

**Supporting Information for Raghavan *et al.*
Incompatibilities in Mismatch Repair Genes *MLH1*-*PMS1* Contribute to a Wide Range of
Mutation Rates in Human Isolates of Baker's Yeast.
DOI: 10.1534/genetics.118.301550**

Figure S1 Incompatibility involving the *MLH1* and *PMS1* MMR genes. We proposed a model for an incompatibility involving *MLH1* and *PMS1* (Heck *et al.* 2006). It is based on the hypothesis that ancestral isolates bearing *MLH1* Gly 761 and *PMS1* Arg 818/822 acquired neutral and beneficial mutations that lead to derived S288c (purple Asp 761, Arg 818/822) and SK1 (green, Gly 761, Lys 818/822) group isolates. Mating between the derived isolates, supported by genetic recombination data presented in Heck *et al.* (2006), yields an incompatible combination (*MLH1* Asp 761, *PMS1* Lys 818/822) that displays negative epistasis, as shown by a mutator phenotype. Sequences of *MLH1* and *PMS1* genes from a worldwide collection (Peter *et al.* 2018) are shown according to their amino acid residues 761 (G or D) in *MLH1* and 818 (R or K) in *PMS1* (Bui *et al.* 2017). Only those homozygous for *MLH1* and *PMS1* sequences are shown. Adapted from Bui *et al.* (2017).

Figure S2 DNA sequence, as shown by chromatogram traces, of the *MLH1* incompatibility site (bp 2282, Gly or Asp at amino acid 761) in the indicated isolates and spore clones.

Figure S3 Efficiency of plating of strains transformed with pEAA611, comparing growth on clon-NAT and clon-NAT + G418 plates. Representative images of EAY1369, EAY1370, YJM521, YJS5845 and YJS5885 isolates and YJS5885 spore clones are shown.

Figure S4 Sequencing analysis of G418 resistant revertants and sensitive control colonies. The homopolymeric A-runs in isolates and spore clones transformed with pEAA613

were sequenced (Materials and Method). The sequencing data from G418 resistant (top) and sensitive (bottom) colonies are presented. Only G418 resistant colonies displayed A₁₄ to A₁₃ frameshift mutations.

Figure S5 Flow cytometry of spore clones. Spore clones of YJS5845 and YJS5885 were prepared for flow cytometry as described in the Materials and Methods. YJS5845 derived spore clones were diploid and YJS5885 derived spore clones were haploid. The black arrows show the position of 1n, 2n, and 4n DNA content. Inset shows the percentage of single cells, small budded and large budded cells in the indicated samples.

Figure S6 Ploidy of YJS5845 and YJS5885 isolates and their spore clones. Whole genome sequencing is presented for YJS5845, YJS5885 and derived spore clones (Materials and Methods). The entire set can be found in Figure 4B and Figure S6.

Table S1 Genotyping of spore clones obtained by dissection of isolate tetrads. *MLH1* and *PMS1* genes were PCR amplified from isolates and derived spore clones and sequenced as described in the Materials and Methods. For YJS5845, three spore clones were genotyped from random spores and 30 were genotyped from spores isolated after tetrad dissection. For YJS5885, all spore clones were genotyped from tetrad dissection. None of the incompatible YJS5845 and YJS5885 spore clones contained the Pro 271 suppressor polymorphism in *MLH1* (Demogines *et al.* 2008). For YJM521, 24 spore clones were genotyped from six four-spore viable tetrads. For YJS4806, 24 spore clones were genotyped from random spores with 22 showing the parental genotype for *MLH1*, and two showing a different segregation pattern (2G:2A, 4G:0A). For YJS4810, 24 spore clones were genotyped from random spores, with all showing the parental genotype for *MLH1*.

Table S2 Genotyping of *MLH1* and *PMS1* loci in YJM and YJS isolates and derived spore clones.

The sequences for the *MLH1* and *PMS1* open reading frames for each of the two parental chromosomes are shown relative to the S288c and SK1 sequences for YJS5845, YJS5885, and YJM521. The parental chromosomes were genotyped as “c” (S288c) or “k” (SK1) based on the amino acid polymorphisms seen at the incompatibility loci (bp 2282 in *MLH1*, bp 2453 in *PMS1*) in the S288c and SK1 sequences (Materials and Methods). The *MLH1*-271P suppressor allele is highlighted at bp 812 in *MLH1*. INS = 12 bp insertion in *PMS1*; NO INS = lacking the insertion.

Table S3 Analysis of *HO*, *PHO80* and *STP22* genes in YJS5845 and YJS5885 for variants using SnpEff.

Table S4 Analysis of resistance to 5-FOA in YJS5885 spore clones. The rate of resistance to 5-FOA, presented with 95% confidence intervals (95% C.I.), was determined for n independent cultures of FY90 and the indicated spore clones of YJS5885 as described in the Materials and Methods. The *URA3* open reading frame (ATG =+1) was sequenced from 7, 2, 1, 1, 1 and 1 independent 5-FOA^r colonies from 5885-9a, 5885-15b, 5885-1a, 5885-14a, 5885-16a, and 5885-19a, respectively. ^a Significantly different from FY90 (p<0.001, Mann-Whitney test); ^b Significantly different from EAY4087 (p<0.001, Mann-Whitney test). YJS5885 compatible and incompatible spore clones are significantly different from each other (p<0.001, Mann-Whitney test).

10 of the 13 spore clones contained single mutations in *URA3*, with the following distribution:
 5885-9a: Two missense (bp287, A>T; bp542, G>A), One nonsense (bp577, G>T), Two single nucleotide deletions (bp178, A deleted; bp629, G deleted), no changes in ORF for two 5-FOA^r mutants.

5885-15b: One missense (bp205, T>C), one nonsense (bp345 G>A).

5885-1a: One nonsense (bp223 A>T).

5885-14a: One nonsense (bp593 T>A).

5885-16a: No changes in ORF for one 5-FOA^r mutant.

5885-19a: One nonsense (bp310 C>T).

Table S5 Sporulation and Lactate growth phenotype. Spore clones were patched on sporulation media and incubated at 30°C for 6 days after which they were examined for evidence of sporulation by light microscopy. Any samples with dyads, triads and tetrads were marked as being able to sporulate (+). Spore clones were also patched on YP-lactate media and scored as able to grow or not (Lactate⁺ or ⁻) after 4 days in 30°C. NT: not tested.

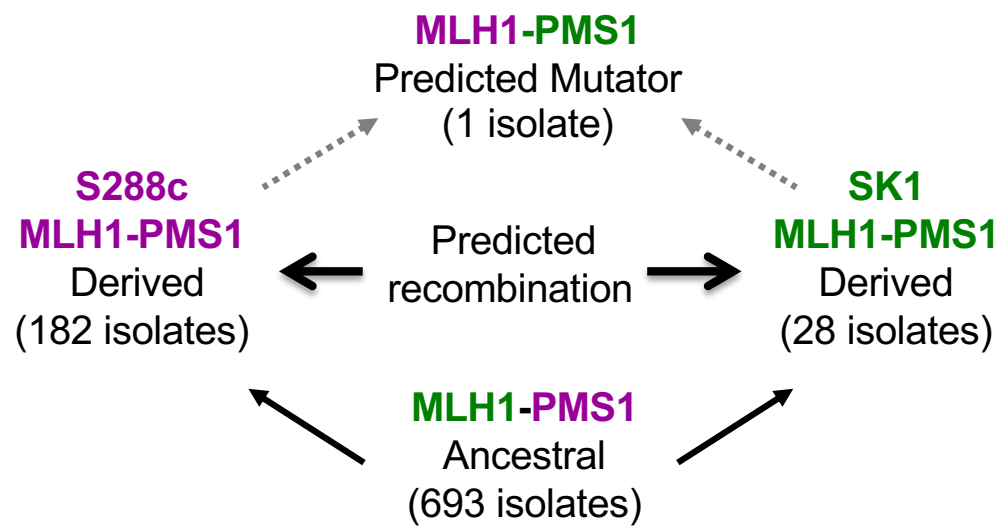
Table S6 Assigning MLH1 polymorphisms found in heterozygous genotypes onto the MLH1 structure-function map. A structure function map for MLH1 was created from an analysis of *MLH1* alanine scan and site-specific mutations, and *mlh1* alleles generated based on homology to HNPCC mutations (Pang *et al.* 1997; Shcherbakova and Kunkel 1999; Tran and Liskay 2000; Welz-Voegele *et al.* 2002; Takahashi *et al.* 2007; Wanat *et al.* 2007; Romanova and Crouse 2013; Smith *et al.* 2013; Smith *et al.* 2015). Alleles that conferred a mutator phenotype in a variety of reporter assays are shown. In MLH1, amino acids 1-335 is referred to as that N-terminal/ATP binding domain, 335-509 as the linker domain, and 510-769 as the C-terminal interaction domain (Gueneau *et al.* 2013). See Table S7 for detailed list of the isolates that contain heterozygous polymorphisms that lie on the MLH1 structure-function map (shown here using their standardized names in the 1011 yeast genome project (Peter *et al.* 2018)).

