Supplemental information

Figures and Legends

Figure S1

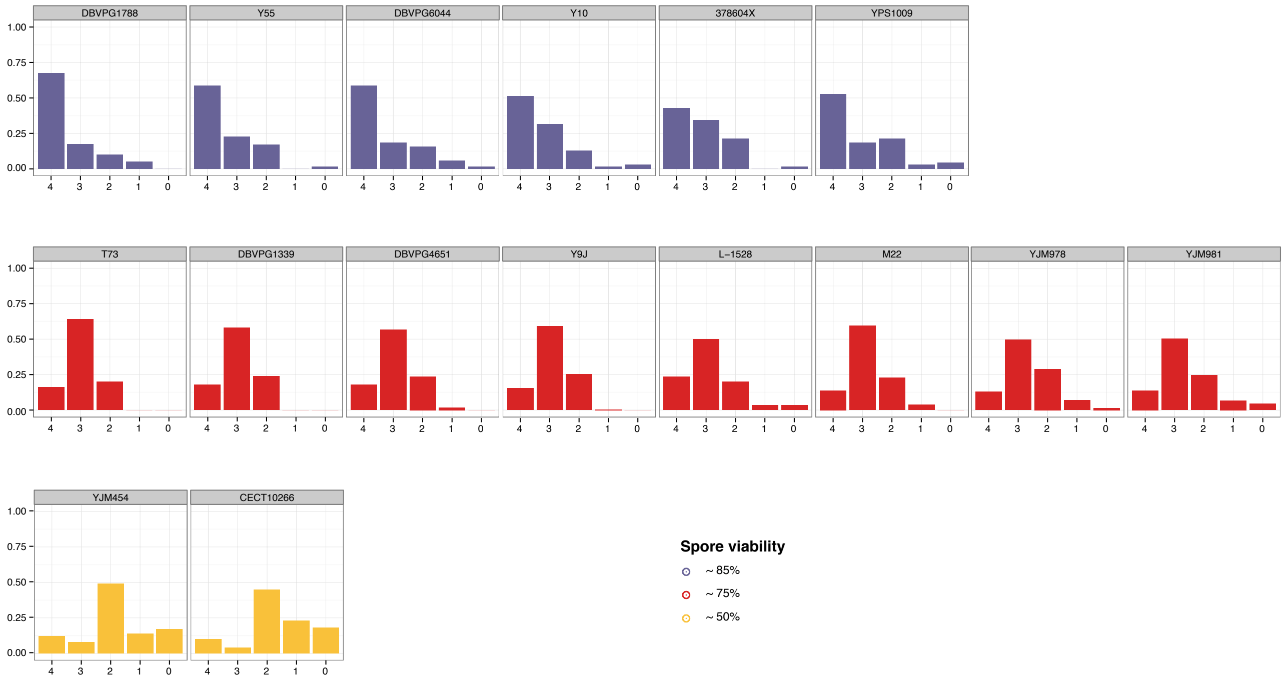

Figure S1, related to Figure 1 - Segregation pattern of the lethal phenotype in identified reproductive isolation cases

Each diagram represents the distribution of tetrad types from crosses between S288c and the strain indicated. Crosses are color coded according to their segregation pattern and the observed offspring viability. The horizontal axis indicates the number of viable spores per tetrad, and the vertical axis indicates the fraction of each type of tetrad observed.

