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Supplemental Data

Nested Inversion Polymorphisms Predispose Chromosome 22q11.2 to Meiotic Rearrangements

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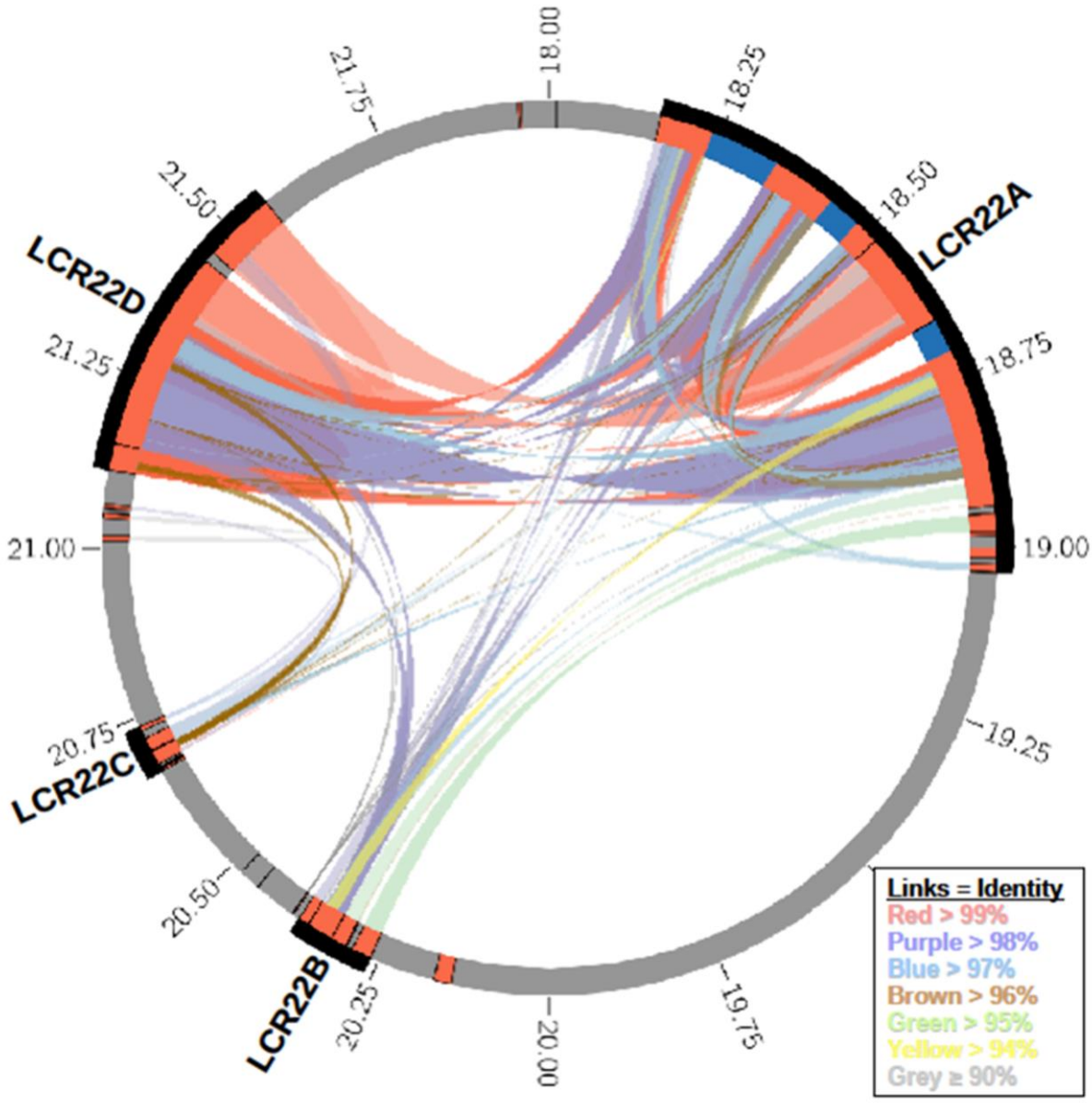

Figure S1

Paralogous relations among the four LCRs of chromosome 22q11.2. Numbers indicate hg38 chromosome 22 coordinates in Mb. Black bars on the outer circle delineate conventional coordinates of LCR22A, LCR22B, LCR22C, and LCR22D. Blue rectangles in LCR22A depict gaps in the reference sequence. Segmental duplicated sequences are shown in orange and the unique sequences in grey. Connecting lines, color-coded by percent identity, show paralogous relations between subunits within and between LCR22s. The plot was generated with Circos v0.64 [1] using segmental duplication definitions [2,3] as downloaded from the UCSC genome browser [4].

