Homology curation at SGD: budding yeast as a model for eukaryotic biology

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Challenge to Biocurators

Promote ways in which [your_organism]

and

research on [your_organism]

can inform genetic medicine

Yeast research informs genetic medicine

- Yeast and human homologs
- Alleles and phenotype variants
- Functional complementation
- Disease associations

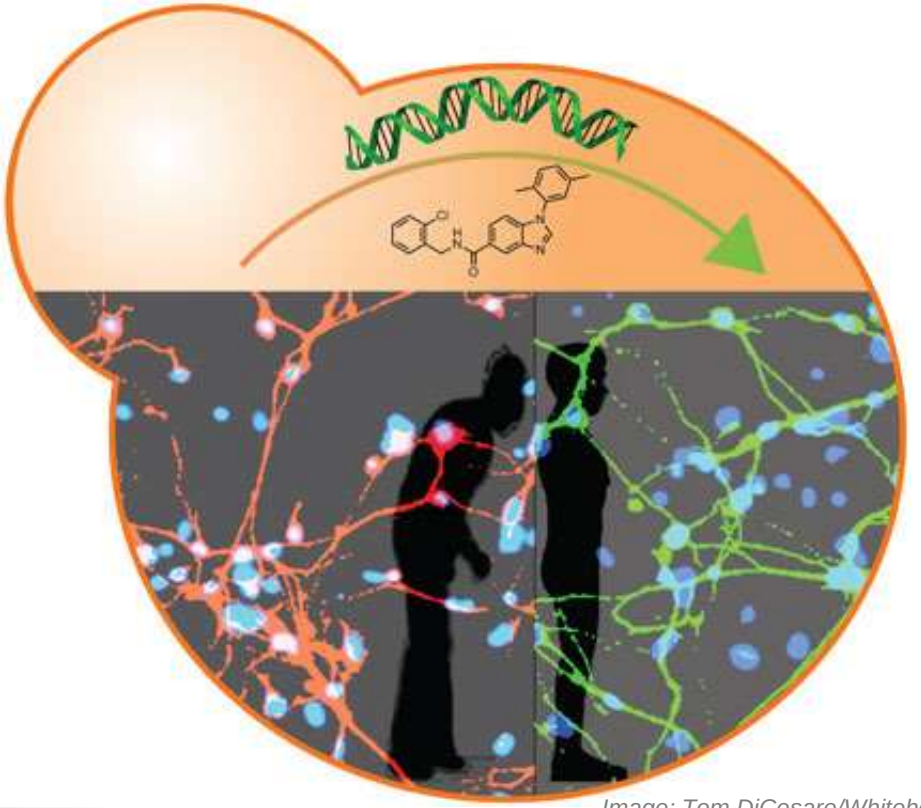
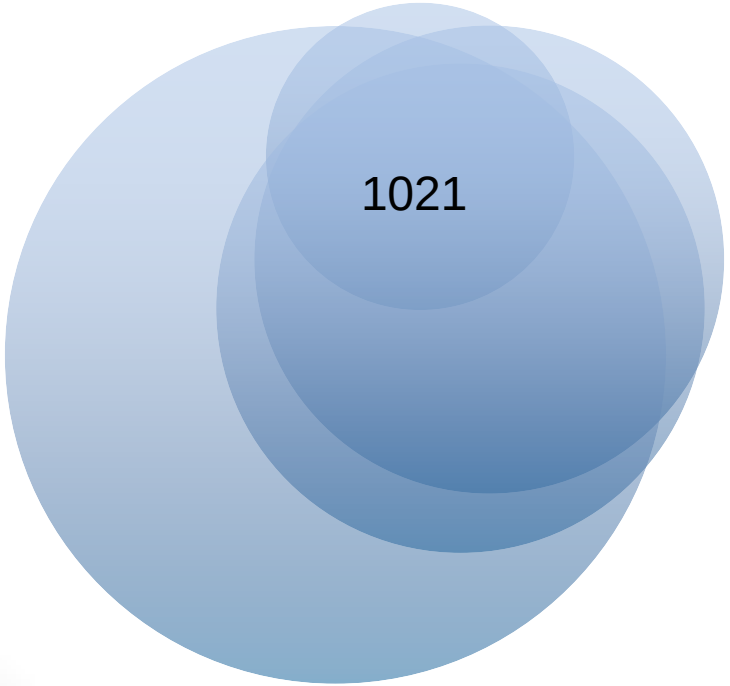