Table S7 Amino acid heterozygosities identified in MLH1 in 107 yeast isolates. Amino acid heterozygosities in the MLH1 open reading frame are shown for 107 isolates (relative to the MLH1 S288c sequence; Peter *et al.* 2018).

Literature Cited

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Homozygous genotypes: 904 isolates



Genotyping at bp 2282 in *MLH1* (G/D at amino acid 761)

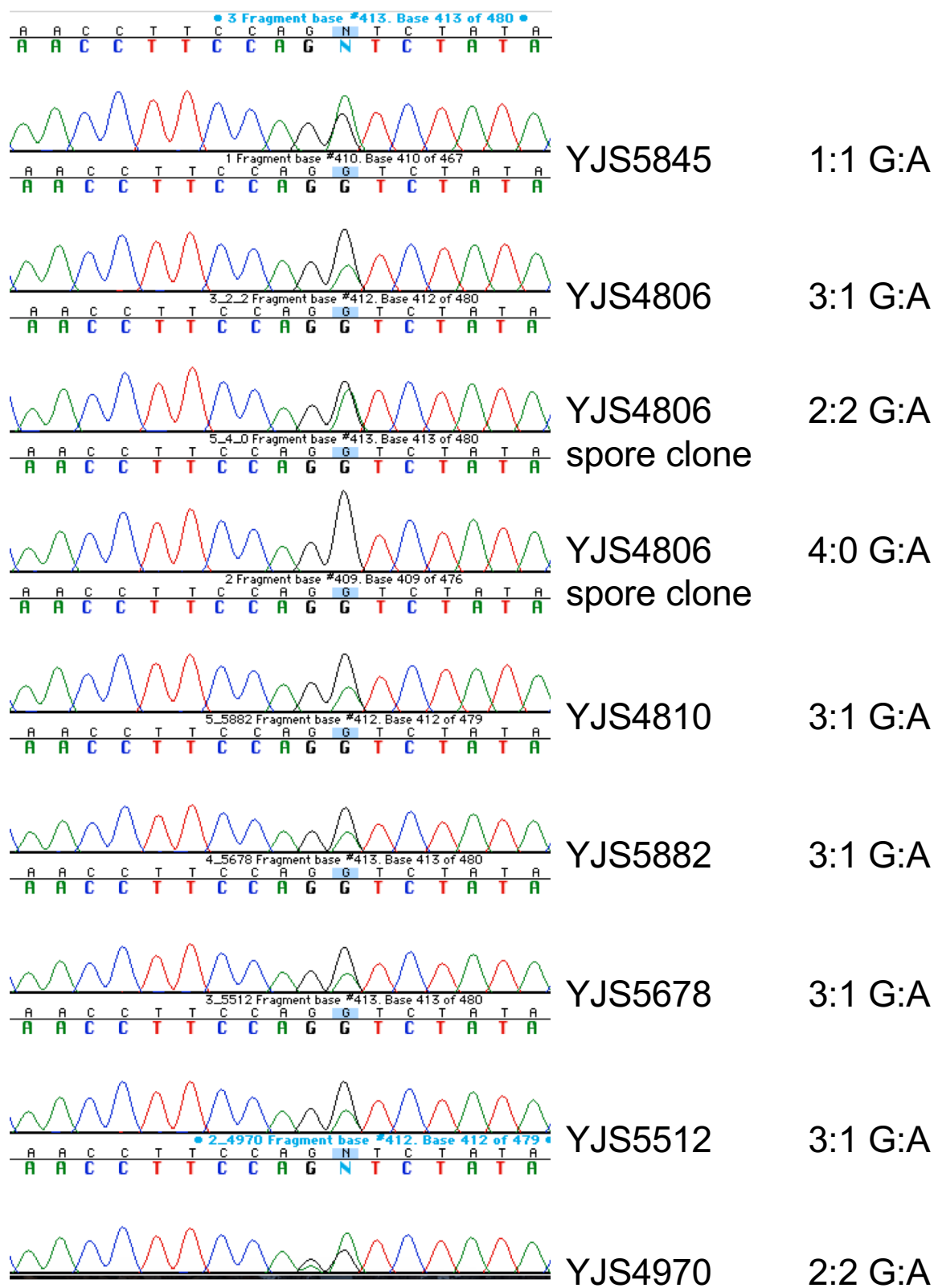


Fig S2

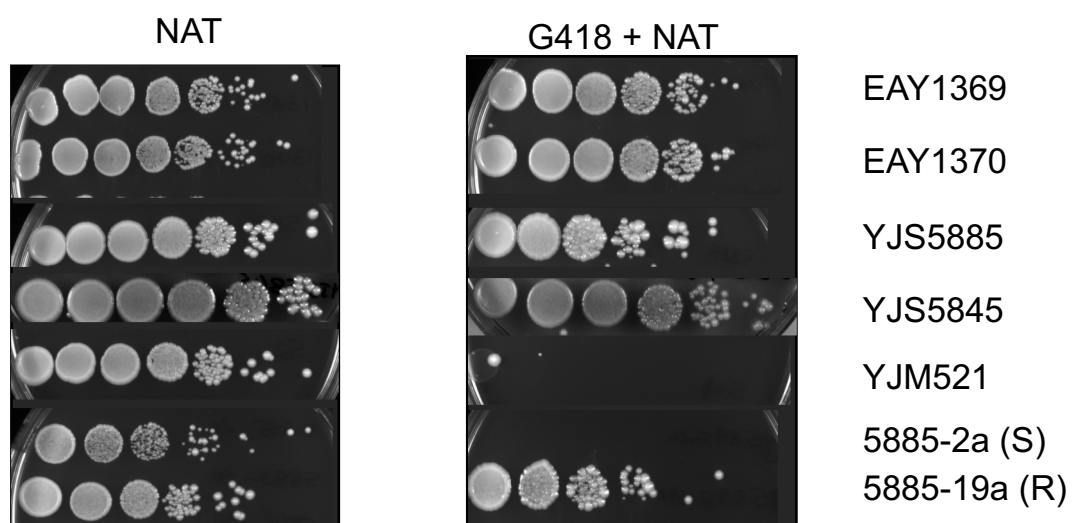
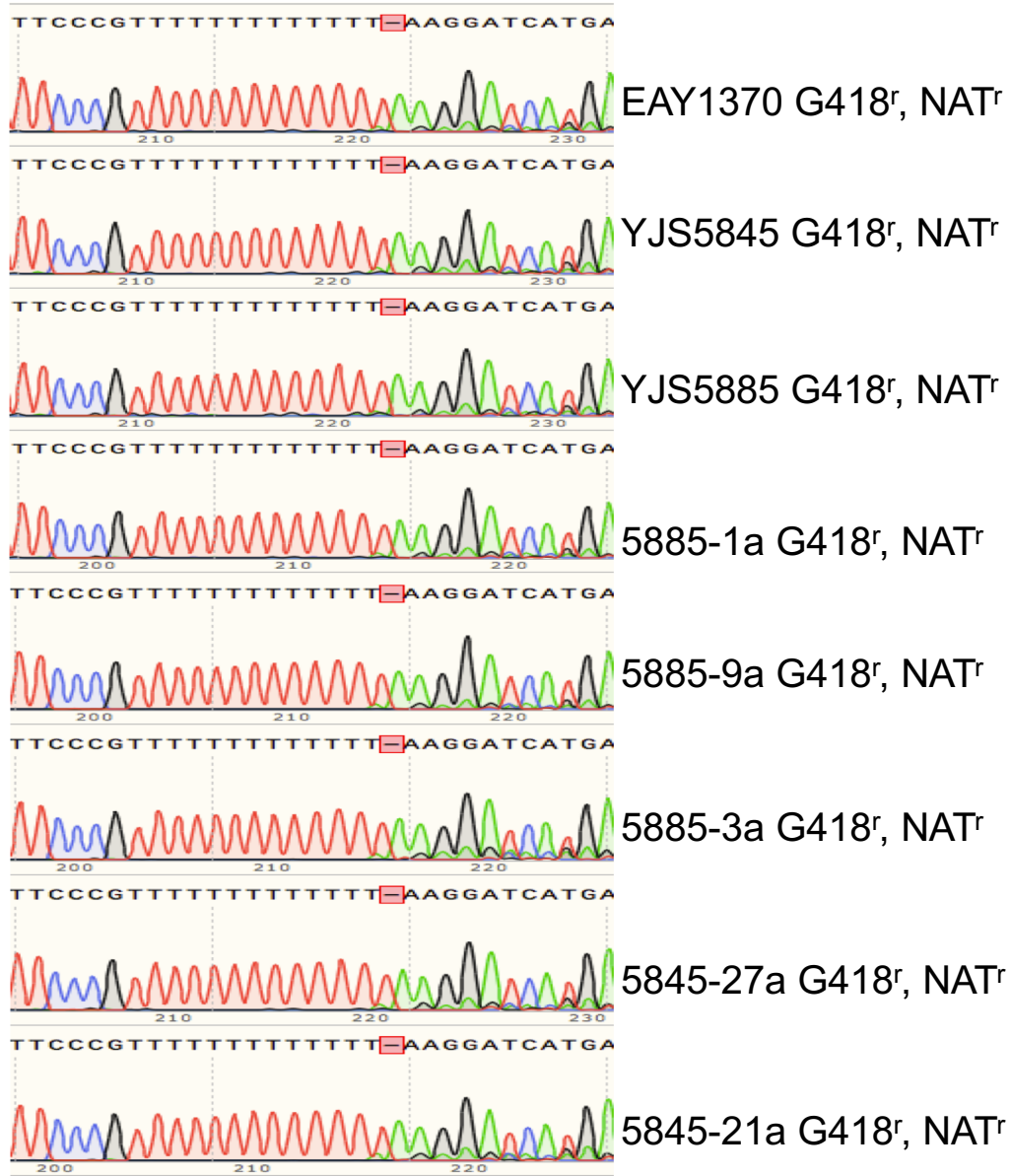


