

Global Linkage Map Connects Meiotic Centromere Function to Chromosome Size in Budding Yeast

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Figure S1 (A) A genetic linkage map for each chromosome was constructed as described in Methods and visualized as a heatmap. The horizontal and the vertical axes of the heatmap represent chromosomal coordinates; a third dimension indicating the SGA-based genetic distance (SGA-GD) between the corresponding chromosomal regions is represented by the intensity of color of each point in the image. Grey corresponds to missing data due to the experimental constrains of the SGA method (Methods). Each chromosome is drawn to scale. Purple dots represent centromeres. Green dots correspond to the top 10 highest double-strand break hotspots as reported by Pan et al., 2011.









 Centro DSB ł 	omere notspot (Pan <i>et</i>	<i>al.</i> , 2011)			
50 I	40 I	30 I	20 I	10 I	N/A
		SGA-based ger	netic distance (S	SGA-GD)	



50	40	30	20	10	N/A		
I	I	I	I	I			
		SGA-based genetic distance (SGA-GD)					

• DSB hotspot (Pan et al., 2011)













7 SI





B Array mutation linked to *MAT* locus:



Figure S3 Chromosome III carries the yeast mating type locus (*MAT*), which determines the mating type of a yeast haploid cell and distinguishes array and query mutants, which are *MAT*a and *MAT*a, respectively. Since SGA selects specifically for *MAT*a meiotic progeny, a query mutant n (**A**, filled black square), located between gene M (**A**, empty red square) and the *MAT* locus (**A**, empty green square), requires a double recombination event to acquire both the array mutation m (**A**, filled red square) and the *MAT*a information (**A**, filled green square). The array mutant n, however, (**B**, filled black square), being already linked to *MAT*a, only requires one recombination event to acquire query mutation m (**B**, filled red square). As a result, query and array mutants linked to the *MAT* locus show different degrees of linkage to nearby genes, and averaging their genetic linkage maps would conceal the true recombination activity occurring within the region.



Figure S4 The overlap between any two datasets is visualized as a heatmap/table, where colors and numbers reflect the fraction of hotspots identified by study 1 (row labels) that are located within 10 kb from a hotspot identified by study 2 (column labels). For example, of all hotspots identified by Gerton *et al.* (row label), 77% were also identified by Borde *et al.* (column label), and, vice versa, of all hotspots identified by Borde *et al.* (row label), 53% were also identified by Gerton *et al.* (column label).

Significant	Centromere linkage				Overall linkage (control)			
Not significant	All chromosomes		All chrs., excl. 4 smallest		All chromosomes		All chrs., excl. 4 smallest	
	R	p-val	R	p-val	R	p-val	R	p-val
This study	0.77	0.01	0.66	0.03	0.74	0.001	0.44	0.15
SGD	0.70	0.002	0.42	0.17	0.64	0.008	0.05	0.87
Gerton <i>et al.</i> , 2000	0.78	0.0003	0.74	0.006	0.46	0.08	-0.07	0.82
Borde <i>et al.</i> , 2004	0.79	0.001	0.92	0.0002	0.25	0.34	0.04	0.89
Buhler <i>et al.</i> , 2007	0.63	0.04	0.72	0.03	0.33	0.22	0.15	0.64
Blitzblau <i>et al.</i> , 2007	0.59	0.02	0.67	0.02	0.62	0.01	0.11	0.74

Figure S5 Pearson correlation coefficients and the corresponding significance p-values were computed between chromosome size and centromere-proximal recombination reported by several published studies, as described in Methods.



Figure S6 Relationship between chromosome size and centromere-associated cohesin clustering, measured from data reported previously (Kugou et al. 2009). Data relative to 1.5 hours after induction of meiosis are shown. Each data point corresponds to a chromosome, labeled by the number. Pearson correlation coefficient is R = 0.73 but not significant (p-value < 0.27).

