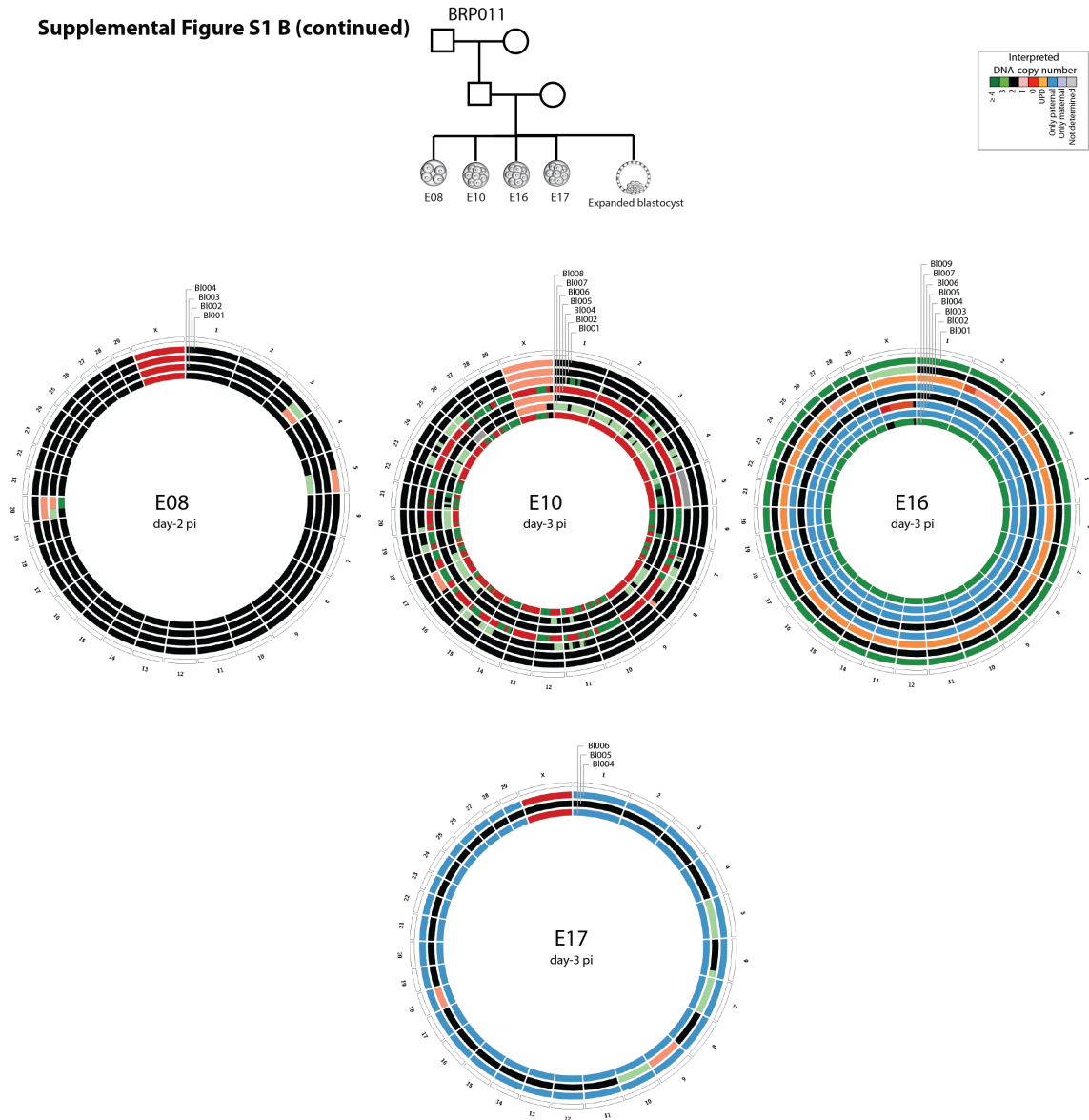
Supplemental Figure S1 B (continued)



BRP010



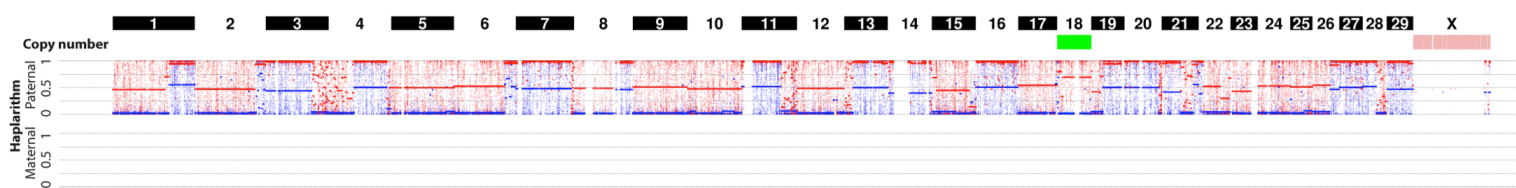
Supplemental Figure S1 B (continued)



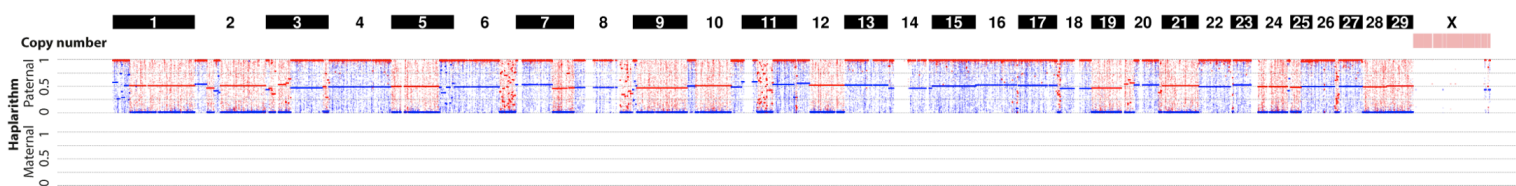
Supplemental Figure S1 | A, Detailed whole genome copy number maps of the bovine single blastomeres. Aberrant logR-segments (> 0.15 or < -0.3) with the length of $> 1\text{Mb}$ corroborated by a characteristic haplarithm pattern are depicted. Aberrant logR-segments not corroborated by a typical haplarithm pattern are shown in grey (see also **panel B** and **Supplemental Fig. S2**). **B,** Overview of all the samples involved in this study per cross, including all BRP pedigrees along with the interpreted copy-number profiles. Each Circos plot illustrates genome-wide interpreted copy-number profiles of the single blastomeres derived from an embryo.

Supplemental Figure S2

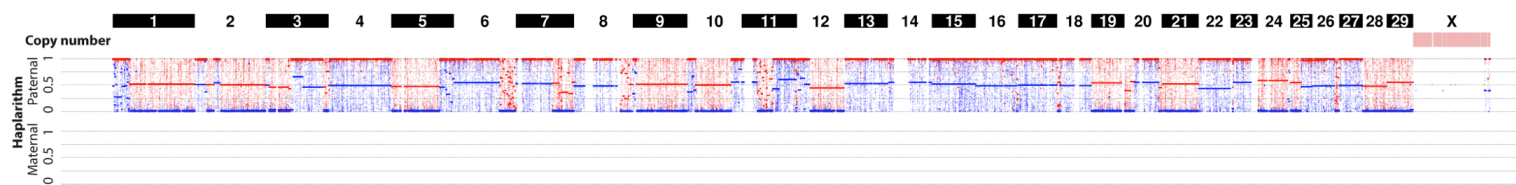
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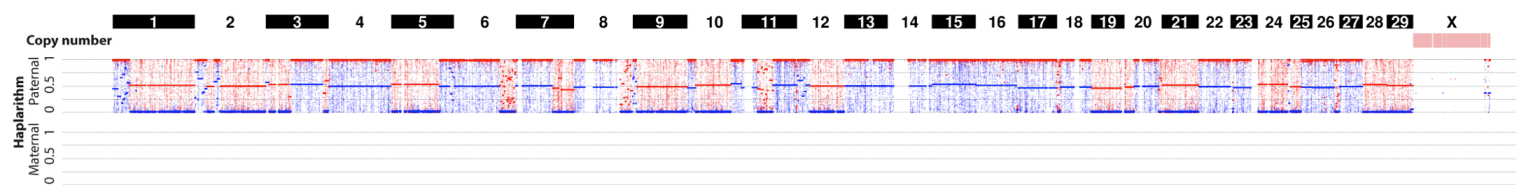
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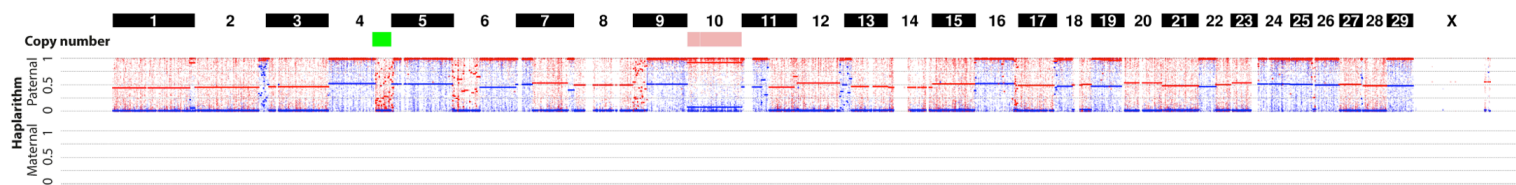
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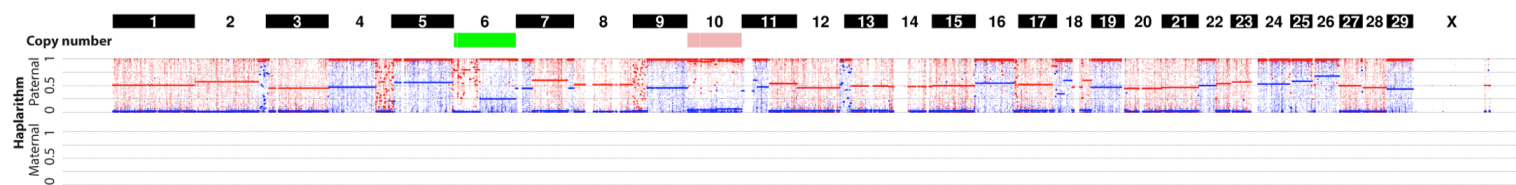
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Whole-genome profile (BRP004_A _ E17_BI001_BRP004)

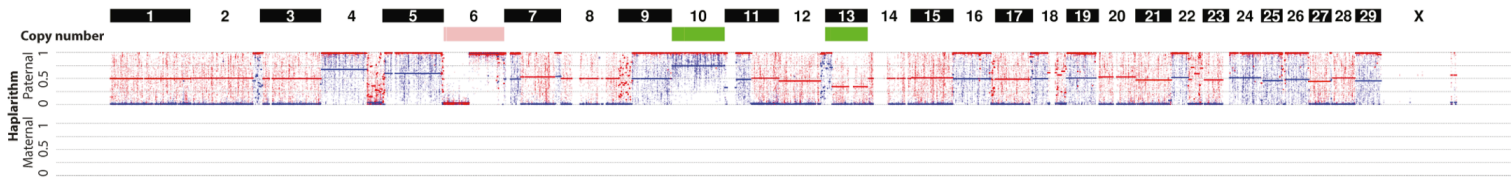


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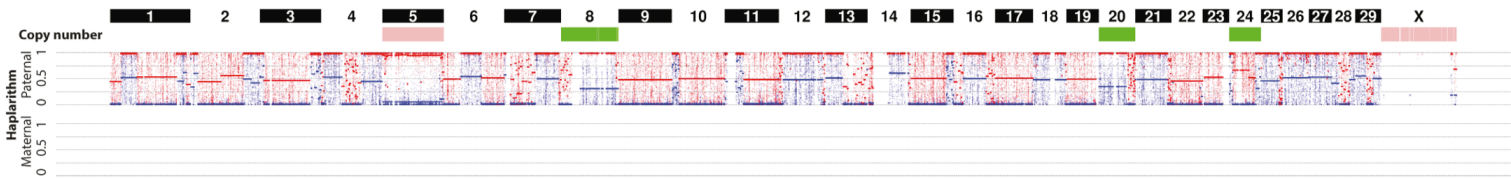


Supplemental Figure S2 (continued)

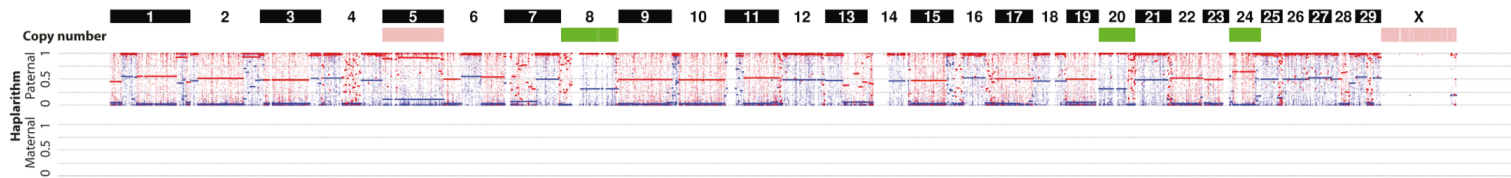
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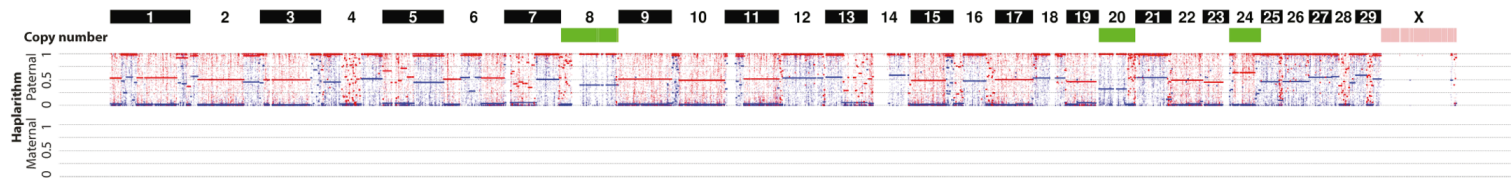
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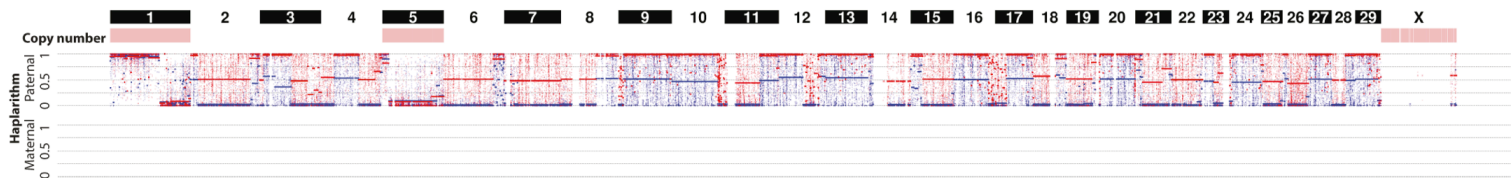
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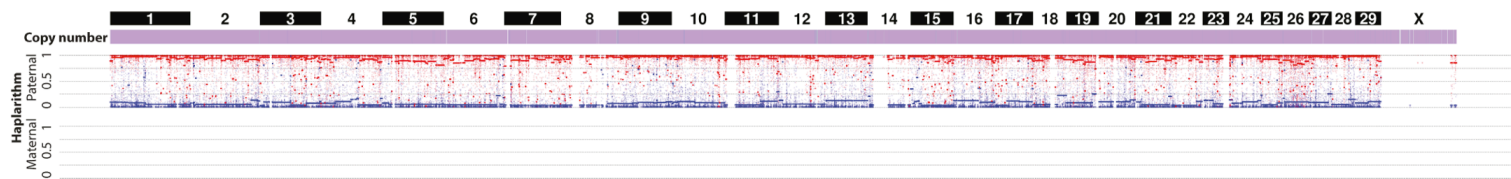
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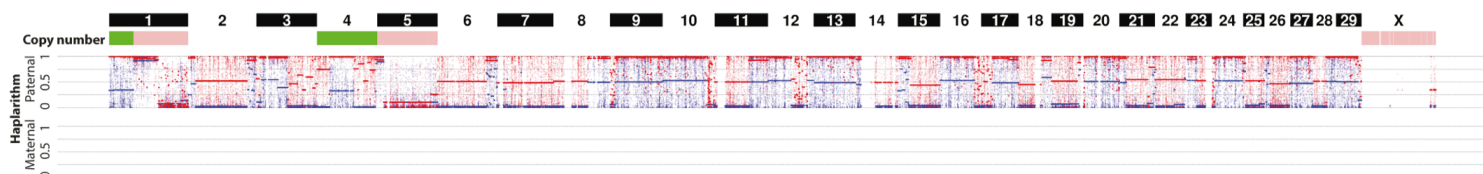


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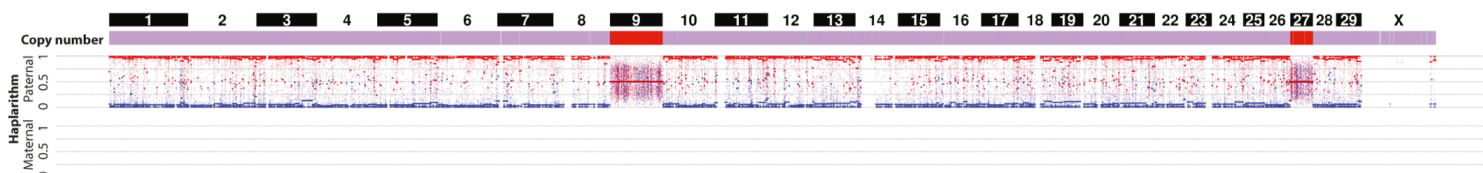


