

Electronic Supplemental Information for

Lindahl, 2019 A comprehensive mechanistic model of iron metabolism in *Saccharomyces cerevisiae*

Table S1. The ironome of *Sacchromyces cerevisiae* circa 2019.

Num.	Name (alias)	Identifier	Location	Iron Center	Description	References
1	Fit1	YDR534C	Cell Wall	Unknown	Promotes Fe ^{III} siderophore import	5, 6, 7, 8, 9
2	Fit2	YOR382W	Cell Wall	Unknown	Promotes Fe ^{III} siderophore import	5, 6, 7, 8, 9
3	Fit3	YOR383C	Cell Wall	Unknown	Promotes Fe ^{III} siderophore import	5, 6, 7, 8, 9
4	Arn1 (Any1)	YHL040C	Plasma membrane (endosomes, trans-Golgi; vacuolar lumen)	Translocates Fe ^{III} siderophore	Transporter for ferrichrome iron chelate	5, 6
5	Arn2 (Taf1)	YHL047C	Plasma membrane	Translocates Fe ^{III} siderophore	Uptake of iron triacetylfulvarinine	5, 6
6	Arn3 (Sit1)	YEL065W	Plasma membrane	Translocates Fe ^{III} siderophore	Ferrioxamine B transporter	5, 6
7	Arn4 (Enb1)	YOL158C	Plasma membrane	Translocates Fe ^{III} siderophore	Endosomal ferric enterobactin transporter	5, 6
8	Fre1	YLR214W	Plasma membrane	Two permanent Heme b (cyt b561) centers; "Bis-heme"	flavo-cytochrome metallo-reductase	5, 12, 14, 15
9	Fre2	YKL220c	Plasma membrane	Probably Bis-heme	Metallo-reductase	238
10	Fre3	YOR381w	Plasma membrane	Probably Bis-heme	Metallo-reductase	239
11	Fre4	YNR060w	Plasma membrane	Probably Bis-heme	Metallo-reductase	239
12	Fre5	YOR384w	Mitochondria ?	Probably Bis-heme	Metallo-reductase?	239
13	Fre7	YOL152w	Plasma membrane	Probably Bis-heme	Copper regulated metallo-reductase	176
14	Fre8	YLR047c	ER/Vacuole?	Probably Bis-heme	Metallo-reductase?	239
15	Fet3	YMR058W	Plasma membrane	Binds Fe ^{II} ; oxidizes it to Fe ^{III} ; then releases Fe ^{III}	Multicopper ferroxidase	12, 14, 15, 16, 17, 18, 19
16	Ftr1	YER145C	Plasma membrane	Fe ^{III} translocates through a channel in the protein	High-affinity nutrient iron permease	5, 16, 17, 18, 19
17	Fet4	YMR319C	Plasma membrane	Fe ^{II} translocates through the protein	Low-affinity nutrient iron importer; dominates during hypoxia	20
18	Smf1	YOL122C	Plasma membrane	Fe ^{II} translocates through the protein	Low-affinity nutrient iron importer; Nramp family	21, 22
19	Cfd1	YIL003W	Cytosol	Dimer binds 2 [Fe ₂ S ₂] clusters; reductively couples to 1 transient [Fe ₄ S ₄]	P-loop NTPase; part of the early CIA complex; interacts with Nbp35	21, 24, 25
20	Nbp35	YGL091C	Cytosol	Dimer binds 2 [Fe ₂ S ₂] clusters;	P-loop NTPase; part of the early CIA complex; interacts with	24, 25, 26

				reductively couples to 1 transient [Fe ₄ S ₄] cluster; also contains 1 permanent [Fe ₄ S ₄] cluster	Cfd1	
21	Dre2 (Ciapin1, anamorsin)	YKR071C	Cytosol (mito IMS; nucleus; membrane bound?)	1[Fe ₂ S ₂] and 1[Fe ₄ S ₄] (or 2[Fe ₂ S ₂])	Reductant for CIA and others	24, 61, 240, 241, 242
22	Tah18 (Ndor1)	YPR048W	Cytosol	none	Flavin containing partner to Dre2	32, 33, 240
23	Nar1 (Narf1; IOP1)	YNL240C	Cytosol	1 permanent [Fe ₄ S ₄] cluster and a second cluster that is surface-exposed and unstable.	Link between early and late CIA complex	32, 33, 34
24	Cia1	YDR267C	Cytosol	None	Late CIA component 1	35
25	Cia2	YHR122W	Cytosol	None	Late CIA component 2	243
26	Mms19	YIL128W	Cytosol	None	Late CIA component	90
27	Lto1	YNL260C	Cytosol	None	Recruits aRli1 to CIA for cluster insertion	35
28	Yae1	YJR067C	Cytosol	None	Recruits aRli1 to CIA for cluster insertion	35
29	Rli1	YDR091C	Cytosol	Two [Fe ₄ S ₄]	ABC protein sub-family E required for activating ribosomes	35
30	Dph1	YIL103W	Cytosol	[Fe ₄ S ₄] (radical SAM)	Diphthamide synthesis; modify His of EF2	36
31	Dph2	YKL191W	Cytosol	[Fe ₄ S ₄] (radical SAM)	Diphthamide biosynthesis; transfers ACP to EF2	36
32	Dph3 (Kti11)	YBL071W-A	Cytosol	Mononuclear Fe ^{II} (cys) ₄	Electron donor to Dph1:Dph2	36, 37, 38
33	Cbr1	YIL043C	Cytosol	None	Cytochrome b5 reductase; NAHH dependent	26, 37, 38
34	Dph4 (Jjj3)	YJR097W	Cytosol	Mononuclear Fe ^{II} (cys) ₄	Involved in Protein synthesis	39, 40
35	Elp3 (Kti8; Tot3; Kat9; HPA1)	YPL086C	Cytosol	[Fe ₄ S ₄] (radical SAM)	Subunit of elongator complex; tRNA modification	41, 42, 43, 44, 45, 46, 47
36	Leu1	YGL009C	Cytosol	[Fe ₄ S ₄]	isopropylmalate isomerase	48
37	Glt1 (GOGAT)	YDL171C	Cytosol	[Fe ₄ S ₄]	Glutamate synthase	49, 50
38	Met8	YBR213W	Cytosol	Fe ^{II} converts to siroheme	Dehydrogenase; siroheme ferrochelatase	54, 55
39	Met5	YJR137C	Cytosol	siroheme + [Fe ₄ S ₄]	Sulfite reductase, β subunit	51, 52, 53, 55, 243
40	Ade4	YMR300C	cytosol	[Fe ₄ S ₄]	Glutamine phosphoribosylpyrophosphate amidotransferase	56, 57
41	Bna1 (HAAO; HAO; HAD)	YJR025C	cytosol	Fe ^{II} (cys)	3-hydroxyanthranilate 3,4-dioxygenase	58
42	Tyw1	YPL207W	cytosol	[Fe ₄ S ₄] (radical SAM)	Wybutosine-modified tRNA biosynthesis	59, 60
43	Rnr4	YGR180C	Cytosol (or nucleus)	none	Stabilizes and activates Rnr2	61, 62, 63, 64, 65
44	Rnr2	YJL026W	Cytosol (or nucleus)	[Fe-O-Fe]	Ribonucleotide Reductase, small R2 subunit	61, 62, 63, 64, 65, 192, 245