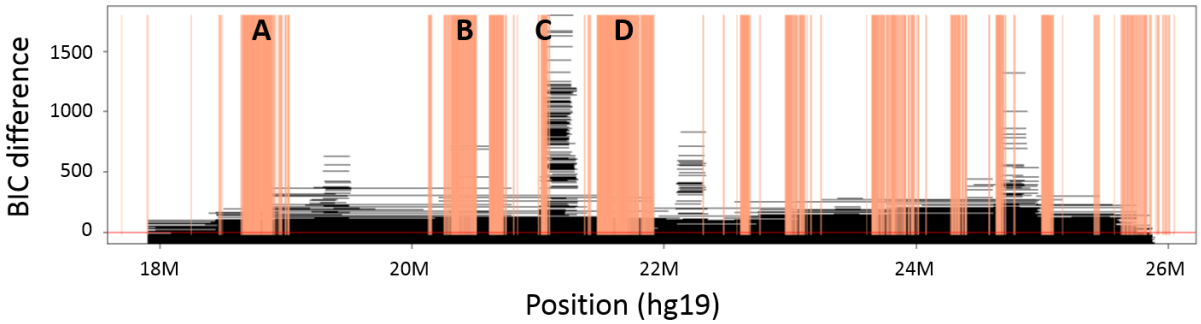

Figure S2

Detailed InveRsion [5] plot of chromosome 22q11 using single nucleotide variation data from the European samples of the 1000G project [6]. Segment sizes ranged from 0.2 to 3 Mb. Orange boxes highlight the location of the LCR blocks. Several putative inversions were found in the region with the strongest signal located between LCR22C and LCR22D

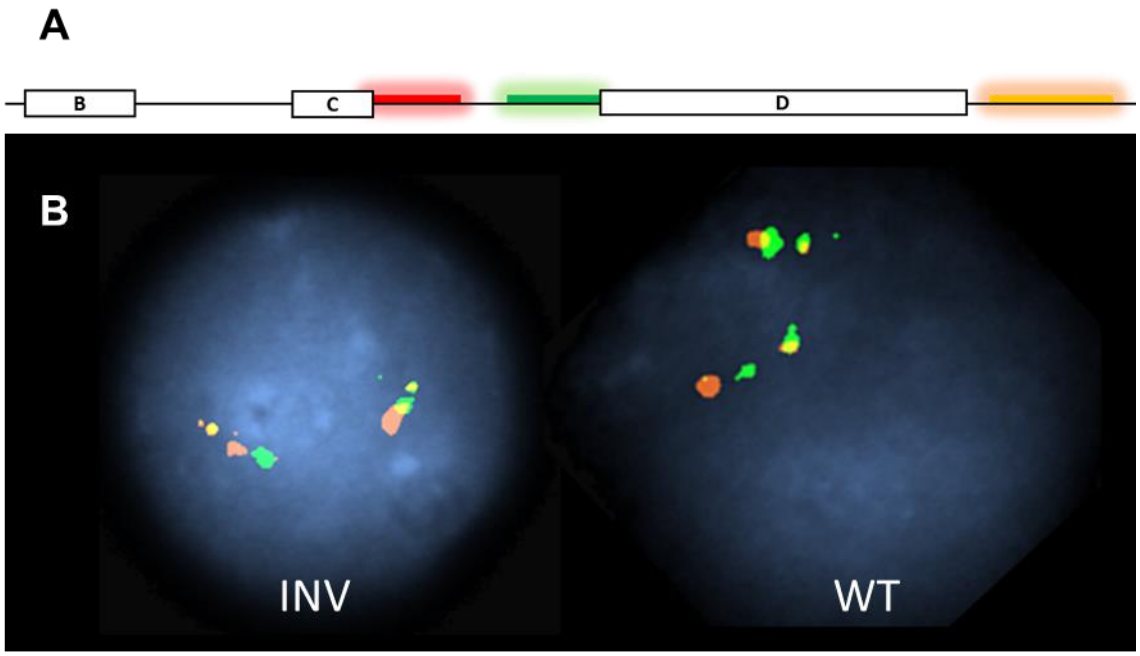

Figure S3

Interphase FISH. **(A)** probe design aligned with schematic representation of the LCR22B-D region. Red (SpectrumOrange labelled) and green (SpectrumGreen labelled) and yellow (a mix of SpectrumOrange and SpectrumGreen) BACs (hg38, RP11-590C5, chr22:20,7260,03-20,906,345, RP11-165F18, chr22:20,934,046-21,099,834 and RP11-354K13, chr22:21,588,266-21,764,059) respectively proximal and distal from LCR22D. Nick Translation (Abbott Molecular, Abbott Park, Illinois, U.S.A.) was used for labelling **(B).** Overlay of three channel recording (DAPI, SpectrumGreen, SpectrumOrange) showcasing an interphase cell heterozygous for an inversion in the LCR22B-C-D region. Detailed image of the signals show probe orders red-green-yellow (WT) and green-red-yellow (INV).