Image: Tom DiCesare/Whitehead Institute

Yeast and human homologs

3193 yeast ORFs have ≥1 reported human homolog

- Homologene: 1341
- Ensembl: 2112
- TreeFam: 2025
- Panther: 2812



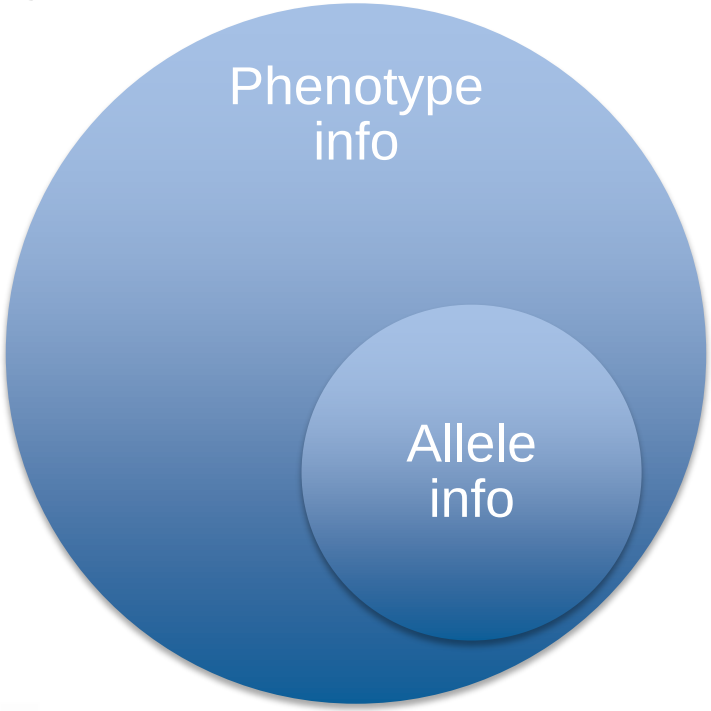
Alleles and phenotype variants

- 6196 ORFs have phenotype annotations (94%)
  - Ascomycete Phenotype Ontology
  - http://bioportal.bioontology.org/ontologies/APO

