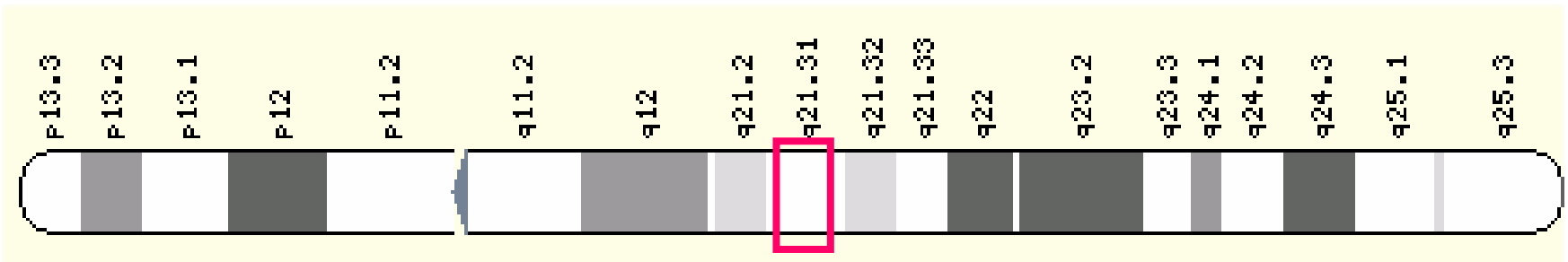
A common inversion under selection in Europeans

Nature Genetics 37:129-137

Stefansson et al. 2005

chr17


p13.3
p13.2
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p12
p11.2
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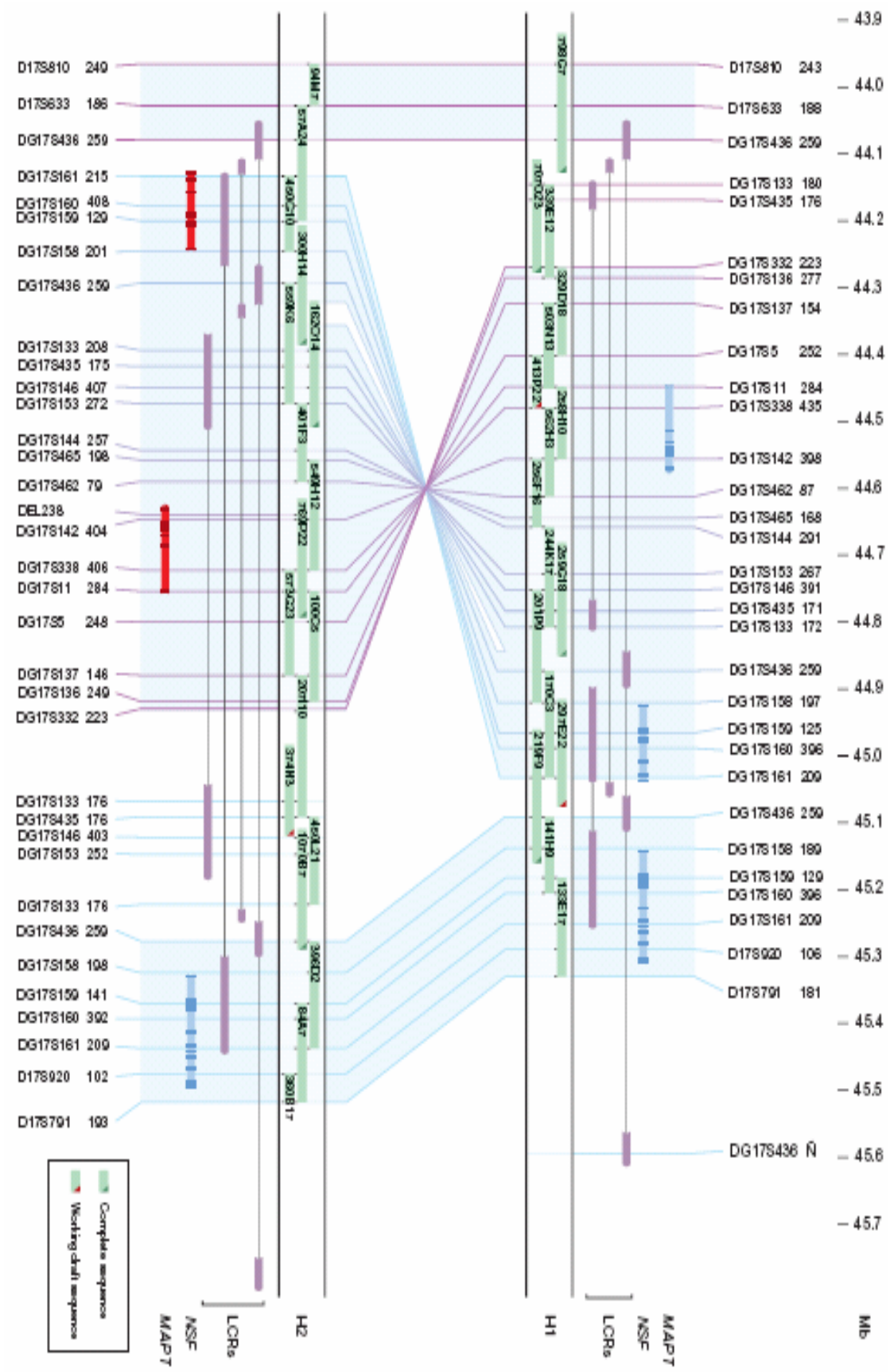
q12
q21.2
q21.31
q21.32
q21.33
q22
q23.2
q23.3
q24.1
q24.2
q24.3
q25.1
q25.3