Figure S2

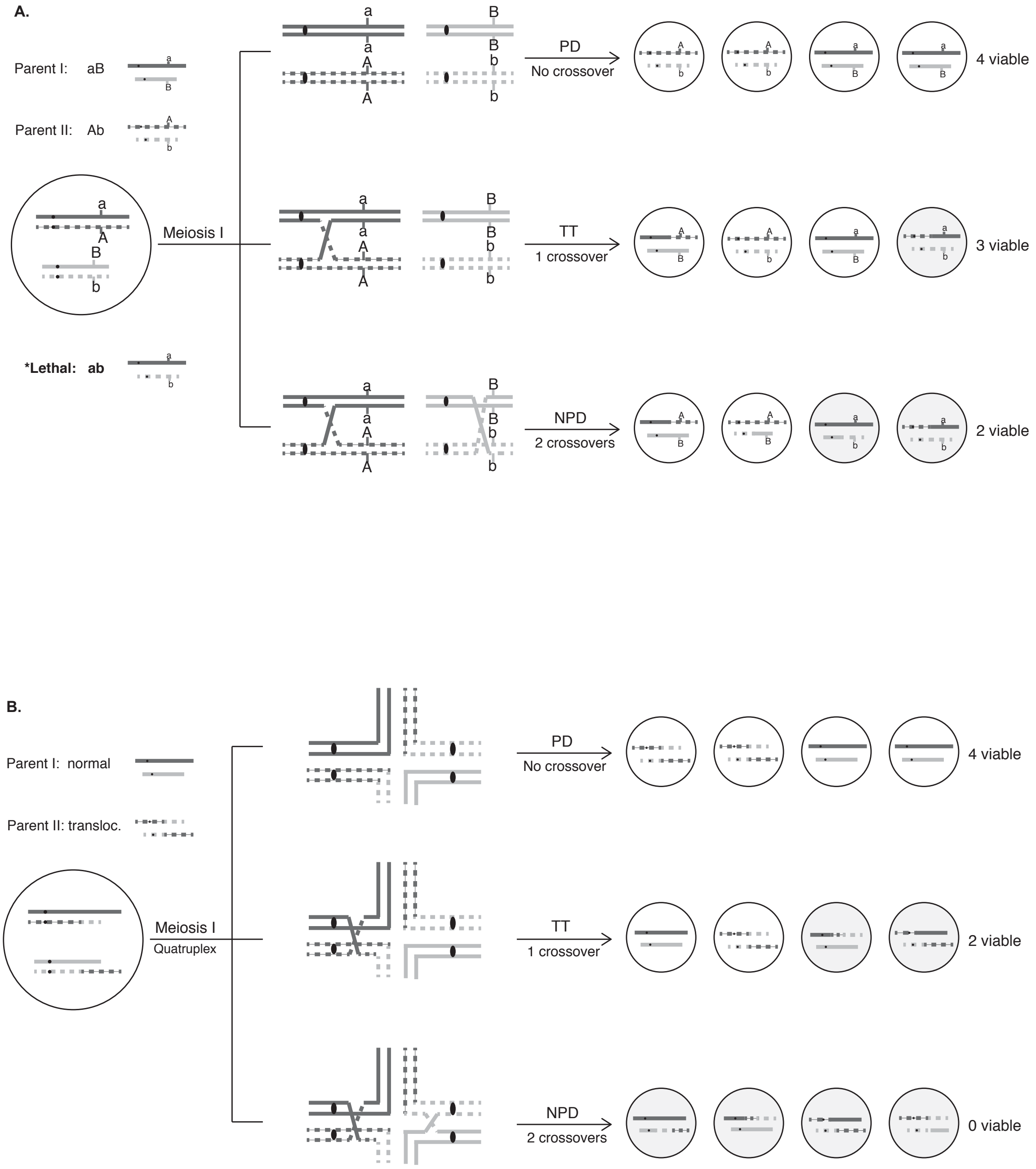

Figure S2, related to Experimental Procedures - Schematics of theoretical tetrad segregation

A. Genic model. Distribution of the tetrad types when two independent genes are involved. Lethal combination will follow Mendelian segregation and be united in 1/4 of the offspring, considering that tetrads with 4 viable spores are parental ditypes (PD), 3 viable spores are tetratypes (TT) and 2 viable spores are non-parental ditypes (NPD).

B. Chromosomal model. Distribution of the tetrad types in the case of diploid heterozygote for a reciprocal translocation. Any recombination will lead to offspring lethality and only progenies with balanced set of either parental chromosomal configuration will be viable. Tetrads with 4 viable spores correspond to PD, 3 viable spores to TT and 2 viable spores to NPD.

