Supplementary Appendix

Generating a curated pathway model using expert knowledge

After an analysis of the relevant literature, the following detailed information was considered to build the networks shown in Figure 2. Bold letters shown parenthetically identify which part of Figure 2 is described:

i) Iron is imported into the mitochondrial matrix. Once at the mitochondrial matrix, iron is loaded directly into the enzyme ferrochelatase [1, 2] and is directed for heme synthesis and ISC biogenesis. Some results show that, \textit{in vitro}, Fe can also be stored by frataxin (Yfh1) for posterior usage [3, 4]. The \textit{in vivo} relevance of this is disputed. To a first approximation one can simplify the reaction network by assuming that a mitochondrial iron pool exists and that the iron from this pool is used for both heme A synthesis and for ISC synthesis. We also consider a production flux that accounts for iron import into that mitochondrial pool and a sink flux that accounts for any other usage or export of iron from the mitochondria. According to the available information, possible alternative roles for Yfh1 in Fe processing are: a) Regulation of Fe import and usage (I) and b) Regulation of ISC synthesis (S), transfer (T) and repair (R) through the regulation of Fe supply [5, 6].

ii) ISC initially assemble in the Isu1, Isu2, Isa1, Isa2, and Nfu1 scaffold dimers, represented by ISS in Figure 2 (e. g. [7]). Scaffolds form homodimers where the initial ISC assembly takes place [6, 8]. ISC synthesis (S) is catalyzed by cysteine desulfurase Nfs1 [9-11] and requires electron balancing. One possible role for Arh1-Yah1 in the ISC synthesis (S) process is that of electron transfer regulation. Recent evidence suggests that, in \textit{E. coli}, the
Isa1/Isa2 homologue protein IscA is important in providing Fe to the Isu1/Isu2 homologue protein [12-15]. In our model, for simplicity’s sake, we will not differentiate between different types of scaffold proteins.

iii) Once a 2Fe-2S ISC is assembled in the scaffold it can be transferred (T) to 2Fe-2S apo-proteins[12, 13, 16-21], represented in Figure 2 by Apo-P1 and Apo_Arh1_Yah1. There is also the possibility that 2Fe-2S clusters are transferred (T) to 4Fe-4S apo-proteins [16, 18, 19]. Two transfer steps would then lead to the formation of the appropriate 4Fe-4S ISC on the apo-protein. The affinity of the clusters for the scaffolds (and thus the transfer of the ISC) is modulated by the reduction state of the cluster [22]. Herein lays another possible role for Arh1-Yah1 in ISC biogenesis. These proteins could provide electrons to regulate the process of ISC transfer (T) to Apo-proteins.

iv) If the ISC remains on the scaffold proteins, it can be transformed into a 4Fe-4S ISC [8, 23]. Roles for Yfh1, Nfs1, and Arh1-Yah1 in this additional ISC synthesis (S) step are similar to those described before.

v) Although we know of no direct evidence for this, one can not rule out the possibility that the 4Fe-4S ISC can be transferred directly to 4Fe-4S apo-proteins, represented in Figure 2 by Apo P2. Arh1-Yah1 could have a role in providing electrons to regulate cluster affinity and transfer (T).

vi) There is a natural turnover of ISC, both in scaffold proteins and in the ISC proteins, for example due to oxidative stress [e. g. [24, 25]]. Nfs1 homologues are able to repair (R) damaged ISC directly in situ [23, 26]. A role for Arh1-Yah1 in providing electrons to facilitate this repair (R) is possible.
vii) Finally, once assembled in the scaffold proteins, the ISC can be transferred to the cytoplasm [27, 28], most likely through Atm1.

viii) Grx5 is a monothiolic reductase that catalyzes the reaction

\[ P - SSG + GSH \leftrightarrow PSH + GSSG \]  

[29]. Because ISC are coordinated between cysteine residues, glutathionylation of such residues would prevent formation of ISC and thus disturb normal ISC biogenesis and ISC dependent protein activity. Thus, Grx5 could be active in regulating the glutathionylation state of cysteine residues in Arh1, Yah1, scaffold or Nfs1 proteins. Grx5 could also be involved in regulating the formation/destruction of disulfide bridges in these proteins [29]. These two modes of action are lumped into one by defining for each ISC assembly protein an inactivated pool that can be reactivated by Grx5.