Uuringu maht

- 17q21.31
- MAPT geen, mikrotuubuliga seotud geen tau, haplotüübid H1 ja H2
- RP11 BAC kloonid ühelt inimeselt, haplotüübid eraldati markeri DG17S142 ja läheduses paikneva deletsiooni põhjal
- 60 mikrosatelliitset markerit paigutati kromosoomispetsiifilistele kontiigidele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DG17S160 392
DG17S161 209
D17S920 102
D17S791 193
Complete sequence
Working draft sequence
MAPT
NSF
LCRs
H2
H1
LCRs
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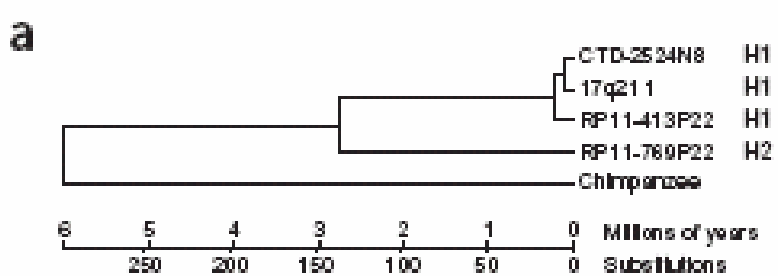
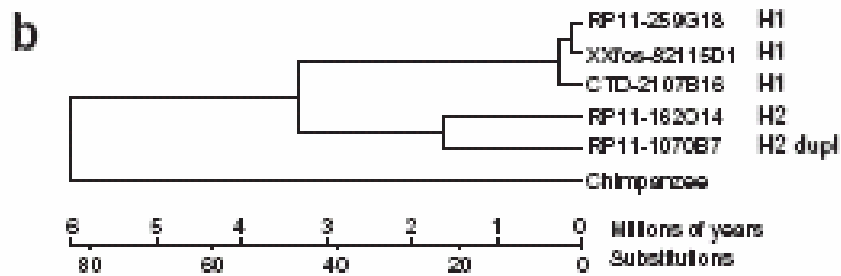
DG17S436 Ñ