45	Grx3	YDR098C	Cytosol (or nucleus)	[Fe ₂ S ₂] (homodimer only)	Monothiol Cytosolic Glutaredoxin 3	66,67
46	Grx4	YER174C	Cytosol (or nucleus)	[Fe ₂ S ₂] (homodimer only)	Monothiol Cytosolic Glutaredoxin 4	66, 67
47	Bol2 (Fra2; Aim15; BolA2)	YGL220W	Cytosol	[Fe ₂ S ₂] (heterodimer with Grx3/4)	Similar to monothiol Glutaredoxins	67, 68, 69
48	Ctt1	YGR088W	Cytosol	Heme b	Catalase T	70, 71, 72
49	Cta1	YDR256C	Peroxisomal membrane and mitochondria	Heme b	Catalase A	72
50	Yhb1	YGR234W	Mito matrix during anoxic conditions; cytosol and mito during aerobic conditions; also found in mito IMS	Heme b	flavo-hemoglobin (or NO dioxygenase)	73, 74, 75, 76, 77
51	Ccp1	YKR066C	Mito IMS	Heme b	Cytochrome c peroxidase	246
52	Ntg2	YOL043C	nucleus	[Fe ₄ S ₄]	Endonuclease III-like 1; bifunctional DNA N-glycosylase/DNA lyase	35, 78, 79, 80, 81, 82, 83, 84, 85
53	Dna2	YHR164C	nucleus	[Fe ₄ S ₄]	Nuclease and Helicase	61, 86, 87, 88
54	Rad3 (TFIIH)	YER171W	Nucleus (also cytosol)	[Fe ₄ S ₄]	Basal transcription factor complex; Helicase XPD subunit; DNA excision repair protein	35, 89, 90, 91, 92
55	Chl1	YPL008W	nucleus	[Fe ₄ S ₄]	Helicase, sister chromatid cohesion, heterochromatin organization	35
56	Pri2	YKL045W	nucleus	[Fe ₄ S ₄]	DNA primase, large subunit	35, 93, 94, 95, 96, 98, 99, 100
57	Pol1 (Cdc17; Crt5; Hpr3)	YNL102W	Nucleus	[Fe ₄ S ₄]	DNA polymerase I alpha-primase, catalytic subunit	35, 93, 96, 97, 98, 99, 100, 101, 102, 103, 233
58	Pol2	YNL262W	nucleus	[Fe ₄ S ₄] (uncertain)	DNA polymerase II epsilon catalytic subunit A	33, 35, 104, 105
59	Pol3	YDL102W	nucleus	[Fe ₄ S ₄]	DNA polymerase delta catalytic subunit	35, 100, 106, 247, 248
60	Rev3	YPL167C	nucleus	[Fe ₄ S ₄]	Catalytic subunit of DNA polymerase zeta	100, 107, 248
61	Tpa1	YER049W	nucleus	Fe ^{II}	2-oxoglutarate-dependent dioxygenase	108, 249
62	Aft1	YGL071W	Nucleus and cytosol	[Fe ₂ S ₂]	Primary Iron Regulon Transcription factor	6, 109, 110, 111, 112, 113, 114, 217
63	Aft2	YPL202C	Nucleus and cytosol	[Fe ₂ S ₂]	Secondary Iron Regulon Transcription factor	62, 110, 112, 118
64	Cth1	YDR151C	Nucleus and cytosol	None	mRNA degradation of respiration-related transcripts	63, 116, 117, 118
65	Cth2 (TIS11)	YLR136C	Nucleus and cytosol	None	mRNA degradation of respiration-related transcripts	63, 116, 117, 118
66	Yap5	YIR018W	nucleus	Two [Fe ₂ S ₂]	Transcriptional Regulator of Ccc1	59, 119, 120, 121, 122, 123, 250
67	Hap1	YLR256W	Nucleus in equilibrium with cytosol	Binds Heme b	Heme regulation	124
68	Hap2	YGL237C	nucleus	Heme activated	Subunit of the Hap2/3/4/5	125