Fig S3

Revertants, G418^r, NAT^r



Controls, NAT^r, G418^s

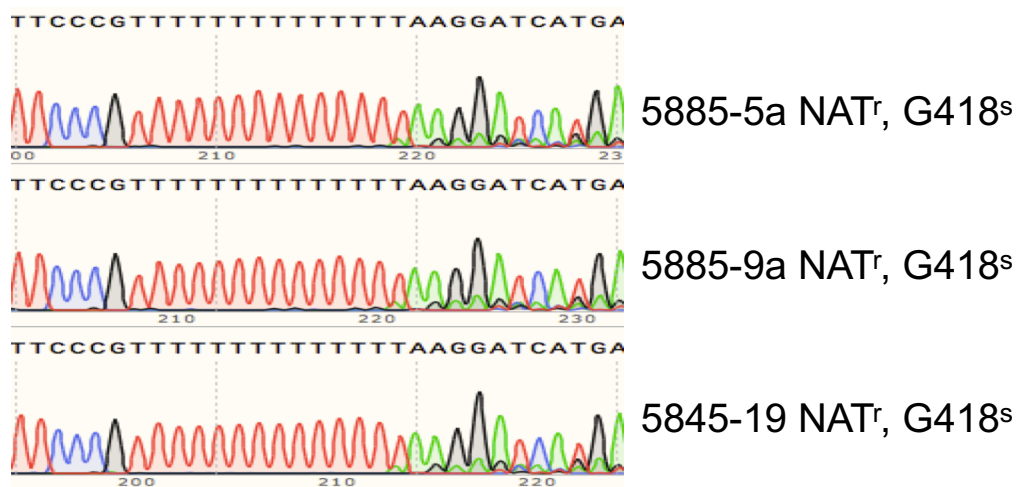


Fig S4

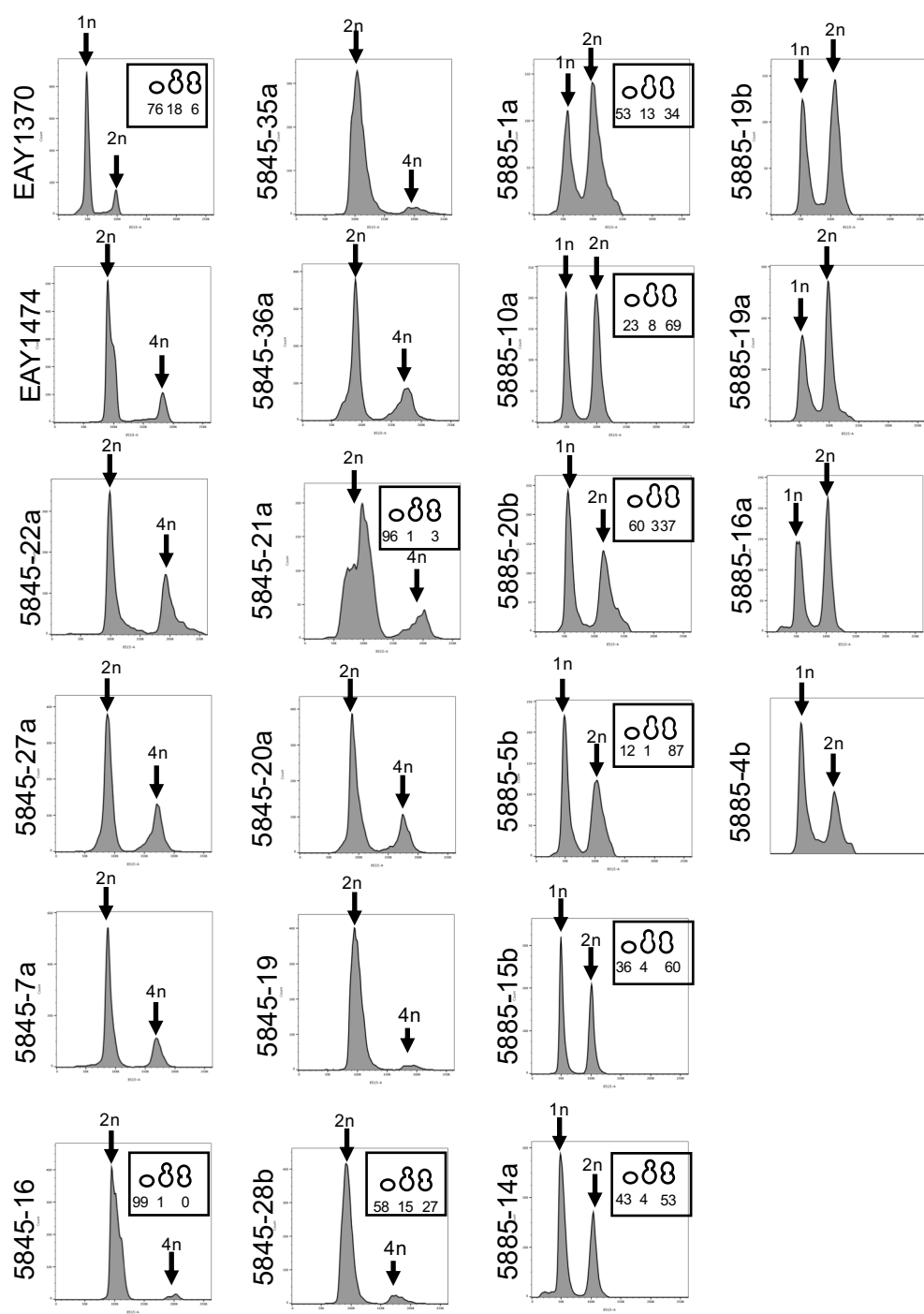
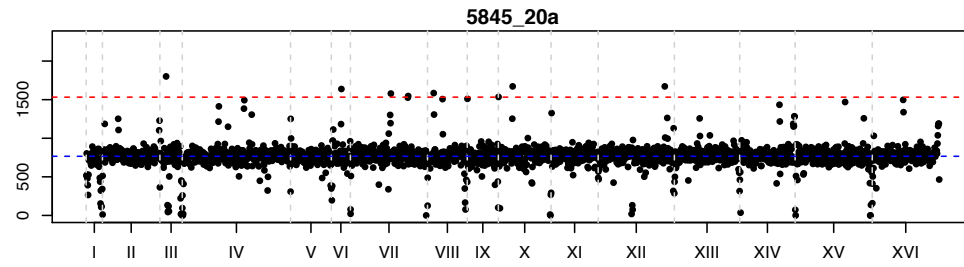
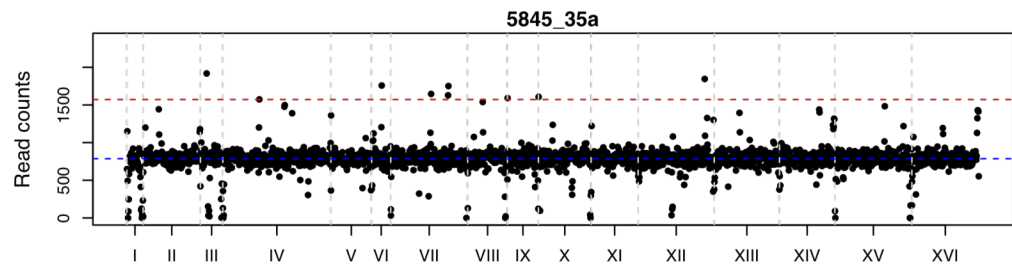
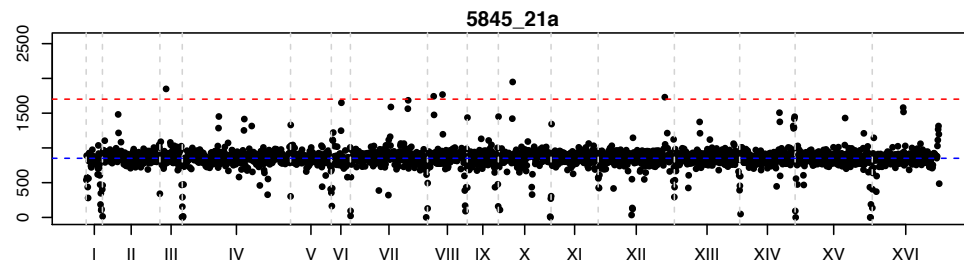