Figure S3.

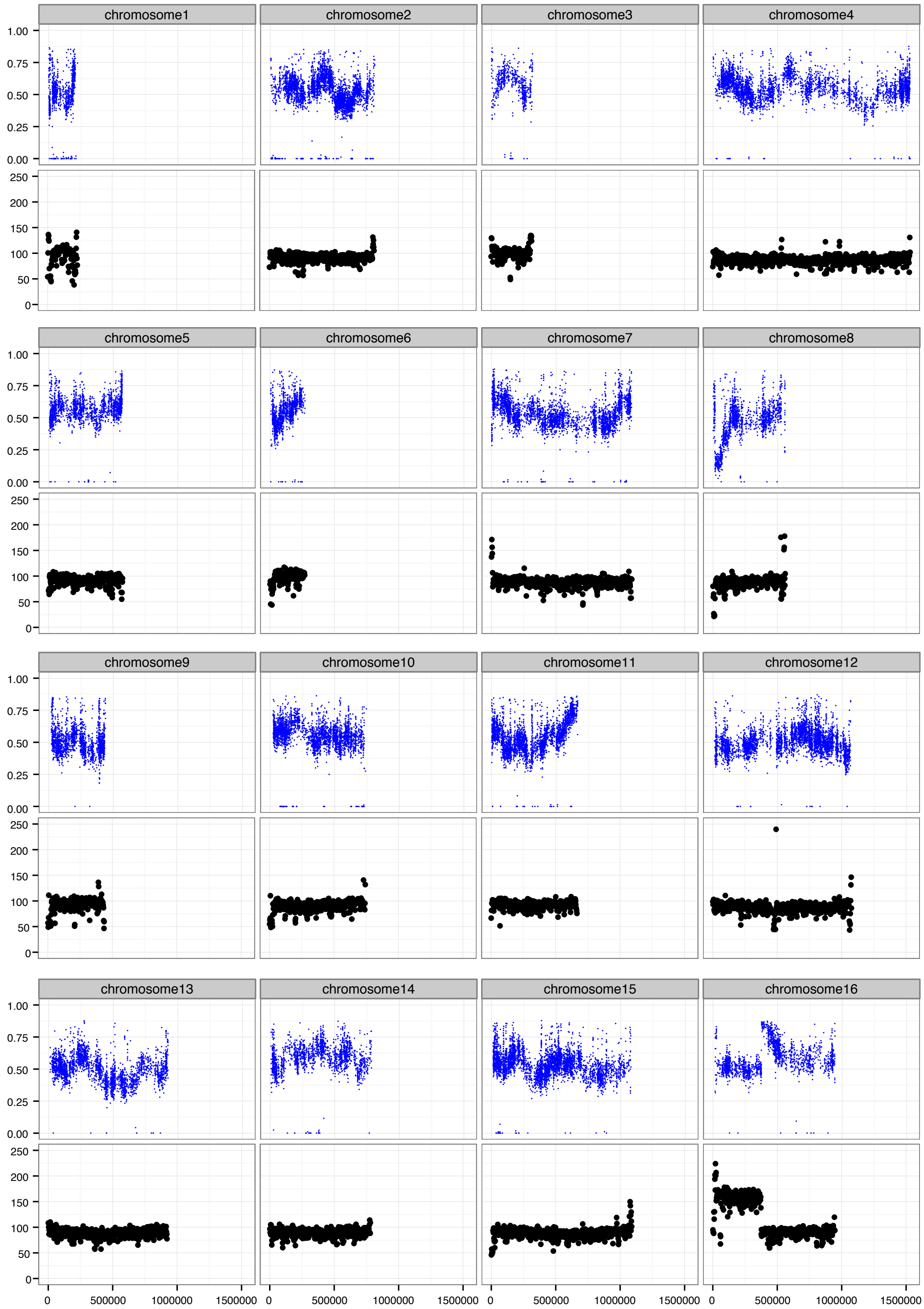

Figure S3, related to Figure 3 - Mapping results using bulk segregant analysis strategy for the cross between DBVPG1339 and S288c

Whole genome mapping result obtained using bulk segregant data from cross between DBVPG1339 and S288c. The upper vertical axis corresponds to allele frequencies of S288c. The lower vertical axis represents the sequencing coverage in a 2 kb window. The theoretical coverage was expected to be 100X if a single copy was present.