H2 kujunemine

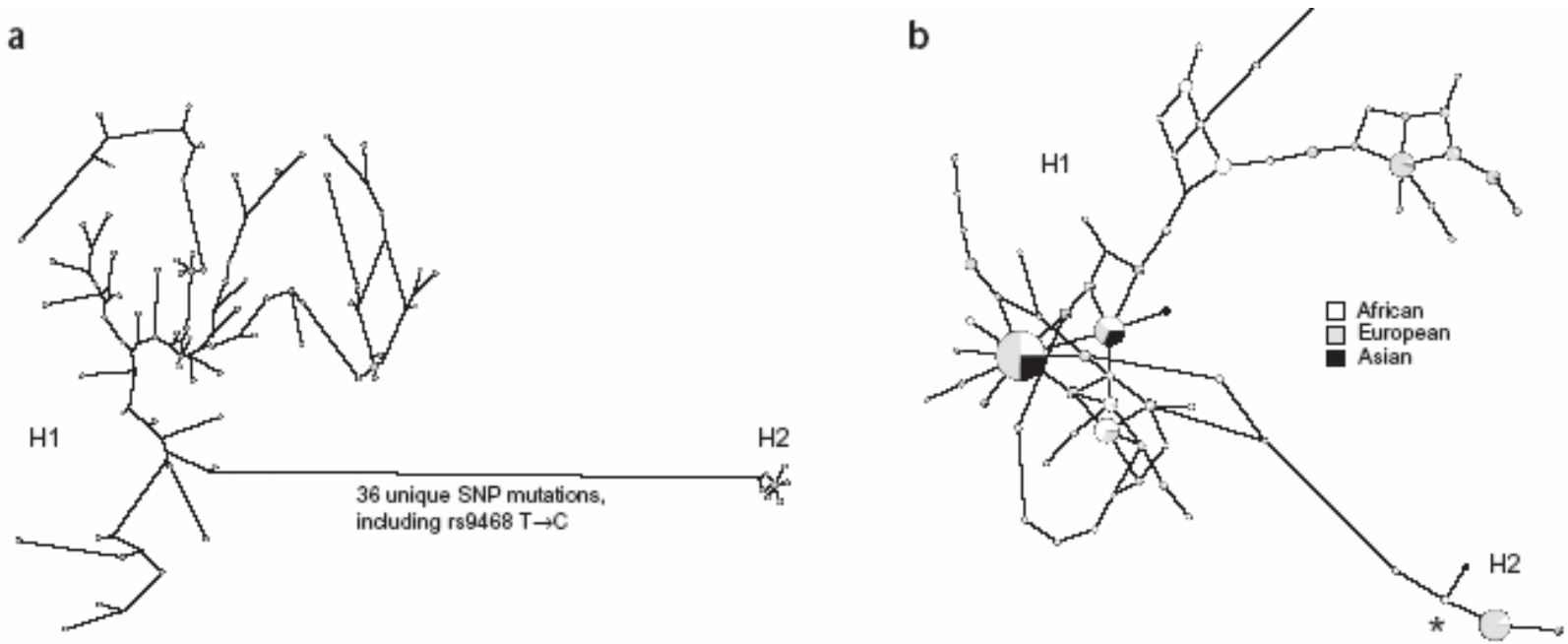
- 77 kb lõik MATP geenist
- H1 ja H2 eristumise tõenäosus 10000 indiviidiga populatsiooni juures, kus keskmine populatsiooni intervall on 30 aastat on 0,006737