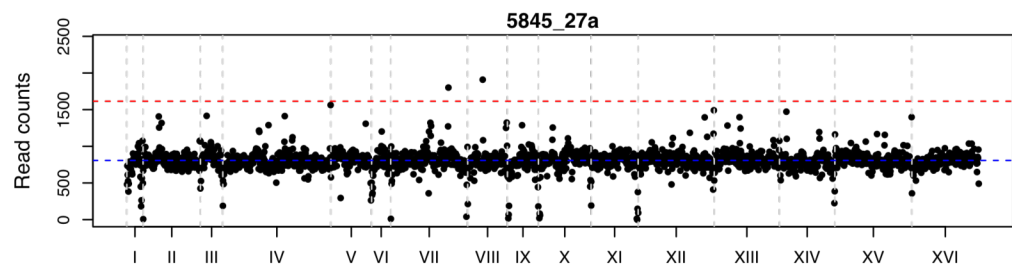
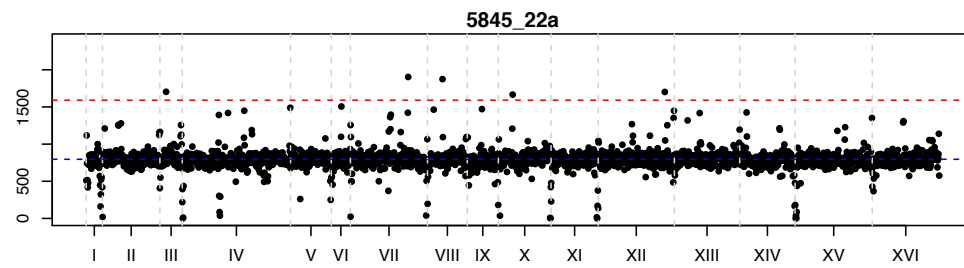
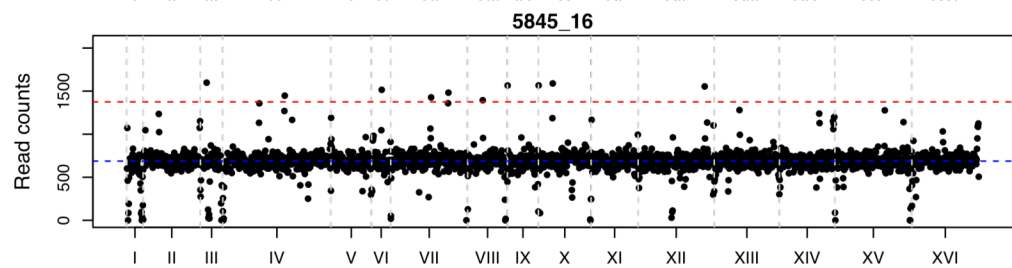
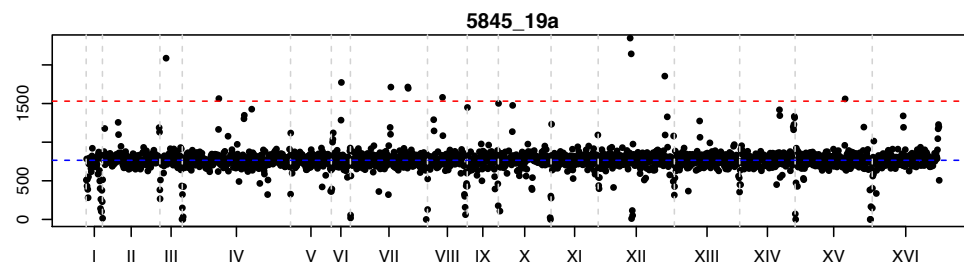
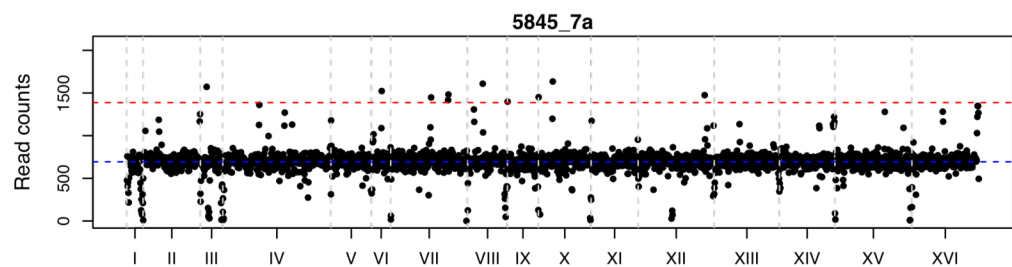
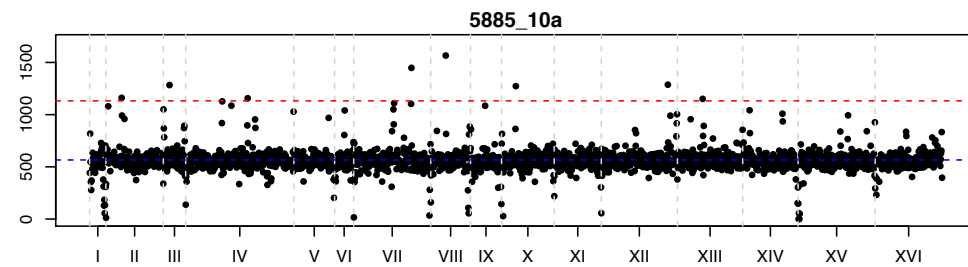