Figure S4.

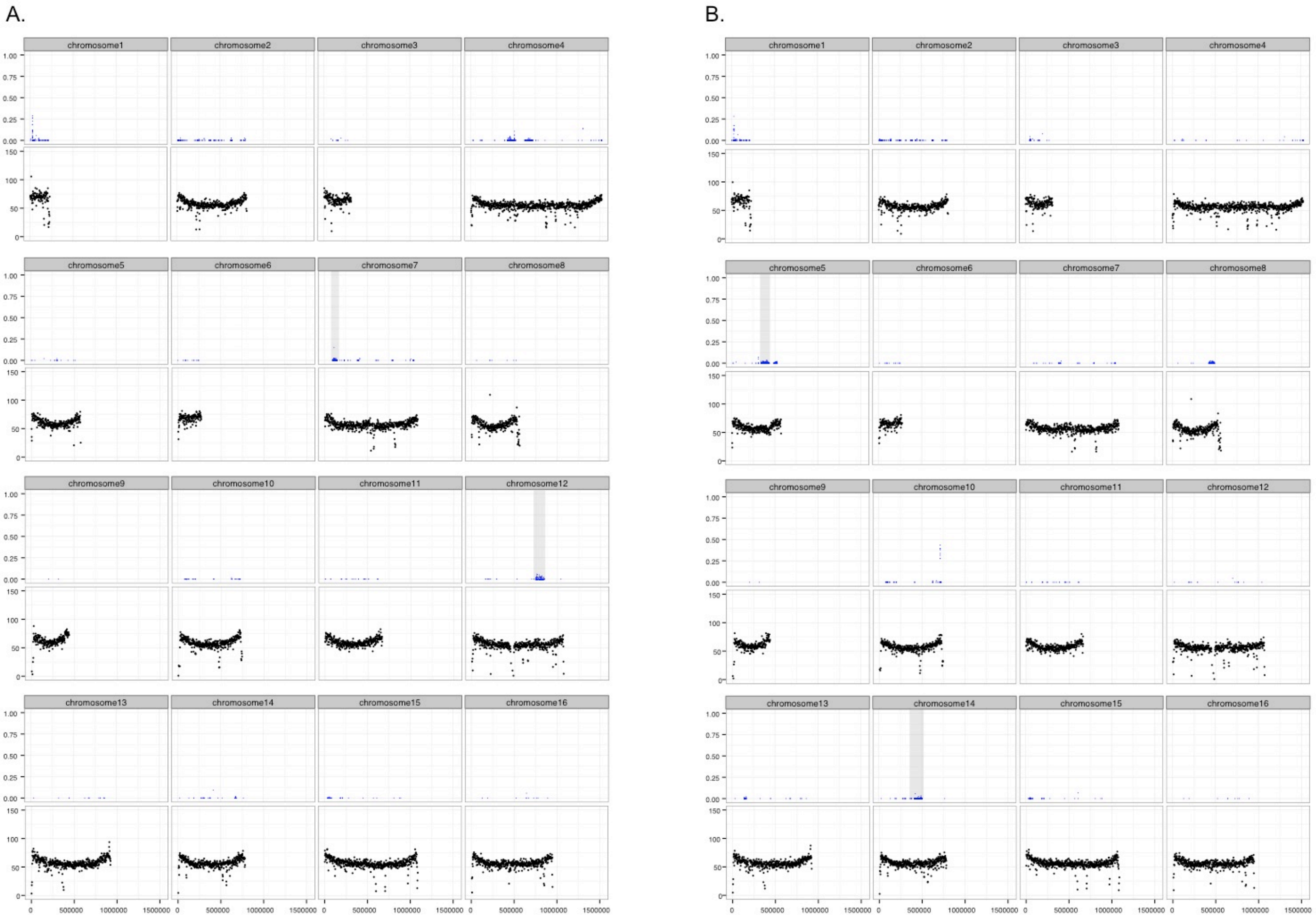

Figure S4, related to Experimental Procedures and Figure 4 - Mapping results for the backcrossed segregants CS-B5 and YS-B5

Allele frequency and coverage from sequencing data of backcrossed segregants CS-B5 (A) and YS-B5 (B). The upper vertical axis corresponds to allele frequencies of S288c. The lower vertical axis represents the sequencing coverage in a 2 kb window. Regions presented continuous allele frequency ~0, which are highlighted in grey boxes.

A. Segregant CS-B5. Two regions were mapped. The first region was approximately 60 kb in length, located on the left-arm of chromosome VII (85000 - 145000) and the second was a 120 kb region on the right-arm of chromosome XII (725000 - 845000). Coverage ~50X indicates the presence of a single genome copy.

B. Segregant YS-B5. Two regions were mapped. The first one was a 105 kb region on the right-arm of chromosome V (385000 - 490000) and the second was a 85 kb region on the left-arm of chromosome XIV (415000 - 500000). Coverage ~50X indicates the presence of a single genome copy.

Table S1.

