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Independent transcriptional reprogramming and apoptosis induction by cisplatin

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Supplementary Table 1. Saccharomyces cerevisiae **knockout strains used in this study.**

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cadmium dichloride (CdCl$_2$).

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Supplementary Table 1. *Saccharomyces cerevisiae* knockout strains used in this study.

Strain	Ploidy	Notes	Ref.
Parental strains			
BY4741	Haploid	*MAT*a; *his3*Δ1; *leu2*Δ0; *met15*Δ0; *ura3*Δ0	1,2
BY4743	Diploid	*MATa/MAT*α; *his3Δ1/his3Δ1*; *leu2Δ0/leu2Δ0*; *MET15/met15Δ0*; *LYS2/lys2Δ0*; *ura3Δ0/ura3Δ0*	1,2
BY4741	Haploid	*rho*^{O}	3
Knockout strains - General apoptosis-related factors			
AIF1 (CPD1)	Haploid	Mitochondrial cell death effector that translocates to the nucleus in response to apoptotic stimuli, homolog of mammalian apoptosis-inducing factor (AIF), putative reductase.	4,5
CYC1	Haploid	Cytochrome *c* isoform 1; electron carrier of the mitochondrial intermembrane space that transfers electrons from ubiquinone-cytochrome c oxidoreductase to cytochrome *c* oxidase during cellular respiration.	6-14
CYC7	Haploid	Cytochrome *c* isoform 2, expressed under hypoxic conditions; electron carrier of the mitochondrial intermembrane space that transfers electrons from ubiquinone-cytochrome *c* oxidoreductase to cytochrome c oxidase during cellular respiration.	15-17
MCA1 (YCA1)	Haploid	Putative cysteine protease similar to mammalian caspases, involved in regulation of apoptosis upon hydrogen peroxide (H_2O_2) treatment.; contributes to clearance of insoluble protein aggregates during normal growth; may be involved in cell cycle progression.	18-22
NDI1	Haploid	NADH:ubiquinone oxidoreductase, transfers electrons from NADH to ubiquinone in the respiratory chain but does not pump protons, in contrast to the higher eukaryotic multisubunit respiratory complex I; phosphorylated; homolog of human AMID.	23-28
NMA111	Haploid	Serine protease and general molecular chaperone; involved in response to heat stress and promotion of apoptosis; may contribute to lipid homeostasis; sequence similarity to the mammalian Omi/HtrA2 family of serine proteases.	29-32
NUC1	Haploid	Major mitochondrial nuclease, has RNAse and DNA endo- and exonucleolytic activities; has roles in mitochondrial recombination, apoptosis and maintenance of polyploidy.	17, 33-36
Knockout strains - Proteases			
PEP4 (yscA; PRA1; PHO9)	Haploid	Vacuolar aspartyl protease (proteinase A), required for the posttranslational precursor maturation of vacuolar proteinases; important for protein turnover after oxidative damage; synthesized as a zymogen, self-activates.	17, 37-43
RIM13 (CPL1)	Haploid	Calpain-like cysteine protease involved in proteolytic activation of Rim101p in response to alkaline pH; has similarity to *Aspergillus nidulans palB*.	44