Supplemental Figure S2 (continued)

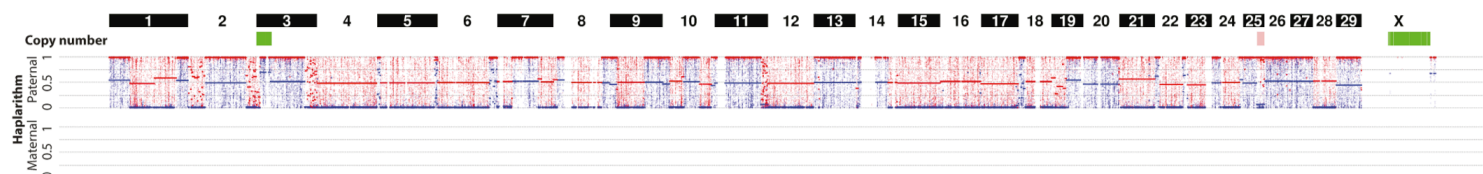
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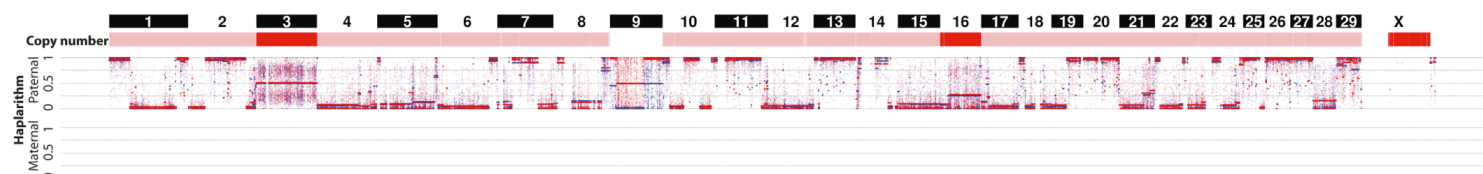
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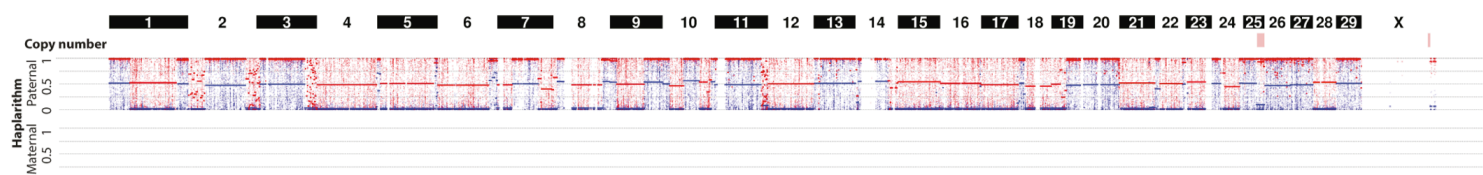
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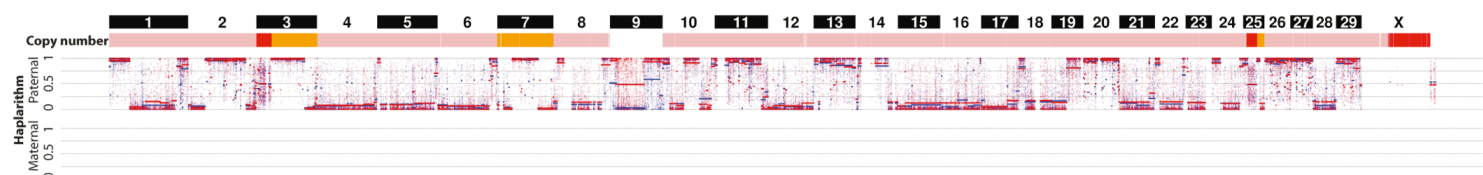
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Whole-genome profile (BRP005 _ E19 BI005 BRP005)

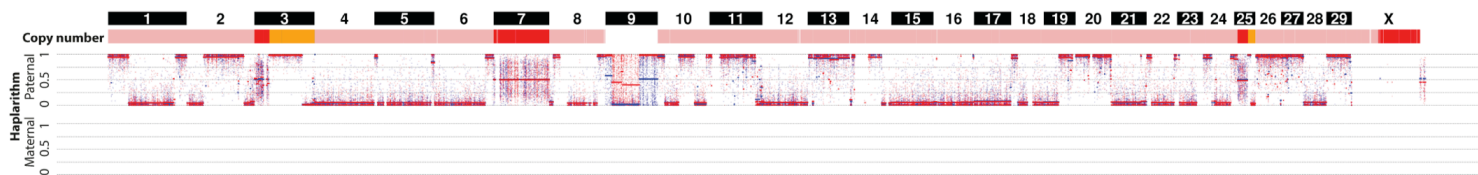


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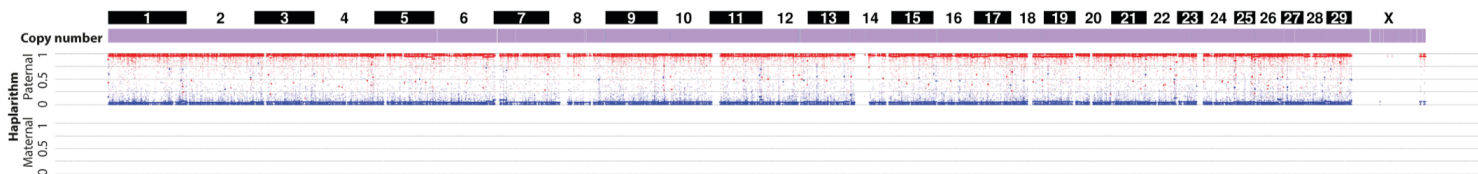


Supplemental Figure S2 (continued)

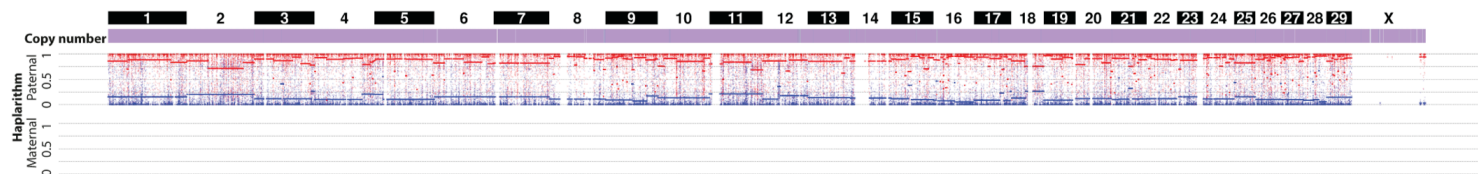
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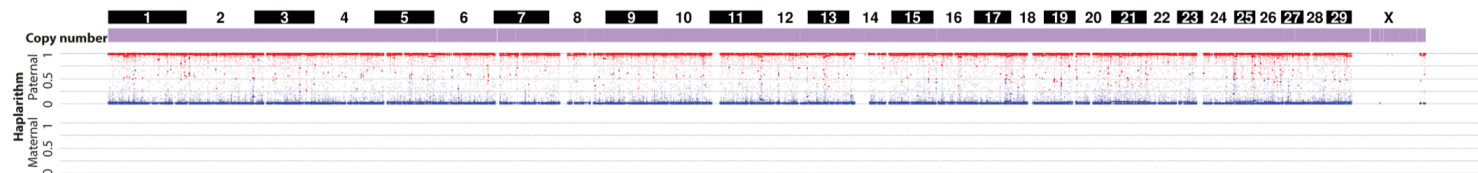
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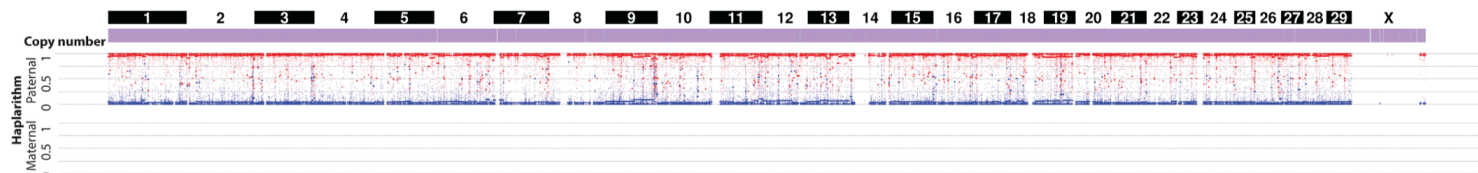
Whole-genome profile (BRP005 _ E20_BI002_BRP005)



Whole-genome profile (BRP005 _ E20_BI003_BRP005)



Whole-genome profile (BRP005 _ E20_BI004_BRP005)



Whole-genome profile (BRP005 _ E20_BI005_BRP005)

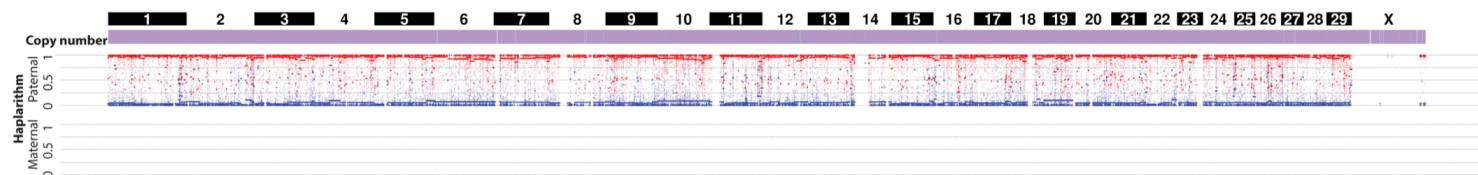
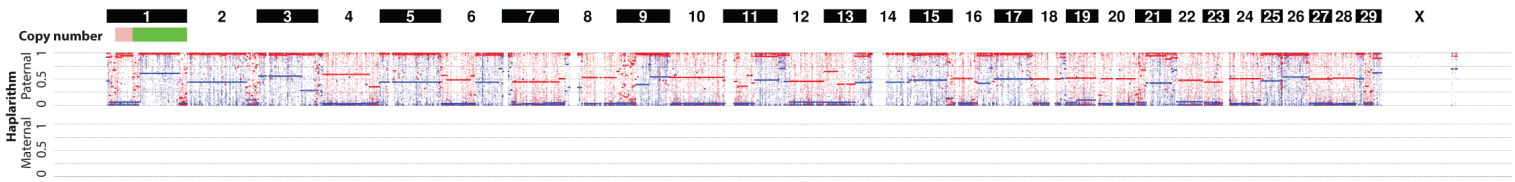
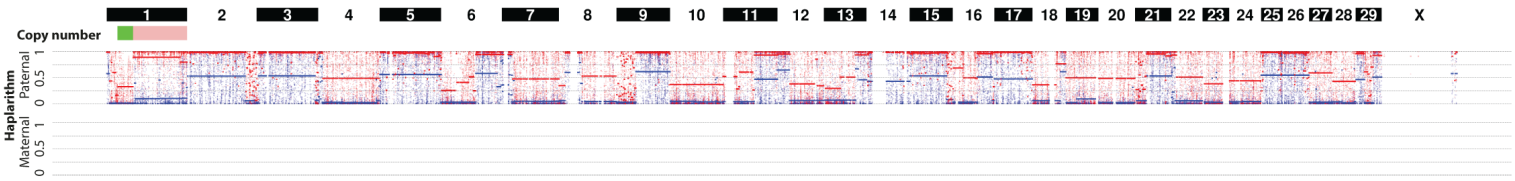


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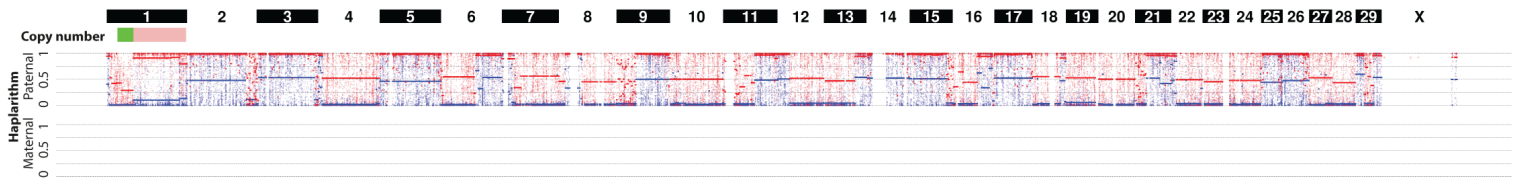
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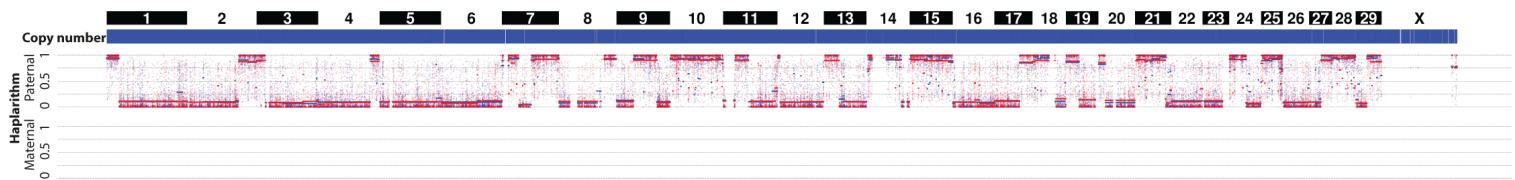
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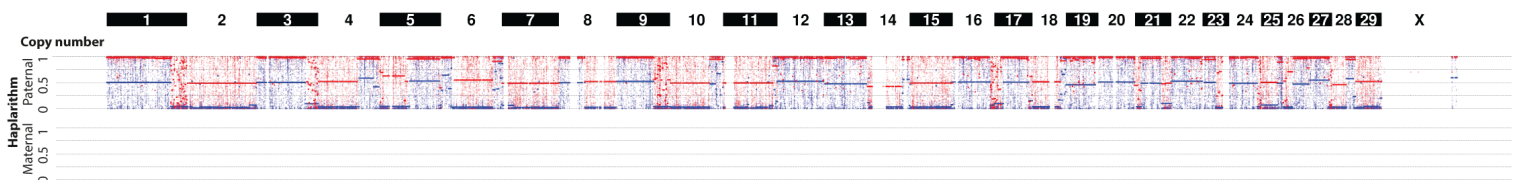
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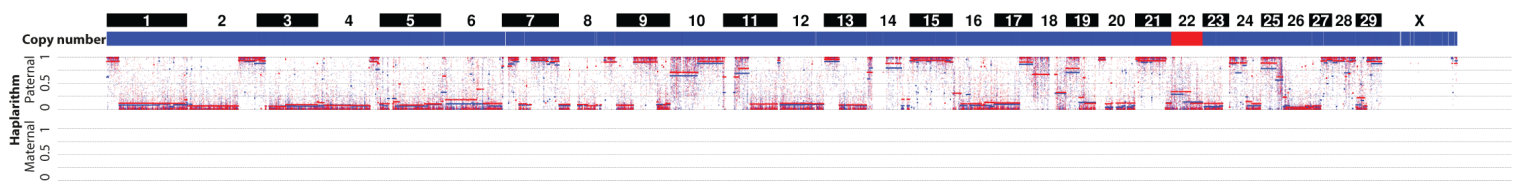
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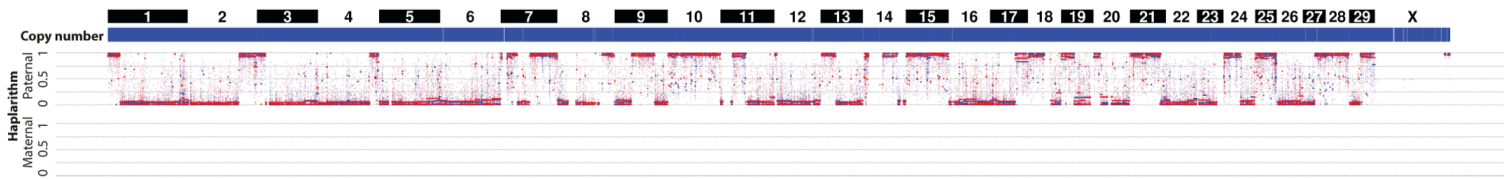


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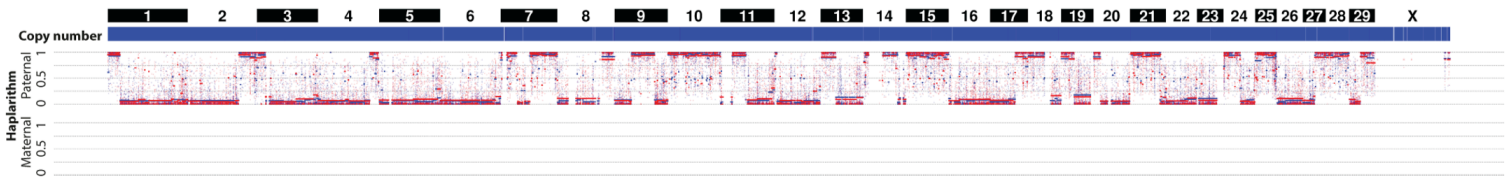