Strains	Source	Location	Offspring viability	Estimated divergence to S288c (%)	Reference
273614X	Clinical	UK	100%	0.34	Schacherer et al. 2009
CLIB192	Baker	France	100%	0.11	Schacherer et al. 2009
CLIB413	Fermented Rice		100%	0.36	Schacherer et al. 2009
T7	Oak tree	US	100%	0.49	Justin Fay*
YJM421	Clinical	US	100%	0.35	Schacherer et al. 2009
EM93_3	Rotting fig	US	98%	0.14	Schacherer et al. 2009
WE372	Wine	South Africa	98%	0.26	Schacherer et al. 2009
YJM320b	Clinical	US	96%	0.32	Schacherer et al. 2009
CLIB272	Beer	US	95%	0.23	Schacherer et al. 2009
DBVPG6861	Polluted water		95%		
YJM434	Clinical	Europe	95%	0.28	Schacherer et al. 2009
YJM678	Clinical		95%		
CLIB483	Fermentation	France	94%	0.29	Schacherer et al. 2009
RM11	Vineyard	US	93%	0.36	Justin Fay*
CLIB154	Wine	Russia	93%	0.21	Schacherer et al. 2009
CLIB382	Beer	Japan	93%	0.25	Schacherer et al. 2009
DBVPG3591	Cocoa beans		93%	0.23	Schacherer et al. 2009
I14	Vineyard	Italy	93%	0.25	Schacherer et al. 2009
UC8	Wine	South Africa	93%	0.28	Schacherer et al. 2009
DBVPG1106	Grapes	Australia	92%	0.35	Skelly et al. 2013
YJM975	Clinical	Italy	92%	0.36	Skelly et al. 2013
CLIB219	Wine	Russia	92%	0.44	Schacherer et al. 2009
YJM280	Clinical	US	92%	0.35	Schacherer et al. 2009
Y9	Ragi	Indonesia	92%	0.34	Schacherer et al. 2009
Y12	Palm wine	Africa	92%	0.35	Schacherer et al. 2009
YJM269	Apple juice		92%	0.38	Schacherer et al. 2009
K12	Sake	Japan	91%	0.25	Schacherer et al. 2009
YJM326	Clinical	US	91%	0.32	Schacherer et al. 2009
BC187	Barrel fermentation	US	91%	0.37	Skelly et al. 2013
L-1374	Wine	Chile	91%	0.36	Skelly et al. 2013
PW5	Palm wine	Nigeria	91%	0.59	Justin Fay*
Y3	Palm wine	Africa	91%	0.38	Schacherer et al. 2009
CBS7960	Sugar cane	South Africa	90%	0.39	Justin Fay*
CECT10109	Prickly pear	Spain	90%	0.31	Schacherer et al. 2009
CLIB294	Fermentation	France	90%	0.25	Schacherer et al. 2009
DBVPG1794	Soil	Finland	90%	0.29	Schacherer et al. 2009
NC_02	Forest	US	90%	0.43	Justin Fay*
UC1	Wine	France	90%	0.24	Schacherer et al. 2009
YJM145	Clinical	US	90%	0.37	Schacherer et al. 2009
YJM413	Clinical		90%	0.33	Schacherer et al. 2009
YJM440	Clinical	US	90%		