					complex	
69	Hap3	YBL021C	nucleus	Heme activated	Subunit of the Hap2/3/4/5 complex	125
70	Hap4	YKL109W	nucleus	Heme activated	Subunit of the Hap2/3/4/5 complex	125
71	Hap5	YOR358W	nucleus	Heme activated	Subunit of the Hap2/3/4/5 complex	125
72	Rox1 (REO1)	YPR065W	nucleus	Hap1-dependent	Heme-dependent repressor of Hap1-dependent genes	125
73	Nfs1	YCL017C	Mito matrix	None	Cysteine Desulfurase	126, 251, 252, 253
74	Isd11	YER048W-A	Mito matrix	None	Complex of cysteine desulfurase	251, 252, 253
75	Acp1	YKL192C	Mito matrix	None	Acyl Carrier Protein	251, 253
76	Isu1	YPL135W	Mito matrix	[Fe ₂ S ₂]	Primary ISC scaffold	251, 252, 253
77	Isu2	YOR226C	Mito matrix	[Fe ₂ S ₂]	Secondary ISC scaffold	132
78	Yfh1 (FXN)	YDL120W	Mito matrix	None or Fe ^{II}	Yeast Frataxin Homolog 1	127, 128, 129, 130
79	Yah1 (FDX2; FDX1L; FDX1; ADX)	YPL252C	Mito matrix	[Fe ₂ S ₂]	ferredoxin	33
80	Arh1	YDR376W	Mito matrix	none	Ferredoxin reductase	33, 131
81	Grx5	YPL059W	Mito matrix	[Fe ₂ S ₂] (can reductively couple forming [Fe ₄ S ₄])	mitochondrial monothiol glutaredoxin 5	67
82	Jac1	YGL018C	Mito matrix	None	DnaJ type chaperone	33, 133
83	Ssq1	YLR369W	Mito matrix	None	HSP70 chaperone	33, 133
84	Mge1	YOR232W	Mito matrix	None	Replaces ADP with ATP on Ssq1	33
85	Isa1	YLL027W	Mito matrix	[Fe ₄ S ₄]	Fe ₄ S ₄ assembly	134
86	Isa2	YPR067W	Mito matrix	[Fe ₄ S ₄]	Fe ₄ S ₄ assembly	134
87	Iba57	YJR122W	Mito matrix	[Fe ₄ S ₄]?	Fe ₄ S ₄ assembly	134, 135, 136, 137, 138, 254
88	Bol1 (BolA1)	YAL044W-A	Mito matrix	[Fe ₂ S ₂] (shared with Grx5)	Fe ₄ S ₄ transfer	67, 121, 134, 135, 136, 137, 138
89	Bol3 (BolA3; Aim1)	YAL046C	Mito matrix	[Fe ₂ S ₂]	Fe ₄ S ₄ chaperone	67, 139
90	Nfu1	YKL040C	Mito matrix	[Fe ₄ S ₄] at homodimer interface	Fe ₄ S ₄ chaperone	67, 139
91	Lys4	YDR234W	Mito matrix	[Fe ₄ S ₄]	homoaconitase	140, 141, 142
92	Ilv3	YJR016C	Mito matrix	[Fe ₄ S ₄] (putative)	Dihydroxyacid dehydratase	143, 144, 162
93	Aco1	YLR304C	Mito matrix	[Fe ₄ S ₄]; one Fe not coordinated	aconitase	139, 255
94	Aco2	YJL200C	Mito matrix	[Fe ₄ S ₄]; one Fe not coordinated	Secondary aconitase	139
95	Sdh2 (SDHB; ACN17)	YLL041C	Mito IM	[Fe ₄ S ₄], [Fe ₃ S ₄], and [Fe ₂ S ₂]	Succinate dehydrogenase, ISC subunit	67
96	Sdh3 (Cyb3; Ykl4)	YKL141W	Mito IM	Heme b shared with Sdh4	Succinate dehydrogenase, heme subunit	67, 256
97	Sdh4	YDR178W	Mito IM	Heme b shared with Sdh3	Succinate dehydrogenase	67, 256
98	Bio2	YGR286C	Mito matrix	[Fe ₄ S ₄] and [Fe ₂ S ₂]	Biotin Synthase	145, 257, 258
99	Lip5	YOR196C	Mito matrix	Two [Fe ₄ S ₄]	Lipoic Acid Synthase	146
100	Mrs3	YJL133W	Mito IM	None (Fe ^{II} transient)	High-affinity iron importer into mitochondria	147