ix) There is a possibility that Grx5 protein-protein disulfide bridge reducing activity could act upon such bridges formed between different ISC proteins. There have been reports that, in the absence of iron on the scaffold dimers, such a bridge forms between Isu and Nfs1 homologues, leading to a dead end complex between the two proteins [30-32]. Grx5 could be active in reducing these bridges and returning both proteins for active duty in ISC assembly.

x) The HSP70-type protein chaperone Ssq1 is important for proper folding of the proteins involved in ISC biogenesis pathway and for the proper functioning of the pathway. Mge1 is used by Ssq1 as a nucleotides exchanging factor. Jac1 is a HSP40-type co-chaperone homologue that is important for the appropriate functioning of Ssq1 in the ISC biogenesis pathway. Ssq1, Mge1 and Jac1 work together and are activated by Isu
homologues [7, 33-39], which suggests that these proteins may be involved in: a) stabilizing (St) ISC assembly in the scaffolds until a productive transfer occurs [7, 40], b) in initial folding (F) of scaffold proteins or other ISC proteins or c) in both processes.

**Derivation of the GMA Model**

**a) The power-law approximation:**

If the flux of a given process is regulated by species $X_1, X_2, \ldots, X_n$ but the functional form of the rate expression is unknown one can write the following equation to describe its rate.

$$v_j = F_j (X_1, X_2, \ldots, X_n) \quad \text{Eq. 1}$$

In general, the exact form of $F$ is unknown. If one assumes that this function is a rational function [7, 40-42], one can write the same equation in logarithmic space and approximate that function using a Taylor series. Then, by truncating the series in the first order term and returning to a Cartesian space, the unknown form of the function can be approximated by a power-law function [43, 44]:

$$v_j \cong \gamma_j \prod_{k=1}^j X_k^{f_{j,k}} \quad \text{Eq. 2}$$

Where $\gamma_j$ is an apparent rate constant and $f_{j,k}$ an apparent kinetic order:

$$\gamma_j = v_{j,0} \prod_{k=1}^j X_{k,0}^{f_{j,k}}$$

$$f_{j,k} = \frac{d\log[v_j]}{d\log[X_k]}_{0}$$
In the case of the ISC biogenesis, the reproduction of experimental results requires that the concentration of several dependent variables decreases steadily until it ultimately is zero, for example when reproducing a Grx5 knock-out cell line. Many of the rate expressions approach zero as the concentrations of different species decrease, which suggest that the Generalized Mass Action (GMA) representation is more adequate for our models. By using such a representation, we ensure that as one protein is knocked out of the model it will affect only the process it is supposedly involved in.

b) Reactions that constitute a base model for ISC biogenesis

The reactions used in the model, together with rate expressions are shown in Supplementary Table 1. The assemble model and differential equations are given as supplementary material in an SBML file. This model is obtained in the following way. First, the mass balance equations for each internal variable are written. For instance, in the case of the pool of scaffold proteins (ISS in Figure 2), we have the following processes:

| Reaction                                                                 | Rate Expression                                                                 |
|--------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| Biogenesis of the Fe2S2 cluster                                          | \( v_3 = \gamma_3 Fe^{2+} ISS \rightarrow Fe^{2+} ISSFe^{2+} \)                 |
| Loss of the Fe2S2 cluster                                                | \( v_4 = \gamma_4 ISSFe^{2+} S_2^{2-} \rightarrow 2 Fe + ISS \)                 |
| Unfolding of the scaffolds                                               | \( v_7 = \gamma_7 ISS \rightarrow \text{ISS} \)                               |
| Folding of the scaffolds                                                 | \( v_8 = a_8 \text{ISS} \)                                                   |
| Transfer of the Fe2S2 cluster                                            | \( v_9 = \gamma_9 \text{ISSFe}^{2+} S_2^{2-} \rightarrow \text{ISSFe}^{2+} P_1 \) |
| Transfer of the Fe4S4 cluster                                            | \( v_{10} = \gamma_{10} \text{ISSFe}^{4+} S_4^{4-} \rightarrow \text{ISSFe}^{4+} P_2 \) |
| Transfer of the Fe2S2 cluster                                            | \( v_{11} = \gamma_{11} \text{ISSFe}^{2+} S_2^{2-} \rightarrow \text{ISSFe}^{2+} P_2 \) |
| Transfer of the Fe2S2 cluster                                            | \( v_{12} = \gamma_{12} \text{ISSFe}^{2+} P_2 \rightarrow \text{ISSFe}^{2+} P_2 \) |
| Glutathionylation of Scaffold                                            | \( v_{13} = \gamma_{13} \text{ISSFe}^{2+} \rightarrow \text{ISSFe}^{2+} \text{Sg} \) |
| Deglutathionylation of Scaffold                                          | \( v_{22} = \gamma_{22} \text{ISS} \rightarrow \text{ISS} \)                  |
| Loss of Fe4S4 cluster from scaffold                                      | \( v_{23} = \gamma_{23} \text{ISS} \rightarrow \text{ISS} \)                  |
| Transfer of the Fe4S4 cluster                                            | \( v_{34} = \gamma_{34} \text{ISSFe}^{4+} \rightarrow \text{ISSFe}^{4+} \)     |