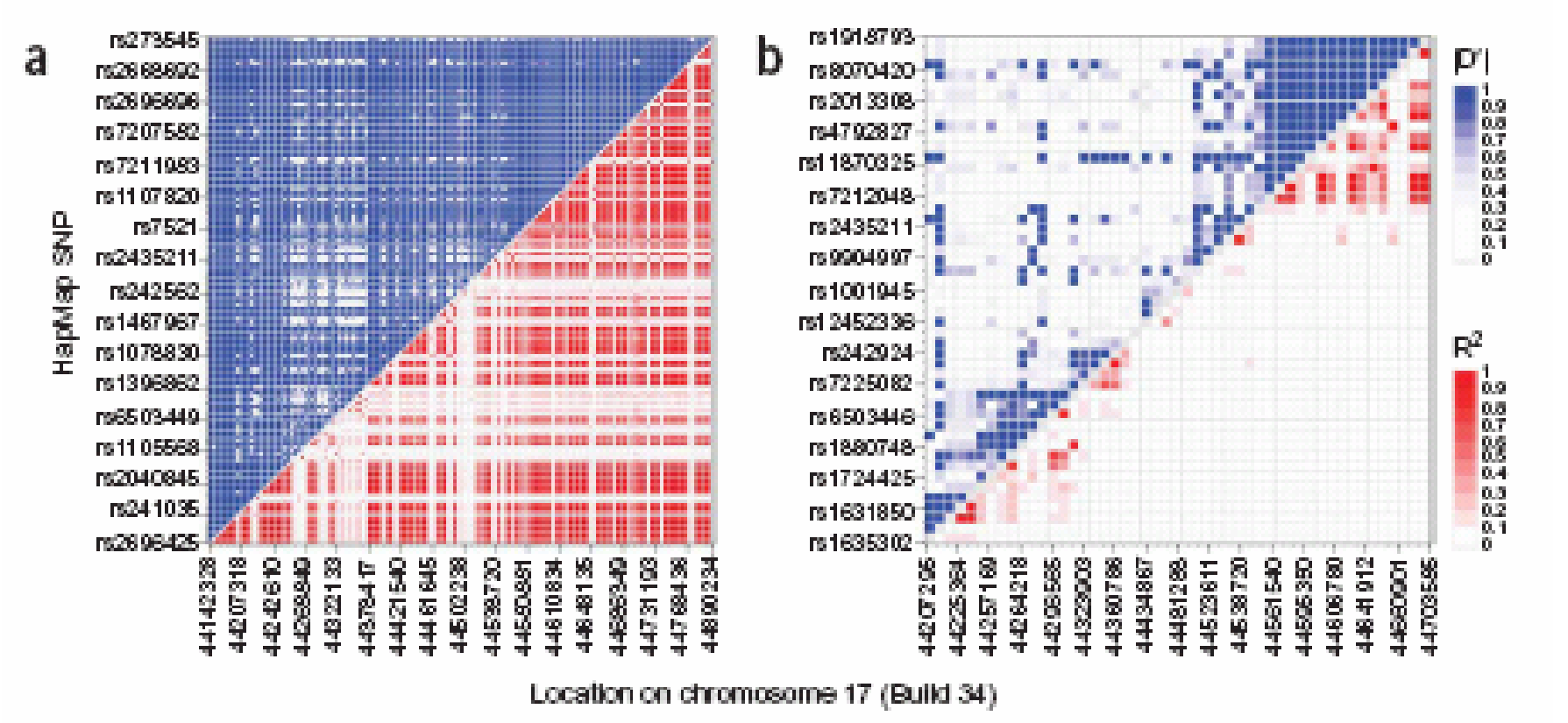


H2 kujunemine

- 6 mikrosatellitse ja 95 SNP markeri põhjal, mis asuvad 424kb pikkuses mitteduplitseerunud regioonis



LD struktuur CEPH ja Yoruba proovidel



rs1800547 genotüüpide sagedused ALFRED andmebaasist

rs9468 genotüüpide sagedused ALFRED andmebaasist

Laste arv H2 kandjatel

Table 1 Relationship between number of children and H2 carrier status

Cohort	Predictor	Estimate	Standard error	*P* value
Combined	Year of birth	−0.0340	0.0008	0.0000
	Carrier of H2	0.0796	0.0259	0.0025
	Sex	0.2360	0.0190	0.0000
Female	Year of birth	−0.0331	0.0010	0.0000
	Carrier of H2	0.0907	0.0338	0.0068
Male	Year of birth	−0.0349	0.0012	0.0000
	Carrier of H2	0.0679	0.0375	0.0719

Results from multiple regression analyses for a cohort of 16,959 females and 12,178 males born between 1925 and 1965, provided for the entire cohort and for the females and males analyzed separately. The regression uses weights that are inversely proportional to the probability that a person will be included in the regression. Standard errors and *P* values are empirically determined based on 10,000 simulations. The estimated effects presented here are statistical; they do not imply causation, as the results could be a consequence of the H2 chromosomes being correlated with some unknown functional variant(s).

Rekombinatsiooni aste vs. H2

Table 2 Relationship between recombination rates and the number of H2 chromosomes carried

Response (recombinations)	Predictor	Estimate	Standard error	*P* value
Total	Number of H2	0.4721 (1.04)	0.1180	0.0002
	Year of birth	−0.0024	0.0064	0.7037
	Average age at birth of offspring	0.0838	0.0152	0.0000
Telomeric	Number of H2	0.0257 (2.24)	0.0092	0.0047
	Year of birth	−0.0006	0.0005	0.2130
	Average age at birth of offspring	0.0077	0.0012	0.0000
Nontelomeric	Number of H2	0.4465 (1.01)	0.1160	0.0004
	Year of birth	−0.0018	0.0062	0.7724
	Average age at birth of offspring	0.0760	0.0149	0.0000

