

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

Stacia R. Engel
Stanford University

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

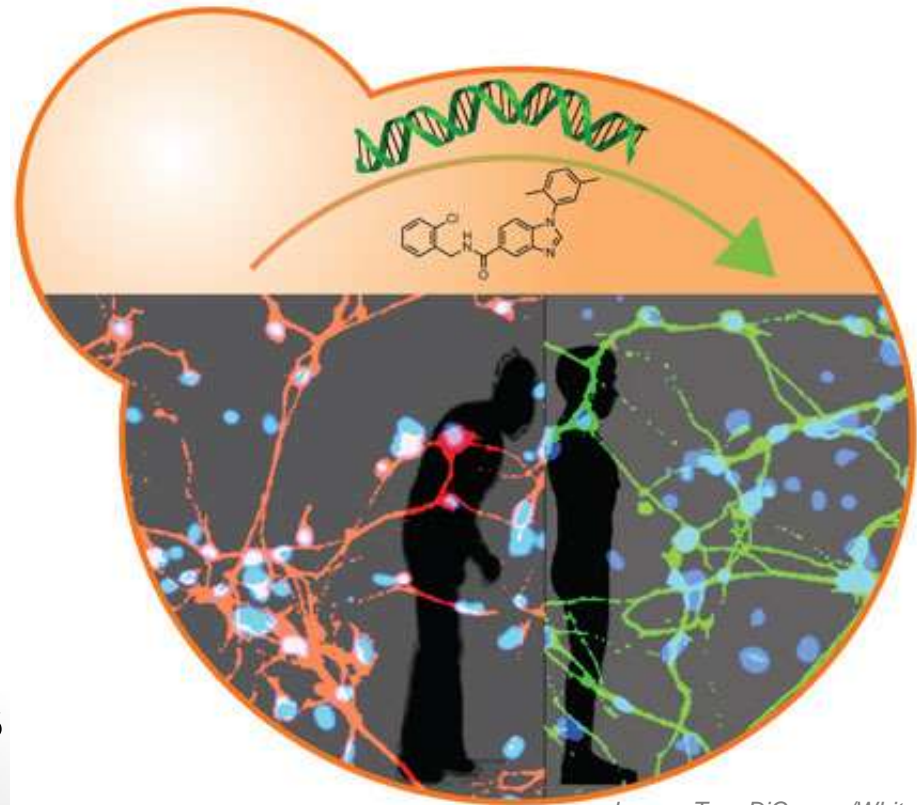
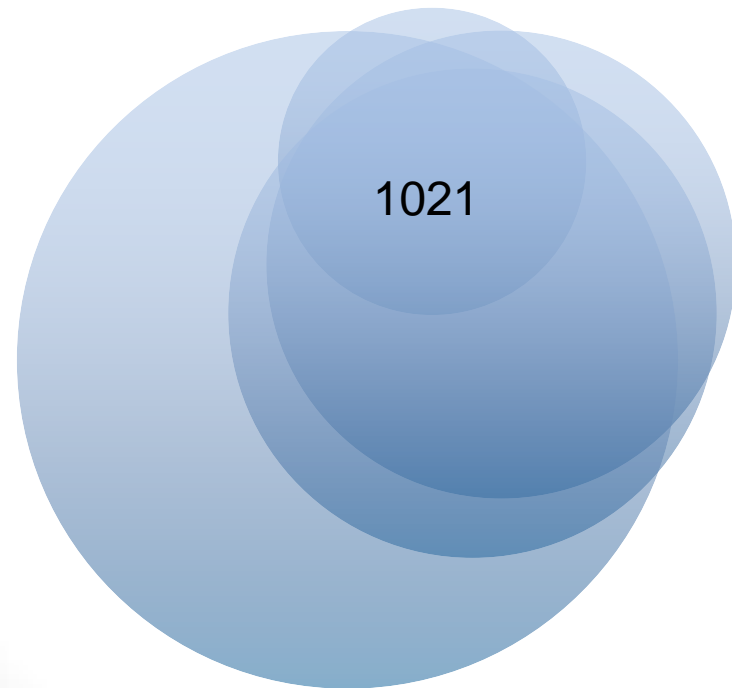


