Table S5. Causal mutant candidates

Mutant strain	Candidate gene	Amino acid change	Causative?	Mutant reads/total read
FY3049 (1.2)	*MOT3*	N388H	Yes	73/74
	GRR1	L181stop	Yes	67/79
	SGM1	L407S	No	79/95
	SGF73	P84L	No	46/69
	TMA108	A458V	No	42/67
	RIM8	P52L	No	46/68
FY3052 (2.3a)	*PTR3*	S363stop	Yes	68/68
	YOR019W	N553K	Weakly	48/97
	MIT1	H187R	Yes	81/81
FY3053 (2.3b)	*PTR3*	N553K	Yes	231/235
	YOR019W	N553K	Weakly	62/259
	MSN2	C652stop	Yes	252/252

Causality was determined by allele replacement for most of the listed mutations as described in Materials and Methods. For three mutations, in *SGF73*, *TMA108*, and *RIM8*, allele replacement was not done. Instead, these mutations were tested during reconstruction of the polygenic mutant and were shown to not confer any mutant phenotype.