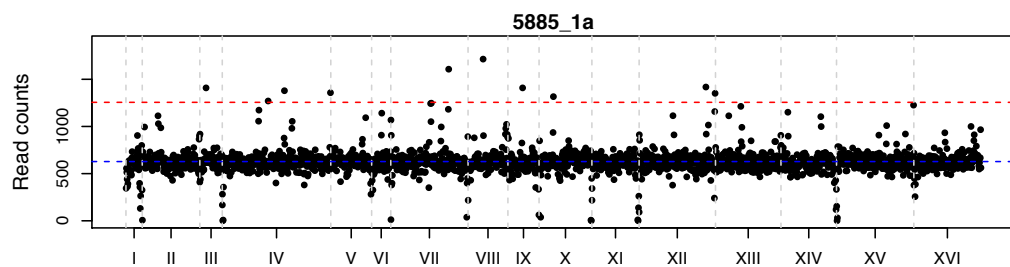
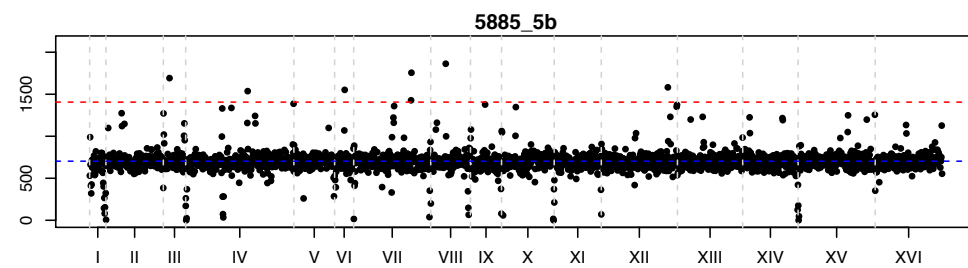
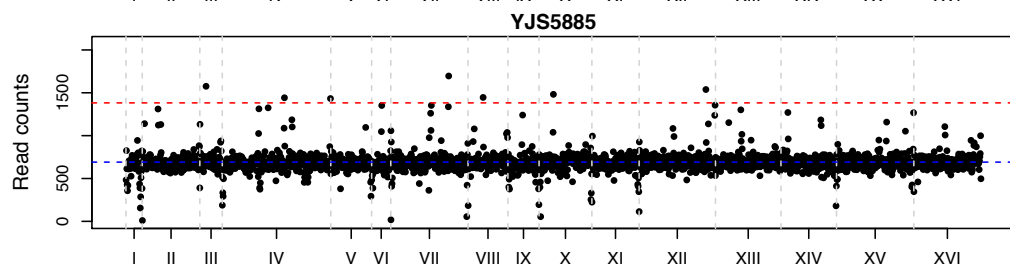
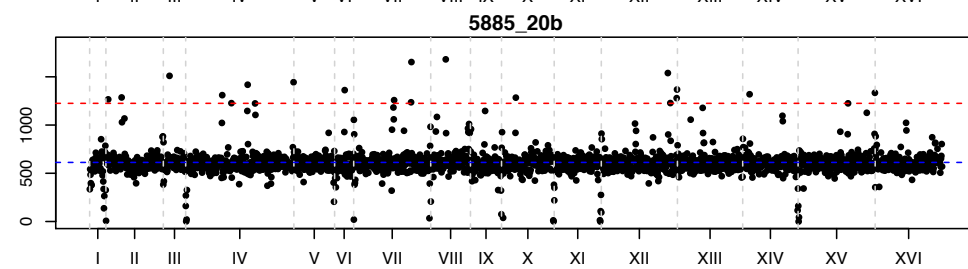
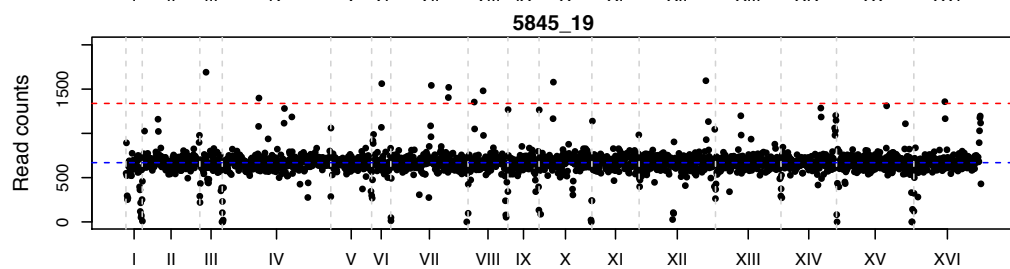
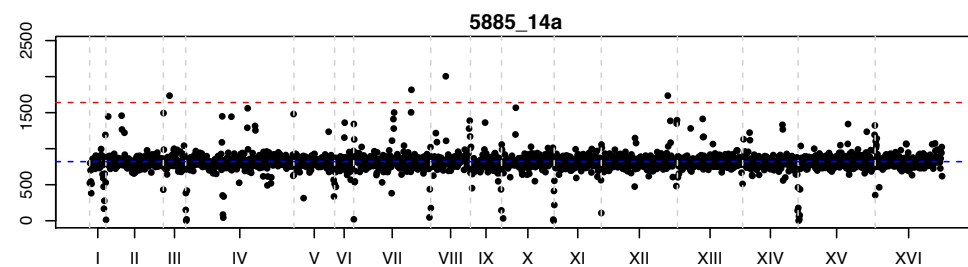
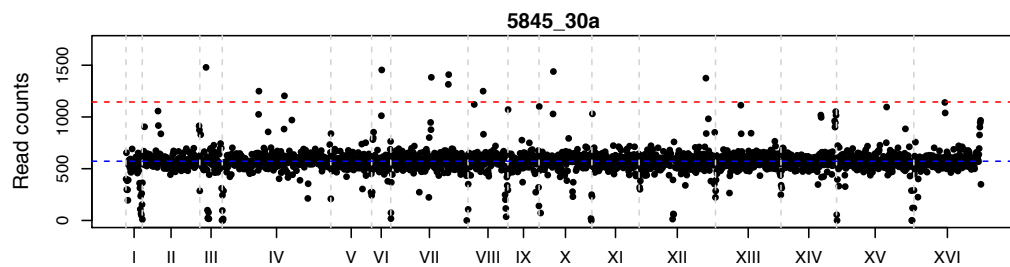