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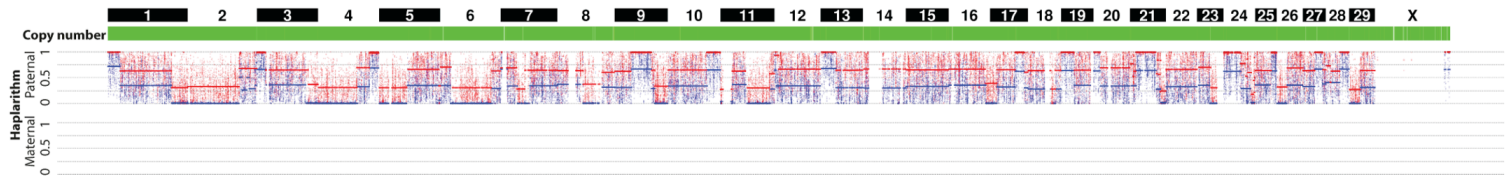
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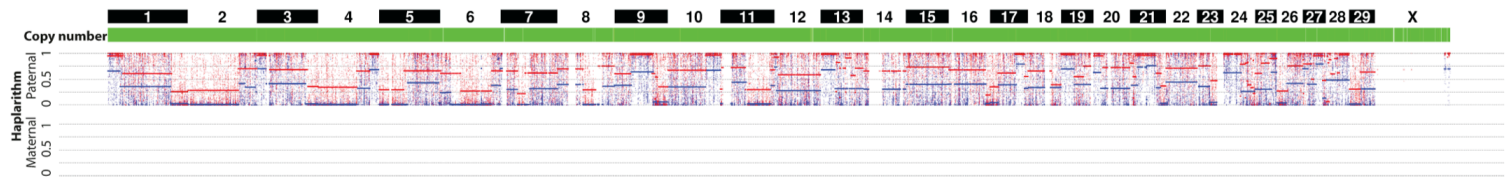
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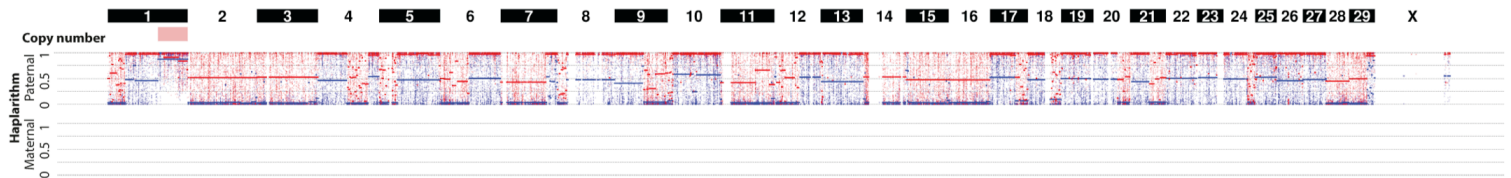
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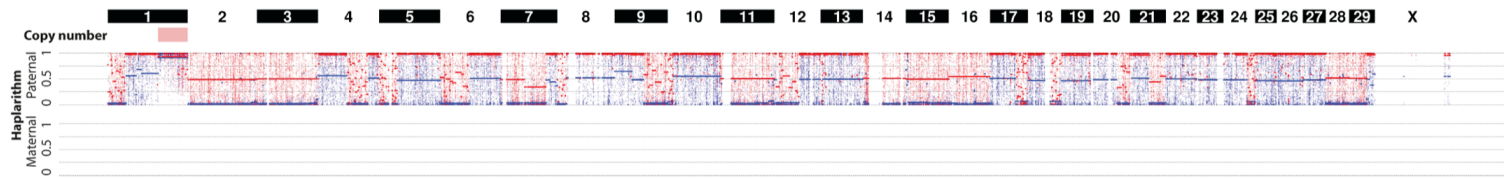
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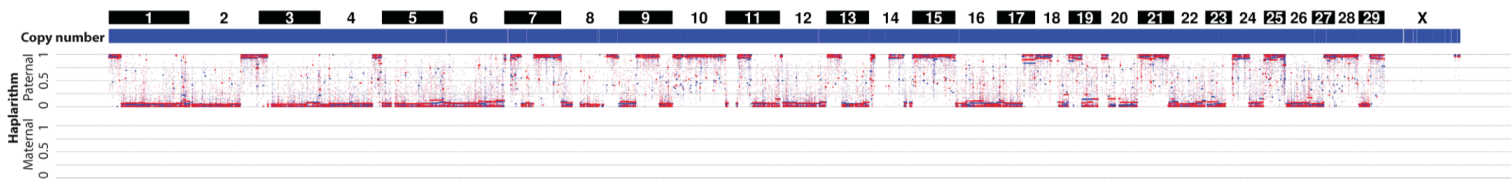


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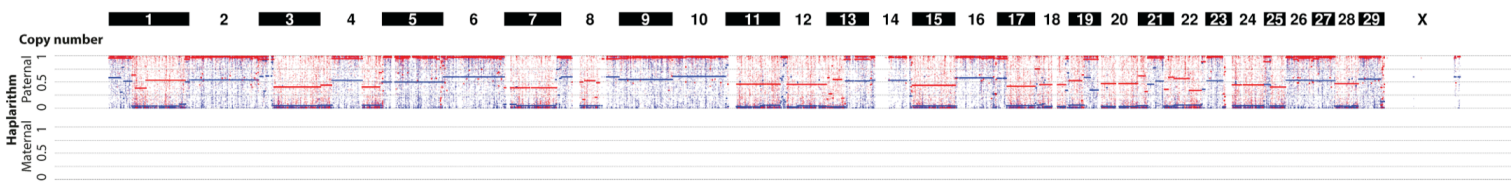


Supplemental Figure S2 (continued)

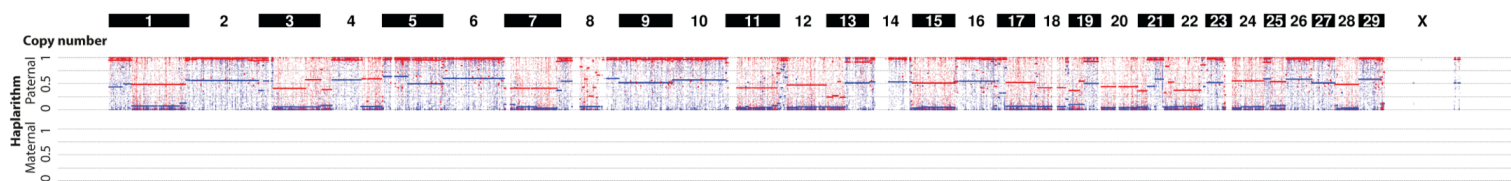
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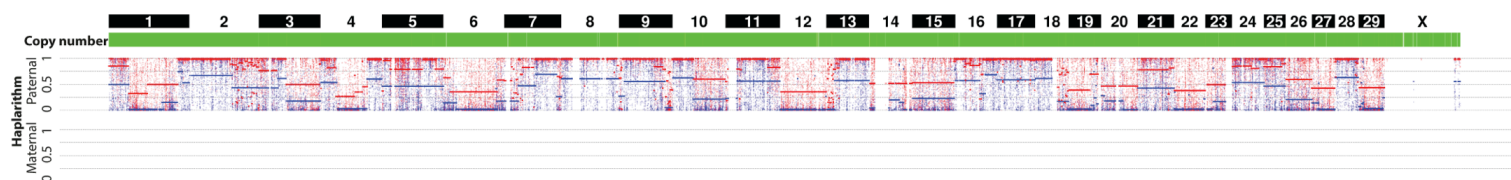
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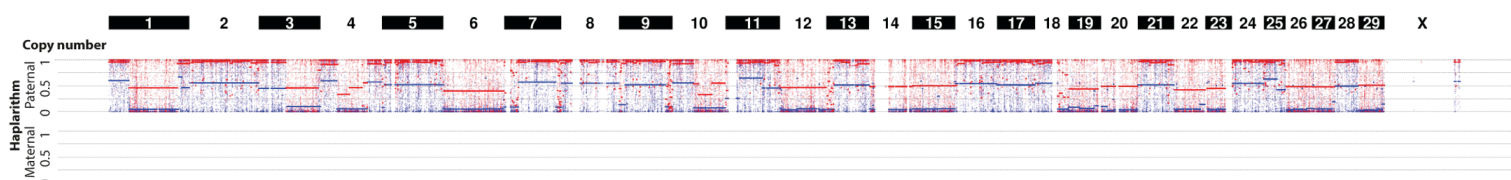
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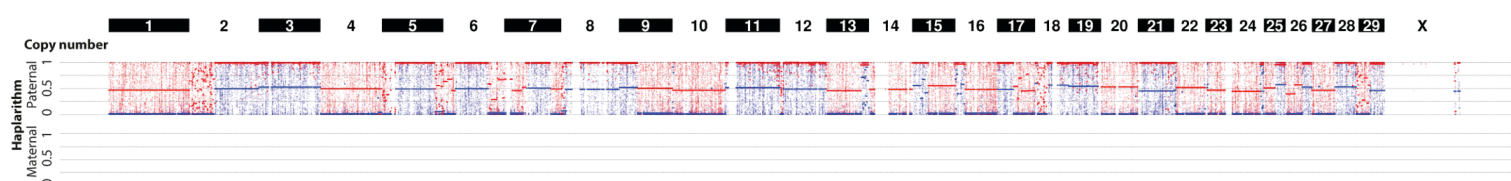
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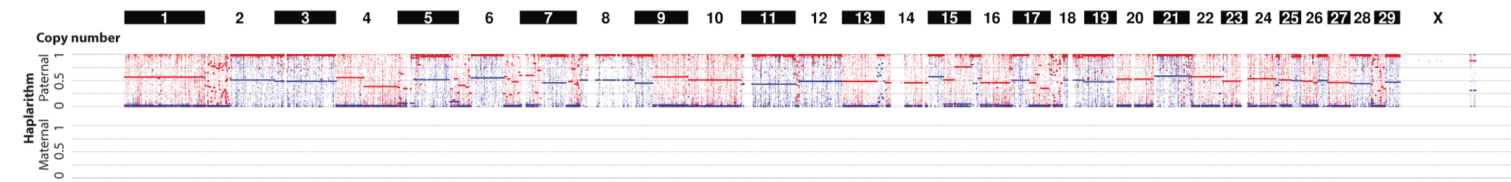


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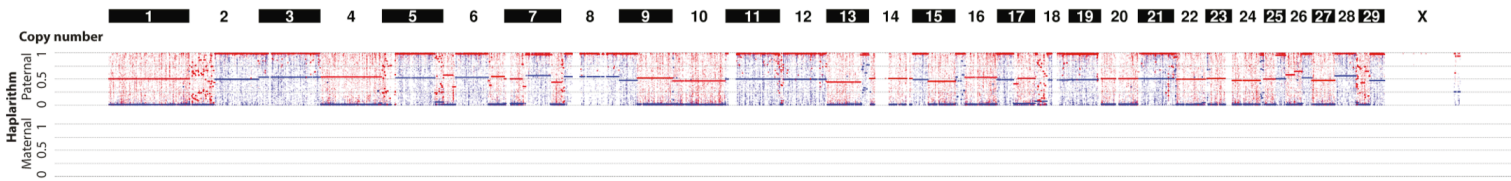


Supplemental Figure S2 (continued)

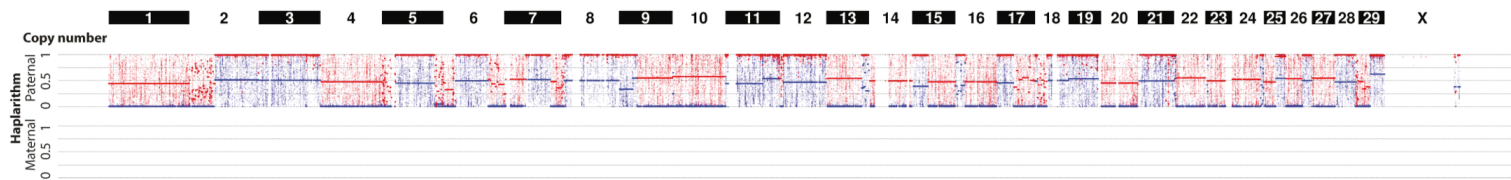
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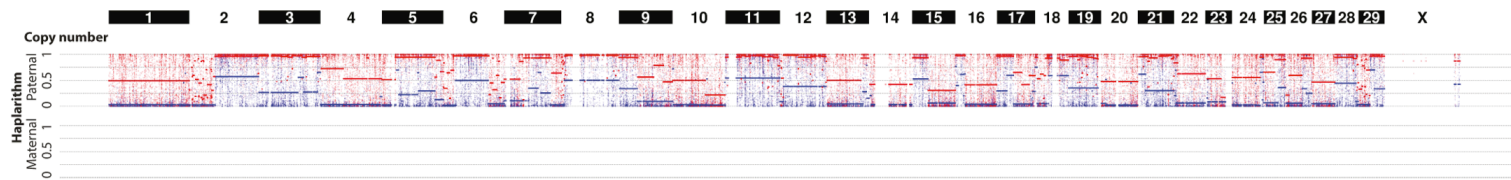
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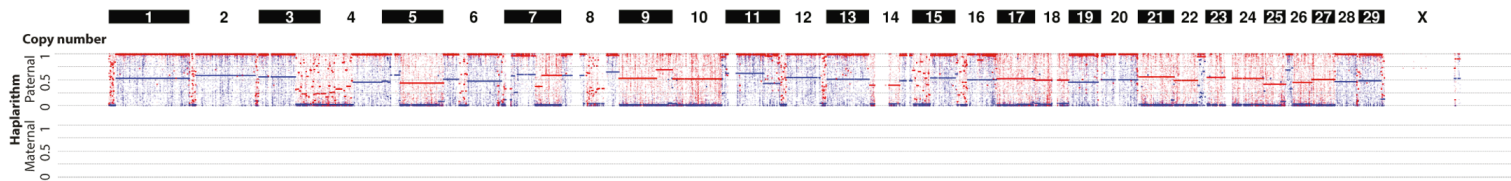
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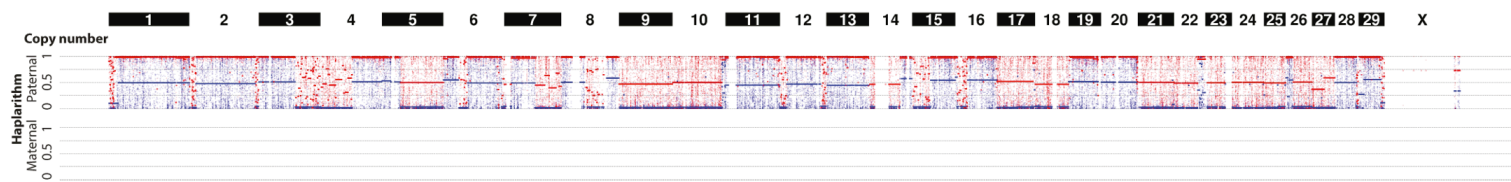
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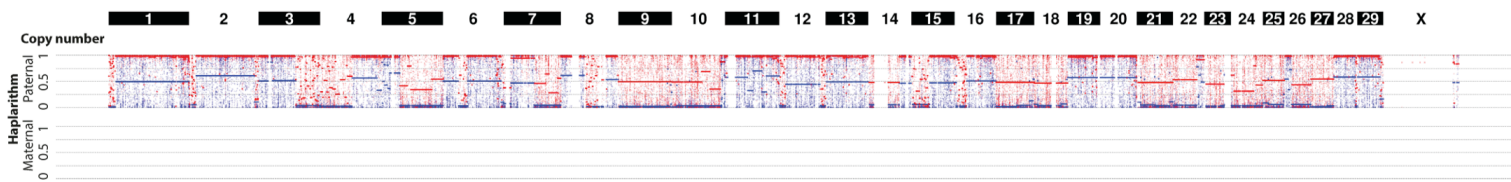


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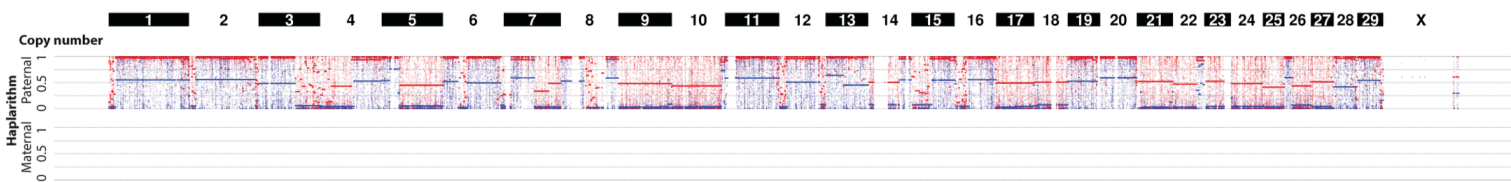


Supplemental Figure S2 (continued)