101	Mrs4	YKR052C	Mito IM	None (Fe ^{II} transient)	High-affinity iron importer into mitochondria	147
102	Rim2 (Pyt1)	YBR192W	Mito IM	None (Fe ^{II} transient)	Low-affinity iron importer into mitochondria	148, 149
103	Coq6	YGR255C	Mito IM (facing matrix)	Heme b	Monooxygenase for CoQ biosynthesis	150,151, 152, 153, 154
104	Coq7	YOR125C	Mito IM	[Fe-O-Fe]	5-demethoxyubiquinone hydroxylase, mitochondrial (DMQ hydroxylase)	150, 151, 153, 154, 155, 156
105	Cyt1 (Ctc1)	YOR065W	Mito IM	1 heme c	Cytochrome bc1; cytochrome c1 subunit	157, 259
106	Cob1 (Cytb)	Q0105	Mito IM	Heme b _H and Heme b _L	Cytochrome bc1; cytochrome b subunit	157, 259
107	Rip1	YEL024W	Mito IM	[Fe ₂ S ₂] (with 2 His ligands)	Cytochrome bc1; Rieske protein	157, 259
108	Cox1 (Oxi3)	Q0045	Mito IM	Heme a and heme a ₃	Cytochrome c oxidase	260
109	Cox15	YER141W	Mito IM	Heme o → heme a (transient)	Heme A synthase	157, 159, 160, 161
110	Cox10	YPL172C	Mito IM	Heme b → heme o (transient)	Heme O synthase	262
111	Mss51	YLR203C	Mito IM (facing matrix)	Heme b	COX1 mRNA translational activator; Cox1 assembly (heme or O ₂ sensor)	49, 162
112	Cyc1	YJR048W	Mito IMS	Heme c	Cytochrome c, isoform 1	162
113	Cyc7	YEL039C	Mito IMS	Heme c	Cytochrome c, isoform 2 Expressed under hypoxic conditions	162
114	Cyc2	YOR037W	Mito IMS	none	Cytochrome c lyase	262
115	Cyb2 (Fcb2)	YML054C	Mito IMS	Heme b2	L-lactate cytochrome c oxidoreductase	163
116	Dld1	YDL174C	Mito IM	Heme b	D-Lactate dehydrogenase	164
117	Hem15	YOR176W	Mito IM	Fe ^{II} → Heme b	Ferrochelatase	5, 49, 51, 52, 162, 165, 125
118	Atm1	YMR301C	Mito IM	None	Sulfur and/or ISC exporter from mitos	27, 28, 33, 166, 167, 169, 170
119	Mmt1	YMR177W	Mito IM	None	Putative iron exporter	171, 172, 173
120	Mmt2	YPL224C	Mito IM	None (Fe ^{II} transiently)	Putative iron exporter	171, 172, 173
121	Ccc1	YLR220W	Vacuolar membrane	None (Fe ^{II} , heme b transiently bound??)	Vacuolar iron importer	59, 174, 175
122	Fet5	YFL041W	Vacuolar membrane	Fe ^{II} /Fe ^{III} (transient)	Vacuolar iron exporter; multicopper oxidase	14, 176, 178
123	Fth1	YBR207W	Vacuolar membrane	Fe ^{III} (transient)	Vacuolar iron exporter	176
124	Fre6	YLL051C	Vacuolar membrane	Two heme b	Vacuolar metalloredutase	12, 14, 178
125	Smf3	YLR034C	Vacuolar membrane	Fe ^{II} (transient)	Vacuolar iron exporter; Nramp family	114, 177, 180
126	Ole1 (Mdm2)	YGL055W	ER membrane	[Fe-O-Fe] + heme b5 (exposed on cytosol face)	Δ9 fatty acid desaturase	181, 182, 183, 184
127	Ncp1	YHR042W	ER membrane	None (flavins)	NADP-cytochrome P450 reductase	201, 202, 203
128	Sur2 (Syr2)	YDR297W	ER membrane	[Fe-O-Fe]	Sphinganine C4-hydroxylase	185, 186, 187
129	Cyb5	YNL111C	ER membrane; cytosolic face	Heme b	Cytochrome b5	188, 190, 205
130	Scs7	YMR272C	ER	[Fe-O-Fe] + heme	Sphingolipid alpha-hydroxylase	172, 183, 184, 186,

	(Fah1)		membrane	b5 (exposed on cytosol face)		263, 264
131	Mpo1	YGL010W	ER membrane	Fe ^{II}	2-hydroxy fatty acid dioxygenase	191
132	Cyp51 (Erg11)	YHR007C	ER membrane facing cytosol	Heme b (cys axial)	Cytochrome P450 Lanosterol C-14 alpha-demethylase	192, 193, 194, 195, 196, 197, 198, 199, 217, 265
133	Erg25	YGR060W	ER membrane	[Fe-O-Fe]	Methylsterol monooxygenase 1	8, 209, 210, 211, 266
134	Erg3 (Pso6; Syr1)	YLR056W	ER membrane	[Fe-O-Fe]	Sterol C5(6)-desaturase	182, 190, 204, 205, 206
135	Erg5	YMR015C	ER membrane	Heme b (cys axial)	C-22 sterol desaturase	8, 207, 208, 209, 210, 211
136	Dap1 (PGRMC1)	YPL170W	ER (lacks a membrane-spanning sequence); endosomes; vacuoles	Heme b (tyrosine axial)	Damage Response protein 1; Membrane-associated progesterone receptor component 1	18, 196, 197, 212, 267
137	Hmx1	YLR205C	ER membrane	Heme b (transient)	Heme oxygenase	109, 213
138	Yno1 (Aim14)	YGL160w	(perinuclear) ER membrane	Bis-heme b	NADPH Oxidase (generates superoxide in an NADPH-dependent fashion. Regulates the actin cytoskeleton.	214
139	Grx6	YDL010W	ER and Golgi membranes; vacuoles	[Fe ₂ S ₂]	Class I 1-C-Grx Monothiol glutaredoxin	68, 194, 215, 216, 217, 218, 219, 220, 268
140	Fe ^{II} _{cyt}	None	Cytosol	Nonheme mononuclear	Low molecular mass nonproteinaceous	269
141	Fe ^{II} _{mit}	None	Mitochondria	Nonheme mononuclear	Low molecular mass nonproteinaceous	112, 113, 227, 228
142	Fe ^{II} _{vac}	None	Vacuoles	Nonheme mononuclear	Low molecular mass nonproteinaceous	230
143	Fe ^{III} _{vac}	None	Vacuoles	Nonheme mononuclear	Low molecular mass polyphosphate	179, 229
144	Heme b	None	Mitochondria, cytosol, ER	Heme b	Axial ligands not defined	270

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Table S2. Model Components. The first 27 components of the model are protein groups. This is followed by 5 iron nonprotein groups and 8 noniron nonprotein groups for a total of 40 components. There are also 3 nutrients and 2 waste products. The prefix ‘a’ on protein groups (e.g. aFET3) means the apo form of the group. The double prefix ‘aa’ indicates an apo protein (e.g. aaCIA) that is metallated in two reactions, affording an intermediate form (aCIA) in which one type of iron center was inserted and the other was not. Subscripts ‘st’ and ‘tr’ mean stationary and transient, respectively. No stoichiometry is suggested for these reactions; substrates, catalysts, and products are indicated but not quantified. The list of reactions is incomplete but serves to illustrate the types of reactions involved.