Results from multiple regressions using inversion count, mother's year of birth and mother's average age at birth of her offspring as predictors, and using the total genome and the genome divided into telomeric and nontelomeric regions as the three different responses. The telomeric region for each chromosome arm is the region including all genotyped markers within 6 cM of the most telomeric marker for that arm. In aggregate, the telomeric regions account for 2.8% of the total genomic length. Data is based on 5,012 mothers born between 1925 and 1965 with at least two children genotyped. For H2, the estimated percentage increase per copy is indicated in parentheses.

Rekombinatsiooni astme tõus

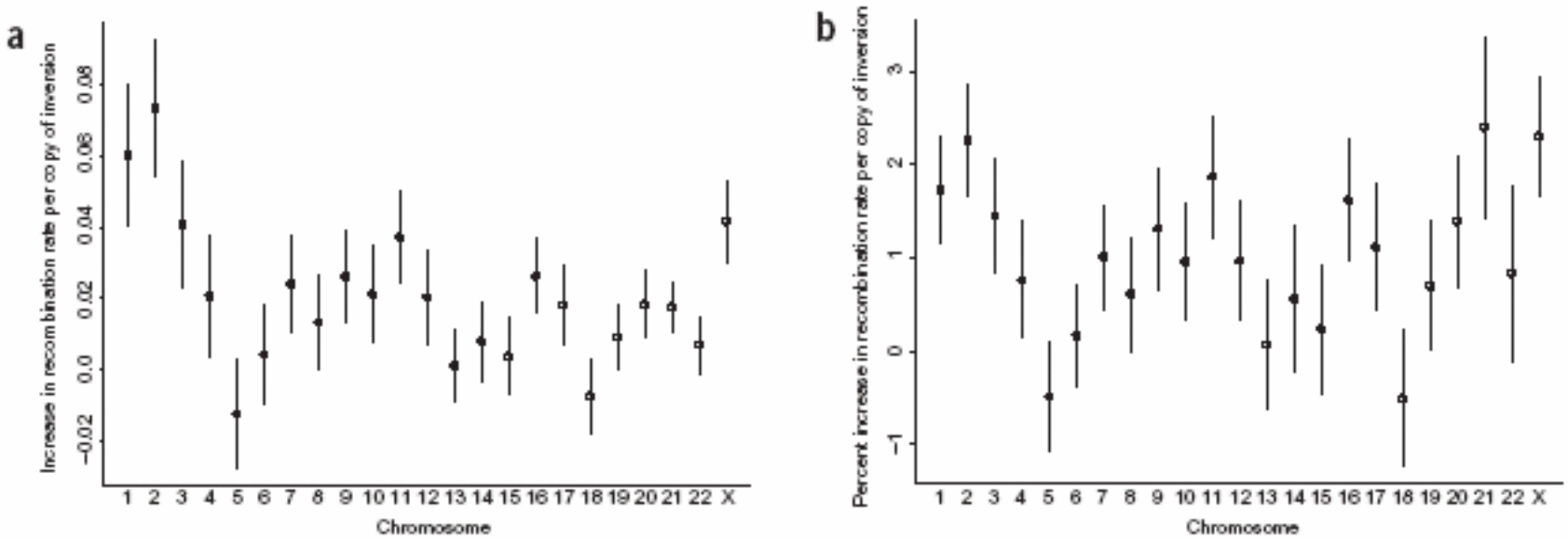
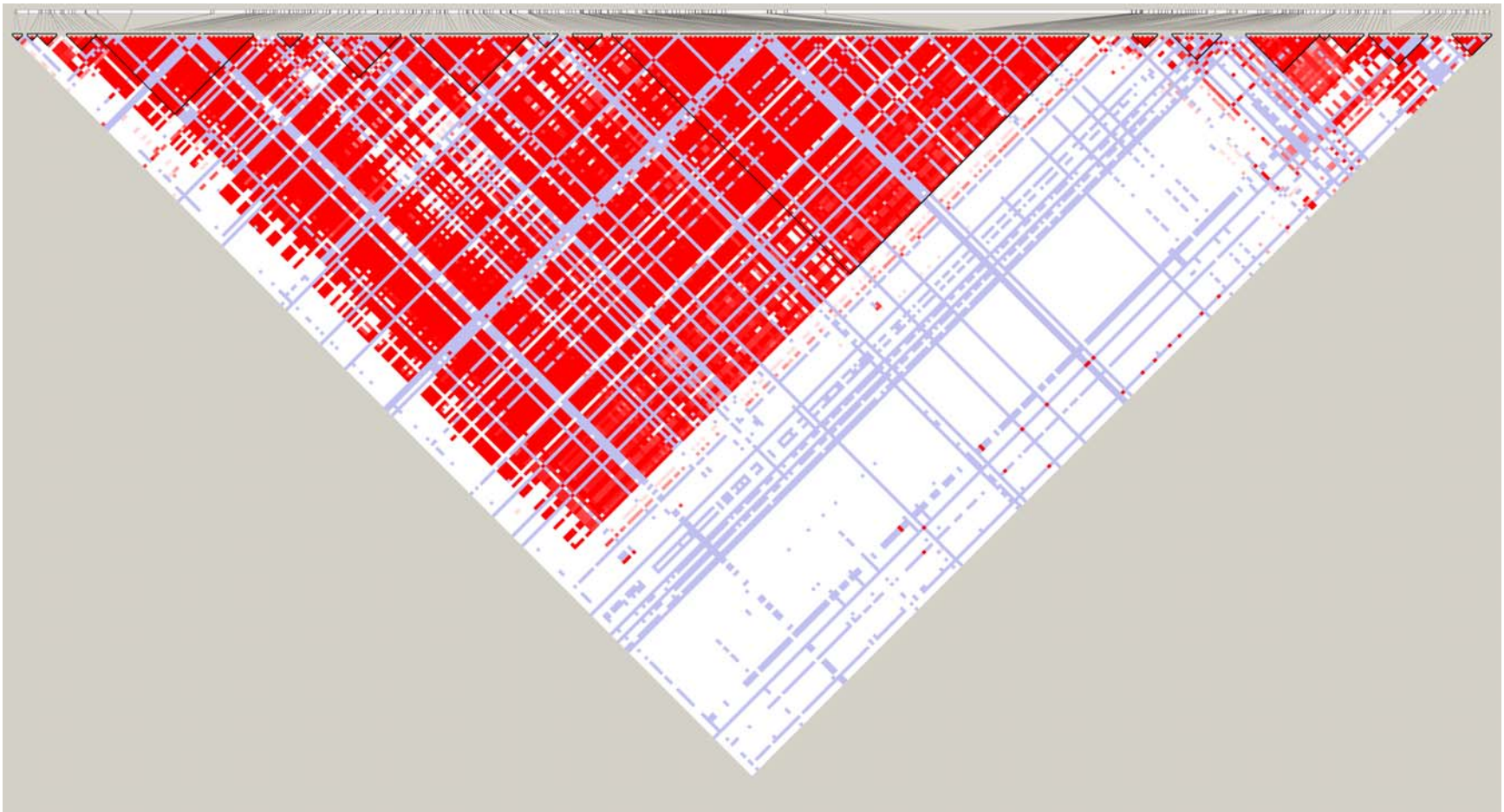