Fig S5





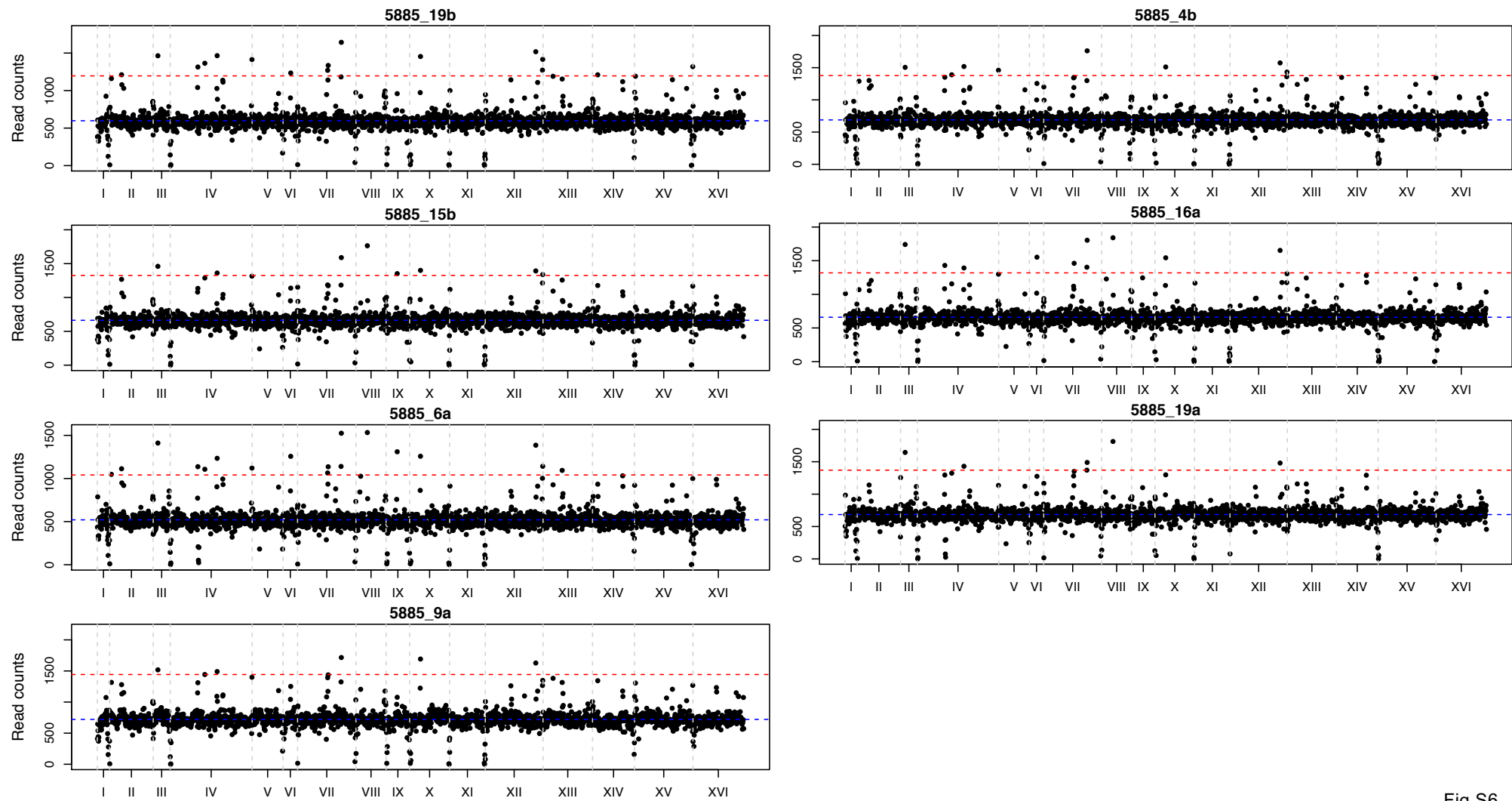


Fig S6

Table S1 Genotyping of spore clones obtained by dissection of isolate tetrads

Lab name	<i>MLH1</i> genotype	<i>PMS1</i> genotype	Number of spore clones genotyped for <i>MLH1-PMS1</i> as:			
			Ancestral	SK1	S288c	Incompatible
YJS5845	SK1/S288c	SK1/S288c	5	17	1	10
YJS5885	SK1/S288c	SK1/S288c	5	6	11	11
YJM521	SK1/S288c	SK1/S288c	5	7	7	5
YJS4806	SK1/S288c (3:1)	SK1	not relevant			
YJS4810	SK1/S288c (3:1)	SK1	not relevant			
YJS5882	SK1/S288c (3:1)	SK1-S288c (2:2)	not relevant			
YJS5678	SK1/S288c (3:1)	SK1/S288c (2:2)	not relevant			
YJS5512	SK1/S288c (3:1)	SK1/S288c (2:2)	not relevant			
YJS4970	SK1/S288c (2:2)	SK1/S288c (2:2)	not relevant			

MLH1 and *PMS1* genes were PCR amplified from isolates and derived spore clones and sequenced as described in the Materials and Methods. For YJS5845, three spore clones were genotyped from random spores and 30 were genotyped from spores isolated after tetrad dissection. For YJS5885, all spore clones were genotyped from tetrad dissection. None of the incompatible YJS5845 and YJS5885 spore clones contained the Pro 271 suppressor polymorphism in *MLH1* (Demogines *et al.* 2008). For YJM521, 24 spore clones were genotyped from six four-spore viable tetrads. For YJS4806, 24 spore clones were genotyped from random spores with 22 showing the parental genotype for *MLH1*, and two showing a different segregation pattern (2G:2A, 4G:0A). For YJS4810, 24 spore clones were genotyped from random spores, with all showing the parental genotype for *MLH1*.

Table S2 Genotyping of *MLH1* and *PMS1* loci in YJM and YJS isolates and derived spore clones

base pair	aa	S288c	SK1	YJS5845c	YJS5845k	YJS5885c	YJS5885k	YJM523	YJM521c	YJM521k
<i>MLH1</i>										
486	162	C, ALA	T, ALA	C	C	C	C	C	C	C
552	184	C, SER	C, SER	C	C	C	C	C	T, SER	C
720	240	C, SER	A, ARG	C	C	C	C	C	C	C
812	271	T, LEU	C, PRO	T	C	T	C	T	C	C
834	278	C, SER	T, SER	C	T	C	T	C	C	T
997	333	G, GLU	A, LYS	G	G	G	G	G	G	G
1044	348	T, ILE	C, ILE	T	C	T	C	T	T	C
1237	413	T, LEU	C, LEU	T	C	T	C	T	T	C
1393	465	G, ASP	G, ASP	G	G	G	G	G	A, ASN	G
1875	625	T, SER	C, SER	T	C	T	C	T	T	C
2032	678	G, ASP	A, ASN	G	A	G	A	G	G	A
2108	703	C, PRO	T, LEU	C	T	C	T	C	C	T
2282	761	A, ASP	G, GLY	A	G	A	G	A	A	G
<i>PMS1</i>										
122	41	A, ASN	G, SER	G	G	G	G	A	A	A
162	54	T, SER	T, SER	T	T	T	C	T	T	T
177	59	T, ASP	T, ASP	T	T	T	T	C, ASP	T	C, ASP
210	70	G, GLU	G, GLU	G	G	G	G	A, GLU	G	A, GLU
213	71	C, PHE	T, PHE	T	T	T	T	T	C	T
258	86	T, ASP	C, ASP	C	C	C	C	C	C	C
333	111	G, VAL	C, VAL	C	C	C	C	C	C	C
335	112	T, ILE	C, THR	C	C	C	C	T	T	T
465	155	C, PRO	T, PRO	T	T	T	T	T	C	T