- 1479 ORFs have allele info

  1063 in broad homolog set

  460 in strict homolog set



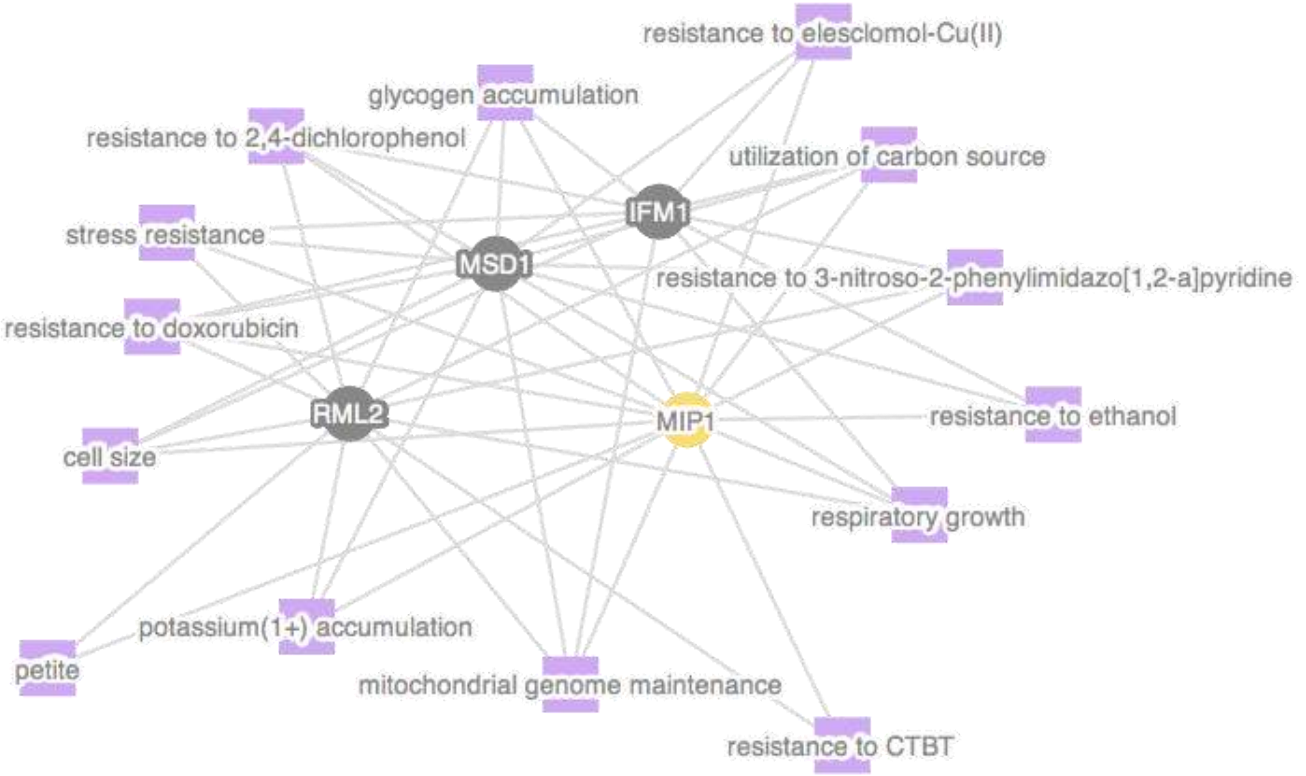
Phenotype	Experiment Type	Mutant Information	Strain Background	Chemical	Details	Reference
mitochondrial genome maintenance: absent	classical genetics					
mitochondrial genome maintenance: decreased						
mutation frequency: increased						
mutation frequency: increased						

Phenotype

Classical Genetics
dominant negative:
null:
gain of function:
conditional:
reduction of function:

Large-scale Survey
null:

unspecified:



- glycogen accumulation: decreased
- haploinsufficient
- mitochondrial genome maintenance: absent
- oxidative stress resistance: decreased
- potassium(1+) accumulation: decreased
- resistance to 2,4-dichlorophenol: decreased
- resistance to 3-nitroso-2-phenylimidazo[1,2-a]pyridine: decreased
- resistance to CTBT: decreased
- resistance to doxorubicin: decreased
- resistance to elesclomol-Cu(II): decreased
- resistance to ethanol: decreased
- resistance to idarubicin: increased
- resistance to toxaphene: decreased
- respiratory growth: absent
- respiratory growth: decreased rate
- stress resistance: increased
- sulfur(1+) accumulation: increased
- toxin resistance: decreased
- utilization of carbon source: decreased
- utilization of carbon source: decreased rate
- utilization of nitrogen source: decreased rate
- vacuolar morphology: abnormal
- vegetative growth: abnormal
- vegetative growth: decreased rate
- viable
- resistance to cycloheximide: increased

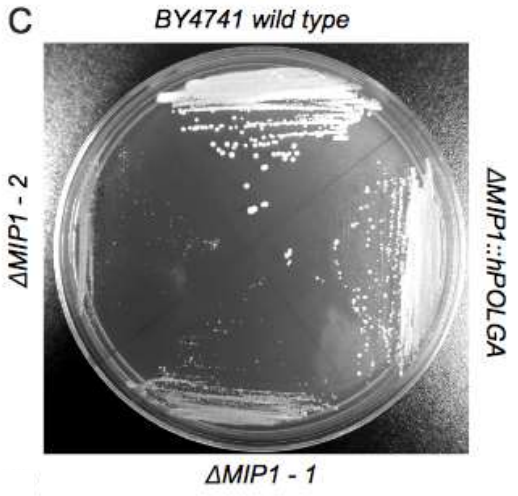
mutations in mitochondrial DNA

SUMMARY: Non-essential gene; null mutants grow slowly, have abnormal vacuolar morphology, accumulate glycogen, cannot respire or use various nitrogen sources, are sensitive to oxidative stress and desiccation, and have shortened lifespan and small cell size; missense mutants that correspond to human Alpers disease mutations show increased mitochondrial DNA point mutations; heterozygous diploid nulls are haploinsufficient