Table S1

Fiber-FISH and parent-of-origin data of 17 families. For individuals screened with the secondary probe set, detected inversion type is indicated. Results of interphase FISH validations are shown in the right column for 12 individuals (marked with *).

family	Sample origin	fiber pattern INVERTED	fiber pattern REFERENCE	% fiber signals INVERTED	Call	Inversion type determined by pattern 2	% interphase signals INVERTED
1	non-transmitting parent	1	11	8,33%	hom REF		
	parent-of-origin	8	7	53,33%	het INV		
2	non-transmitting parent	0	10	0,00%	hom REF		
	parent-of-origin	4	16	20,00%	het INV	Type B-D	
3	non-transmitting parent	0	11	0,00%	hom REF		
	parent-of-origin	0	12	0,00%	hom REF		
4	non-transmitting parent	4	6	40,00%	het INV		
	parent-of-origin	14	15	48,28%	het INV		
	patient	0	8	0,00%	REF		
5	non-transmitting parent	4	19	17,39%	hom REF		
	parent-of-origin	9	8	52,94%	het INV		
6	non-transmitting parent	1	13	7,14%	hom REF		
	parent-of-origin	4	8	33,33%	het INV		
7	non-transmitting parent	1	10	9,09%	hom REF		
	parent-of-origin	3	10	23,08%	het INV		
8	non-transmitting parent	5	15	25,00%	het INV	Type B-D	
	parent-of-origin	3	7	30,00%	het INV	Type B-D	
	patient	0	8	0,00%	REF		
9	non-transmitting parent	7	6	53,85%	het INV		
	parent-of-origin	4	10	28,57%	het INV		
	patient	0	9	0,00%	REF		
10	non-transmitting parent	4	8	33,33%	het INV		
	parent-of-origin	6	15	28,57%	het INV	Type B-D	
	patient	0	8	0,00%	REF		
11	non-transmitting parent *	6	32	15,79%	hom REF		14,29%
	parent-of-origin *	2	8	20,00%	het INV		44,12%
	patiënt *	0	9	0,00%	REF		13,73%
12	non-transmitting parent *	6	9	40,00%	het INV		43,24%
	parent-of-origin	2	8	20,00%	het INV	Type B-D	
	patiënt *	1	11	8,33%	REF		11,11%
13	non-transmitting parent	3	9	25,00%	het INV	Type B-D	
	parent-of-origin	5	5	50,00%	het INV	Type C-D	
	patient	0	13	0,00%	REF		
14	non-transmitting parent	4	6	40,00%	het INV	Type C-D	
	parent-of-origin	5	8	38,46%	het INV	Type B-D	
	patient	0	10	0,00%	REF		
15	non-transmitting parent *	11	23	32,35%	het INV		40,28%
	parent-of-origin	4	4	50,00%	het INV		
16	non-transmitting parent *	0	13	0,00%	hom REF		10,20%
	parent-of-origin *	12	18	40,00%	het INV		46,30%
	patient (deletion LCR22A-B) *	9	10	47,37%	het INV		36,11%
17	non-transmitting parent *	0	9	0,00%	hom REF		14,29%
	parent-of-origin *	4	6	40,00%	het INV		42,86%
	patient (duplication LCR22A-D)	7	4	63,64%	het INV		
Population samples	RANDOM 1	3	7	30,00%	het INV	Type B-D	
	RANDOM 2	3	6	33,33%	het INV	Type B-D	
	RANDOM 3	2	7	22,22%	het INV		
	RANDOM 4	1	9	10,00%	hom REF		
	RANDOM 5	1	9	10,00%	hom REF		
	RANDOM 6	1	10	9,09%	hom REF		
	RANDOM 7	2	8	20,00%	het INV		
	HAPMAP - GM19238	1	10	9,09%	hom REF		
	HAPMAP - GM19239	1	9	10,00%	hom REF		
	HAPMAP - GM19240 *	11	20	35,48%	het INV	Type C-D	40,91%
	HAPMAP - GM12878	7	8	46,67%	het INV		
	Hydatiform mole - CHM1	0	8	0,00%	REF		
	Hydatiform mole - CHM13	0	10	0,00%	REF		

Supplementary references

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