Number	Component	Members	Location	Iron center(s)	Reactions that influence the component	Reactions influenced by the component
1	FET3	Fet3 Ftr1 Fre1 Fre2 Fre3 Fre4 Fre5 Fre7 Fre8 Fit1 Fit2 Fit3 Arm1 Arm2 Arm3 Arm4	Plasma membrane Exceptions: Fit1; wall Fit2, wall Fit3, wall Fre5? Fre8?	2 heme b; Fre1 2 heme b; Fre2 2 heme b; Fre3 2 heme b; Fre4 2 heme b; Fre5 2 heme b; Fre7 2 heme b; Fre8	amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ aFET3 (biosynthesis) aFET3 + DAP $\xrightarrow{[Membrane]}$ FET3 + aDAP (metallation)	$Fe^{II}_{env} + O_2 + NAH \xrightarrow{[FET3][Membrane]} Fe^{II}_{cyt}$ (import of environmental iron into cytosol)
2	FET4	Fet4 Smf1	Plasma membrane	none	amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ FET4 FET4 $\xrightarrow{[O_2]}$ (inhibition by O ₂)	$Fe^{II}_{env} \xrightarrow{[FET4][Membrane]} Fe^{II}_{cyt}$ (import of environmental iron into cytosol)
3	CCC	Ccc1	Vacuolar membrane	none	amino acids + ATP $\xrightarrow{[DNA][RIB][AFT]}$ CCC	$Fe^{II}_{cyt} \xrightarrow{[CCC][Membrane]} Fe^{II}_{vac}$ (transfer of cytosolic iron into vacuoles)
4	FET5	Fet5 Fth1 Fre6	Vacuolar membrane	2 Heme b; Fre6	amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ aFET5 aFET5 + DAP $\xrightarrow{[Membrane]}$ FET5 + aDAP	$Fe^{II}_{vac} + O_2 + NAH \xrightarrow{[FET5][Membrane]} Fe^{II}_{cyt}$ (transfer of vacuolar iron into cytosol)
5	SMF	Smf3	Vacuolar membrane	none	amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ SMF SMF $\xrightarrow{[O_2]}$	$Fe^{II}_{vac} \xrightarrow{[SMF][Membrane]} Fe^{II}_{cyt}$ (transfer of vacuolar iron into cytosol)
6	CIA	Cfd1 Nbp35 Nar1 Cia1 Cia2 Mms19	cytosol	[Fe ₄ S ₄] _{tr} ; Cfd1 [Fe ₄ S ₄] _{tr} ; Nbp35 [Fe ₄ S ₄] _{st} ; Nbp35 [Fe ₄ S ₄] _{st} ; Nar1 [Fe ₄ S ₄] _{tr} ; Nar1 2[Fe ₂ S ₂] _{tr} ; Cfd1 2[Fe ₂ S ₂] _{tr} ; Nbp35	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaCIA aaCIA + CIA \longrightarrow 2aCIA (autocatalysis) aCIA + 2GRX + NAH $\xrightarrow{[DRE]}$ CIA + 2aGRX (reductive coupling of 2Fe ₂ S ₂)	CIA + aLEU \longrightarrow aCIA + LEU (metallating a cytosolic protein) CIA + aPOL \longrightarrow aCIA + POL (metallating a nuclear protein)
7	DRE	Dre2 Tah18	cytosol	2 [Fe ₂ S ₂]; Dre2	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aDRE GRX + aDRE \longrightarrow aGRX + DRE (metallating DRE)	aCIA + 2GRX + NAH $\xrightarrow{[DRE]}$ CIA + 2aGRX DRE catalyzing the reductive coupling of [Fe ₂ S ₂] clusters on the CIA. Plus other reduction reactions...
8	LEU	Leu1 Glt1 Met8 Met5	cytosol	[Fe ₄ S ₄]; Leu1 [Fe ₄ S ₄]; Glt1 [Fe ₄ S ₄] and Fe ^{II} siroheme; Met5	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaLEU CIA + aaLEU \longrightarrow aCIA + aLEU Fe ^{II} cyt + aLEU \longrightarrow LEU	TCAM + ATP $\xrightarrow{[LEU]}$ amino acids (synthesis of amino acids by LEU)
9	RIB	Rli1 Yae1 Lto1 Dph1 Dph2 Dph3 Cbr1 Dph4	cytosol	[Fe ₄ S ₄]; Rli1 [Fe ₄ S ₄]; Dph1 [Fe ₄ S ₄]; Dph2 Fe ^{II} ; Dph3 Fe ^{II} ; Dph4 [Fe ₄ S ₄]; Elp3	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaRIB CIA + aaRIB \longrightarrow aCIA + aRIB Fe ^{II} cyt + aRIB \longrightarrow RIB (collectively autocatalytic synthesis of RIB)	amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ proteins of the iron regulon amino acids + ATP $\xrightarrow{[DNA][RIB]}$ all other proteins (RIB catalyzes the synthesis of all proteins in the cell)