Image: Tom DiCesare/Whitehead Institute

Yeast and human homologs

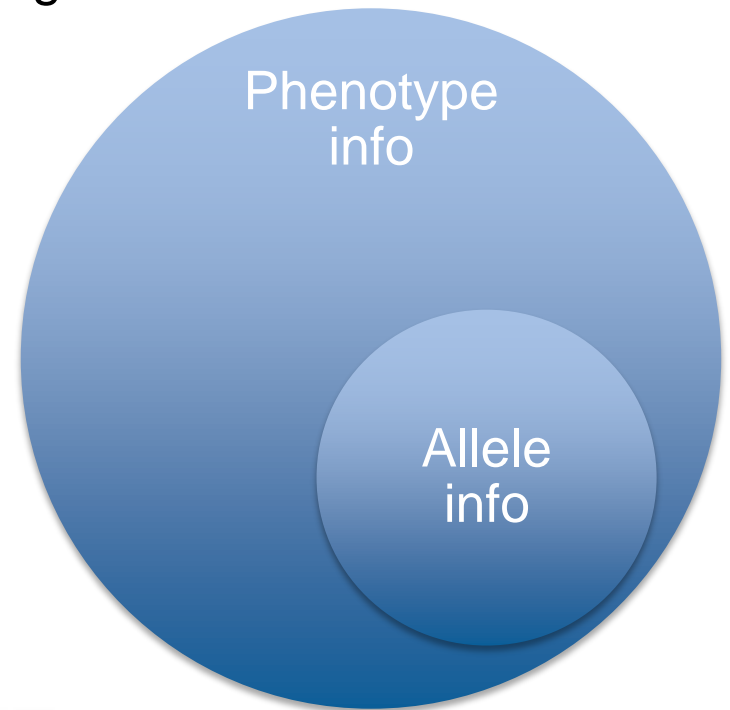
3193 yeast ORFs have ≥ 1 reported human homolog