552	184	T, ALA	A, ALA	T	A	T	A	T	T	T
558	186	T, ILE	C, ILE	C	C	C	C	C	T	C
708	236	A, LEU	G, LEU	G	G	G	G	G	A	G
711	237	T, ASN	C, ASN	C	C	C	C	C	T	C
810	270	G, SER	C, SER	G	C	G	C	G	G	G
855	285	G, VAL	A, VAL	G	A	G	A	G	G	G
858	286	T, ASN	T, ASN	T	T	T	T	C, ASN	T	C, ASN
918	306	C, PHE	C, PHE	C	C	C	C	C	T, PHE	C
925	309	G, VAL	G, VAL	G	G	G	G	G	T, PHE	G
939	313	T, ALA	A, ALA	A	A	A	A	A	T	A
1150	384	T, PHE	G, VAL	G	G	G	G	G	T	G
1175	392	A, GLU	A, GLU	A	A	A	A	T, ASP	A	T, ASP
1191	397	C, ASN	C, ASN	T, ILE	C	T, ILE	C	T, ILE	C	T, ILE
1199	400	C, THR	G, SER	G	G	G	G	G	C	G
1201	401	G, ALA	G, ALA	T, SER	G	T, SER	G	T, SER	G	T, SER
1249	416	NO INS	INS	INS	INS	INS	INS	INS	NO INS	INS
1329	443	C, ILE	C, ILE	T, ILE	C	C	C	T, ILE	C	T, ILE
1538	513	A, TYR	T, PHE	A	T	A	T	A	A	A
1575	525	G, ALA	C, ALA	G	C	G	C	G	G	G
1691	564	C, ALA	C, ALA	C	C	C	C	T, VAL	C	T, VAL
1782	594	T, TYR	C, TYR	C	C	C	C	C	T	C
1821	607	A, GLU	G, GLU	G	G	G	G	G	A	G
2076	692	T, ASP	T, ASP	C, ASP	T	T	T	T	T	T
2303	768	A, LYS	A, LYS	A	A	A	A	G, ARG	A	G, ARG
2322	774	T, THR	G, THR	G	G	G	G	G	T	G
2364	788	G, LEU	A, LEU	A	A	A	A	A	G	A
2453	818	G, ARG	A, LYS	G	A	G	A	A	G	A

The sequences for the *MLH1* and *PMS1* open reading frames for each of the two parental chromosomes are shown relative to the S288c and SK1 sequences for YJS5845, YJS5885, and YJM521. The parental chromosomes were genotyped as “c” (S288c) or “k” (SK1) based on the amino acid polymorphisms seen at the incompatibility loci (bp 2282 in *MLH1*, bp 2453 in *PMS1*) in the S288c and SK1 sequences (Materials and Methods). The MLH1-271P suppressor allele is highlighted at bp 812 in *MLH1*. INS = 12 bp insertion in *PMS1*; NO INS = lacking the insertion.

Table S3 Analysis of *HO*, *PHO80* and *STP22* genes in YJS5845 and YJS5885 for variants using SnpEff.

YJS5845				
Gene Name	Mutation	Type of mutation	Amino acid change	Predicted effect of missense mutation by SnpEff
<i>HO</i> gene in Chromosome IV	1756T>C	missense	Cys586Arg	Deleterious
	1740C>T	synonymous	Asn580Asn	
	1722T>C	synonymous	His574His	
	1718C>T	missense	Pro573Leu	Tolerated
	1710C>T	synonymous	Val570Val	
	1635C>T	synonymous	Gly545Gly	
	1214C>T	missense	Ser405Leu	Tolerated
	1059T>C	synonymous	Val353Val	
	1026C>A	synonymous	Gly342Gly	
	789A>G	synonymous	Leu263Leu	
	667A>G	missense	Ser223Gly	Tolerated
	565G>A	missense	Ala189Thr	Tolerated
	369G>A	synonymous	Arg123Arg	
<i>PHO80</i> in Chromosome XV	21A>C	missense	Glu7Asp	Tolerated
	111G>A	synonymous	Val37Val	
<i>STP22</i> in Chromosome III	1000C>A	missense	Gln334Lys	Tolerated
	546A>G	synonymous	Pro182Pro	
	528T>C	synonymous	Asn176Asn	
	525G>A	synonymous	Gln175Gln	
	492C>G	synonymous	Pro164Pro	
	36G>A	synonymous	Ala12Ala	
YJS5885				
Gene Name	Mutation	Type of mutation	Amino acid change	Predicted effect of missense mutation by SnpEff
<i>HO</i> gene Chromosome IV	1740C>T	synonymous	Asn580Asn	
	1710C>T	synonymous	Val570Val	
	1635C>T	synonymous	Gly545Gly	
	1424T>A	missense	Leu475His	Tolerated
	1214C>T	missense	Ser405Leu	Tolerated
	667A>G	missense	Ser223Gly	Tolerated
	369G>A	synonymous	Arg123Arg	

YJS5885

Gene Name	Mutation	Type of mutation	Amino acid change	Predicted effect of missense mutation by SnpEff
<i>PHO80</i> gene in Chromosome XV	21A>C	missense	Glu7Asp	Tolerated
	111G>A	synonymous	Val37Val	
	266C>T	missense	Ser89Phe	Tolerated
	375A>G	synonymous	Thr125Thr	
	739C>T	missense	Pro247Ser	Tolerated
<i>STP22</i> gene in Chromosome III	1000C>A	missense	Gln334Lys	Tolerated
	528T>C	synonymous	Asn176Asn	
	525G>A	synonymous	Gln175Gln	
	492C>G	synonymous	Pro164Pro	
	123T>A	missense	Asn41Lys	Tolerated
	78C>A	missense	Asn26Lys	Tolerated
	36G>A	synonymous	Ala12Ala	

Table S4 Analysis of resistance to 5-FOA in YJS5885 spore clones.

Strain or spore clone	Incompatible/Compatible	Rate 5-FOA ^r (10 ⁻⁷), (95% C.I.), n	Relative rate
FY90	C	0.79 (0.26-2.6), 22	1
EAY4087 (<i>mlh1Δ</i>)	Not applicable	16 ^a (9.5-18), 20	20
5885-1a	C	1.9 ^b (0.72-5.2), 15	2.4
5885-14a	C	0.98 ^b (0.53-2.1), 15	1.2
5885-15b	C	0.48 ^b (0.37-3.2), 15	0.61
5885-6a	C	0.68 ^b (0.32-1.5), 15	0.86
5885-9a	I	6.0 ^{a, b} (4.7-9.7), 15	7.6
5885-16a	I	1.5 ^b (0.92-1.9), 15	1.9
5885-19a	I	6.4 ^{a, b} (2.9-7.9), 15	8.1

The rate of resistance to 5-FOA, presented with 95% confidence intervals (95% C.I.), was determined for n independent cultures of FY90 and the indicated spore clones of YJS5885 as described in the Materials and Methods. The *URA3* open reading frame (ATG =+1) was sequenced from 7, 2, 1, 1, 1 and 1 independent 5-FOA^r colonies from 5885-9a, 5885-15b, 5885-1a, 5885-14a, 5885-16a, and 5885-19a, respectively. ^a Significantly different from FY90 (p<0.001, Mann-Whitney test); ^b Significantly different from EAY4087 (p<0.001, Mann-Whitney test). YJS5885 compatible and incompatible spore clones are significantly different from each other (p<0.001, Mann-Whitney test).

10 of the 13 spore clones contained single mutations in *URA3*, with the following distribution:
 5885-9a: Two missense (bp287, A>T; bp542, G>A), One nonsense (bp577, G>T), Two single nucleotide deletions (bp178, A deleted; bp629, G deleted), no changes in ORF for two 5-FOA^r mutants.
 5885-15b: One missense (bp205, T>C), one nonsense (bp345 G>A).
 5885-1a: One nonsense (bp223 A>T).
 5885-14a: One nonsense (bp593 T>A).
 5885-16a: No changes in ORF for one 5-FOA^r mutant.
 5885-19a: One nonsense (bp310 C>T).