SGD Saccharomyces GENOME DATABASE

Functional complementation

- Manually curated gene pairs: yeast human
- 1st set: ~400 papers
  - Previously tagged for ‘potential information’
  - 106: no experimental info
  - 136: didn’t test
  - 16: tested, but negative
  - 140: found evidence
- Result: 142 gene pairs



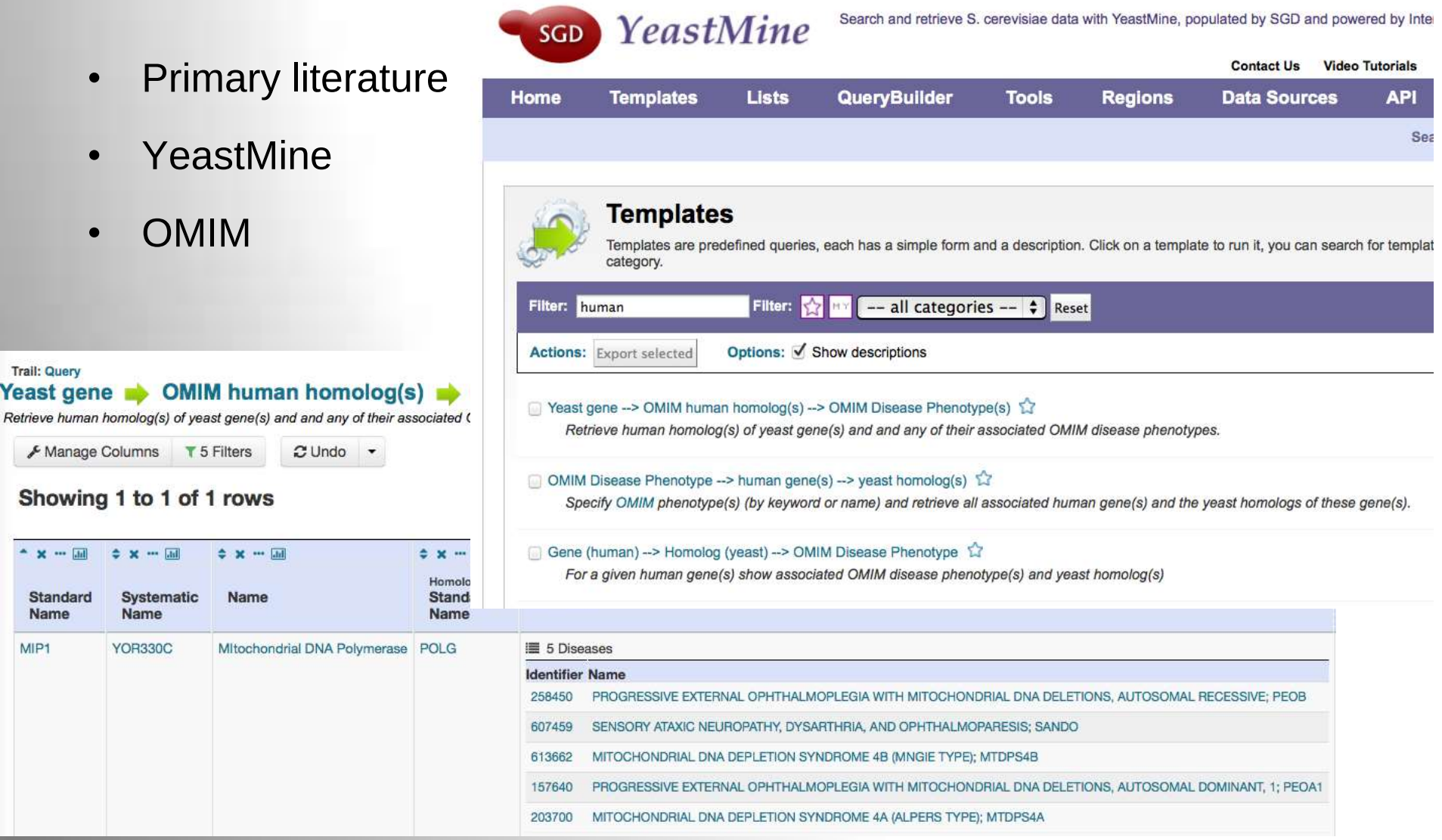
Qian Y, *et al*. 2014, PMID: 24398692

Functional complementation set

Yeast	Human	OMIM	Complementation
ACO1	ACO2	100850	human -> yeast
AFG3	AFG3L2	604581	human -> yeast
AGC1	SLC25A13	603859	human -> yeast
AGX1	AGXT	604285	human -> yeast
AKR1	ZDHHC15	300576	human -> yeast
AKR1	ZDHHC17	607799	human -> yeast
AKR1	ZDHHC21	614605	human -> yeast
AKR1	ZDHHC5	614586	human -> yeast
AKR1	ZDHHC7	614604	human -> yeast
AKR1	ZDHHC8	608784	human -> yeast
AKR1	ZDHHC9	300646	human -> yeast
ALA1	AARS	601065	human -> yeast
ALG1	ALG1	605907	human -> yeast
ALG12	ALG12	607144	human -> yeast
ALG3	ALG3	608750	human -> yeast
ALG5	ALG5	604565	human -> yeast
ALG6	ALG6	604566	human -> yeast
ALG8	ALG8	608103	human -> yeast
ALG9	ALG9	606941	human -> yeast
ALR1	MAGT1	300715	human -> yeast
ALR1	TUSC3	601385	human -> yeast
ARD1	NAA10	300013	human -> yeast
ATM1	ABCB7	300135	human -> yeast
ATP12	ATPAF2	608918	human -> yeast
BCS1	BCS1L	603647	human -> yeast
BET5	TRAPPC1	610969	human -> yeast
CAR2	OAT	613349	human -> yeast
CCA1	TRNT1	612907	human -> yeast
CCC2	ATP7A	300011	human -> yeast
CCC2	ATP7B	606882	human -> yeast
CCS1	CCS	603864	human -> yeast
CDC48	VCP	601023	human -> yeast
CIN2	RP2	300757	human -> yeast
COQ2	COQ2	609825	human -> yeast
COQ6	COQ6	614647	human -> yeast
COQ8	ADCK3	606980	human -> yeast
COQ9	COQ9	612837	human -> yeast
COX10	COX10	602125	human -> yeast