Knockout strains – Proteins related to the permeability transition pore complex (PTPC)			
AAC1	Haploid	Mitochondrial inner membrane ADP/ATP translocator, exchanges cytosolic ADP for mitochondrially synthesized ATP; phosphorylated; Aac1p is a minor isoform while Pet9p is the major ADP/ATP translocator.	17, 45-47
AAC3 (ANC3)	Haploid	Mitochondrial inner membrane ADP/ATP translocator, exchanges cytosolic ADP for mitochondrially synthesized ATP; expressed under anaerobic conditions; similar to Pet9p and Aac1p; has roles in maintenance of viability and in respiration.	17, 48-50
POR1 (OMP2)	Haploid	Mitochondrial porin (voltage-dependent anion channel), outer membrane protein required for the maintenance of mitochondrial osmotic stability and mitochondrial membrane permeability; phosphorylated.	17, 51-57
POR2	Haploid	Putative mitochondrial porin (voltage-dependent anion channel), related to Por1p but not required for mitochondrial membrane permeability or mitochondrial osmotic stability.	17,40, 55,58,59
Knockout strains – Autophagy-related proteins			
ATG5 (APG5)	Haploid	Conserved protein involved in autophagy and the Cvt pathway; undergoes conjugation with Atg12p to form a complex involved in Atg8p lipidation; conjugated Atg12p also forms a complex with Atg16p that is essential for autophagosome formation.	60-65
ATG10 (APG10)	Haploid	Conserved E2-like conjugating enzyme that mediates formation of the Atg12p-Atg5p conjugate, which is a critical step in autophagy.	66-68
ATG12 (APG12)	Haploid	Conserved ubiquitin-like modifier involved in autophagy and the Cvt pathway; conjugated to Atg5p to form a complex involved in Atg8p lipidation; Atg12p-Atg5p also forms a complex with Atg16p that is required for autophagosome formation.	65, 67-70
VPS30 (VPT30; ATG6; APG6)	Haploid	Subunit of phosphatidylinositol (PtdIns) 3-kinase complexes I and II; Complex I is essential in autophagy and Complex II is required for vacuolar protein sorting; ortholog of the higher eukaryotic gene Beclin 1.	71-73
VPS34 (PEP15, STT8, VPL7, VPS7, VPT29)	Haploid	Phosphatidylinositol 3-kinase responsible for the synthesis of phosphatidylinositol 3-phosphate; forms membrane-associated signal transduction complex with Vps15p to regulate protein sorting; activated by the GTP-bound form of Gpa1p.	74-79
Knockout strains – Proteins involved in mitochondrial fusion and fission			
DNM1	Haploid	Dynamin-related GTPase required for mitochondrial fission and the maintenance of mitochondrial morphology, assembles on the cytoplasmic face of mitochondrial tubules at sites at which division will occur; also participates in endocytosis and regulating peroxisome abundance.	80-90
FIS1 (MDV2)	Haploid	Protein involved in mitochondrial membrane fission and peroxisome abundance; required for localization of Dnm1p and Mdv1p during mitochondrial division; mediates ethanol-induced apoptosis and ethanol-induced mitochondrial fragmentation.	55,82,85, 87,91-95
MDM10 (FUN37)	Haploid	Subunit of both the ERMES complex that links the ER to mitochondria, and of the mitochondrial sorting and assembly machinery (SAM complex) that functions in import and assembly of outer membrane beta-barrel proteins.	55,79, 96-99