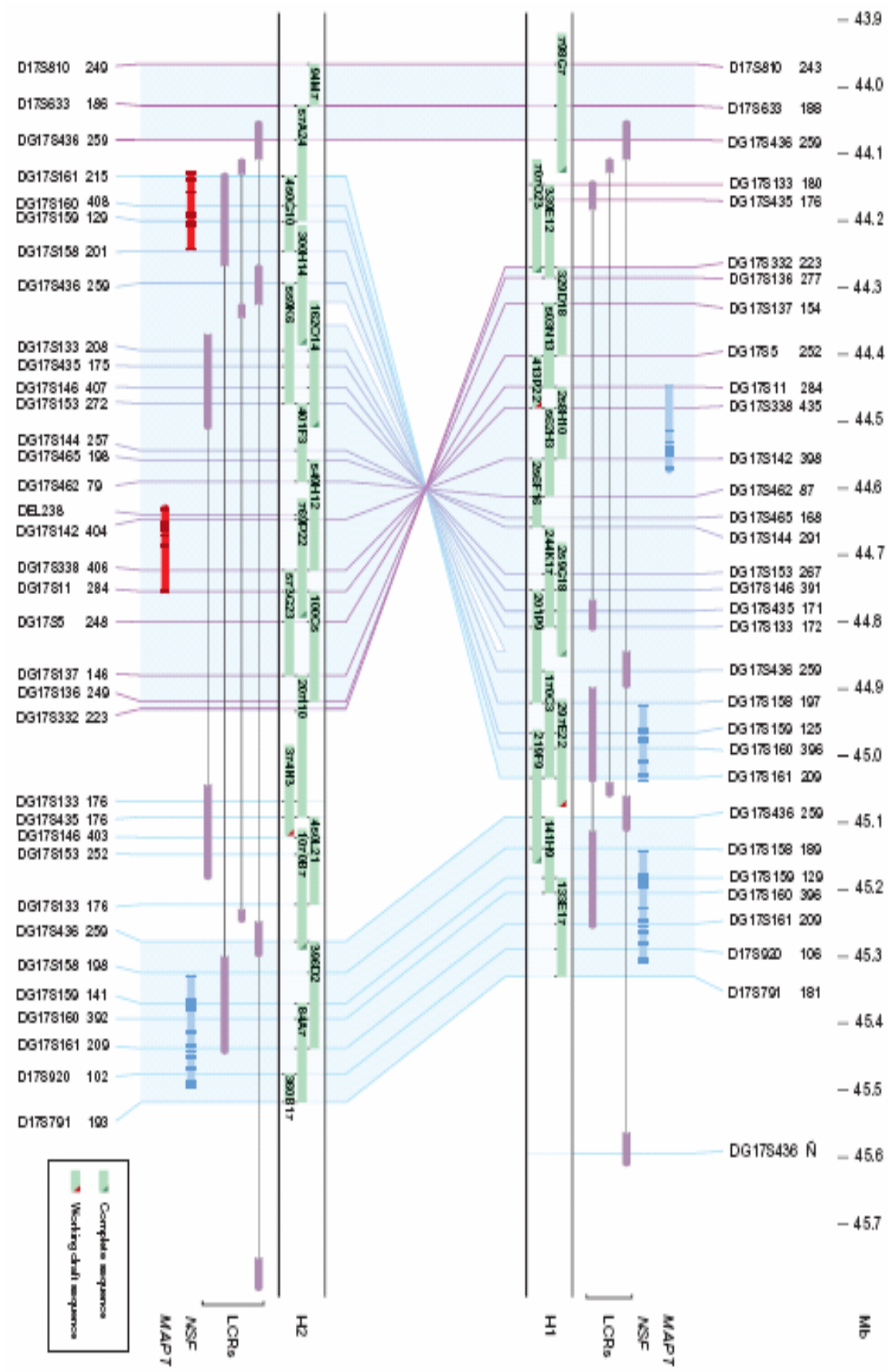
Figure 6 The genome-wide impact of the number of H2 copies on the rate of recombination in mothers. (a) Increase in Morgans. (b) Percentage increase. Error bars represent s.e.