10	GRX	Elp3 Grx3 Grx4 Bol2	cytosol	[Fe ₂ S ₂]; Grx3 [Fe ₂ S ₂]; Grx4 [Fe ₂ S ₂]; Bol2	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aGRX aGRX + ISU + ATP \xrightarrow{ATM} GRX + aISU (GRX is metallated by the ATM-dependentr export of [Fe ₂ S ₂] from mitos to cytosol)	2GRX + aCIA+NAH \xrightarrow{DRE} 2aGRX + CIA GRX + aAFT \longrightarrow aGRX + AFT GRX + aDRE \longrightarrow aGRX + DRE (GRX metallates proteins in the cytosol)
11	NUC	Rnr2 Rnr4 Ade4 Tyw1 Bna1	cytosol	[Fe-O-Fe]; Rnr2 [Fe ₄ S ₄]; Ade4 [Fe ₄ S ₄]; Tyw1 Fe ^{II} ; Bna1	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaNUC Fe ^{II} cyt + aaNUC $\xrightarrow{[DRE]}$ aNUC CIA + aNUC \longrightarrow aCIA + NUC	amino acids + ATP $\xrightarrow{[NUC]}$ nucleotides (NUC catalyzes the synthesis of nucleotides from amino acids)
12	CAT	Cta1 Ctt1 Yhb1 Ccp1 Grx6	cytosol	Heme b; Cta1 (5) Heme b; Ctt1 Heme b; Yhb1 Heme b; Ccp1 [Fe ₂ S ₂]; Grx6	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaCAT aaCAT + DAP \longrightarrow aCAT+ DAP aCAT + GRX \longrightarrow CAT + aGRX	ROS $\xrightarrow{[CAT]}$ (CAT catalyzes the decomposition of ROS)
13	CTH	Cth1 Cth2	cytosol	none	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ CTH	aaaETC (or aaETC or aETC or ETC) $\xrightarrow{[CTH]}$ (CTH catalyzes the degradation of ETC)
14	AFT	Aft1 Aft2 Yap5	nucleus/ cytosol	[Fe ₂ S ₂] _n ; Aft1 [Fe ₂ S ₂] _n ; Aft2 [Fe ₂ S ₂]; Yap5	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aAFT GRX + aAFT _n \rightleftharpoons aGRX + AFT _c	amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ proteins of the iron regulon (aAFT catalyzes the expression of the iron regulon)
15	DAP	Dap1	Cytosol	Heme b; Dap1	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aDAP aDAP + heme b \rightarrow DAP	aHAP + DAP \rightleftharpoons HAP + aDAP aMEM + DAP $\xrightarrow{[Membrane]}$ MEM + aDAP (DAP transfers a heme onto aHAP and aMEM)
16	HAP	Hap1 Hap2 Hap3 Hap4 Hap5 Rox1	Nucleus	Heme b; Hap1	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aHAP aHAP + DAP \rightleftharpoons HAP + aDAP	amino acids + ATP $\xrightarrow{[DNA][RIB][HAP]}$ aaaETC (HAP catalyzes the synthesis of aaaETC)
17	POL	Ntg2 Dna2 Pri2 Pol1 Pol2 Pol3 Rad3 Chl1 Rev3 Tpa1	Nucleus	[Fe ₄ S ₄]; Ntg2 [Fe ₄ S ₄]; Dna2 [Fe ₄ S ₄]; Pri2 [Fe ₄ S ₄]; Pol1 [Fe ₄ S ₄]; Pol2 [Fe ₄ S ₄]; Pol3 [Fe ₄ S ₄]; Rad3 [Fe ₄ S ₄]; Chl1 [Fe ₄ S ₄]; Rev3 Fe ^{II} ; Tpa1	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aPOL CIA + Fe ^{II} cyt + aPOL+ NAH $\xrightarrow{[DRE]}$ aCIA + POL	nucleotides $\xrightarrow{[POL][DNA]}$ DNA
18	ISU	Isu1 Isu2 Yfh1 Nfs1 Isd11 Acp1 Jac1 Ssq1 Mge1 Grx5 Yah1 Arh1	Mito matrix	[Fe ₂ S ₂] _n ; Grx5 [Fe ₂ S ₂] _n ; Isu1 [Fe ₂ S ₂] _n ; Isu2 [Fe ₂ S ₂]; Yah1	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aISU Fe ^{II} _{mit} + ATP + NAH + aISU \longrightarrow ISU	ISU + ATP + aGRX $\xrightarrow{[ATM][Membrane]}$ GRX + aISU 2ISU + aISA + NAH \longrightarrow 2aISU + ISA 2ISU + aaTCA \longrightarrow 2aISU + aTCA
19	ISA	Isa1 Isa2 Iba57 Bol1 Bol3 Nfu1	Mito matrix	Isa1 [Fe ₄ S ₄] Isa2 [Fe ₄ S ₄] Bol1 [Fe ₂ S ₂] Bol3 [Fe ₂ S ₂] Nfu1 [Fe ₄ S ₄]	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaISA ISA + aaISA \longrightarrow 2aISA (autocatalytic) 2ISU + aISA + NAH \longrightarrow 2aISU + ISA (reductive coupling)	ISA +aaaTCA \longrightarrow aISA + aaTCA ISA +aLYS \longrightarrow aISA + LYS (ISA metallates [Fe ₄ S ₄] containing proteins in mitochondria)
20	LYS	Lys4 Ilv3	Mito matrix	[Fe ₄ S ₄] (Lys4) [Fe ₄ S ₄] putative (Ilv3)	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aLYS ISA +aLYS \longrightarrow aISA + LYS	TACM + ATP $\xrightarrow{[LYS]}$ amino acids (LYS catalyzes the synthesis of amino acids)
21	TCA	Aco1 Aco2 Sdh2 Sdh3 Sdh4 Bio2 Lip5	Mito matrix	[Fe ₄ S ₄]; Aco1 [Fe ₄ S ₄]; Aco2 [Fe ₄ S ₄]; [Fe ₂ S ₂]; [Fe ₂ S ₂]; Sdh2 heme b; Sdh3 [Fe ₄ S ₄]; [Fe ₂ S ₂]; Bio2 2[Fe ₄ S ₄]; Lip5	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ aaaTCA ISA +aaaTCA \longrightarrow aISA + aaTCA ISU +aaTCA \longrightarrow aISU + aTCA DAP + aTCA \longrightarrow TCA	acetyl-CoA $\xrightarrow{[TCA][TCAM]}$ CO ₂ + NAH (TCA catalyzes the TCA cycle) acetyl-CoA $\xrightarrow{[TCA]}$ TCAM (TCA also catalyzes the TCA filling reaction)
22	MRS	Mrs3 Mrs4	Mito IM	none	amino acids +	Fe ^{II} cyt $\xrightarrow{[MRS][Membrane][ETC]}$ Fe ^{II} mit

