PNAS
www.pnas.org

Jing Hou[1], Guihong Tan[1], Gerald R. Fink[2], Brenda J. Andrews[1], Charles Boone[1]

[1]*Donnelly Centre for Cellular and Biomolecular Research, University of Toronto, 160 College Street, Toronto, Ontario M5S 3E1, Canada.*
[2]*Whitehead Institute for Biomedical Research, 9 Cambridge Center, Cambridge 02142 MA, USA*

Supplementary Information for

The complex modifier landscape underlying genetic background effects

Jing Hou, Guihong Tan, Gerald R. Fink, Brenda J. Andrews, Charles Boone

Brenda Andrews, Charles Boone
Emails: brenda.andrews@utoronto.ca; charlie.boone@utoronto.ca

This PDF file includes:

Figs. S1 and S2
Captions for tables S1 and S2

www.pnas.org/cgi/doi/10.1073/pnas.1820915116

Supplementary materials

Figure S1- Allele frequency variation and segregation patterns for 7 conditional essential genes. A-G. Raw allele frequencies (in grey) are presented for each segregant pool, with the y-axis indicating the allele frequency of S288c and x-axis the chromosome coordinates. Average allele frequency within a 20 kb window is indicated in blue for simplification. The segregation patterns in heterozygous deletion hybrids, homozygous deletion hybrids and the final segregation patterns in the bulk segregant pools are presented in bar plots. Schematic illustrations of modifier segregation modes are presented for *CYS3*, *LSM6*, *SWI6* and *OST4*. For cases with fitness variation, the upper panel corresponds to the segregant pool with normal fitness and the lower panel corresponds to the pool with low fitness segregants. **H.** Allele frequency distribution across all bulk segregant pools. K-smoothed allele frequency values are combined across different chromosomes for all tested pools. Vertical dashed lines indicate the mean allele frequency value (0.52, green) and ±2.5X standard deviations from the mean (0.29 and 0.75, orange). Genomic regions with allele frequency deviations surpassing the cutoffs of ±2.5X standard deviations and spanning more than 10 kb in size are considered as significant, as highlighted in **A-G**.

Figure S2- Sequence alignments. A. DNA alignment of the promoter region of *OPT1* in S288c and Σ1278b. **B.** Allelic variations of *MET1* in S288c, Σ1278b, Y12, K12 and K12_2. Protein sequence alignments are shown.

Table S1- Segregation patterns observed in S288c/Σ1278b hybrids with deletions of 57 conditional essential genes.

Table S2- Yeast strains used in this study. Origin of the wild isolates and their fitness ratios after deletion of *CYS3* are indicated. Strains generated in this study and their genotypes are also included.