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

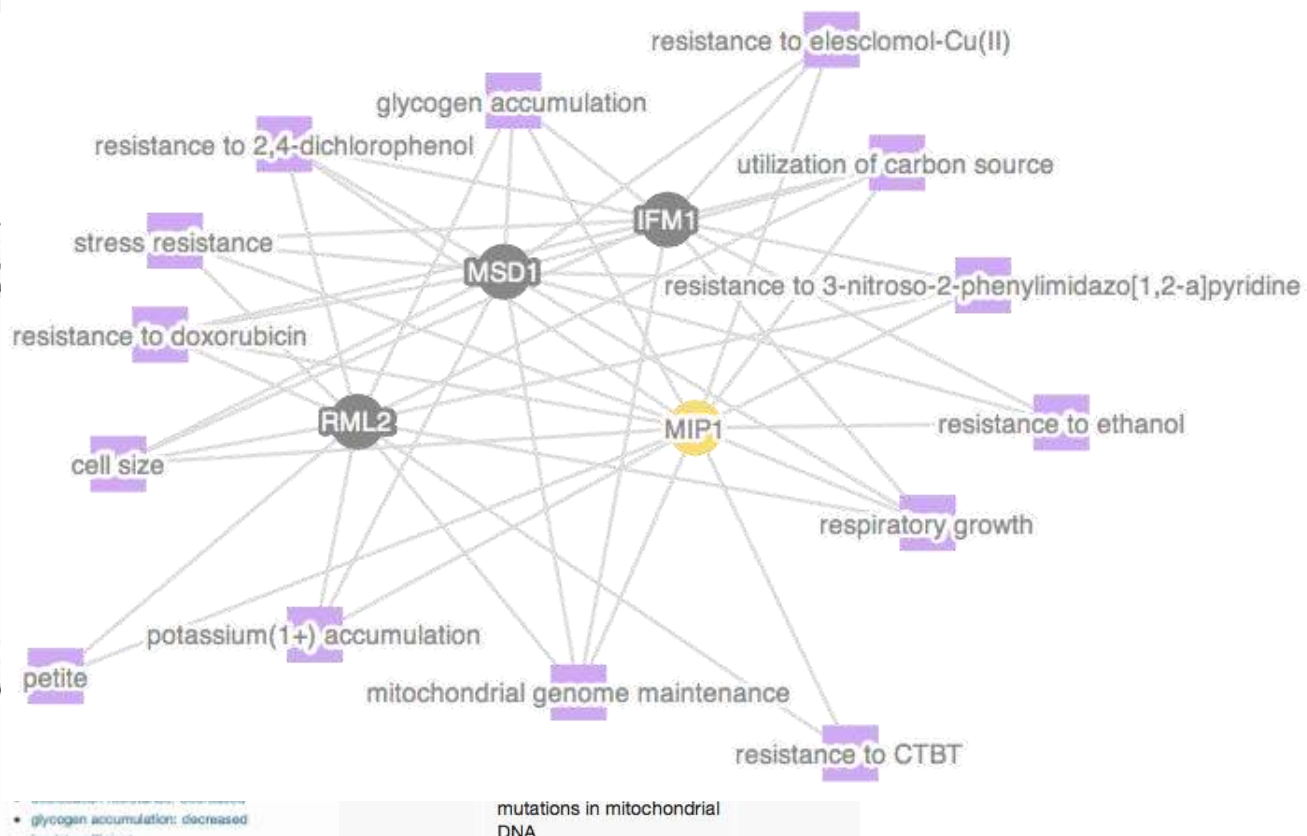


Alleles and phenotype variants

- 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



mitochondrial genome maintenance: absent	classical genetics
mitochondrial genome maintenance: decreased	Classical Geneti dominant negative
mutation frequency: increased	null: gain of function: conditional: reduction of function:
mutation frequency: increased	Large-scale Sun null:

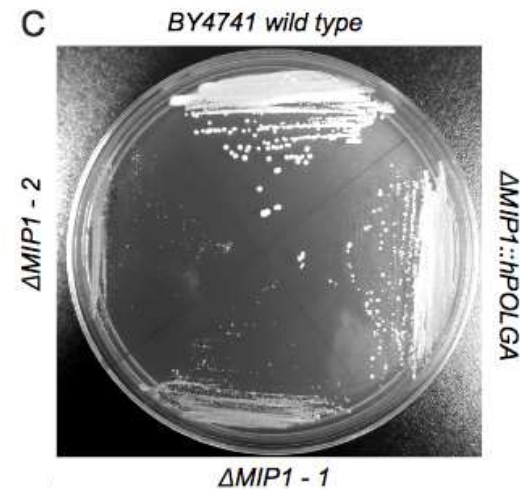
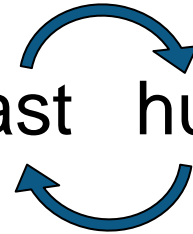


- glycogen accumulation: decreased
- haploinsufficient
- mitochondrial genome maintenance: absent
- oxidative stress resistance: decreased
- potassium(1+) accumulation: decreased
- resistance to 2,4-dichlorophenol: decreased
- resistance to 3-nitroso-2-phenylimidazo[1,2-a]pyridine: decreased
- resistance to CTBT: decreased
- resistance to doxorubicin: decreased
- resistance to elesclomol-Cu(II): decreased
- resistance to ethanol: decreased
- resistance to idarubicin: increased
- resistance to taxaphene: 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
- unspecified:
- resistance to cycloheximide: increased