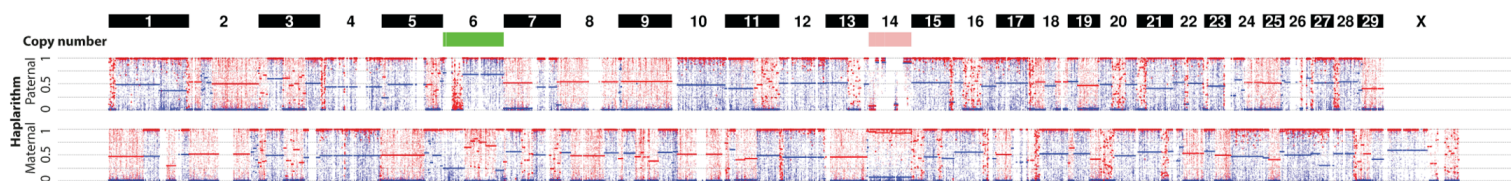
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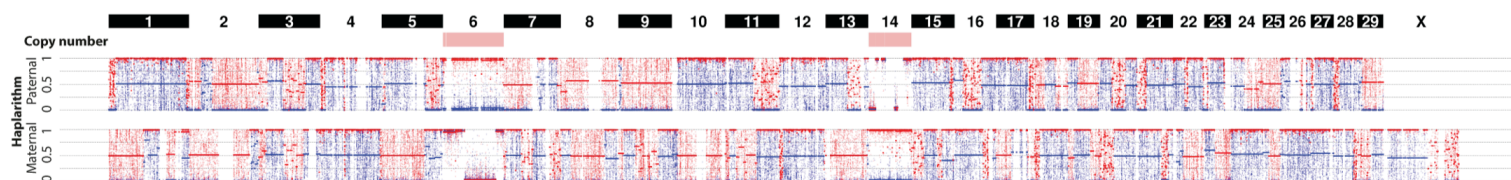
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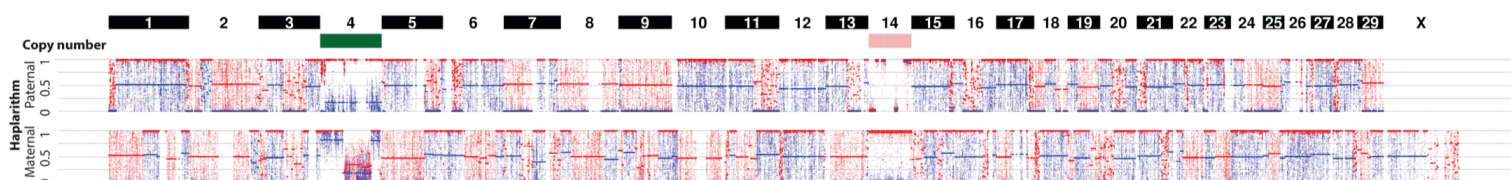
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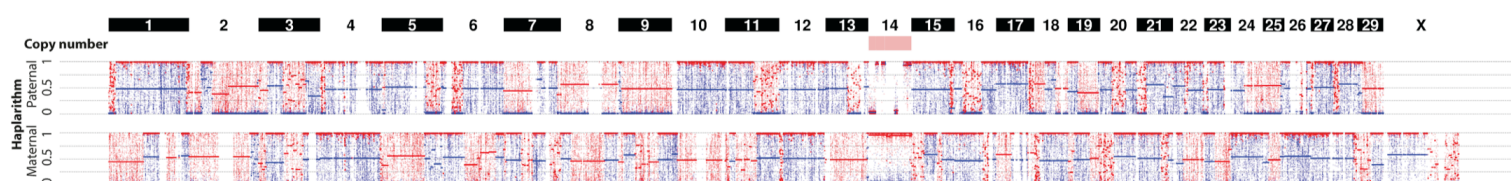
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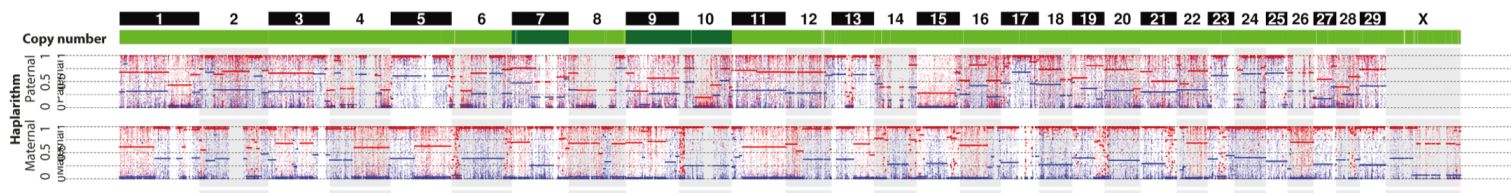


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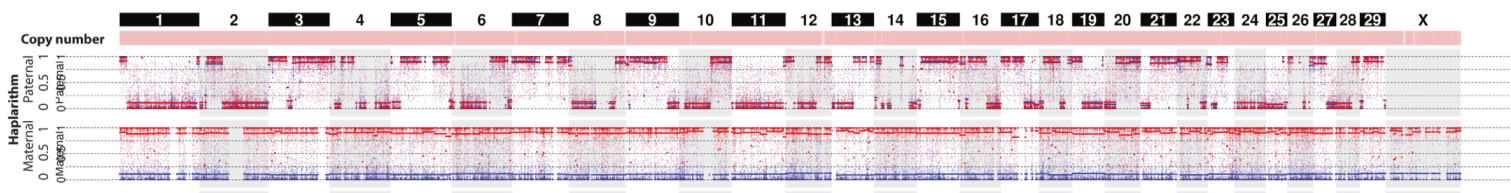


Supplemental Figure S2 (continued)

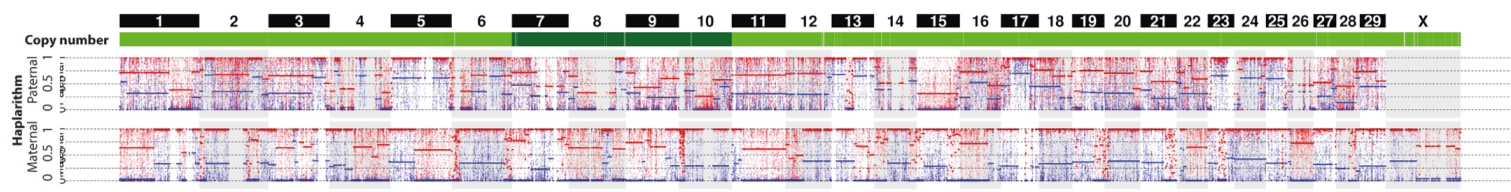
Whole-genome profile (E04_BI002_BRP010)



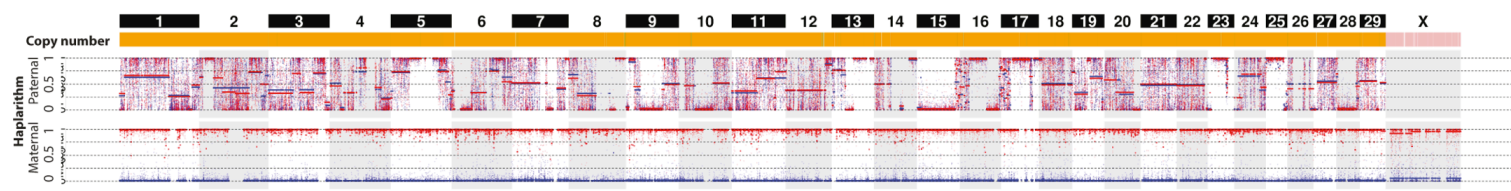
Whole-genome profile (E04_BI003_BRP010)



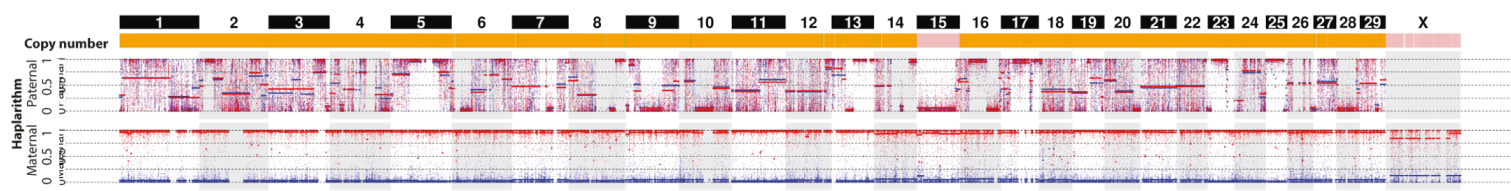
Whole-genome profile (E04_BI004_BRP010)



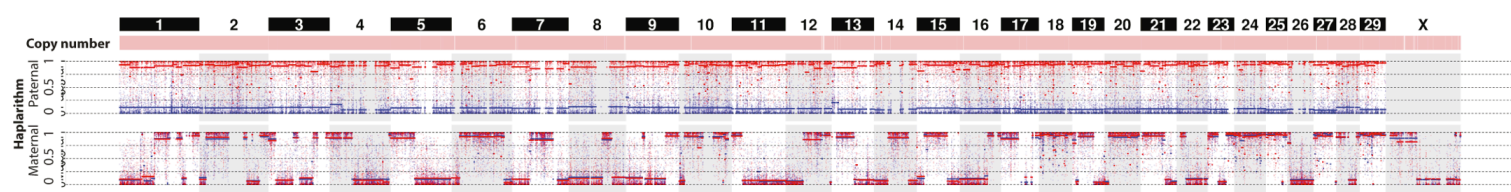
Whole-genome profile (E04_BI005_BRP010)



Whole-genome profile (E04_BI006_BRP010)

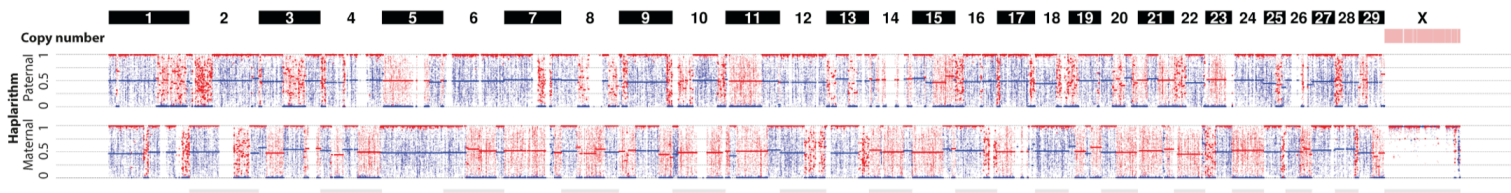


Whole-genome profile (E04_BI007_BRP010)

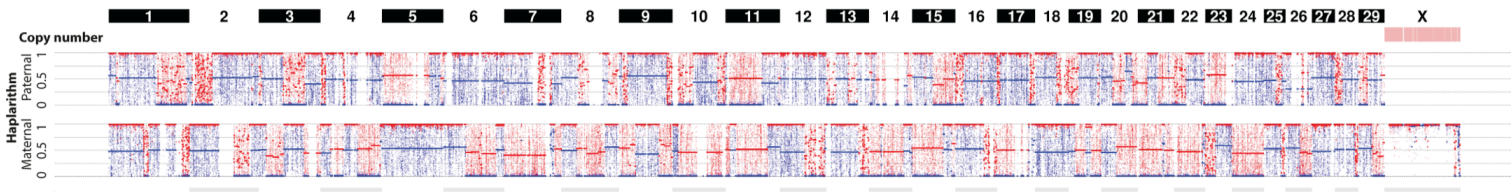


Supplemental Figure S2 (continued)

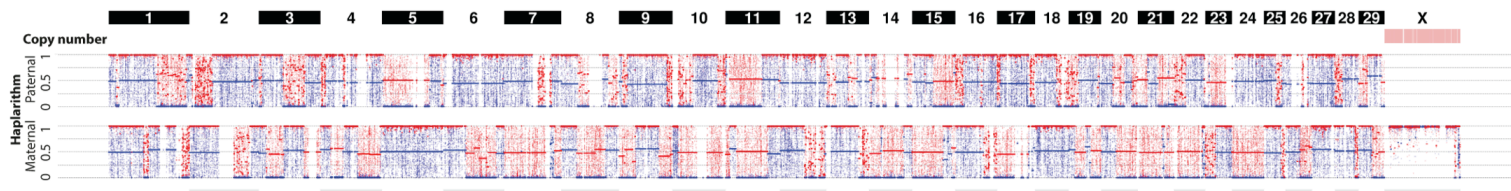
Whole-genome profile (BRP010 _ E11_BI001_BRP010)



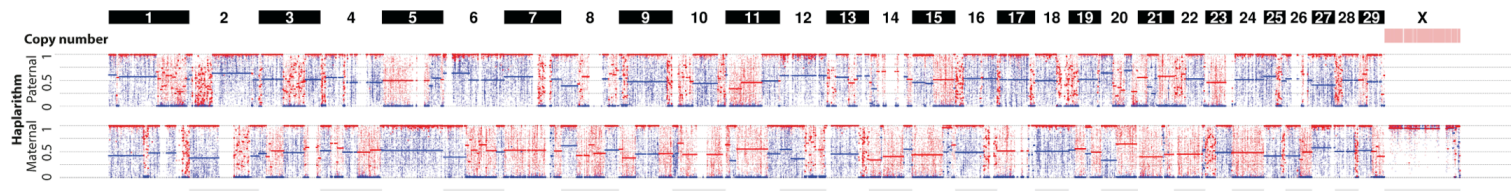
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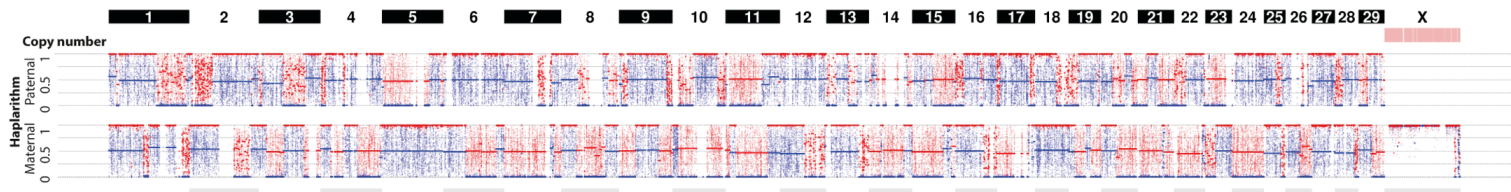
Whole-genome profile (BRP010 _ E11_BI003_BRP010)



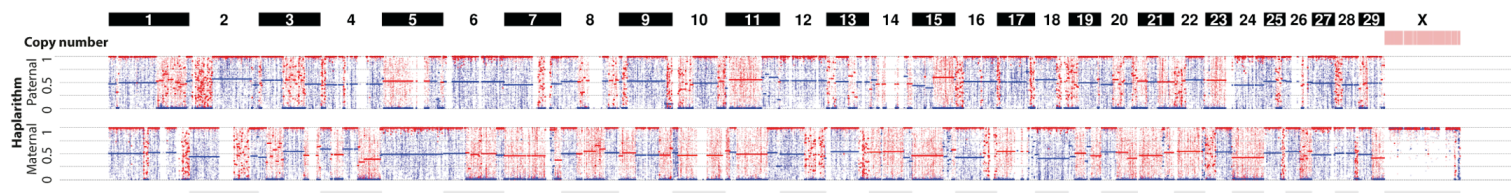
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Whole-genome profile (BRP010 _ E11_BI005_BRP010)

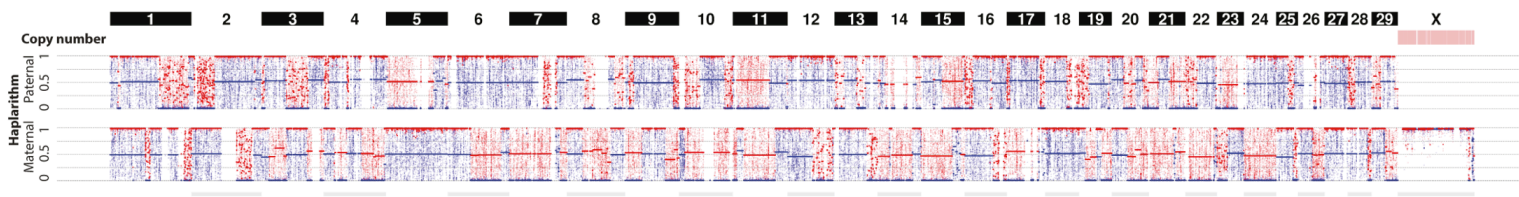


Whole-genome profile (BRP010 _ E11_BI006_BRP010)

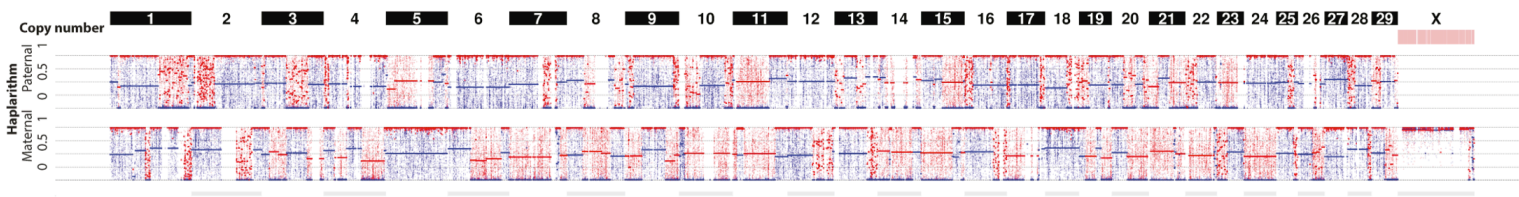


Supplemental Figure S2 (continued)

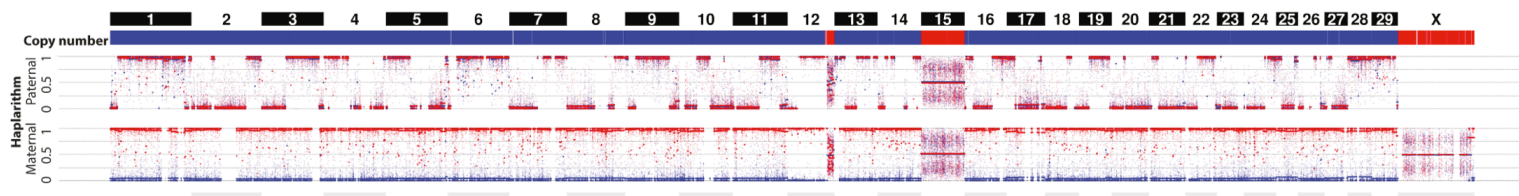
Whole-genome profile (BRP010 _ E11_BI007_BRP010)