Figure S1

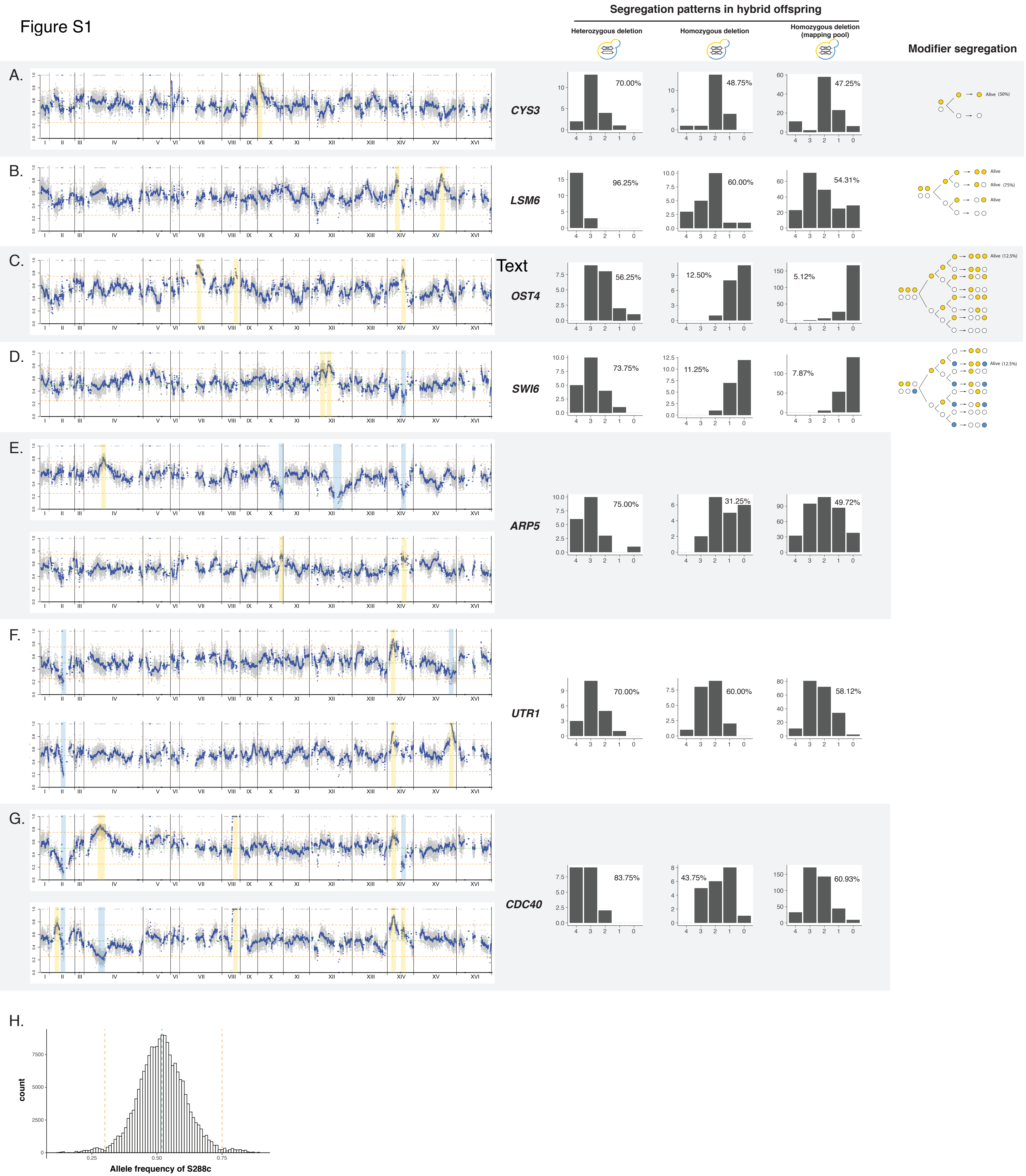
Segregation patterns in hybrid offspring
Heterozygous deletion
Homozygous deletion
Homozygous deletion (mapping pool)
Modifier segregation
A.
CYS3
70.00%
48.75%
47.25%
Alive (50%)
B.
LSM6
96.25%
60.00%
54.31%
Alive
Alive (75%)
Alive
C.
Text
OST4
56.25%
12.50%
5.12%
Alive (12.5%)
D.
SWI6
73.75%
11.25%
7.87%
Alive (12.5%)
E.
ARP5
75.00%
31.25%
49.72%
F.
UTR1
70.00%
60.00%
58.12%
G.
CDC40
83.75%
43.75%
60.93%
I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
XIII
XIV
XV
XVI
4
3
2
1
0
H.
count
Allele frequency of S288c
0.25
0.50
0.75
0
2500
5000
7500

Figure S2

A.

```
                  1 [        .         .         .         .         :         .         .         . 80
1 OPT1PR_sigma      CTTAGCAATCGTTGTTGAAGAAAGAGAGCTCTTATCATCATGGGGTGCCCATCATTTTTTTTTTTTTTTTCAAATTTTGG
2 OPT1PR_S288c      CTTAGCAATCGTTGTTGAAGAAAGAGAGCTCTTATCATCATGGGGTGCCCATCA-TTTTTCTTTTTTTTTCAAATTTTGG

                 81          .         1         .         .         .         .         :         . 160
1 OPT1PR_sigma      GCTATTCAATGAATCGTTTCGACTATATATGGACAATCATCGGAAGCTGTGTATTCTTGGTAAAAAGTTTTCGACTGTGT
2 OPT1PR_S288c      GCTATTCAATGAATTGTTTCGACTATATATGGACAATCATCGGAAGCTGTGTATTCTTGGTAAAAAGTTTTCGACTGTGT

                161          .         .         .         2    ] 205
1 OPT1PR_sigma      GGCAGAAAATAACCGCAACAATTATATAACGTCACAGAACACATG
2 OPT1PR_S288c      GGCAGAAAATAACCGCAACAATTATATAACGTCACAGAACACATG
```