COX17	COX17	604813	human -> yeast
CRC1	SLC25A20	604515	human -> yeast
CUE5	TOLLIP	606277	human -> yeast
CYC3	HCCS	300056	human -> yeast
CYS4	CBS	608531	human -> yeast
DFG10	SRD5A3	611715	human -> yeast
ERG26	NSDHL	300275	human -> yeast
ESS1	PIN1	601052	human -> yeast
FLD1	BSCL2	606158	human -> yeast
FLX1	SLC25A32	610815	human -> yeast
FOL2	GCH1	600225	human -> yeast
GAL1	GALK2	137028	human -> yeast
GAL10	GALE	606953	human -> yeast
GDT1	TMEM165	614726	human -> yeast
GET1	CAMLG	601118	human -> yeast
GET1	WRB	602915	human -> yeast
GET2	CAMLG	601118	human -> yeast
GET2	WRB	602915	human -> yeast
GRS1	GARS	600287	human -> yeast
HAM1	ITPA	147520	yeast -> human
HMG1	HMGCR	142910	human -> yeast
HRT1	RBX1	603814	human -> yeast
HRT1	RBX1	603814	human -> yeast
HUB1	UBL5	606849	human -> yeast
IRA1	NF1	613113	human -> yeast
IRA2	NF1	613113	human -> yeast
ISM1	IARS2	612801	human -> yeast
ISU1	ISCU	611911	human -> yeast
ISU2	ISCU	611911	human -> yeast
LAS17	WAS	300392	human -> yeast
LEU5	SLC25A16	139080	human -> yeast
LPD1	DLD	238331	human -> yeast
MDM38	LETM1	604407	human -> yeast
MEP1	RHCG	605381	human -> yeast
MET14	PAPSS2	603005	human -> yeast
MET22	BPNT1	604053	human -> yeast
MET3	PAPSS2	603005	human -> yeast
MIP1	POLG	174763	human -> yeast
MLH1	MLH1	120436	human -> yeast
MNL1	EDEM1	607673	human -> yeast
MPC1	MPC1	614738	human -> yeast
MSB3	USP6NL	605405	human -> yeast
MSB4	USP6NL	605405	human -> yeast
MTO1	MTO1	614667	human -> yeast
NAM2	LARS2	604544	human -> yeast
NAT1	NAA15	608000	human -> yeast
NCR1	NPC1	607623	yeast -> human
NDI1	MT-ND4	516003	yeast -> human
NPC2	NPC2	601015	yeast -> human
NUS1	NUS1	610463	human -> yeast
PAH1	LPIN1	605518	human -> yeast
PAH1	LPIN2	605519	human -> yeast