5
Thus, the mass action term for ISS is:

\[
\frac{d\text{ISS}}{dt} = v_4 - v_3 + v_7 - v_8 + v_9 + v_{10} + v_{11} + v_{12} + v_{13} - v_{22} + v_{23} + v_{35}
\]

Then, each velocity is substituted by its power-law form according to the information provided in the Supplementary Table 1. Protein and metabolite levels are considered at their basal steady-state. Then, the apparent rate constants are also normalized. This allows for a more appropriate comparison of the different results.

c) Scanning procedure

The scanning procedure considers different values for the parameters as indicated in Supplementary Table 2. A value of 0 in the corresponding kinetic-order removes the considered variable from the model. Results are computed using Mathematica®. The values for the scanned parameters are given in Supplementary Table 2. Due to the combinatorial explosion of possibilities some simplifying assumptions were made for the scanning. Rate constants for similar processes are scanned as being the same. The same applies to the kinetic orders. This is all indicated in Supplementary Table 2. Another simplifying assumption that we made was that while scanning for the role of one protein, the kinetic orders for the remaining proteins remained constant. Thus, for example when studying the role of Arh1-Yah1, the kinetic orders that regard the role of Grx5 were left untouched and with a value of 1. The rate constant for the sink reaction of Arh1 was set to 0.1 while the rate constants for all other sink reactions were zero. The values for the rate constants of reactions in which Arh1-Yah1 was not involved were left at their basal values which are reported in the SBML file supplied as
supplementary material. We performed in excess of two and half million simulations curves for the scanning.
### Supplementary Table 1: Set of Reactions in the complete model