B.

```
                  1 [        .         .         .         .         :         .         .         . 80
1 MET1_S288c        MVRDLVTLPSSLPLITAGFATDQVHLLIGTGSTDSVSVCKNRIHSILNAGGNPIVVNPSSPSHTKQLQLEFGKFAKFEIV
2 MET1_sigma        MVRDLVTLPSSLPLITAGFATDQVHLLIGTGSTDSVSVCKNRIHSILNAGGNPIVVNPSSPSHTKQLQLEFGKFAKFEIV
3 MET1_K12_2        MVRDLVTLPSSLPLITAGFATDQVHLLIGTGSTDSVSVCKNRIHSILNAGGNPIVVNPSSPSHTKQLQLEFGKFAKFEIV
4 MET1_Y12          MVRDLVTLPSSLPLITAGFATDQVHLLIGTGSTDSVSVCKNRIHSILNAGGNPIVVNPSSPSHTKQLQLEFGKFAKFEIV
5 MET1_K12          MVRDLVTLPSSLPLITAGFATDQVHLLIGTGSTDSVSVCKNRIHSILNAGGNPIVVNPSSPSHTKQLQLEFGKFAKFEIV

                 81          .         1         .         .         .         .         :         . 160
1 MET1_S288c        EREFRLSDLTTLGRVLVCKVVDRVFVDLPITQSRLCEEIFWQCQKLRIPINTFHKPEFSTFNMIPTWVDPKGSGLQISVT
2 MET1_sigma        EREFRLSDLTTLGRVLVCKVVDRVFVDLPITQSRLCEEIFWQCQKLRIPINTFHKPEFSTFNMIPTWVDPKGSGLQISVT
3 MET1_K12_2        EREFRLSDLTTLGRVLVCKVVDRVFVDLPITQSRLCEEIFWQCQKLRIPINTFHKPEFSTFNMIPTWVDPKGSGLQISVT
4 MET1_Y12          EREFRLSDLTTLGRVLVCKVVDRVFVDLPITQSRLCEEIFWQCQKLRIPINTFHKPEFSTFNMIPTWVDPKGSGLQISVT
5 MET1_K12          EREFRLSDLTTLGRVLVCKVVDRVFVDLPITQSRLCEEIFWQCQKLRIPINTFHKPEFSTFNMIPTWVDPKGSGLQISVT

                161          .         .         .         2         .         .         .         . 240
1 MET1_S288c        TNGNGYILANRIKRDIISHLPPNISEVVINMGYLKDRIINEDHKALLEEKYYQTDMSLPGFGYGLDEDGWESHKFNKLIR
2 MET1_sigma        TNGNGYILANRIKRDIISHLPPNISEVVINMGYLKDRIINEDHKALLEEKYYQTDMSLPGFGYGLDEDGWESHKFNKLIR
3 MET1_K12_2        TNGNGYILANRIKRDIISHLPPNISEVVINMGYLKDRIINEDHKALLEEKYYQTDMSLPGFGYGLDEDGWESHKFNKLIR
4 MET1_Y12          TNGNGYILANRIKRDIISQLPPNISEVVINMGYLKDRIINEDHKALLEEKYYQTDMSLPGFGYGLDEDGWESHKFNKLIR
5 MET1_K12          TNGNGYILANRIKRDIISQLPPNISEVVINMGYLKDRIINEDHKALLEEKYYQTDMSLPGFGYGLDEDGWESHKFNKLIR

                241          :         .         .         .         .         3         .         . 320
1 MET1_S288c        EFEMTSREQRLKRTRWLSQIMEYYPMNKLSDIKLEDFETSSSPNKKTKQETVTEGVVPPTDENIENGTKQLQLSEVKKEE
2 MET1_sigma        EFEMTSREQRLKRTRWLSQIMEYYPMNKLSDIKLEDFETSSSPNKKTKQETVTEGAVPPTDENIENGTKQLQLSEVKKEE
3 MET1_K12_2        EFEMTSREQRLKRTRWLSQIMEYYPMNKLSDIKLEDFETSSSPNKKTKQETVTEGVVPPTDENIENGTKQLQLSEVKKEE
4 MET1_Y12          EFEMTSREQRLKRTRWLSQIMEYYPMNKLSDIKLEDFETSSSPNKKTKQETVTEGVVPPTDENIENGTKQLQLSEVKKEE