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

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	Yeast	Human	OMIM	Complementation	Yeast	Human	OMIM	Complementation	Yeast	Human	OMIM	Complementation
ACO1	ACO2	100850	human -> yeast	COQ9	COQ9	612837	human -> yeast	MEP1	RHCG	605381	human -> yeast	RPL10	RPL10	312173	human -> yeast
AFG3	AFG3L2	604581	human -> yeast	COX10	COX10	602125	human -> yeast	MET14	PAPSS2	603005	human -> yeast	SAC6	LCP1	153430	human -> yeast
AGC1	SLC25A13	603859	human -> yeast	COX17	COX17	604813	human -> yeast	MET22	BPNT1	604053	human -> yeast	SAC6	PLS3	300131	human -> yeast
AGX1	AGXT	604285	human -> yeast	CRC1	SLC25A20	604515	human -> yeast	MET3	PAPSS2	603005	human -> yeast	SEC59	DOLK	610746	human -> yeast
AKR1	ZDHC15	300576	human -> yeast	CUE5	TOLLIP	606277	human -> yeast	MIP1	POLG	174763	human -> yeast	SGF73	ATXN7	607640	human -> yeast
AKR1	ZDHC17	607799	human -> yeast	CYC3	HCCS	300056	human -> yeast	MLH1	MLH1	120436	human -> yeast	SGS1	BLM	604610	human -> yeast
AKR1	ZDHC21	614605	human -> yeast	CYS4	CBS	608531	human -> yeast	MNL1	EDEM1	607673	human -> yeast	SGS1	WRN	604611	human -> yeast
AKR1	ZDHC5	614586	human -> yeast	DFG10	SRD5A3	611715	human -> yeast	MPC1	MPC1	614738	human -> yeast	SLM3	TRMU	610230	human -> yeast
AKR1	ZDHC7	614604	human -> yeast	ERG26	NSDHL	300275	human -> yeast	MSB3	USP6NL	605405	human -> yeast	SMT3	SUMO1	601912	human -> yeast
AKR1	ZDHC8	608784	human -> yeast	ESS1	PIN1	601052	human -> yeast	MSB4	USP6NL	605405	human -> yeast	SOD1	SOD1	147450	human -> yeast
AKR1	ZDHC9	300646	human -> yeast	FLD1	BSCL2	606158	human -> yeast	MTO1	MTO1	614667	human -> yeast	SPT15	TBP	600075	yeast -> human
ALA1	AARS	601065	human -> yeast	FLX1	SLC25A32	610815	human -> yeast	NAM2	LARS2	604544	human -> yeast	STE24	ZMPSTE24	606480	human -> yeast
ALG1	ALG1	605907	human -> yeast	FOL2	GCH1	600225	human -> yeast	NAT1	NAA15	608000	human -> yeast	SYM1	MPV17	137960	human -> yeast
ALG12	ALG12	607144	human -> yeast	GAL1	GALK2	137028	human -> yeast	NCR1	NPC1	607623	yeast -> human	TAZ1	TAZ	300394	human -> yeast
ALG3	ALG3	608750	human -> yeast	GAL10	GALE	606953	human -> yeast	NDI1	MT-ND4	516003	yeast -> human	THS1	TARS	187790	human -> yeast
ALG5	ALG5	604565	human -> yeast	GDT1	TMEM165	614726	human -> yeast	NPC2	NPC2	601015	yeast -> human	TIM13	TIMM13	607383	human -> yeast
ALG6	ALG6	604566	human -> yeast	GET1	CAMLG	601118	human -> yeast	NUS1	NUS1	610463	human -> yeast	TIM8	TIMM8A	300356	human -> yeast