MGM1 (MNA1)	Haploid	Mitochondrial GTPase, present in complex with Ugo1p and Fzo1p; required for mt morphology and genome maintenance; exists as long and short form with different distributions; homolog of human OPA1 involved in autosomal dominant optic atrophy.	96, 100-104
MIR1	Haploid	Mitochondrial phosphate carrier, imports inorganic phosphate into mitochondria; functionally redundant with Pic2p but more abundant than Pic2p under normal conditions; phosphorylated.	17,40, 56,59, 105-107
OXA1	Haploid	Mitochondrial inner membrane insertase, mediates the insertion of both mitochondrial- and nuclear-encoded proteins from the matrix into the inner membrane, interacts with mitochondrial ribosomes; conserved from bacteria to animals.	17, 108-116
PCP1 (MDM37, RBD1)	Haploid	Mitochondrial serine protease required for the processing of various mitochondrial proteins and maintenance of mitochondrial DNA and morphology; belongs to the rhomboid-GlpG superfamily of intramembrane peptidases.	77, 117,118
SAM37 (MAS37, PET3027, TOM37)	Haploid	Component of the Sorting and Assembly Machinery (SAM or TOB complex) of the mitochondrial outer membrane, which binds precursors of beta-barrel proteins and facilitates their outer membrane insertion; contributes to SAM complex stability.	17,55, 119,120
TIM18	Haploid	Component of the mitochondrial TIM22 complex involved in insertion of polytopic proteins into the inner membrane; may mediate assembly or stability of the complex.	17,121
Knockout strains – Cell cycle regulators			
CHK1	Haploid	Serine/threonine kinase and DNA damage checkpoint effector, mediates cell cycle arrest via phosphorylation of Pds1p; phosphorylated by checkpoint signal transducer Mec1p; homolog of *Saccharomyces pombe* and mammalian Chk1 checkpoint kinase.	122-125
MBP1	Haploid	Transcription factor involved in regulation of cell cycle progression from G1 to S phase, forms a complex with Swi6p that binds to MluI cell cycle box regulatory element in promoters of DNA synthesis genes.	59, 126-130
Knockout strains – Proteins involved in DNA replication and repair			
MCM2	Diploid	Protein involved in DNA replication; component of the Mcm2-7 hexameric complex that binds chromatin as a part of the pre-replicative complex.	131-140
MCM3	Diploid	Protein involved in DNA replication; component of the Mcm2-7 hexameric complex that binds chromatin as a part of the pre-replicative complex.	59,131-135, 138-140
MCM5 (BOB1, CDC46)	Diploid	Component of the hexameric MCM complex, which is important for priming origins of DNA replication in G1 and becomes an active ATP-dependent helicase that promotes DNA melting and elongation when activated by Cdc7p-Dbf4p in S-phase.	138, 140-147
MCM6	Diploid	Protein involved in DNA replication; component of the Mcm2-7 hexameric complex that binds chromatin as a part of the pre-replicative complex.	131-135, 138140, 148,149

MSH6 (PMS3)	Haploid	Protein required for mismatch repair in mitosis and meiosis, forms a complex with Msh2p to repair both single-base and insertion-deletion mispairs; potentially phosphorylated by Cdc28p.	30, 150-158
PSF2 (CDC102)	Diploid	Subunit of the GINS complex (Sld5p, Psf1p, Psf2p, Psf3p), which is localized to DNA replication origins and implicated in assembly of the DNA replication machinery.	159-161
Knockout strains – Proteins involved in chromatin structure			
NHP6A	Haploid	High-mobility group (HMG) protein that binds to and remodels nucleosomes; involved in recruiting FACT and other chromatin remodelling complexes to the chromosomes; functionally redundant with Nhp6Bp; homologous to mammalian HMGB1 and HMGB2.	162-165
NHP6B (YBR090C-A)	Haploid	High-mobility group (HMG) protein that binds to and remodels nucleosomes; involved in recruiting FACT and other chromatin remodelling complexes to the chromosomes; functionally redundant with Nhp6Ap; homologous to mammalian HMGB1 and HMGB2.	162-166
Knockout strains – Kinases			
ADK1 (AKY1, KY2)	Haploid	Adenylate kinase, required for purine metabolism; localized to the cytoplasm and the mitochondria; lacks cleavable signal sequence.	17, 167-169
ADK2 (AKY3, PAK3)	Haploid	Mitochondrial adenylate kinase, catalyzes the reversible synthesis of GTP and AMP from GDP and ADP; may serve as a back-up for synthesizing GTP or ADP depending on metabolic conditions; 3' sequence of ADK2 varies with strain background.	17, 170,171
GLK1 (HOR3)	Haploid	Glucokinase, catalyzes the phosphorylation of glucose at C6 in the first irreversible step of glucose metabolism; one of three glucose phosphorylating enzymes; expression regulated by non-fermentable carbon sources.	30, 172-175
HXK1	Haploid	Hexokinase isoenzyme 1, a cytosolic protein that catalyzes phosphorylation of glucose during glucose metabolism; expression is highest during growth on non-glucose carbon sources; glucose-induced repression involves the hexokinase Hxk2p.	30,173, 174,176, 177
HXK2 (HEX1, HKB, SCI2)	Haploid	Hexokinase isoenzyme 2 that catalyzes phosphorylation of glucose in the cytosol; predominant hexokinase during growth on glucose; functions in the nucleus to repress expression of HXK1 and GLK1 and to induce expression of its own gene.	56, 173,174, 176-185
TOR1 (DRR1)	Haploid	PIK-related protein kinase and rapamycin target; subunit of TORC1, a complex that controls growth in response to nutrients by regulating translation, transcription, ribosome biogenesis, nutrient transport and autophagy; involved in meiosis.	186-211
Knockout strains – Chaperons (members of the heat-shock protein family)			
ECM10 (SSC3)	Haploid	Heat shock protein of the HSP70 family, localized in mitochondrial nucleoids, plays a role in protein translocation, interacts with Mge1p in an ATP-dependent manner; overexpression induces extensive mitochondrial DNA aggregations.	17,40, 212,213