YPS1000	Oak exudate	US	90%	0.41	Schacherer et al. 2009
YPS128	Oak	US	90%	0.53	Skelly et al. 2013
YPS163	Oak exudate	US	90%	0.36	Schacherer et al. 2009
DBVPG1788	Soil	Finland	86%	0.36	Justin Fay*
Y55	Wine	France	86%	0.54	Skelly et al. 2013
DBVPG6044	Bili wine	West Africa	86%	0.60	Justin Fay*
378604X	Clinical	UK	84%	0.41	Skelly et al. 2013
YPS1009	Oak tree	US	84%	0.50	Justin Fay*
Y10	Coconut	Philippines	83%	0.49	Justin Fay*
YJM981	Clinical	Italy	73%	0.29	Schacherer et al. 2009
T73	Wine	Spain	73%	0.23	Schacherer et al. 2009
Y9J	Wine	Japan	73%	0.28	Schacherer et al. 2009
L-1528	Wine	Chile	72%	0.35	Justin Fay*
M22	Wine	Italy	71%	0.24	Schacherer et al. 2009
YJM978	Clinical	Italy	71%	0.26	Schacherer et al. 2009
DBVPG4651	Tuber Magnatum	Italy	71%	0.28	Schacherer et al. 2009
DBVPG1339	Grape must	Netherland	70%	0.24	Schacherer et al. 2009
CECT10266	Tanning Liquor	Spain	48%	0.44	This study
YJM454	Clinical	US	44%	0.48	This study
FY5	Lab	US	98%	0	This study

Table S1, related to Figure 1 - List of strains used in this study

The offspring viability for crosses between listed strains and FY4 (isogenic to S288c) was estimated by dissecting 20 tetrads. Cross between FY4 and FY5 (isogenic to S288c) was performed as a control.

* Publically available sequences from the Fay lab: http://www.genetics.wustl.edu/jflab/

Table S2.

Strains	Segregations					N° of tetrad analyzed	% viability
	4 viable	3 viable	2 viable	1 viable	0 viable		
DBVPG1788	27	7	4	2	0	40	87%
Y55	41	16	12	0	1	70	84%
DBVPG6044	41	13	11	4	1	70	82%
Y10	36	22	9	1	2	70	82%
378604X	30	24	15	0	1	70	79%
YPS1009	37	13	15	2	3	70	78%
T73	8	32	10	0	0	50	74%
DBVPG1339	51	165	68	0	0	284	74%
DBVPG4651	50	158	66	5	0	279	73%
Y9J	42	161	69	1	0	273	72%
L-1528	7	15	6	1	1	30	72%
M22	29	125	48	8	0	210	71%
YJM978	26	99	58	14	3	200	66%
YJM981	41	149	73	20	13	296	66%
YJM454	12	8	49	14	17	100	46%
CECT10266	10	4	45	23	18	100	41%

Table S2, related to Figure S1 - Lethal phenotype segregation in reproductive isolated strains

Additional tetrads were dissected for strains with low offspring viability and the segregation of the lethal phenotype were listed.