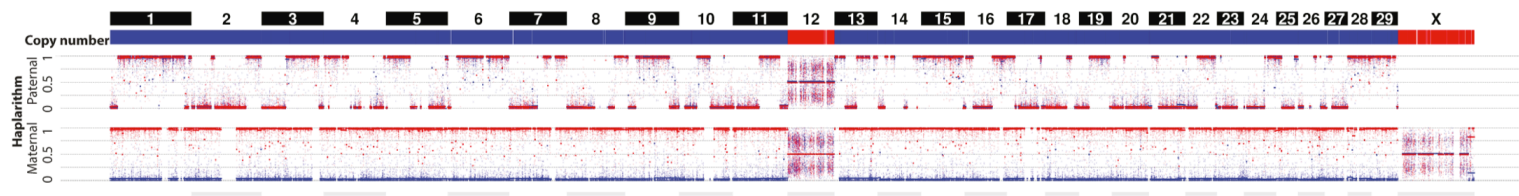
Whole-genome profile (BRP010 _ E11_BI008_BRP010)



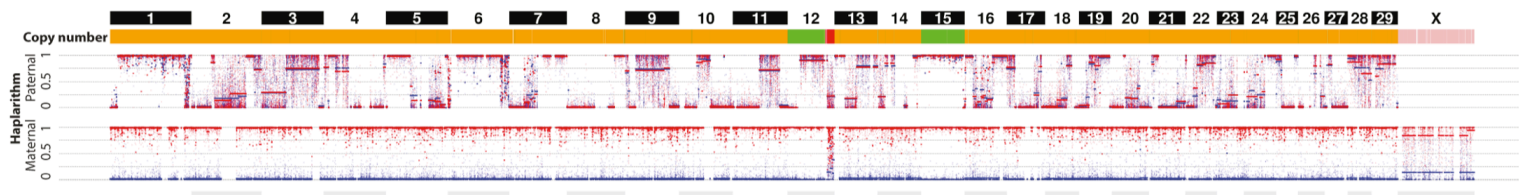
Whole-genome profile (BRP010 _ E12_BI001_BRP010)



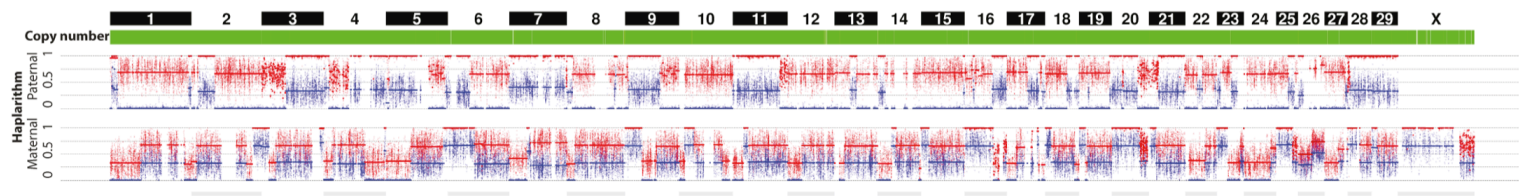
Whole-genome profile (BRP010 _ E12_BI002_BRP010)



Whole-genome profile (BRP010 _ E12_BI004_BRP010)

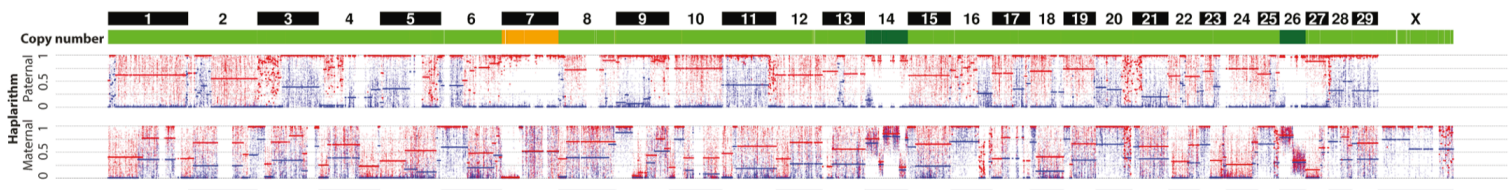


Whole-genome profile (BRP010 _ E12_BI005_BRP010)

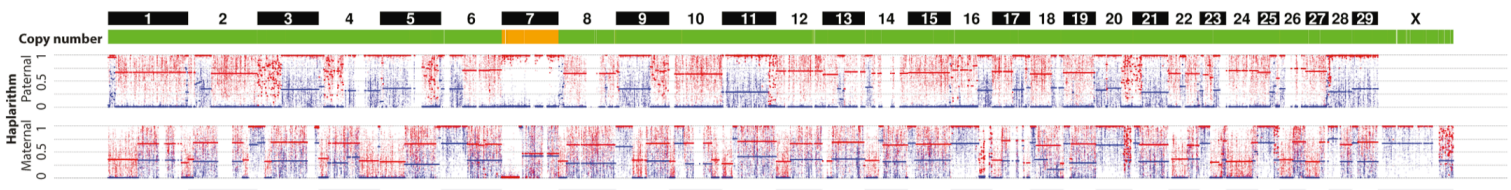


Supplemental Figure S2 (continued)

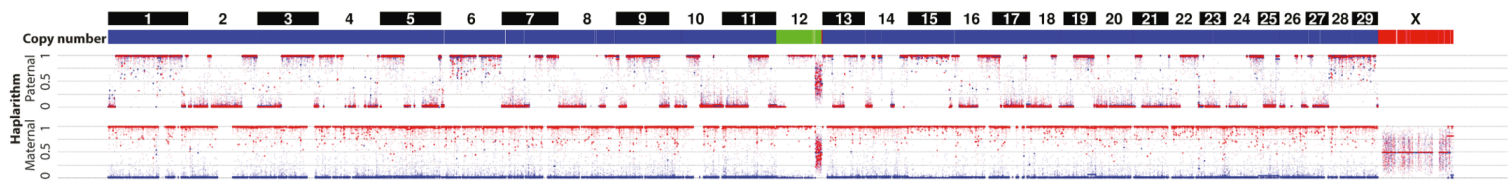
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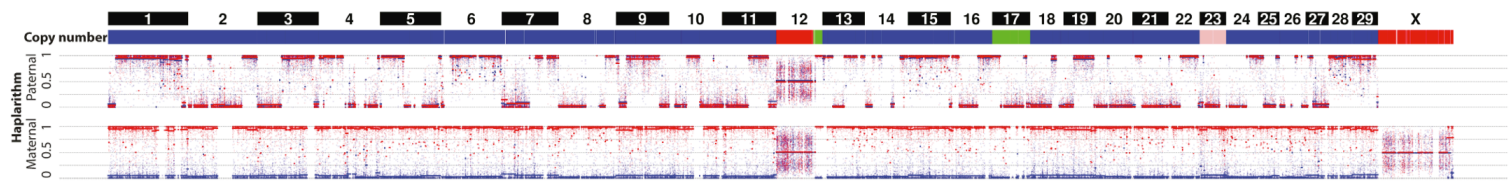
Whole-genome profile (BRP010 _ E12_BI007_BRP010)



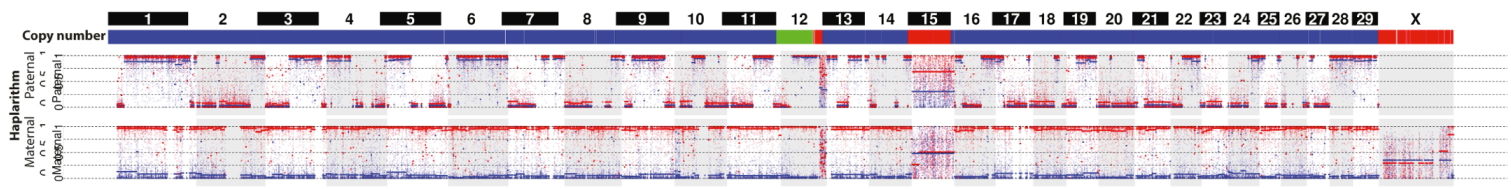
Whole-genome profile (BRP010 _ E12_BI008_BRP010)



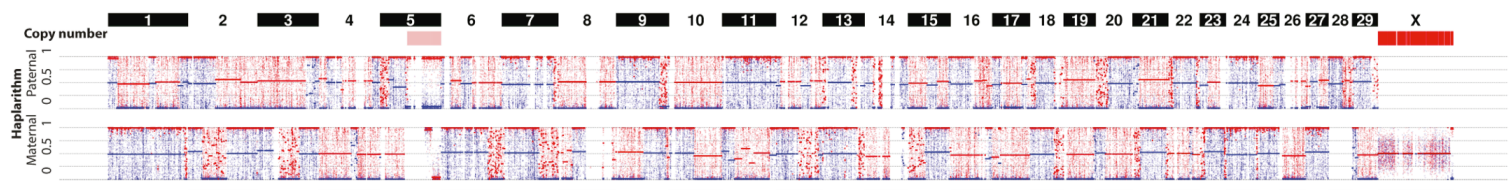
Whole-genome profile (BRP010 _ E12_BI010_BRP010)



Whole-genome profile (BRP010 _ E12_BI011_BRP010)

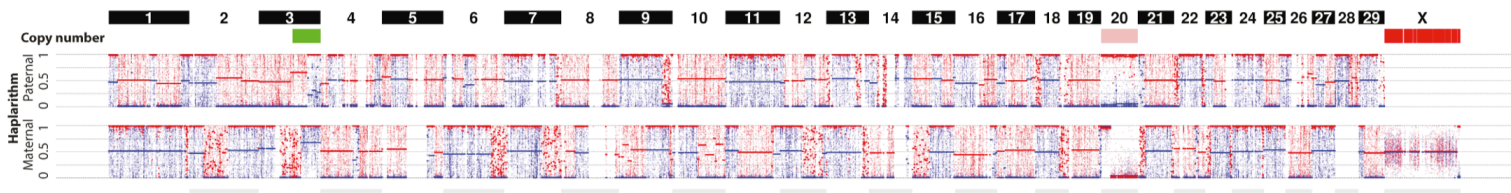


Whole-genome profile (BRP011 _ E08_BI001_BRP011)

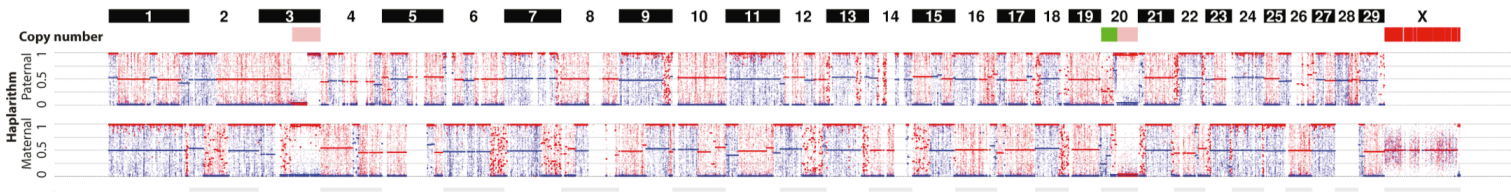


Supplemental Figure S2 (continued)

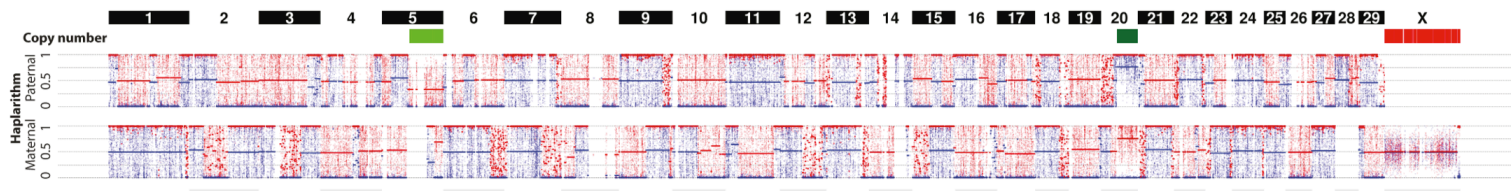
Whole-genome profile (BRP011 _ E08_BI002_BRP011)



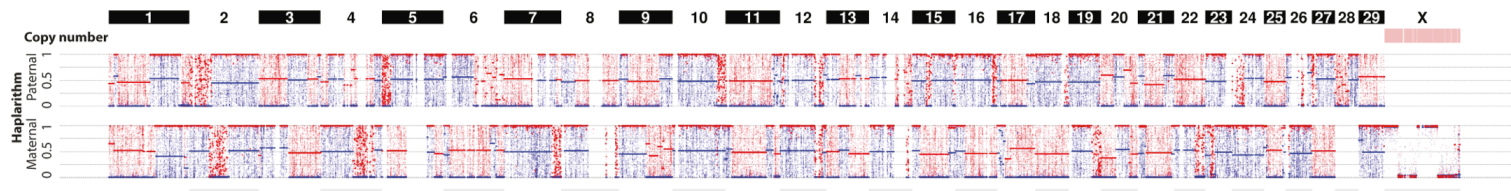
Whole-genome profile (BRP011 _ E08_BI003_BRP011)



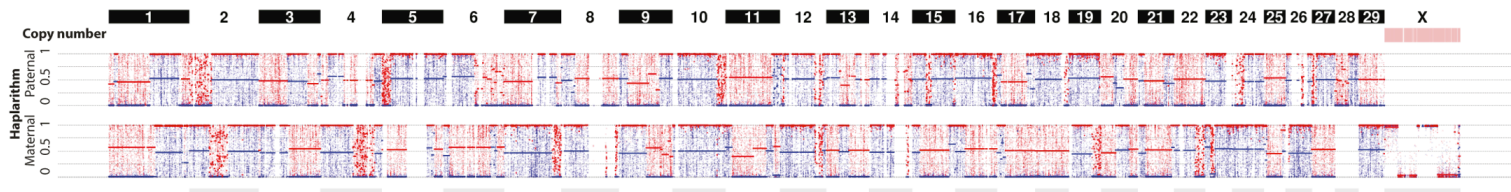
Whole-genome profile (BRP011 _ E08_BI004_BRP011)



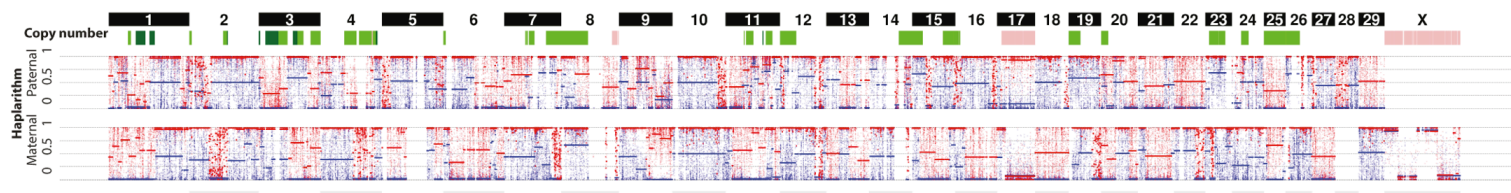
Whole-genome profile (BRP011 _ E10_BI001_BRP011)



Whole-genome profile (BRP011 _ E10_BI002_BRP011)

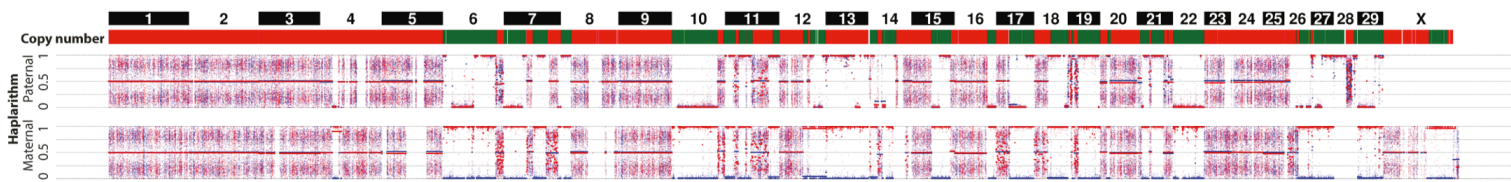


Whole-genome profile (BRP011 _ E10_BI004_BRP011)

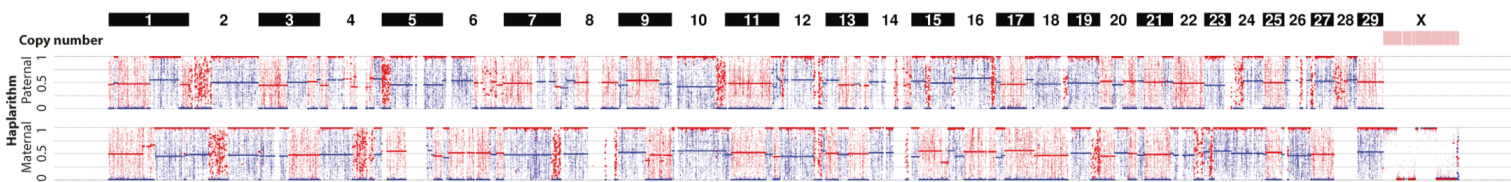


Supplemental Figure S2 (continued)

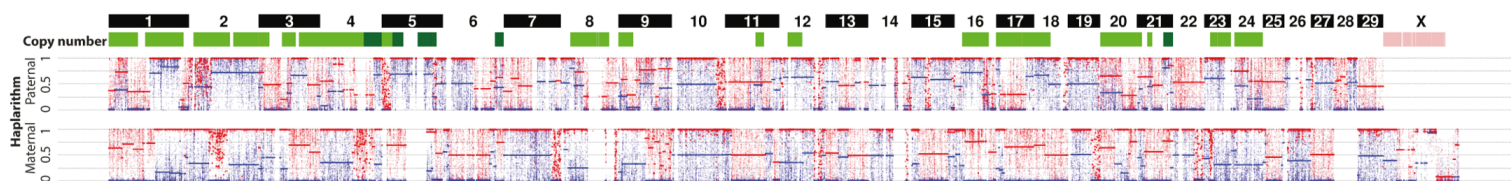
Whole-genome profile (BRP011 _ E10_BI005_BRP011)