PAH1	LPIN3	605520	human -> yeast
PCK1	PCK1	614168	human -> yeast
PET9	SLC25A4	103220	human -> yeast
PEX13	PEX13	601789	human -> yeast
PFY1	PFN1	176610	human -> yeast
PHO85	CDK5	123831	human -> yeast
PHO92	YTHDF2	610640	human -> yeast
PMR1	ATP2C1	604384	human -> yeast
PMS1	PMS1	600258	human -> yeast
PUT2	ALDH4A1	606811	human -> yeast
PXA1	ABCD1	300371	human -> yeast
PXA1	ABCD2	601081	human -> yeast
PXA2	ABCD1	300371	human -> yeast
PXA2	ABCD2	601081	human -> yeast
RAD5	HLTF	603257	human -> yeast
RAD53	CHEK2	604373	human -> yeast
RPL10	RPL10	312173	human -> yeast
SAC6	LCP1	153430	human -> yeast
SAC6	PLS3	300131	human -> yeast
SEC59	DOLK	610746	human -> yeast
SGF73	ATXN7	607640	human -> yeast
SGS1	BLM	604610	human -> yeast
SGS1	WRN	604611	human -> yeast
SLM3	TRMU	610230	human -> yeast
SMT3	SUMO1	601912	human -> yeast
SOD1	SOD1	147450	human -> yeast
SPT15	TBP	600075	yeast -> human
STE24	ZMPSTE24	606480	human -> yeast
SYM1	MPV17	137960	human -> yeast
TAZ1	TAZ	300394	human -> yeast
THS1	TARS	187790	human -> yeast
TIM13	TIMM13	607383	human -> yeast
TIM8	TIMM8A	300356	human -> yeast
TOP2	TOP2A	126430	human -> yeast
TPI1	TPI1	190450	human -> yeast
TRM7	FTSJ1	300499	human -> yeast
TRM732	THADA	611800	human -> yeast
TRS20	TRAPPC2	300202	human -> yeast
TSC13	TECR	610057	human -> yeast
ULP2	PML	102578	human -> yeast
VAS1	VARS2	612802	human -> yeast
VMA2	ATP6V1B1	192132	human -> yeast
VPH1	ATP6V0A4	605239	human -> yeast
VPS30	BECN1	604378	human -> yeast
VPS35	VPS35	601501	human -> yeast
YFH1	FTL	134790	human -> yeast
YFH1	FXN	606829	human -> yeast
YHC3	CLN3	607042	human -> yeast
YME1	YME1L1	607472	human -> yeast
YTA12	AFG3L2	604581	human -> yeast
YTA12	SPG7	602783	human -> yeast