5 MET1_K12          EFEMTSREQRLKRTRWLSQIMEYYPMNKLSDIKLEDFETSSSPNKKTKQETVTEGVVPPTDENIENGTKQLQLSEVKKEE

                321          .         .         :         .         .         .         .         4 400
1 MET1_S288c        GPKKLGKISLVGSGPGSVSMLTIGALQEIKSADIILADKLVPQAILDLIPPKTETFIAKKFPGNAERAQQELLAKGLESL
2 MET1_sigma        GPKKLGKISLVGSGPGSVSMLTIGALQEIKSADIILADKLVPQAILDLIPPKTETFIAKKFPGNAERAQQELLAKGLESL
3 MET1_K12_2        GPKKLGKISLVGSGPGSVSMLTIGALQEIKSADIILADKLVPQAILDLIPPKTETFIAKKFPGNAERAQQELLAKGLESL
4 MET1_Y12          GPKKLEKISLVGSGPGSVSMLTIGALQEIKSADIILADKLVPQAILDLIPPKTETFIAKKFPGNAERAQQELLAKGLESL
5 MET1_K12          GPKKLEKISLVGSGPGSVSMLTIGALQEIKSADIILADKLVPQAILDLIPPKTETFIAKKFPGNAERAQQELLAKGLESL

                401          .         .         .         .         :         .         .         . 480
1 MET1_S288c        DNGLKVVRLKQGDPYIFGRGGEEFNFFKDHGYIPVVLPGISSSLACTVLAQIPATQRDIADQVLICTGTGRKGALPIIPE
2 MET1_sigma        DNGLKVVRLKQGDPYIFGRGGEEFNFFKDHGYIPVVLPGISSSLACTVLAQIPATQRDIADQVLICTGTGRKGALPIIPE
3 MET1_K12_2        DNGLKVVRLKQGDPYIFGRGGEEFNFFKDHGYIPVVLPGISSSLACTVLAQIPATQRDIADQVLICTGTGRKGALPIIPE
4 MET1_Y12          DNGLKVVRLKQGDPYIFGRGGEEFNFFKDHGYIPVVLPGISSSLACTVLAQIPATQRDIADQVLICTGTGRKGALPIIPE
5 MET1_K12          DNGLKVVRLKQGDPYIFGRGGEEFNFFKDHGYIPVVLPGISSSLACTVLAQIPATQRDIADQVLICTGTGRKGALPIIPE

                481          .         5         .         .         .         .         :         . 560
1 MET1_S288c        FVESRTTVFLMALHRANVLITGLLKHGWDGDVPAAIVERGSCPDQRVTRTLLKWVPEVVEEIGSRPPGVLVVGKAVNALV
2 MET1_sigma        FVESRTTVFLMALHRANVLITELLKHGWDGDVPAAIVERGSCPDQRVTRTLLKWVPEVVEEIGSRPPGVLVVGKAVNALV
3 MET1_K12_2        FVESRTTVFLMALHRANVLITELLKHGWDGDVPAAIVERGSCPDQRVTRTLLKWVPEVVEEIGSRPPGVLVVGKAVNALV
4 MET1_Y12          FVESRTTVFLMALHRANVLITELLKHGWDSDVPAAIVERGSCPDQRVTRTLLKWVPEVVEEIGSRPPGVLVVGKAVNALV
5 MET1_K12          FVESRTTVFLMALHRANVLITELLKHGWDSDVPAAIVERGSCPDQRVTRTLLKWVPEVVEEIGSRPPGVLVVGKAVNALV

                561          .         .         .   ] 594
1 MET1_S288c        EKDLINFDESRKFVIDEGFREFEVDVDSLFKLYX
2 MET1_sigma        EKDLINFDESRKFVIDEGFREFEVDVDSLFKLYX
3 MET1_K12_2        EKDLINFDESRKFVIDEGFREFEVDVDSLFKLYX
4 MET1_Y12          EKDLINFDESRKFVIDEGFREFEVDVDSLFKXYX
5 MET1_K12          EKDLINFDESRKFVIDEGFREFEVDVDSLFKXYX
```