| Reaction | Description | Chemical Equation | Rate Expression |
|----------|-------------|-------------------|-----------------|
| 1        | Iron entry into the mitochondria | $\text{Fe} \rightarrow \text{Fe}$ | $v_1 \equiv \gamma_1 \left[\text{Fe}\right]^{11}$ |
| 2        | Iron sink for other processes and export | $\text{Fe} \rightarrow \text{Fe}$ | $v_2 \equiv \gamma_2 \left[\text{Fe}\right]^{21}$ |
| 3        | Biogenesis of the Fe2S2 cluster | $2 \text{Fe} + \text{ISS} \rightarrow \text{ISSFe2S2}$ | $v_3 \equiv \gamma_3 \left[\text{ISS}\right]^{31} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{32} \left[\text{Nfs}\right]^{33} \left[\text{Yfh}\right]^{34} \left[\text{Arh}\right]^{35}$ |
| 4        | Loss of the Fe2S2 cluster | $\text{ISSFe2S2} \rightarrow 2 \text{Fe} + \text{ISS}$ | $v_4 \equiv \gamma_4 \left[\text{ISSFe2S2}\right]^{41} \left[\text{SqJac}\right]^{42}$ |
| 5        | Biogenesis of the Fe4S4 cluster | $\text{ISSFe2S2} + 2 \text{Fe} \rightarrow \text{ISSFe4S4}$ | $v_5 \equiv \gamma_5 \left[\text{Fe}\right]^{51} \left[\text{ISSFe2S2}\right]^{52} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{53} \left[\text{Nfs}\right]^{54} \left[\text{Yfh}\right]^{55}$ |
| 6        | Loss of the Fe4S4 cluster | $\text{ISSFe4S4} \rightarrow \text{ISSFe2S2} + 2 \text{Fe}$ | $v_6 \equiv \gamma_6 \left[\text{ISSFe4S4}\right]^{61} \left[\text{SqJac}\right]^{62}$ |
| 7        | Unfolding of the scaffolds | $\text{U\_ISS} \rightarrow \text{ISS}$ | $v_7 \equiv \gamma_7 \left[\text{ISS}\right]^{71} \left[\text{SqJac}\right]^{72}$ |
| 8        | Folding of the scaffolds | $\text{ISS} \rightarrow \text{U\_ISS}$ | $v_8 \equiv \alpha \left[\text{ISS}\right]$ |
| 9        | Transfer of the Fe2S2 cluster | $\text{ISSFe2S2} + \text{Apo\_P1} \rightarrow \text{ISS} + \text{P1}$ | $v_9 \equiv \gamma_9 \left[\text{ISSFe2S2}\right]^{91} \left[\text{Apo\_P1}\right]^{92} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{93} \left[\text{Nfs}\right]^{94}$ |
| 10       | Transfer of the Fe4S4 cluster | $\text{ISSFe4S4} + \text{Apo\_P2} \rightarrow \text{ISS} + \text{P2}$ | $v_{10} \equiv \gamma_{10} \left[\text{ISSFe4S4}\right]^{101} \left[\text{Apo\_P2}\right]^{102} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{103} \left[\text{Nfs}\right]^{104}$ |
| 11       | Transfer of the Fe2S2 cluster | $\text{ISSFe2S2} + \text{Apo\_P2} \rightarrow \text{ISS} + \text{Apo1\_P2}$ | $v_{11} \equiv \gamma_{11} \left[\text{ISSFe2S2}\right]^{111} \left[\text{Apo\_P2}\right]^{112} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{113} \left[\text{Nfs}\right]^{114}$ |
| 12       | Transfer of the Fe2S2 cluster | $\text{ISSFe2S2} + \text{Apo1\_P2} \rightarrow \text{ISS} + \text{P2}$ | $v_{12} \equiv \gamma_{12} \left[\text{ISSFe2S2}\right]^{121} \left[\text{Apo1\_P2}\right]^{122} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{123} \left[\text{Nfs}\right]^{124}$ |
| 13       | Transfer of the Fe2S2 cluster | $\text{ISSFe2S2} + \text{Apo\_Arh1\_Yah1} \rightarrow \text{ISS} + \text{Arh1\_Yah1}$ | $v_{13} \equiv \gamma_{13} \left[\text{ISSFe2S2}\right]^{131} \left[\text{Apo\_Arh1\_Yah1}\right]^{132} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{133} \left[\text{Nfs}\right]^{134}$ |
| 14       | Partial degradation of the Fe2S2 cluster | $\text{Arh1\_Yah1} \rightarrow \text{D\_Arh1\_Yah1}$ | $v_{14} \equiv \gamma_{14} \left[\text{Arh1\_Yah1}\right]^{141} \left[\text{D\_Arh1\_Yah1}\right]^{142}$ |
| 15       | Repair of the Fe2S2 cluster | $\text{D\_Arh1\_Yah1} \rightarrow \text{Arh1\_Yah1}$ | $v_{15} \equiv \gamma_{15} \left[\text{D\_Arh1\_Yah1}\right]^{151} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{152} \left[\text{Nfs}\right]^{153} \left[\text{SqJac}\right]^{154}$ |
| 16       | Partial degradation of the Fe2S2 cluster | $\text{P1} \rightarrow \text{D\_P1}$ | $v_{16} \equiv \gamma_{16} \left[\text{P1}\right]^{161}$ |
| 17       | Repair of the Fe2S2 cluster | $\text{D\_P1} \rightarrow \text{P1}$ | $v_{17} \equiv \gamma_{17} \left[\text{D\_P1}\right]^{171} \left[\text{Arh1}_1 \_ \text{Yah1}_1\right]^{172} \left[\text{Nfs}\right]^{173} \left[\text{SqJac}\right]^{174}$ |
| 18       | Loss of inactive Fe2S2 cluster | $\text{Apo1\_P2} \rightarrow \text{Apo\_P2} + 2\text{Fe}$ | $v_{18} \equiv \gamma_{18} \left[\text{Apo1\_P2}\right]^{181} \left[\text{Apo\_P2}\right]^{182} \left[\text{Fe}\right]^{183}$ |
19 Loss of inactive Fe2S2 cluster D_Arh1_Yah1 → Apo_Arh1_Yah1 + 2 Fe
20 Loss of inactive Fe2S2 cluster D_P1 → Apo_P1 + 2 Fe
21 Loss of inactive Fe4S4 cluster D_P2 → Apo_P2 + 4 Fe
22 Glutathionylation of Scaffold ISS → ISS_SG
23 Deglutathionylation of Scaffold ISS_SG → ISS
24 Glutathionylation of P1 Apo_P1 → P1_SG
25 Deglutathionylation of P1 P1_SG → Apo_P1
26 Glutathionylation of P2 Apo_P2 → P2_SG
27 Deglutathionylation of P2 P2_SG → Apo_P2
28 Glutathionylation of Arh1_Yah1 Apo_Arh1_Yah1 → Arh1_Yah1_SG
29 Deglutathionylation of Arh1_Yah1 Arh1_Yah1_SG → Apo_Arh1_Yah1
30 Formation of dead-end complex Nfs1 + ISS → Nfs1_ISS
31 Recovery of the dead-end complex Nfs1_ISS → Nfs1 + ISS
32 Glutathionylation of Nfs1 Nfs1 → Nfs1_SG
33 Deglutathionylation of Nfs11 Nfs1_SG → Nfs1
34 Loss of Fe4S4 cluster from scaffold ISSFe4S4 → ISS + 4 Fe
35 Partial degradation of the Fe4S4 cluster P2 → D_P2
36 Repair of the Fe4S4 cluster D_P2 → P2
37 Export of Fe2S2 cluster to the cytoplasm ISSFe2S2 →
38 Export of Fe4S4 cluster to the cytoplasm ISSFe4S4 →
39 Formation of Heme Fe → Heme_Fe
40 Destruction of Heme Heme_Fe → Fe
41 Depletion of Yfh1 for Δyfh1 cells
Yfh1 →