SSQ1 (SSC2, SSH1)	Haploid	Mitochondrial HSP70-type molecular chaperone, required for assembly of iron/sulfur clusters into proteins at a step after cluster synthesis, and for maturation of Yfh1p, which is a homolog of human frataxin implicated in Friedreich's ataxia.	17, 214-217
Knockout strains – Others			
CPR3 (CYP3)	Haploid	Mitochondrial peptidyl-prolyl cis-trans isomerase (cyclophilin), catalyzes the cis-trans isomerization of peptide bonds N-terminal to proline residues; involved in protein refolding after import into mitochondria.	17,40, 218
CYB5	Haploid	Cytochrome b5, involved in the sterol and lipid biosynthesis pathways; acts as an electron donor to support sterol C5-6 desaturation.	219,220
GTT2	Haploid	Glutathione S-transferase capable of homodimerization; functional overlap with Gtt2p, Grx1p, and Grx2p.	17,40, 221-223
NNT1	Haploid	Putative nicotinamide N-methyltransferase, has a role in rDNA silencing and in lifespan determination.	224,225
SOD2	Haploid	Mitochondrial manganese superoxide dismutase, protects cells against oxygen toxicity; phosphorylated.	17,40,59, 226-233
TDH1 (GLD3)	Haploid	Glyceraldehyde-3-phosphate dehydrogenase, isozyme 1, involved in glycolysis and gluconeogenesis; tetramer that catalyzes the reaction of glyceraldehyde-3-phosphate to 1,3 bis-phosphoglycerate; detected in the cytoplasm and cell-wall.	17, 234-236
TDH2 (GLD2)	Haploid	Glyceraldehyde-3-phosphate dehydrogenase, isozyme 2, involved in glycolysis and gluconeogenesis; tetramer that catalyzes the reaction of glyceraldehyde-3-phosphate to 1,3 bis-phosphoglycerate; detected in the cytoplasm and cell-wall.	56,59, 234-236
TDH3 (GLD1, SP35, HSP36, SSS2)	Haploid	Glyceraldehyde-3-phosphate dehydrogenase, isozyme 3, involved in glycolysis and gluconeogenesis; tetramer that catalyzes the reaction of glyceraldehyde-3-phosphate to 1,3 bis-phosphoglycerate; detected in the cytoplasm and cell-wall.	17,56,59, 234-236
TRX3	Haploid	Mitochondrial thioredoxin, highly conserved oxidoreductase required to maintain the redox homeostasis of the cell, forms the mitochondrial thioredoxin system with Trr2p, redox state is maintained by both Trr2p and Glr1p.	17,40, 237,238
YNL305C (YBH3)	Haploid	Hypothetical protein; green fluorescent protein (GFP)-fusion protein localizes to the vacuole; YNL305C is not an essential gene.	30,239

S. cerevisiae mutant strains were obtained from Euroscarf (Frankfurt, Germany). When gene deletion resulted in the inviability of haploid cells (BY4741 strain), the analysis was performed on the corresponding heterozygous knockouts (in the diploid strain BY4743). Official gene symbols and notes were found in the NCBI – Entrez Gene Database (http://www.ncbi.nlm.nih.gov/sites/entrez).

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