ALG8	ALG8	608103	human -> yeast	GET1	WRB	602915	human -> yeast	PAH1	LPIN1	605518	human -> yeast	TOP2	TOP2A	126430	human -> yeast
ALG9	ALG9	606941	human -> yeast	GET2	CAMLG	601118	human -> yeast	PAH1	LPIN2	605519	human -> yeast	TPI1	TPI1	190450	human -> yeast
ALR1	MAGT1	300715	human -> yeast	GET2	WRB	602915	human -> yeast	PAH1	LPIN3	605520	human -> yeast	TRM7	FTSJ1	300499	human -> yeast
ALR1	TUSC3	601385	human -> yeast	GRS1	GARS	600287	human -> yeast	PCK1	PCK1	614168	human -> yeast	TRM732	THADA	611800	human -> yeast
ARD1	NAA10	300013	human -> yeast	HAM1	ITPA	147520	yeast -> human	PET9	SLC25A4	103220	human -> yeast	TRS20	TRAPPC2	300202	human -> yeast
ATM1	ABCB7	300135	human -> yeast	HMG1	HMGCR	142910	human -> yeast	PEX13	PEX13	601789	human -> yeast	TSC13	TECR	610057	human -> yeast
ATP12	ATPAF2	608918	human -> yeast	HRT1	RBX1	603814	human -> yeast	PFY1	PFN1	176610	human -> yeast	ULP2	PML	102578	human -> yeast
BCS1	BCS1L	603647	human -> yeast	HRT1	RBX1	603814	human -> yeast	PHO85	CDK5	123831	human -> yeast	VAS1	VARS2	612802	human -> yeast
BET5	TRAPPC1	610969	human -> yeast	HUB1	UBL5	606849	human -> yeast	PHO92	YTHDF2	610640	human -> yeast	VMA2	ATP6V1B1	192132	human -> yeast
CAR2	OAT	613349	human -> yeast	IRA1	NF1	613113	human -> yeast	PMR1	ATP2C1	604384	human -> yeast	VPH1	ATP6V0A4	605239	human -> yeast
CCA1	TRNT1	612907	human -> yeast	IRA2	NF1	613113	human -> yeast	PMS1	PMS1	600258	human -> yeast	VPS30	BECN1	604378	human -> yeast
CCC2	ATP7A	300011	human -> yeast	ISM1	IARS2	612801	human -> yeast	PUT2	ALDH4A1	606811	human -> yeast	VPS35	VPS35	601501	human -> yeast
CCC2	ATP7B	606882	human -> yeast	ISU1	ISCU	611911	human -> yeast	PXA1	ABCD1	300371	human -> yeast	YFH1	FTL	134790	human -> yeast
CCS1	CCS	603864	human -> yeast	ISU2	ISCU	611911	human -> yeast	PXA1	ABCD2	601081	human -> yeast	YFH1	FXN	606829	human -> yeast
CDC48	VCP	601023	human -> yeast	LAS17	WAS	300392	human -> yeast	PXA2	ABCD1	300371	human -> yeast	YHC3	CLN3	607042	human -> yeast
CIN2	RP2	300757	human -> yeast	LEU5	SLC25A16	139080	human -> yeast	PXA2	ABCD2	601081	human -> yeast	YME1	YME1L1	607472	human -> yeast
COQ2	COQ2	609825	human -> yeast	LPD1	DLD	238331	human -> yeast	RAD5	HLTF	603257	human -> yeast	YTA12	AFG3L2	604581	human -> yeast
COQ6	COQ6	614647	human -> yeast	MDM38	LETM1	604407	human -> yeast	RAD53	CHEK2	604373	human -> yeast	YTA12	SPG7	602783	human -> yeast
COQ8	ADCK3	606980	human -> yeast												