		Rim2			$ATP \xrightarrow{[DNA][RIB][Membrane]} MRS$	(MRS catalyzes the transfer of cytosolic iron into the mitochondria)
23	ATM	Atm1 Mmt1 Mmt2	Mito IM	none	amino acids + $ATP \xrightarrow{[DNA][RIB][Membrane]} ATM$	$ISU + aGRX + ATP \xrightarrow{[ATM][Membrane]} GRX + aISU$ (ATM catalyzes the transfer of $[Fe_2S_2]$ clusters from the mito to the cytosol, where it coordinates aGRX)
24	ETC	Cyt1 Cob1 Rip1 Coq6 Coq7 Cox10 Cox15 Mss51 Cox1 Cyc1 Cyc7 Cyc2 Cyb2 Dld1 Yno1	Mito IM	heme c; Cyt1 heme b _H /b _L ; Cob1 $[Fe_2S_2]$; Rip1 heme b; Coq6 $[Fe-O-Fe]$; Coq7 Heme b → o; Cox10 Heme o → a; Cox15 Heme b; Mss51 heme a; Cox1 heme c; Cyc1 heme c; Cyc7 heme b → e; Cyc2 heme b; Cyb2 heme b; Dld1 heme b; Yno1	amino acids + ATP $\xrightarrow{[DNA][RIB][Membrane][HAP]} aaaETC$ heme b + aaaETC $\xrightarrow{[Membrane]} aaETC$ $GRX + aaETC \xrightarrow{[Membrane]} aGRX + aETC$ $Fe^{II}cyt + aETC \xrightarrow{[Membrane]} ETC$	$NAH + O_2 \xrightarrow{[ETC][Membrane]} ATP + ROS$ (ETC catalyzes the reduction of O_2 by NAH to generate ATP and ROS)
25	HEM	Hem15	Mito IM	$Fe^{II}_{mit} \rightarrow$ heme b	amino acids + $ATP \xrightarrow{[DNA][RIB][Membrane]} aHEM$	$Fe^{II}_{mit} + TCAM \xrightarrow{[HEM][Membrane]} heme\ b$ HEM catalyzes the synthesis of heme b from TCAM
26	MEM	Ole1 Ncp1 Sur2 Scs7 Cyp51 Erg25 Erg5 Erg3 Cyb5 Mpo1	ER membrane	$[Fe-O-Fe]$, Heme b; Ole1 $[Fe-O-Fe]$; Sur2 $[Fe-O-Fe]$, heme b; Scs7 Heme b; Cyp51 $[Fe-O-Fe]$; Erg25 Heme b; Erg5 $[Fe-O-Fe]$; Erg3 Heme b; Cyb5 Fe^{II} ; Mpo1	amino acids + ATP $\xrightarrow{[DNA][RIB]} aaMEM$ $aaMEM + Fe^{II}cyt \xrightarrow{[Membrane]} aMEM$ $aMEM + DAP \xrightarrow{[Membrane]} MEM + aDAP$	acetyl-CoA + NAH + $O_2 \xrightarrow{[MEM][membrane]} Membrane$ (MEM catalyzes the synthesis of membrane)
27	HMX	Hmx1	ER membrane	Heme b → Fe^{II} ; Hmx1	amino acids + ATP $\xrightarrow{[DNA][RIB]} HMX$	$MEM + O_2 + NAH \xrightarrow{[HMX]} Fe^{II}_{cyt}$ $Heme\ b + O_2 + NAH \xrightarrow{[HMX]} Fe^{II}_{cyt}$ (HMX catalyzes the degradation of hemes to generate cytosolic iron)
28	Fe^{II}_{cyt}	Iron nonprotein	Cytosol	LMM Nonheme high-spin Fe^{II}	$Fe^{env} + O_2 + NAH \xrightarrow{[FET3][Membrane]} Fe^{II}_{cyt}$ $Fe^{env} \xrightarrow{[FET4][Membrane]} Fe^{II}_{cyt}$ $Fe^{III}_{vac} + NAH + O_2 \xrightarrow{[FET5][Membrane]} Fe^{II}_{cyt}$ $Fe^{II}_{vac} \xrightarrow{[SMF3][Membrane]} Fe^{II}_{cyt}$ $MEM + O_2 + NAH \xrightarrow{[HMX]} Fe^{II}_{cyt}$ $DAP + O_2 + NAH \xrightarrow{[HMX]} Fe^{II}_{cyt}$	$Fe^{II}_{cyt} + aRIB + NAH + O_2 \xrightarrow{[DRE]} RIB$ (Fe^{II}_{cyt} metallates many cytosolic proteins) $Fe^{II}_{cyt} \xrightarrow{[MRS][Membrane][ETC]} Fe^{II}_{mit}$ $Fe^{II}_{cyt} \xrightarrow{[CCC][Membrane]} Fe^{II}_{vac}$ (Fe^{II}_{cyt} is transported to mitochondria and vacuoles) $Fe^{II}_{cyt} + aaMEM \xrightarrow{[Membrane]} aMEM$ (Cytosolic iron metallates aaMEM located in the ER) $Fe^{II}_{cyt} + O_2 \rightarrow NP + ROS$ (Cytosolic iron reacts with O_2 to generate nanoparticles and ROS)
29	Fe^{II}_{mit}	Iron nonprotein	Mito Matrix	LMM Nonheme high-spin Fe^{II}	$Fe^{II}_{cyt} \xrightarrow{[MRS][Membrane][ETC]} Fe^{II}_{mit}$	$Fe^{II}_{mit} + ATP + NAH + aISU \xrightarrow{YAH} ISU$ (Fe^{II}_{mit} is a substrate for the synthesis of $[Fe_2S_2]$ clusters in the mitochondria) $Fe^{II}_{mit} + TCAM \xrightarrow{[HEM][Membrane]} heme\ b$ (Fe^{II}_{mit} is a substrate for the synthesis of heme b)
30	Fe^{II}_{vac}	Iron nonprotein	Vacuole lumen	LMM Nonheme high-spin Fe^{II}	$Fe^{II}_{cyt} \xrightarrow{[CCC][Membrane]} Fe^{II}_{vac}$	$Fe^{II}_{vac} \xrightarrow{[SMF3][Membrane]} Fe^{II}_{cyt}$ (Fe^{II}_{vac} can be exported into the cytosol) $Fe^{II}_{vac} + O_2 \rightarrow Fe^{III}_{vac}$ (Fe^{II}_{vac} can get oxidized to Fe^{III}_{vac} by O_2)
31	Fe^{III}_{vac}	Iron nonprotein	Vacuole lumen	LMM Nonheme high-spin Fe^{III}	$Fe^{II}_{vac} + O_2 \rightarrow Fe^{III}_{vac}$	$Fe^{III}_{vac} + NAH + O_2 \xrightarrow{[FET5][Membrane]} Fe^{II}_{cyt}$ (Fe^{III}_{vac} must become reduced and then transferred into the cytosol)
32	Heme b	Iron nonprotein	Mito IM	Heme b	$Fe^{II}_{mit} + TCAM \xrightarrow{[HEM][Membrane]} Heme\ b$	Heme b + aDAP → DAP (Heme b is used to metallate aDAP, which then leaves the mito to metallate other proteins in the cell) Heme b + aTCA → TCA (Heme b can directly metallate mito proteins)