Supplementary Table 3. The distribution of number of children for 82,992 Icelandic males and for 79,811 Icelandic females born between 1925 and 1965. Included in the table is the number of males and females, respectively that have one, two, three, four, five and six or more children according to the Icelandic genealogy database and the corresponding fraction of the total number of males and females. Individuals that have six or more children have been pooled into one bin. Also included in the table are the corresponding numbers for the 12178 males and 16959 females that have been genotyped for the inversion markers.

Number of Children	In the genealogy database				Genotyped for the inversion			
	Males	Fraction	Females	Fraction	Males	Fraction	Females	Fraction
0	16566	0.200	10544	0.132	1177	0.097	764	0.045
1	8145	0.098	8374	0.105	943	0.077	1235	0.073
2	18521	0.223	18631	0.233	2639	0.217	3701	0.218
3	20889	0.252	22533	0.282	3623	0.298	5400	0.318
4	11109	0.134	11745	0.147	2097	0.172	3202	0.189
5	4567	0.055	4620	0.058	952	0.078	1461	0.086
6+	3195	0.038	3364	0.042	747	0.061	1196	0.071
Total	82992	1.00	79811	1.00	12178	1.00	16959	1.00

LD HapMap-i CEPH andmetel

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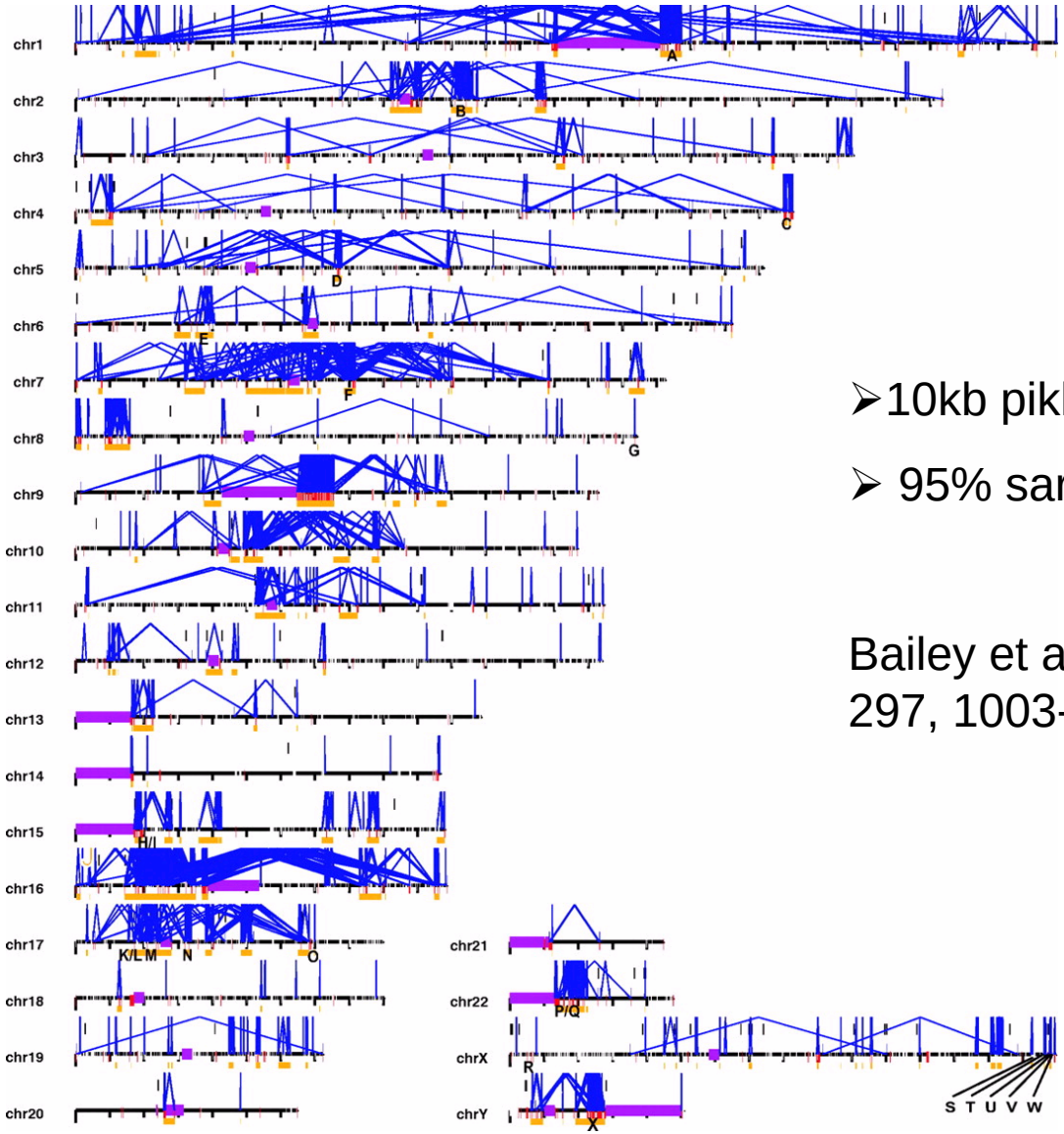
Duplitseerunud piirkonnad inimesel



- 10kb pikkust
- 95% sarnasust

Bailey et al. Science 297, 1003-1007 (2002)

Palju on veel