Disease associations

- Primary literature
- YeastMine
- OMIM



Search and retrieve *S. cerevisiae* data with YeastMine, populated by SGD and powered by InterMine

[Contact Us](#) [Video Tutorials](#)

[Home](#) [Templates](#) [Lists](#) [QueryBuilder](#) [Tools](#) [Regions](#) [Data Sources](#) [API](#)



Templates

Templates are predefined queries, each has a simple form and a description. Click on a template to run it, you can search for template category.

Filter: Filter:

Actions: Options: Show descriptions

- Yeast gene --> OMIM human homolog(s) --> OMIM Disease Phenotype(s) ☆
Retrieve human homolog(s) of yeast gene(s) and any of their associated OMIM disease phenotypes.
- OMIM Disease Phenotype --> human gene(s) --> yeast homolog(s) ☆
Specify OMIM phenotype(s) (by keyword or name) and retrieve all associated human gene(s) and the yeast homologs of these gene(s).
- Gene (human) --> Homolog (yeast) --> OMIM Disease Phenotype ☆
For a given human gene(s) show associated OMIM disease phenotype(s) and yeast homolog(s)

Trail: Query
Yeast gene → **OMIM human homolog(s)** →
 Retrieve human homolog(s) of yeast gene(s) and any of their associated (

Showing 1 to 1 of 1 rows

Standard Name	Systematic Name	Name	Homolo Stand Name
MIP1	YOR330C	Mitochondrial DNA Polymerase	POLG

5 Diseases

Identifier	Name
258450	PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA WITH MITOCHONDRIAL DNA DELETIONS, AUTOSOMAL RECESSIVE; PEOB
607459	SENSORY ATAXIC NEUROPATHY, DYSARTHRIA, AND OPHTHALMOPARESIS; SANDO
613662	MITOCHONDRIAL DNA DEPLETION SYNDROME 4B (MNGIE TYPE); MTDPS4B
157640	PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA WITH MITOCHONDRIAL DNA DELETIONS, AUTOSOMAL DOMINANT, 1; PEOA1
203700	MITOCHONDRIAL DNA DEPLETION SYNDROME 4A (ALPERS TYPE); MTDPS4A

Yeast research informs genetic medicine

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

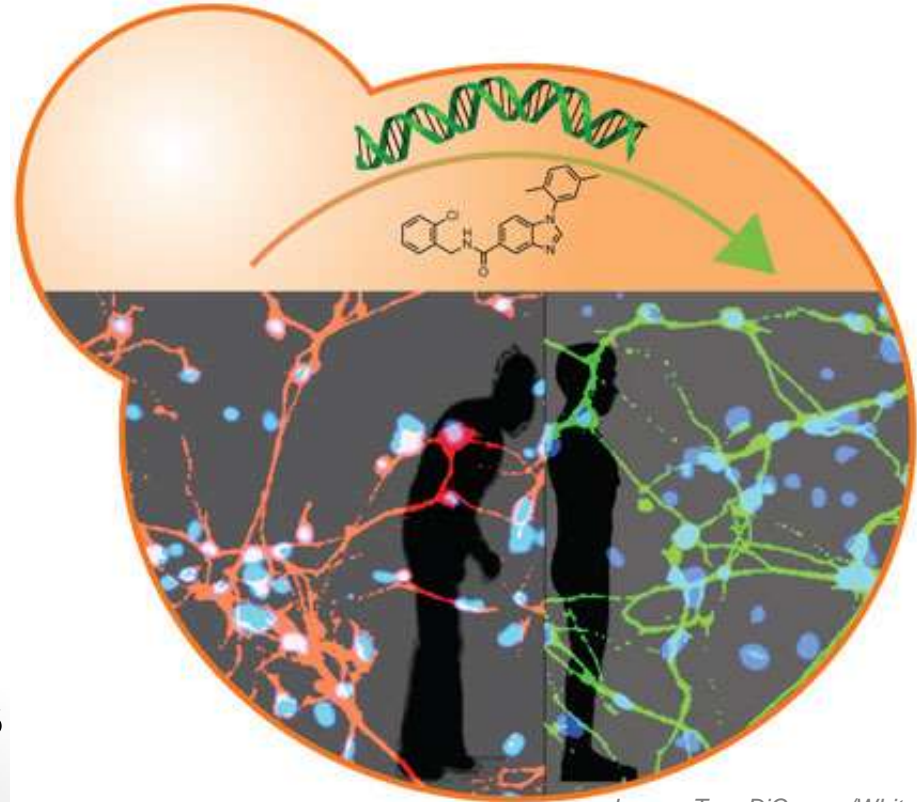


Image: Tom DiCesare/Whitehead Institute

Locus Overview

Standard Name: MIP1¹
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 Polymerase¹

Functional complementation

Yeast and human homologs

Disease associations

Alleles and phenotype variants

Annotations 65 entries for 41 phenotypes

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) PMID:25419700
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) PMID:20693824
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) PMID:20693824
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) PMID:20693824

Homology curation at SGD



www.yeastgenome.org