						Heme b + O ₂ + NAH $\xrightarrow{[HMX]}$ Fe ^{II} _{cyt} (Heme b can be degraded by HMX)
33	ATP	nonprotein	All regions	none	NAH + O ₂ $\xrightarrow{[ETC][Membrane]}$ ATP + ROS (ATP is generated by the ETC)	TCAM + ATP $\xrightarrow{[LEU]}$ amino acids amino acids + ATP $\xrightarrow{[DNA][RIB][aAFT]}$ all iron regulon proteins (ATP is used to drive anabolic processes) ISU + ATP + aGRX $\xrightarrow{[ATM][Membrane]}$ GRX + aISU (ATP is used to drive the export of [Fe ₂ S ₂] clusters from mitos)
34	NAH	nonprotein	All regions	none	Acetyl-CoA $\xrightarrow{[TCA]}$ CO ₂ + NAH	Fe ^{env} + O ₂ + NAH $\xrightarrow{[FET3][Membrane]}$ Fe ^{II} _{cyt} Acetyl-CoA + NAH + O ₂ $\xrightarrow{[MEM]}$ Membrane aCIA + 2GRX + NAH $\xrightarrow{[DRE]}$ CIA + 2 aGRX (reductive coupling of 2Fe ₂ S ₂)
35	TCAM	nonprotein	Mito matrix	none	acetyl-CoA $\xrightarrow{[TCA]}$ TCAM	Fe ^{II} _{mit} + TCAM $\xrightarrow{[Hem15][Membrane]}$ heme b TCAM + ATP $\xrightarrow{[LYS]}$ amino acids
36	amino acids	nonprotein	Mito matrix and cytosol	none	TCAMe + ATP $\xrightarrow{[LEU]}$ amino acids	amino acids + ATP $\xrightarrow{[DNA][RIB]}$ other soluble proteins (amino acids are substrates for protein synthesis) amino acids + ATP $\xrightarrow{[NUC]}$ nucleotides (amino acids are substrates for synthesis of nucleotides)
37	Nucleotides	nonprotein	Cytosol/nucleus	none	amino acids + ATP $\xrightarrow{[NUC]}$ nucleotides	nucleotides $\xrightarrow{[DNAR][DNA]}$ DNA
38	DNA	nonprotein	nucleus	None	nucleotides $\xrightarrow{[POL][DNA]}$ DNA	DNA + ROS \longrightarrow
39	ROS	nonprotein	All compartments	none	NAH + O ₂ $\xrightarrow{[ETC][Membrane]}$ ATP + ROS	ROS $\xrightarrow{[CAT]}$ DNA + ROS \longrightarrow
40	Membrane	nonprotein	Plasma, Vacuole, and Mito membranes	none	Acetyl-CoA + NAH + O ₂ $\xrightarrow{[MEM][membrane]}$ Membrane	Fe ^{env} + O ₂ + NAH $\xrightarrow{[FET3][Membrane]}$ Fe ^{II} _{cyt} amino acids + ATP $\xrightarrow{[DNA][RIB][Membrane]}$ membrane bound proteins (Membrane is a catalyst for reactions that take place at membranes) Fe ^{II} _{cyt} $\xrightarrow{[MRS][Membrane][ETC?]}$ Fe ^{II} _{mit} NAH + O ₂ $\xrightarrow{[ETC][Membrane]}$ ATP + ROS Membrane + ROS \longrightarrow (Membrane is damaged by ROS)
	Fe ^{env}	nutrient				Fe ^{env} + O ₂ + NAH $\xrightarrow{[FET3][Membrane]}$ Fe ^{II} _{cyt} Fe ^{env} $\xrightarrow{[FET4][Membrane]}$ Fe ^{II} _{cyt}
	Acetyl-CoA	nutrient				Acetyl-CoA $\xrightarrow{[TCA]}$ TCAM Acetyl-CoA + NAH + O ₂ $\xrightarrow{[MEM]}$ Membrane Acetyl-CoA $\xrightarrow{[TCA][TCAM]}$ NAH + CO ₂
	O ₂	nutrient				NAH + O ₂ $\xrightarrow{[ETC][Membrane]}$ ATP + ROS Many others
	CO ₂	waste				Acetyl-CoA $\xrightarrow{[TCA][TCAM]}$ NAH + CO ₂
	NP	waste				Fe ^{II} _{mit} + O ₂ \rightarrow NP + ROS

					$\text{Fe}^{\text{II}}_{\text{cyt}} + \text{O}_2 \rightarrow \text{NP} + \text{ROS}$	
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