42 Depletion of Arh1_Yah1 for Δarh1 and Δyah1 cells
Apo_Arh1_Yah1 →

43 Depletion of scaffold for Δssq1 and Δjac1 cells
SsqJac →

44 Depletion of Nfs1 for Δnfs1 cells
Nfs1 →

45 Depletion of Grx5 for Δgrx5 cells
Grx5 →

46 Depletion of scaffold for Δiss cells
Iiss →

47 Depletion of scaffold for Δissfe2s2 and Δissfe4s4 cells
Iissfe2s2, Iissfe4s4 →

48 Depletion of scaffold with a Fe2S2 and a Fe4S4 ISC cluster assembled, respectively
Fe2s2, Fe4s4 →

49 Depletion of mitochondrial iron
Fe →

50 Depletion of generic protein that needs a Fe2S2 ISC to be functional
P1_SG →

51 Depletion of generic protein that needs a Fe4S4 ISC to be functional
P2_SG →

52 Depletion of electron donor (either Arh1 or Yah1; see text for an explanation)
Arh1_Yah1_SG →

53 Depletion of apo forms of P1, P2 and Arh1_Yah1 respectively
Apo_P1, Apo_P2, Apo_Arh1_Yah1 →

54 Depletion of glutathionylated forms of P1, P2, Arh1_Yah1, Nfs1 and Isu, respectively
P1_SG, P2_SG, Arh1_Yah1_SG, Nfs1_SG, Isu_SG →

55 Depletion of forms of P1, P2 and Arh1_Yah1, respectively, with a damaged and repairable ISC
Ap01_P2 – P2 form with an intermediate Fe2S2 cluster assembled; Heme_Fe →

56 Species in parenthesis and brackets in the equations are modifiers and are not represented in the flux diagram because they contribute to the catalysis of the reaction but are neither produced nor consumed in the reaction