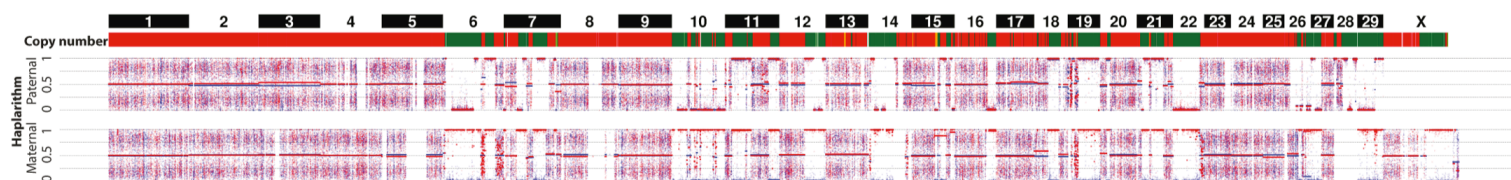
Whole-genome profile (BRP011 _ E10_BI006_BRP011)



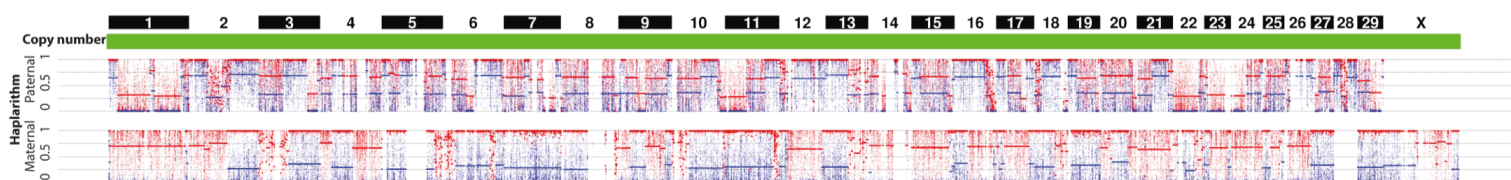
Whole-genome profile (BRP011 _ E10_BI007_BRP011)



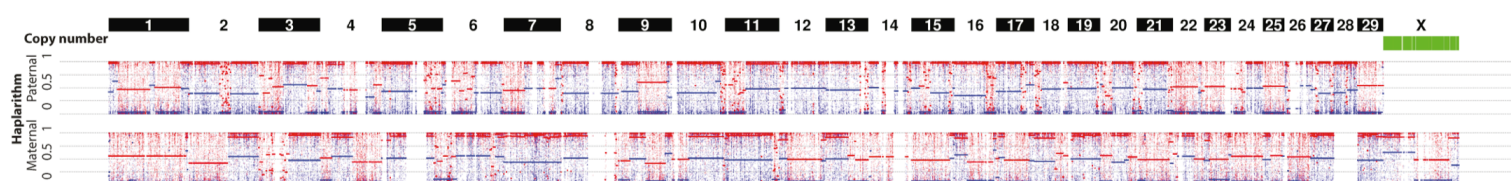
Whole-genome profile (BRP011 _ E10_BI008_BRP011)



Whole-genome profile (BRP011 _ E16_BI001_BRP011)

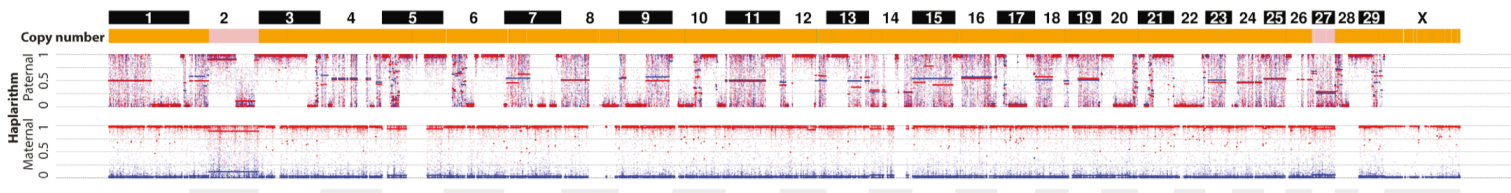


Whole-genome profile (BRP011 _ E16_BI002_BRP011)

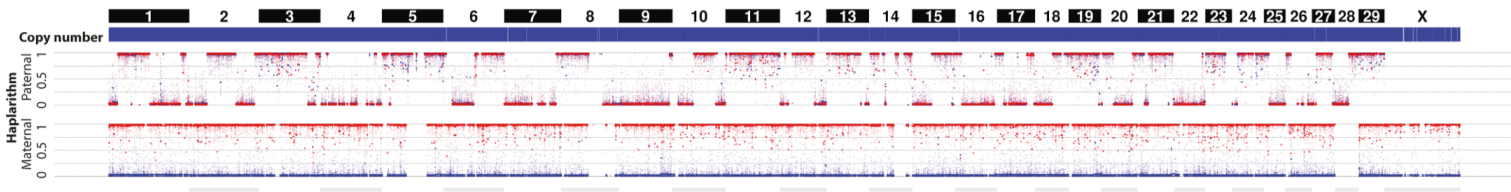


Supplemental Figure S2 (continued)

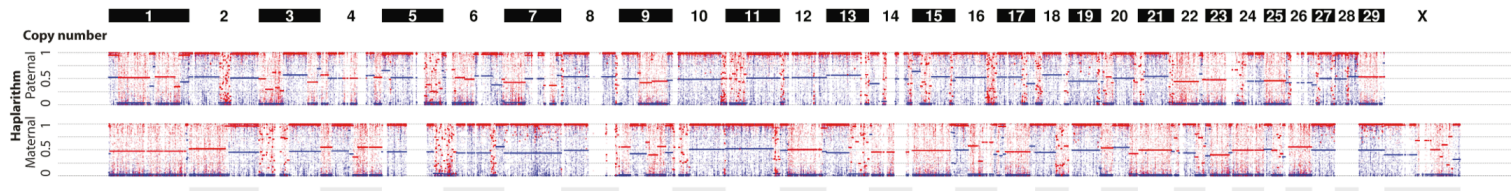
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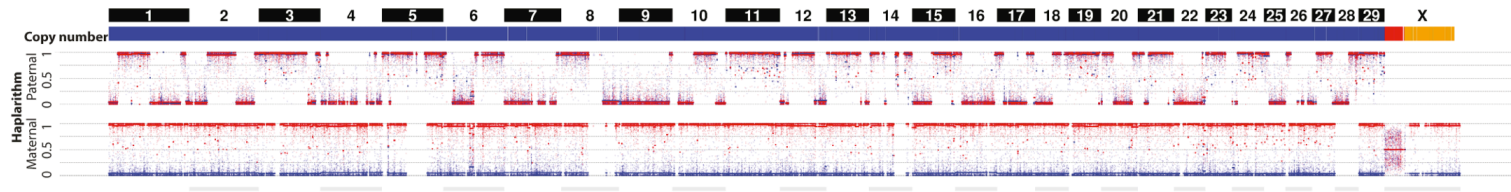
Whole-genome profile (BRP011 _ E16_BI004_BRP011)



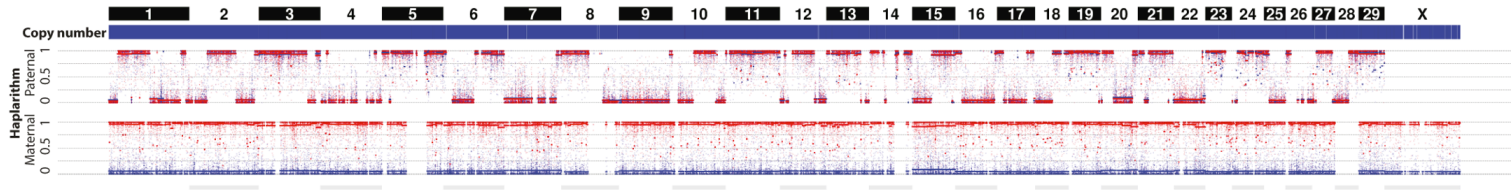
Whole-genome profile (BRP011 _ E16_BI005_BRP011)



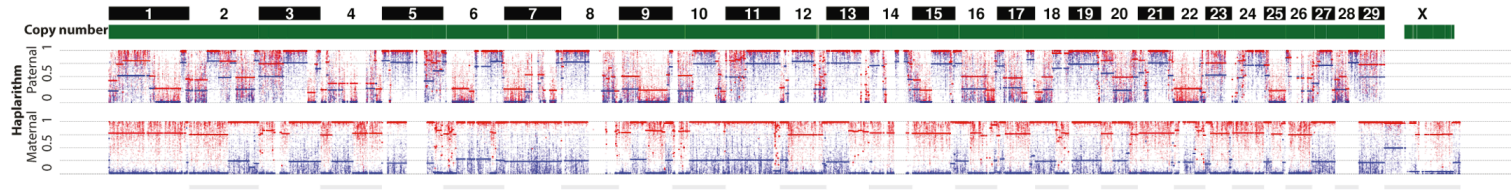
Whole-genome profile (BRP011 _ E16_BI006_BRP011)



Whole-genome profile (BRP011 _ E16_BI007_BRP011)

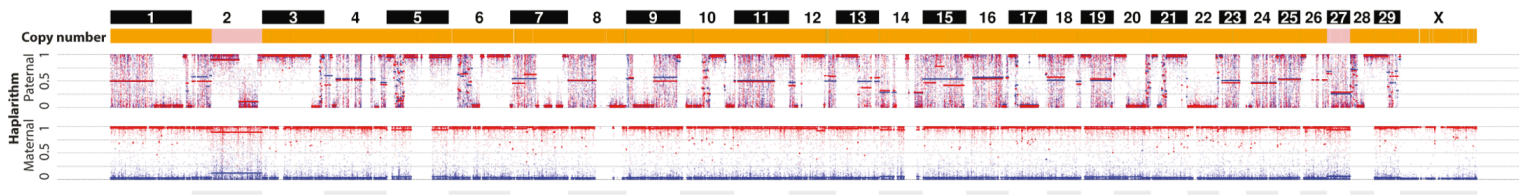


Whole-genome profile (BRP011 _ E16_BI009_BRP011)

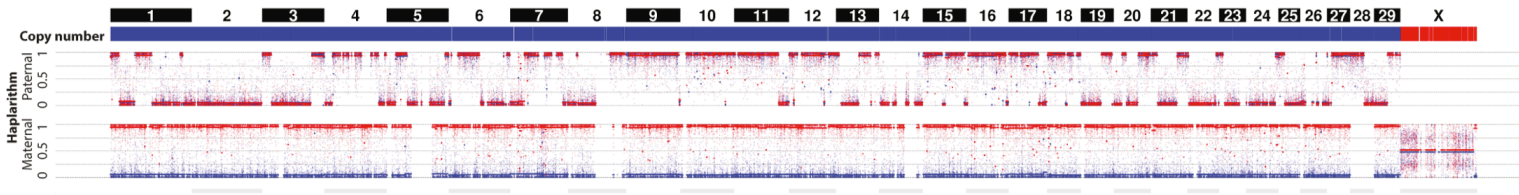


Supplemental Figure S2 (continued)

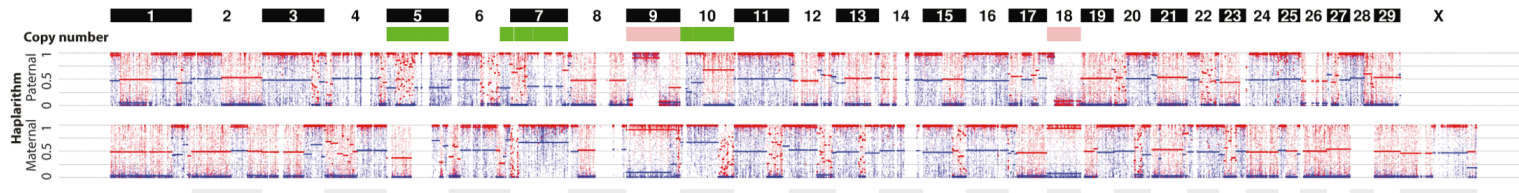
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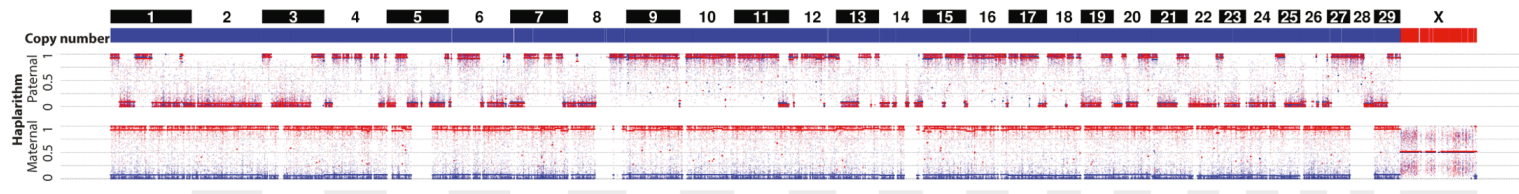
Whole-genome profile (BRP011 _ E17_BI004_BRP011)



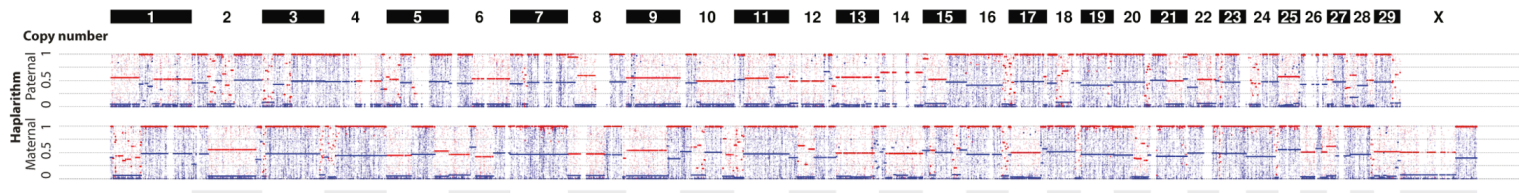
Whole-genome profile (BRP011 _ E17_BI005_BRP011)



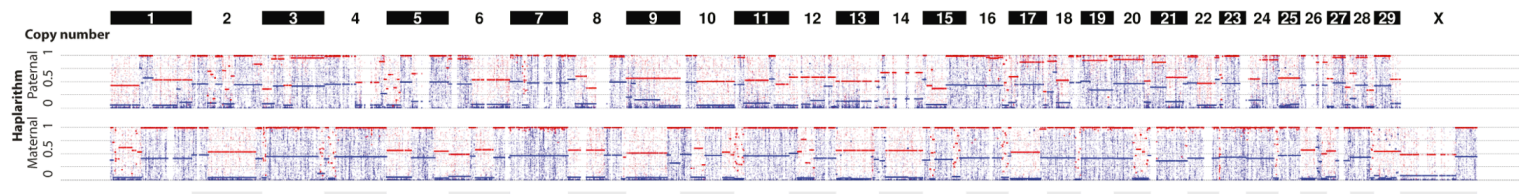
Whole-genome profile (BRP011 _ E17_BI006_BRP011)



Whole-genome profile (BRP012_E07 _ E07_BI001_BRP012)

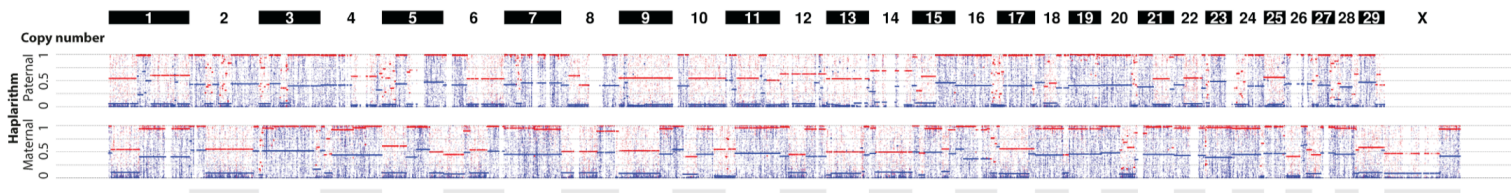


Whole-genome profile (BRP012_E07 _ E07_BI002_BRP012)

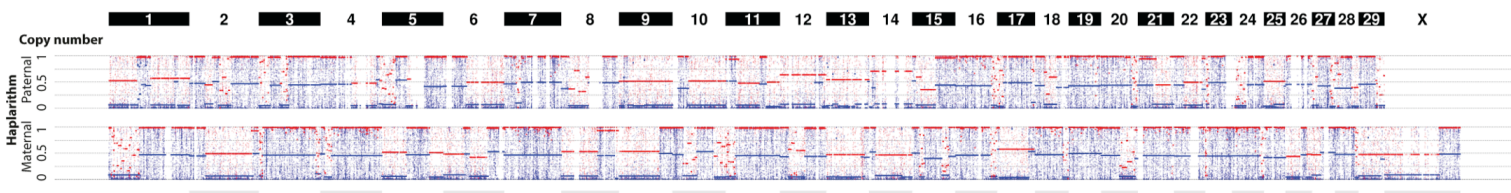


Supplemental Figure S2 (continued)