Disease associations

- Primary literature
- YeastMine
- OMIM



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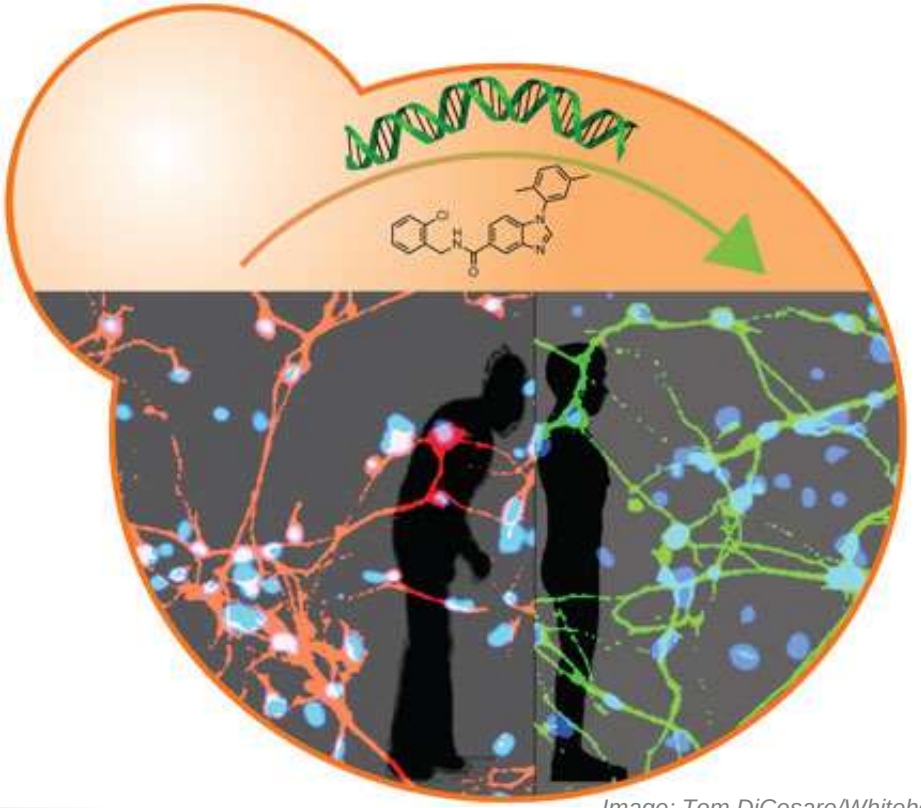

Image: Tom DiCesare/Whitehead Institute

Locus Overview

Standard Name: MIP1 [1]
Systematic Name: YOR330C
SGD ID: S000005857
Feature Type: ORF , Verified
Description: Mitochondrial DNA polymerase gamma subunit; single subunit of mitochondrial DNA polymerase in yeast, in contrast to metazoan complex of catalytic and accessory subunits; polymorphic in yeast, petites occur more frequently in some lab strains; human ortholog POLG complements yeast mip1 mutant; mutations in human POLG associated with Alpers-Huttenlocher syndrome (AHS), progressive external ophthalmoplegia (PEO), parkinsonism, other mitochondrial diseases [2 3 4 5 6 7 8 9]
Name Description: Mitochondrial DNA Polymerase [1]

Annotations

65 entries for 41 phenotypes

disease

Phenotype	Experiment Type	Mutant Information	Strain Background	Chemical	Details	Reference
mutation frequency: increased	heterozygous diploid	dominant negative **Allele:** mip1-Q264H	Other	3mM methyl methanesulfonate		Stumpf JD and Copeland WC (2014)
respiratory growth: decreased	classical genetics	reduction of function **Allele:** mip1-C261R	Other	2% ethanol	mip1-R467W, and mip1-P513R alleles corresponding to mutations in human ortholog associated with Alpers' disease	Baruffini E, et al. (2011)
mitochondrial genome maintenance: decreased	classical genetics	reduction of function **Allele:** mip1-C261R	Other		**Details:** similar phenotype observed for mip1-I334H, mip1-R467W, and mip1-P513R alleles corresponding to mutations in human ortholog associated with Alpers' disease	Baruffini E, et al. (2011)
mutation frequency: increased	classical genetics	reduction of function **Allele:** mip1-C261R	Other		**Details:** similar phenotype observed for mip1-I334H, mip1-R467W, and mip1-P513R alleles corresponding to mutations in human ortholog associated with Alpers' disease; increased frequency of point mutations in mitochondrial DNA	Baruffini E, et al. (2011)

Corresponds to human mutation, Q308H. Associated with PEO disease

Functional complementation

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