Table S1 Data sources for large-scale recombination and cohesin binding studies

Publication	Data source					
(Gerton <i>et al.</i> 2000)	Table 1					
(Borde et al. 2004)	Table S2					
(Buhler et al. 2007)	Table S5 (5X background)					
(Blitzblau <i>et al.</i> 2007)	Table S2					
(Mancera et al. 2008)	Supplementary information 2: hot_spots.txt					
(Pan <i>et al.</i> 2011)	Table S2 (signal intensity > 1000)					
(Glynn <i>et al.</i> 2004)	Mitotic cohesin subunit (Scc1/Mcd1): Supplementary dataset 8 Meiotic cohesin subunit (Rec8): Supplementary dataset 9					
(Kiburz et al. 2005)	Supp Raw Data.doc					
(Kugou <i>et al.</i> 2009)	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE8422					

SGA-based genetic distances

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A set of 16 files, one for each chromosome, contain the SGA-based genetic distances (SGA-GD; Methods) for the indicated loci. Rows and columns correspond to query and array mutants, respectively. Multiple experiments, involving the same query locus, appear as duplicated rows in each file.

Supplementary references

- Anscombe, F. J., 1973 Graphs in Statistical Analysis. The American Statistician 27: 17-21.
- Bishop, D. K., and D. Zickler, 2004 Early decision; meiotic crossover interference prior to stable strand exchange and synapsis. Cell **117**: 9-15.
- Blitzblau, H. G., G. W. Bell, J. Rodriguez, S. P. Bell and A. Hochwagen, 2007 Mapping of meiotic single-stranded DNA reveals double-stranded-break hotspots near centromeres and telomeres. Current biology : CB **17**: 2003-2012.
- Borde, V., W. Lin, E. Novikov, J. H. Petrini, M. Lichten *et al.*, 2004 Association of Mre11p with double-strand break sites during yeast meiosis. Molecular cell **13**: 389-401.
- Buhler, C., V. Borde and M. Lichten, 2007 Mapping meiotic single-strand DNA reveals a new landscape of DNA double-strand breaks in Saccharomyces cerevisiae. PLoS biology 5: e324.
- Cherry, J. M., E. L. Hong, C. Amundsen, R. Balakrishnan, G. Binkley *et al.*, 2012 Saccharomyces Genome Database: the genomics resource of budding yeast. Nucleic acids research **40**: D700-705.
- Gerton, J. L., J. Derisi, R. Shroff, M. Lichten, P. O. Brown *et al.*, 2000 Global mapping of meiotic recombination hotspots and coldspots in the yeast Saccharomyces cerevisiae. Proceedings of the National Academy of Sciences of the United States of America **97**: 11383-11390.
- Glynn, E. F., P. C. Megee, H. G. Yu, C. Mistrot, E. Unal *et al.*, 2004 Genome-wide mapping of the cohesin complex in the yeast Saccharomyces cerevisiae. PLoS biology **2:** E259.
- Jones, G. H., 1987 Chiasmata, pp. 213-244 in *Meiosis*, edited by P. B. MOENS. Academic Press, Orlando, FL.
- Kaback, D. B., D. Barber, J. Mahon, J. Lamb and J. You, 1999 Chromosome sizedependent control of meiotic reciprocal recombination in Saccharomyces cerevisiae: the role of crossover interference. Genetics **152**: 1475-1486.
- Kaback, D. B., V. Guacci, D. Barber and J. W. Mahon, 1992 Chromosome sizedependent control of meiotic recombination. Science **256**: 228-232.
- Kiburz, B. M., D. B. Reynolds, P. C. Megee, A. L. Marston, B. H. Lee *et al.*, 2005 The core centromere and Sgo1 establish a 50-kb cohesin-protected domain around centromeres during meiosis I. Genes & development **19**: 3017-3030.

- Kugou, K., T. Fukuda, S. Yamada, M. Ito, H. Sasanuma *et al.*, 2009 Rec8 guides canonical Spo11 distribution along yeast meiotic chromosomes. Mol Biol Cell 20: 3064-3076.
- Mancera, E., R. Bourgon, A. Brozzi, W. Huber and L. M. Steinmetz, 2008 Highresolution mapping of meiotic crossovers and non-crossovers in yeast. Nature 454: 479-485.
- Pan, J., M. Sasaki, R. Kniewel, H. Murakami, H. G. Blitzblau *et al.*, 2011 A hierarchical combination of factors shapes the genome-wide topography of yeast meiotic recombination initiation. Cell 144: 719-731.
- Pinsky, B. A., and S. Biggins, 2005 The spindle checkpoint: tension versus attachment. Trends in cell biology **15**: 486-493.
- Stahl, F. W., H. M. Foss, L. S. Young, R. H. Borts, M. F. Abdullah *et al.*, 2004 Does crossover interference count in Saccharomyces cerevisiae? Genetics **168**: 35-48.