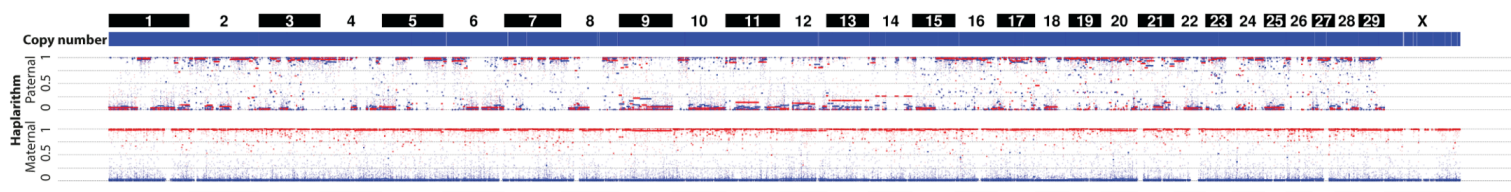
Whole-genome profile (BRP012_E07 _ E07_BI003_BRP012)



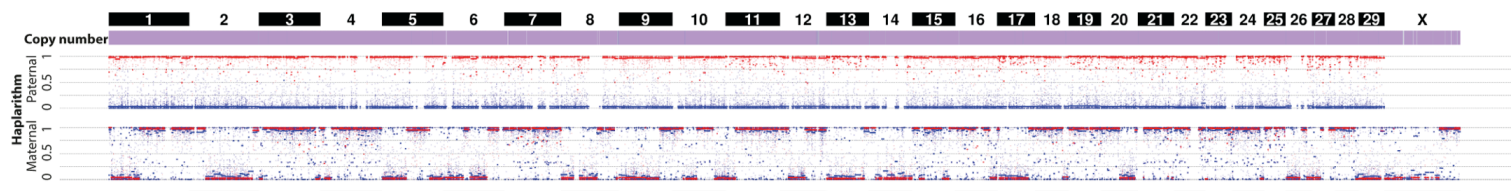
Whole-genome profile (BRP012_E07 _ E07_BI004_BRP012)



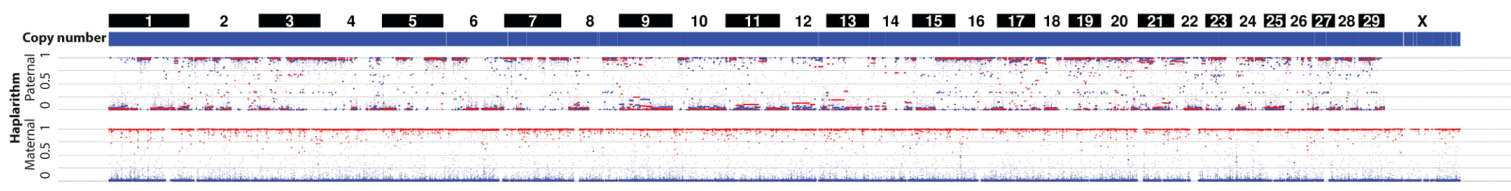
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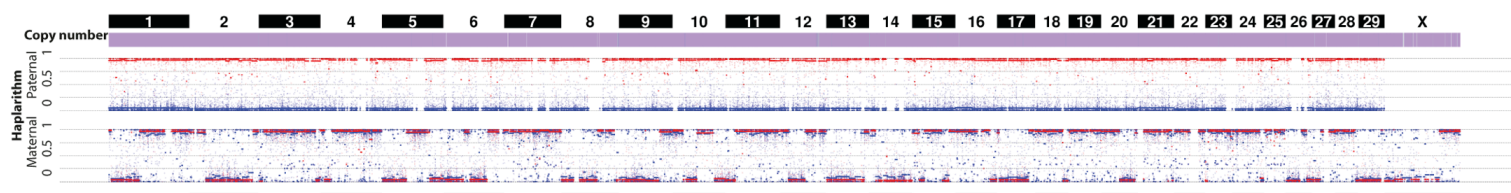
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Whole-genome profile (BRP012_E19 _ E19_BI003_BRP012)

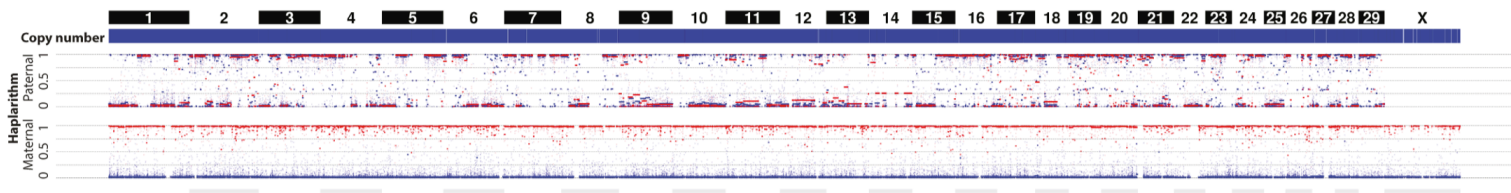


Whole-genome profile (BRP012_E19 _ E19_BI004_BRP012)

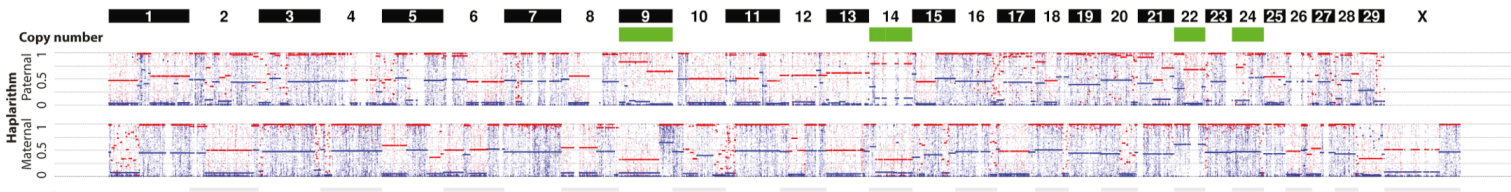


Supplemental Figure S2 (continued)

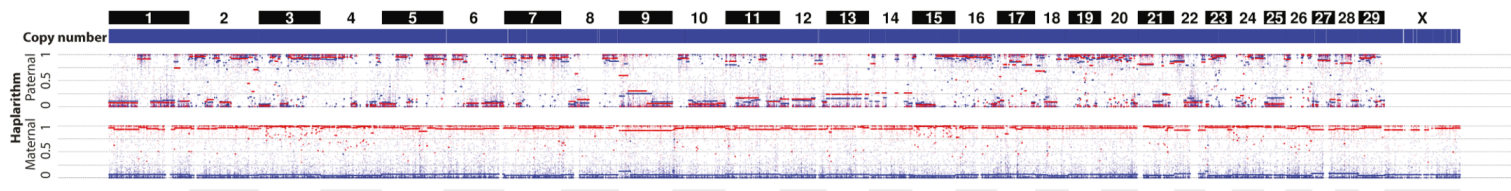
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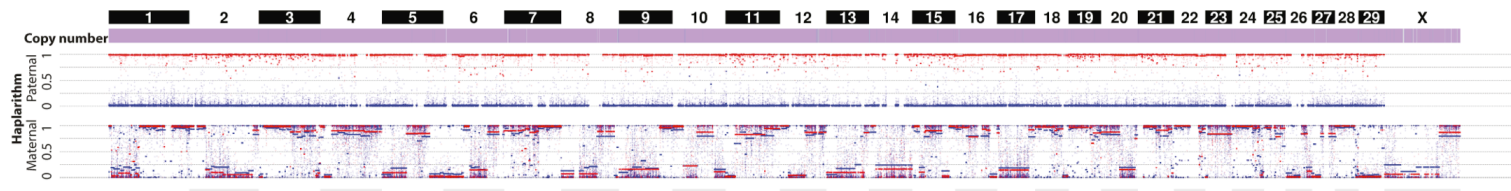
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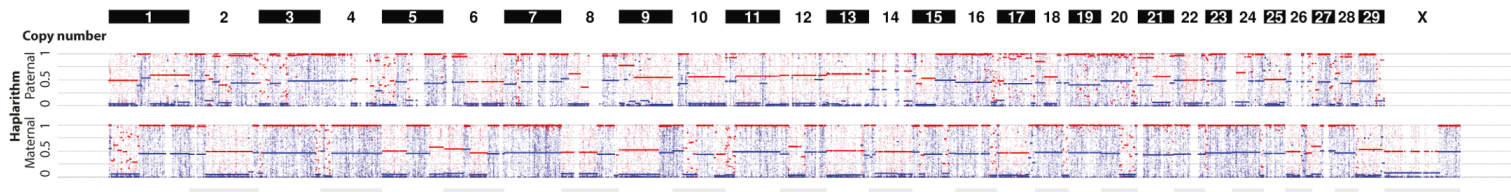
Whole-genome profile (BRP012_E19 _ E19_BI007_BRP012)



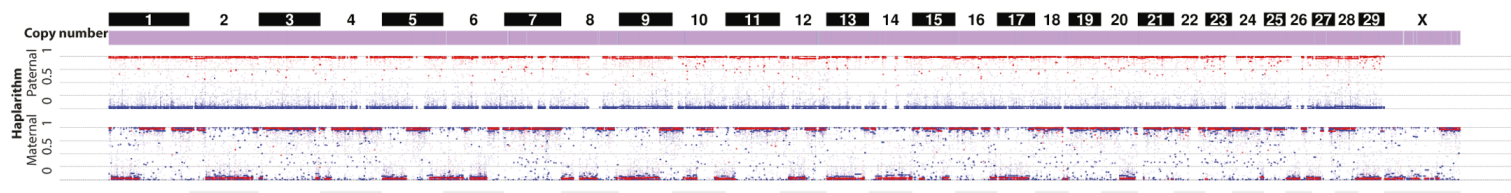
Whole-genome profile (BRP012_E19 _ E19_BI009_BRP012)



Whole-genome profile (BRP012_E19 _ E19_BI010_BRP012)

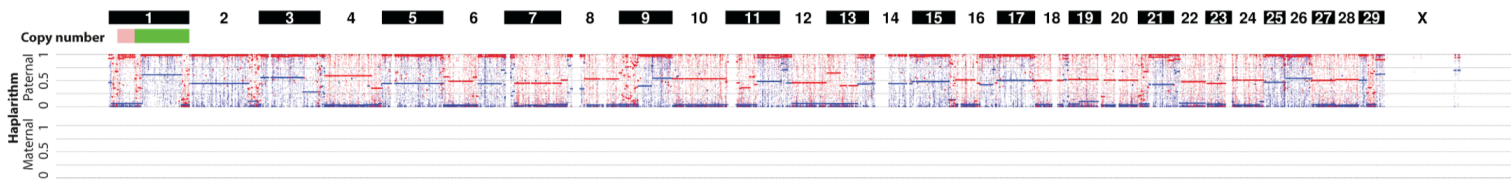


Whole-genome profile (BRP012_E19 _ E19_BI011_BRP012)

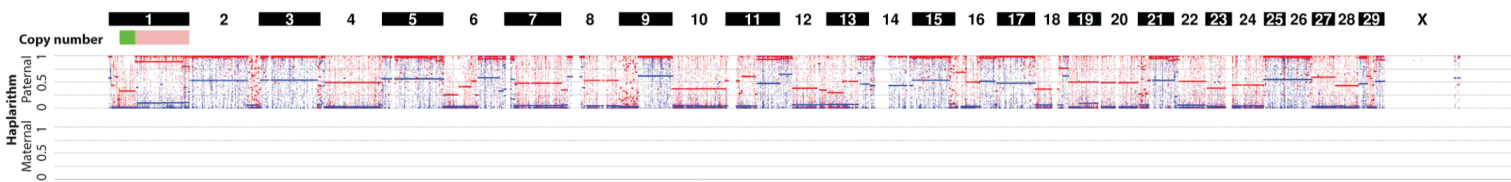


Supplemental Figure S2 (continued)

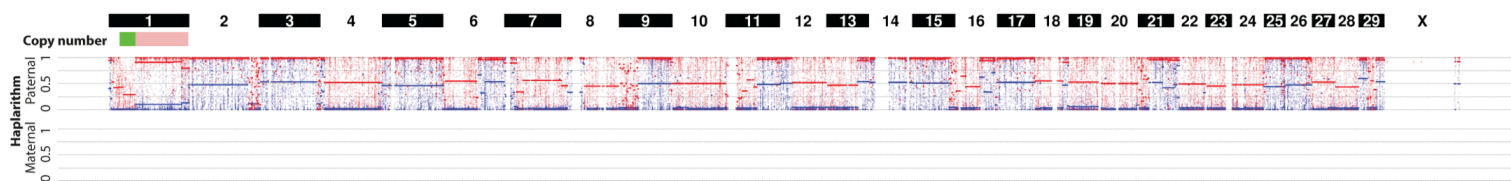
Whole-genome profile (BRP006_A _ E13_BI002_BRP006)



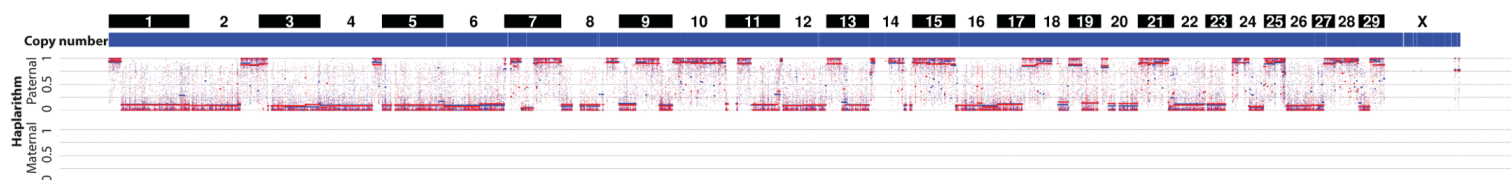
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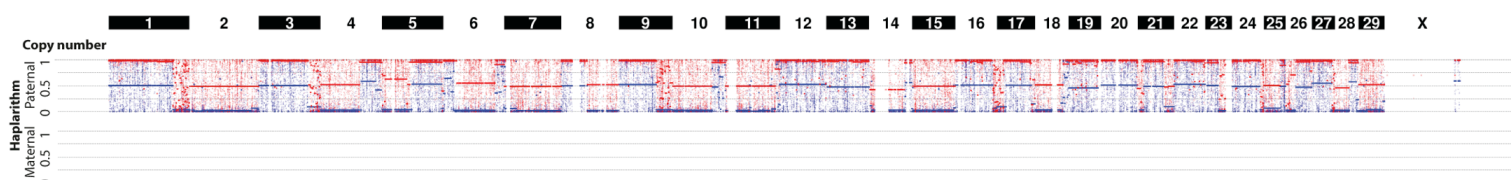
Whole-genome profile (BRP006_A _ E13_BI004_BRP006)



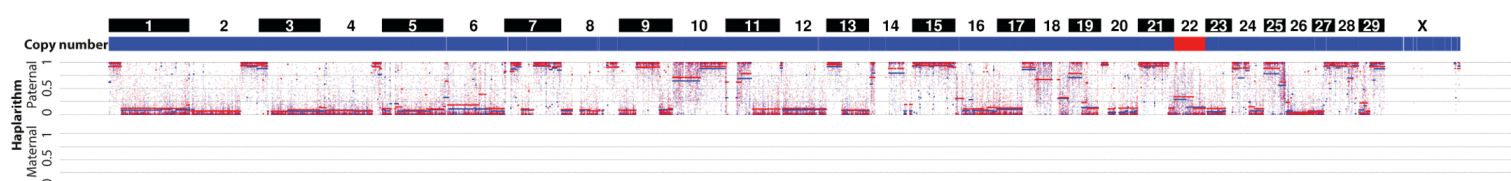
Whole-genome profile (BRP006_A _ E21_BI001_BRP006)



Whole-genome profile (BRP006_A _ E21_BI003_BRP006)

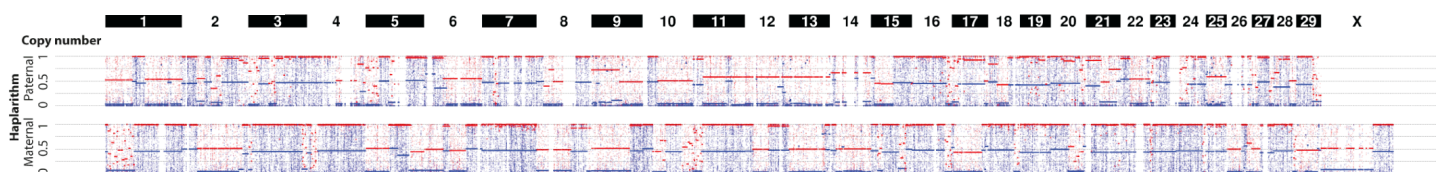


Whole-genome profile (BRP006_A _ E21_BI004_BRP006)



Supplemental Figure S2 (continued)

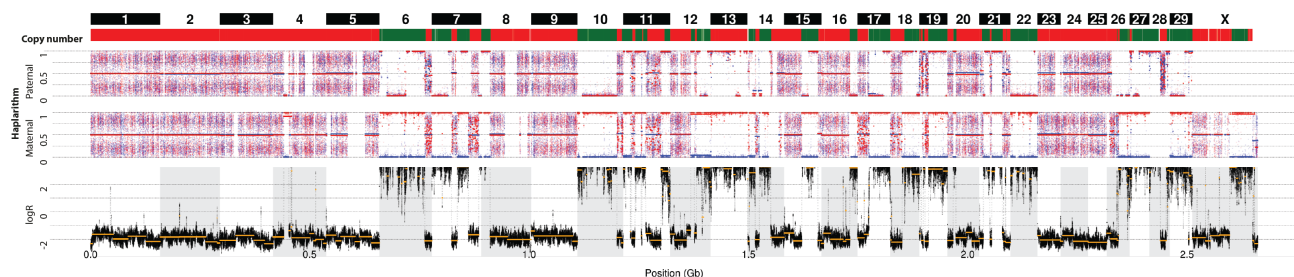
Whole-genome profile (BRP012_E19 _ E19_BI012_BRP012)



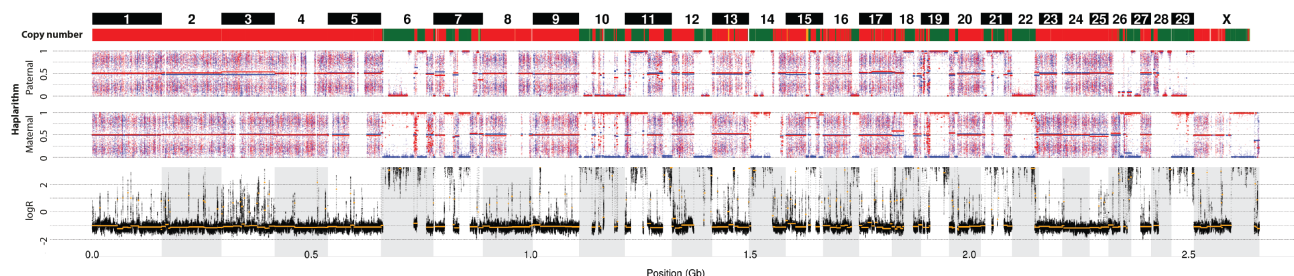
Supplemental Figure S2 | Whole-genome haplarithm profiles of all the single blastomeres involved in this study. In each panel we show the interpreted copy number, and the paternal and the maternal haplarithms.