Table S5 Sporulation and lactate growth phenotype

	Sporulation	Lactate+ or -		Sporulation	Lactate + or -
5885-1a	-	+	5845-19a	-	-
5885-6a	-	+	5845-22a	+	+
5885-10a	-	-	5845-27a	+	+
5885-20b	-	+	5845-7a	+	+
5885-5b	-	+	5845-28b	+	+
5885-15b	-	-	5845-29a	+	+
5885-14a	-	+	5845-41a	-	-
5885-19b	-	-	5845-16	+	+
5885-6b	-	+	5845-35a	poor growth- few dyads	+
5885-5a	-	+	5845-18a	+	+
5885-11a	-	+	5845-21a	-	+
5885-12a	-	-	5845-20a	+	+
5885-18a	-	-	5845-30a	+	-
5885-9a	-	-	5845-19	+	+
5885-4b	-	+	5845-36b	+	NT
5885-19a	-	-			
5885-16a	-	-			
5885-3a	-	+			
5885-12b	-	-			
5885-1b	-	NT			
5885-2a	-	NT			
5885-4a	-	NT			
5885-7a	+	NT			
5885-8a	-	NT			
5885-13a	-	NT			
5885-17a	+	NT			

Spore clones were patched on sporulation media and incubated at 30°C for 6 days after which they were examined for evidence of sporulation by light microscopy. Any samples with dyads, triads and tetrads were marked as being able to sporulate (+). Spore clones were also patched on YP-lactate media and scored as able to grow or not (Lactate⁺ or ⁻) after 4 days in 30°C. NT: not tested.

Table S6 Assigning MLH1 polymorphisms found in heterozygous genotypes onto the MLH1 structure-function map.

<i>mlh1</i> allele (Reference)	Amino acid position: isolate(s) with heterozygous genotype
N-terminal/ATP binding	
I22T (Wanat <i>et al.</i> 2007)	22-ILE/LEU: APL, CFI, CFN
Linker (Argueso <i>et al.</i> 2003)	
R390A,K391A	391-LYS/ASN: BHL, BMQ
K393A,R394A (Argueso <i>et al.</i> 2003)	393-LYS/GLU: CPN, CPR
R401A,D403A	402-ILE/LEU: ASN, BGB, BGI, BGM, BGS
C-terminal interaction (Argueso <i>et al.</i> 2003)	
E603A,D605A,E606A	605-ASP/ASN: BHL, BMQ
K648A,K650A	650-LYS/THR: ADL, AKT, BFE, BFG, BFM, BML, BMM, BTB, BTE, CKK, CKS, CLA
E680A,D681A,E682A	681-ASP/ASN: CPN, CPR

A structure function map for MLH1 was created from an analysis of *MLH1* alanine scan and site-specific mutations, and *mlh1* alleles generated based on homology to HNPCC mutations (Pang *et al.* 1997; Shcherbakova and Kunkel 1999; Tran and Liskay 2000; Welz-Voegele *et al.* 2002; Takahashi *et al.* 2007; Wanat *et al.* 2007; Romanova and Crouse 2013; Smith *et al.* 2013; Smith *et al.* 2015). Alleles that conferred a mutator phenotype in a variety of reporter assays are shown. In MLH1, amino acids 1-335 is referred to as that N-terminal/ATP binding domain, 335-509 as the linker domain, and 510-769 as the C-terminal interaction domain (Gueneau *et al.* 2013). See Table S7 for detailed list of the isolates that contain heterozygous polymorphisms that lie on the MLH1 structure-function map (shown here using their standardized names in the 1011 yeast genome project (Peter *et al.* 2018)).

Table S7 Amino acid heterozygotes identified in MLH1 in 107 yeast isolates

Origin		Position of amino acid heterozygosity (amino acid 1/amino acid 2) in MLH1		285	329	366	391	393	400	402	409	417	421	430	436	442	443	445	470	488	489	501	507	542	595	596	605	607	616	650	655	657	678	681	694	703	716	722	761					
AAI	Val1336-4	Bakery, France	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
ABV	OPV95861	Water, Brazil	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
ADN	CL1834_2	Bakery, Netherlands	Pro	Thr	Ile	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
AE8	CB1121	Beer, Netherlands	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
AEK	CE1348	Beer	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
AEV	CE1394	Citellary	Ala	Ile	Thr	Ile	Pro	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys	Lys	Asp	Asp	Ser	Pro	Glu	Asn	Gly		
AF5	VS5216	Water, Netherlands	Ala	Ile	Thr	Ile	Pro	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys	Lys	Asp	Asp	Ser	Pro	Glu	Asn	Gly		
AF5	CE8794	Rainbow trout, Sweden	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
AF5	CE1171	Citellary	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
AF5	CE1480	Citellary	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
AKN	C15.1	Palm nut, Cameroon	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Pha	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
AKT	CUCC_10-003	Singapore bee, Ecuador	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
ALV	21-4-126	Water, Slovakia	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
AMN	51153	True Leaf, Taiwan	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
ANP	UNOP93-883-2	Onopeltia, Neavosa island, S. Amer.	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
APV	ML1	Dissidia, Brazil	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
APL	YS1211	Bakery, Turkey	Ala	Ile/Leu	Thr	Ile	Lau/Pro	Thr	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys	Lys	Asp	Asp	Ala/Ser	Pro	Glu	Asn	Gly	
ARE	CE7957	Industrial Brazil	Ala	Ile	Thr	Ile	Leu	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala/Ser	Pro	Glu	Asn	Gly	
ARE	CE1398	Eucalyptus leaf	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Ser	Pro	Glu	Asn	Gly		
ARE	CE1246	Spudum, human clinical, Netherlands	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
ASC	CE4555	Katiri Beer, South America	Ala	Ile	Thr	Ile	Leu	Thr	Pro	Gln/Lys	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
ASC	CU227	Beer, Netherlands	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
ASN	CU8836	Dairy cheese, France	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Met	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val/Asp	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly		
AT5	CECT1031	Flower, Spain	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys	Lys	Asp	Asp	Ala/Ser	Pro	Glu	Asn	Gly	
ATV	CECT1462	Beer, United Kingdom	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp/Asn	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BBC	CO_21-4-88	Mushroom, Slovakia	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BBB	CO_21-4-97	Water, Slovakia	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BBE	CO_21-4-98	Water, Slovakia	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BBS	CO_21-4-106	Water, Slovakia	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BBP	1663	Flower, Spain	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala/Ser	Pro	Glu	Asn	Gly	
BDA	#34	Evolution Canyon, Israel	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BDB	163	Evolution Canyon, Israel	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly	
BDE	EXF-5734	Gooseberry, Israel	Ala	Ile	Thr	Ile	Pro	Thr	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys/Thr	Lys	Lys	Asp	Asp	Ala/Ser	Pro	Glu	Asn	Gly
BFG	EXF-5869	Wood	Ala	Ile	Thr	Ile	Pro	Thr	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys/Thr	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly
BFG	EXF-6835	Industrial, Slovenia	Ala	Ile	Thr	Ile	Pro	Thr	Pro/Ser	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile/Thr	Lys/Thr	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly
BGL	CU8550	Dairy cheese, France	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Met	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly		
BGI	CU8552	Leuconine, France	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Met	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly		
BGI	CU8553	Leuconine, France	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Met	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly		
BGM	CU8560	Dairy cheese, France	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp/Lys	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Met	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly
BGS	CU8563	Dairy cheese, France	Ala	Ile	Thr	Ile	Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Met	Thr	Gln	Ser/Gly	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val/Asp	Asp	Leu/Pro	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly
BHD	CU8109	Cider, France	Ala	Ile	Thr	Ile	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp	Leu	Ile	Lys	Lys	Asp	Asp	Ala	Pro	Glu	Asn	Gly			
BHL	CU8102	Cider, France	Ala	Ile	Thr	Ile	Lau/Pro	Thr	Pro	Gln	Asp	Lys	Lys	Val	Ile	Ile	Gln	Pro	Lau	Thr	Gln	Ser	Asp	Pro	Glu	Lys	Arg	Val	Val	Ile	Val	Asp												