a ISS – Scaffold for initial ISC assembly; ISSFe2S2, ISSFe4S4 – Scaffold with a Fe2S2 and a Fe4S4 ISC cluster assembled, respectively; Fe – Mitochondrial iron; P1 – generic protein that needs a Fe2S2 ISC to be functional; P2 – generic protein that needs a Fe4S4 ISC to be functional; Arh1_Yah1 – electron donor (either Arh1 or Yah1; see text for an explanation); Apo_P1, Apo_P2, Apo_Arh1_Yah1 –apo forms of P1, P2 and Arh1_Yah1 respectively; P1_SG, P2_SG, Arh1_Yah1_SG, Nfs1_SG, Isu_SG – glutathionylated forms of P1, P2, Arh1_Yah1, Nfs1 and Isu, respectively; D_P1, D_P2, D_Arh1_Yah1, - Forms of P1, P2 and Arh1_Yah1, respectively, with a damaged and repairable ISC; Ap01_P2 – P2 form with an intermediate Fe2S2 cluster assembled; Heme – heme molecules synthesized in the mitochondrial matrix; Heme_Fe – Heme molecules with iron.
Supplementary Table 2: Parameters that were scanned and ranges of values for the scanning. A total of 5647152 simulations were done.

| Parameters | Type of parameter | Scanning Range | Controlled processes |
|------------|------------------|----------------|---------------------|
| $\gamma_3 = \gamma_5$ | Rate constant | $10^{-2} - 10^2$ | Assembly of ISC in scaffold |
| $\gamma_4 = \gamma_6 = \gamma_{35}$ | Rate constant | $10^{-2} - 10^2$ | Loss of ISC from scaffold |
| $\gamma_8$ | Rate constant | $10^{-2} - 10^2$ | Rate of appropriate folding for scaffolds |
| $\gamma_9 = \gamma_{10} = \gamma_{11} = \gamma_{12} = \gamma_{13}$ | Rate constant | $10^{-2} - 10^2$ | ISC transfer to Apo-Proteins |
| $\gamma_{23} = \gamma_{25} = \gamma_{27} = \gamma_{29} = \gamma_{31} = \gamma_{33}$ | Rate constant | $10^{-2} - 10^2$ | Recovery of glutathionylated proteins |
| $\gamma_{37} = \gamma_{38}$ | Rate constant | $10^{-2} - 10^2$ | Export of ISC to the cytoplasm |
| $\tau_{41}$ | Rate constant | 0, 0.1 | Depletion of Yfh1 |
| $\tau_{42}$ | Rate constant | 0, 0.1 | Depletion of Arh1_Yah1 |
| $\tau_{43}$ | Rate constant | 0, 0.1 | Depletion of Ssq1 and Jac1 |
| $\tau_{44}$ | Rate constant | 0, 0.1 | Depletion of Nfs1 |
| $\tau_{45}$ | Rate constant | 0, 0.1 | Depletion of Grx5 |
| $f_33 = f_{53}$ | Kinetic order | 0, 1, 2 | Assembly of ISC in scaffold |
| $f_35 = f_{55}$ | Kinetic order | 0, 1, 2 | Assembly of ISC in scaffold |
| $f_{72}$ | Kinetic order | 0, 1, 2 | Correct folding of scaffolds |
| $f_{93} = f_{103} = f_{113} = f_{123} = f_{133}$ | Kinetic order | 0, 1, 2 | Transfer of ISC to apo-proteins |
| $f_{94} = f_{104} = f_{114} = f_{124} = f_{134}$ | Kinetic order | 0, 1, 2 | Transfer of ISC to apo-proteins |
| $f_{42} = f_{62}$ | Kinetic order | 0, 1, 2 | Stability of ISC in scaffolds |
| $f_{52} = f_{72} = f_{362}$ | Kinetic order | 0, 1, 2 | In situ Repair of damaged clusters |
| $f_{53} = f_{73} = f_{363}$ | Kinetic order | 0, 1, 2 | In situ Repair of damaged clusters |
| $f_{54} = f_{74} = f_{364}$ | Kinetic order | 0, 1, 2 | In situ Repair of damaged clusters |
| $f_{555} = f_{755} = f_{365}$ | Kinetic order | 0, 1 | Deglutathionylation of scaffold |
| $f_{532}$ | Kinetic order | 0, 1 | Deglutathionylation of P1 |
| $f_{525}$ | Kinetic order | 0, 1 | Deglutathionylation of P2 |
| $f_{272}$ | Kinetic order | 0, 1 | Deglutathionylation of Arh1_Yah1 |
| $f_{292}$ | Kinetic order | 0, 1 | Recovery of dead-end complex |
| $f_{312}$ | Kinetic order | 0, 1 | Deglutathionylation of Nfs1 |
| $f_{332}$ | Kinetic order | 0, 1 | Deglutathionylation of Nfs1 |
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