Supplemental Figure S3

Whole-genome profile (BRP011 _ E10_BI005_BRP011)



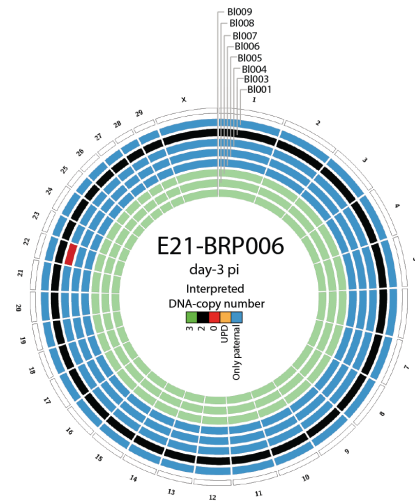
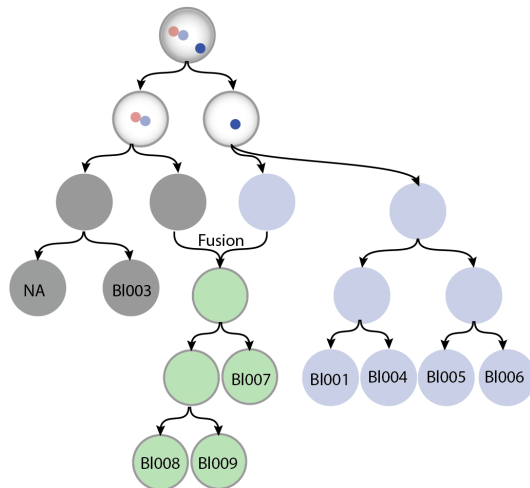
Whole-genome profile (BRP011 _ E10_BI008_BRP011)



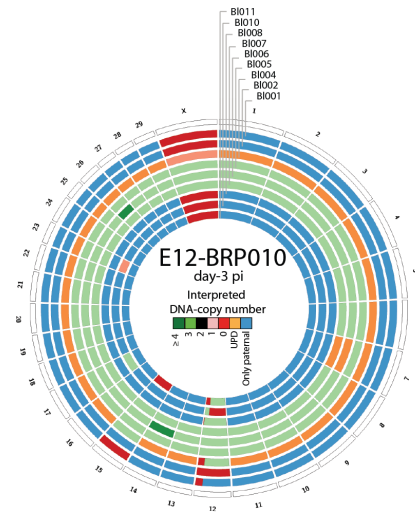
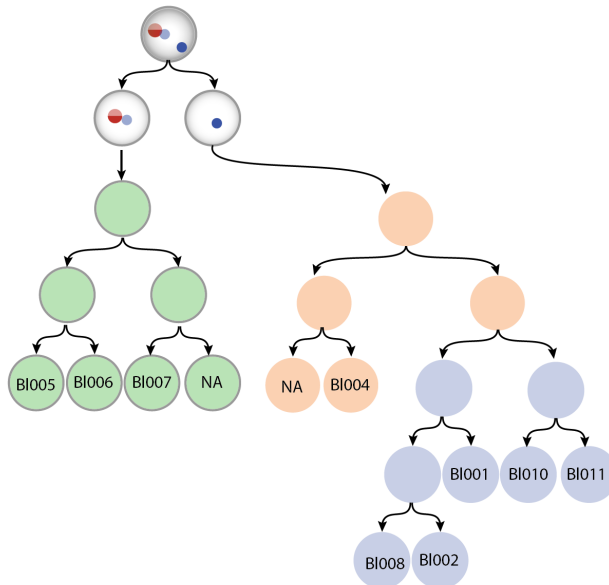
Supplemental Figure S3 | Amplified fragments of the paternal genome in two blastomeres. The top and bottom panels illustrate genome-wide haplarithms of two blastomeres (BI005 and BI008) derived from E10_BRP011. In each panel we show the interpreted copy number (top), the paternal and the maternal haplarithms (middle) and the logR plot (bottom).

Supplemental Figure S4

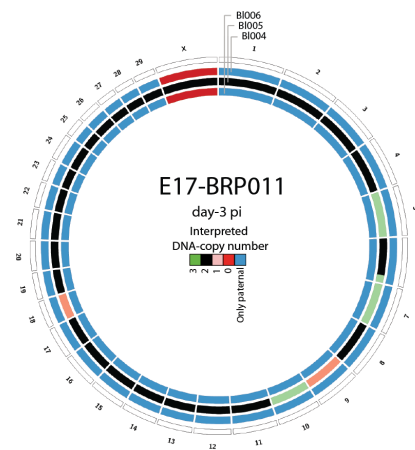
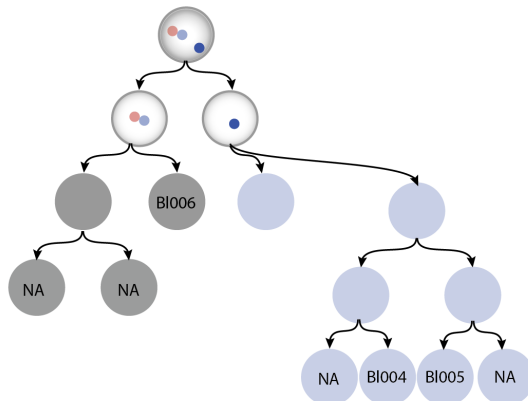
A



B

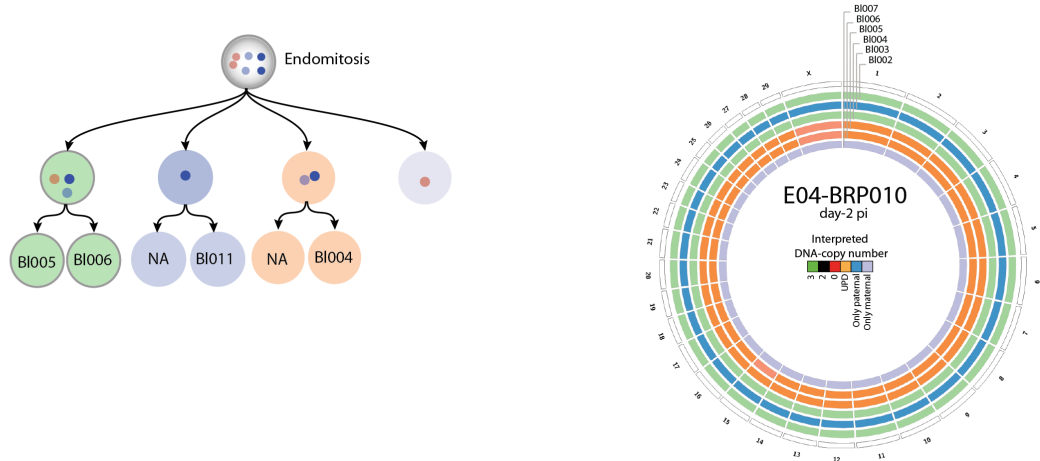


C



Supplemental Figure S4 (continued)

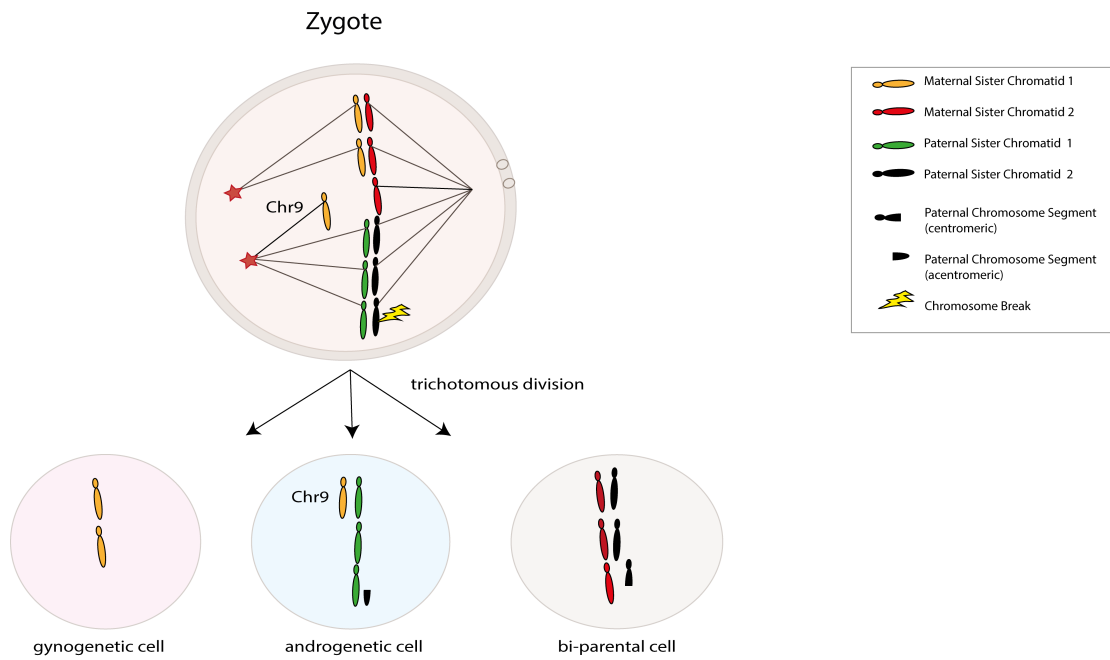
D



Supplemental Figure S4 | Hypothetical models for the first zygotic divisions in dispermic embryos.

The hypothetical cleavage histories of the dispermic embryos are illustrated on the left panels. On the right, each Circos plot represents the interpreted DNA copy number heatmap across the 29 autosomes and ChrX for every analysed blastomere derived from each embryo. **A-C**, The model is based on an atypical division of the triploid zygote before syngamy (grey circle with three pronuclei: 1 maternal (red) and 2 paternal (blue and light blue)) in two blastomeres. One blastomere contains both parental genomes and the second contains the excess paternal genome. These two progenitors give rise in one biparental cell line (black) and an androgenetic one (blue). **A**, Emergence of the triploid blastomeres (green) via the fusion of a biparental with an androgenetic cell. The substandard cells failed to be analysed are indicated by NA. **B**, Biparental, and androgenetic. **C**, The green blastomeres are burdened with triploidy attributed to an MII maternal error and contain one of the two paternal sperm genomes. The second paternal genome is distributed into a second blastomere; the yellow star indicates that the segmental imbalances in chromosome 12 and the whole chromosome imbalances in chromosome 15 affecting exclusively the androgenetic blastomeres, probably occurred after the first cleavage. **D**, A model based on endomitosis followed by stochastic allocation of the nuclei in four blastomeres.

Supplemental Figure S5



Supplemental Figure S5 | The gonameric spindle-based heterogoneic cleavage divisions in E19_BRP005. A model of the gonameric spindle with distinct microtubules attached to each parental genome, which occupy separate space on the metaphase plate. The spindle becomes tripolar after losing centrosome integrity at one pole (red stars). The paternal chromosomes are affected by DNA breaks (yellow thunder). The zygote cleaves directly into three blastomeres.

Supplemental Table S1 | Characteristics of the embryo cohort .

Embryo	Time of blastomere isolation (# days pi)	Embryo content (# cells)	Successful amplification (# cells)	Successful hybridization (# cells)	QC passed (# cells)
E09_BRP004	2	4	4	4	1
E10_BRP004	2	4	4	4	0
E16_BRP004	3	8	7	7	4
E17_BRP004	3	6	6	6	4
E18_BRP004	3	6	6	6	3
E11_BRP005	2	4	4	4	3
E19_BRP005	3	8	8	8	6
E20_BRP005	3	5	5	5	5
E21_BRP006	3	9	9	9	8
E13_BRP006	2	4	4	4	3
E07_BRP007	2	4	4	4	2
E04_BRP008	2	4	4	4	2
E05_BRP008	2	4	4	4	2
E22_BRP009	3	8	8	8	5
E23_BRP009	3	8	8	8	4
E03_BRP010	2	4	4	4	4
E11_BRP010	3	8	8	8	8
E12_BRP010	3	11	11	11	9
E04_BRP010	2	7	7	7	6
E08_BRP011	2	4	4	4	4
E16_BRP011	3	10	10	8	8
E17_BRP011	3	7	7	6	3
E10_BRP011	3	8	8	8	7
E19_BRP012	3	12	12	12	11
E07_BRP012	2	4	4	4	4
Total		161	160	157	116

(%)		na	99.38	97.51	72.04
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Supplemental Table S2 | Nature and frequency of chromosome aberrations per analysed blastomere *

Bovine Cross	Embryo ID	Blastomere ID	Full Chromosome Aberrations					Segmental Abnormalities	
			Monosomy	Trisomy	Nullisomy	Amplification	UPD	Simple	Complex
BRP004	E09	BI002	0	1	0	0	0		
	E16	BI003	0	0	0	0	0		
		BI004	0	0	0	0	0		
		BI005	0	0	0	0	0		
		BI008	0	0	0	0	0		
	E17	BI001	1	0	0	0	0	1	
		BI002	1	1	0	0	0		
		BI005	1	2	0	0	0		
		BI006	2	0	0	0	0		
	E18	BI001	1	3	0	0	0		
		BI002	1	3	0	0	0		
		BI004	0	3	0	0	0		
BRP005	E11	BI002	2	0	0	0	0		
		BI004	1	1	0	0	0		1
	E19	BI001	0	0	2	0	0		
		BI002	0	0	0	0	0	3	
		BI003	0	1	2	0	1	1	
		BI005	0	0	0	0	0	1	
		BI006	0	1	0	0	0	1	2
		BI008	0	1	1	0	0	1	2
BRP006	E13	BI002	0	0	0	0	0		1
		BI003	0	0	0	0	0		1
	E21	BI006	0	0	1	0	0		
BRP007	E07	BI002	0	0	0	0	0	1	
		BI004	0	0	0	0	0	1	
BRP008	E04	BI002	0	0	0	0	0		
		BI003	0	0	0	0	0		
	E05	BI002	0	0	0	0	0		
BRP009	E22	BI001	0	0	0	0	0		
		BI002	0	0	0	0	0		
		BI004	0	0	0	0	0		
		BI007	0	0	0	0	0		
		BI008	0	0	0	0	0		
	E23	BI004	0	0	0	0	0		

		BI005	0	0	0	0	0		
		BI006	0	0	0	0	0		
		BI008	0	0	0	0	0		
BRP010	E03	BI001	1	1	0	0	0		
		BI002	2	0	0	0	0		
		BI003	1	0	0	1	0		
		BI004	1	0	0	0	0		
	E11	BI001	0	0	0	0	0		
		BI002	0	0	0	0	0		
		BI003	0	0	0	0	0		
		BI004	0	0	0	0	0		
		BI005	0	0	0	0	0		
		BI006	0	0	0	0	0		
		BI007	0	0	0	0	0		
		BI008	0	0	0	0	0		
	E12	BI001	0	0	2	0	0	1	0
		BI002	0	0	2	0	0		0
		BI004	2	0	0	0	0		1
		BI006	0	0	0	2	1		
		BI007	0	0	0	0	1		
		BI008	0	0	1	0	0		0
		BI010	0	0	1	0	0		1
		BI011	0	0	2	0	0		1
	E04	BI005	1	0	0	0	0		
		BI006	1	0	0	0	0		1
BRP011	E08	BI001	0	0	1	0	0	1	
		BI002	1	0	1	0	0	1	
		BI003	0	0	1	0	0	1	1
		BI004	0	0	1	0	0	2	
	E16	BI002	0	0	0	0	0		
		BI003	1	0	0	0	0		1
		BI005	0	0	0	0	0		
		BI006	0	0	0	0	0		1
		BI009	0	0	0	0	0		
	E17	BI005	2	2	0	0	0		
	E10	BI001	0	0	0	0	0		
		BI002	0	0	0	0	0		
		BI005	0	0	10	1	0		

		BI006	0	0	0	0	0		
		BI008	0	0	10	0	0		
BRP012	E19	BI006	0	4	0	0	0		

* see Methods for a detail explanation of the rules applied to the blastomeres included in frequency and nature of chromosome aberrations calculations.