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Title: **Molecular pathways of generation and detoxification of reactive oxygen species and induction of apoptosis in yeasts**

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**Supplementary data (Figures)**



**Figure S1**: Structure of glutathione (GSH) consisting of glutamate, cysteine and glycine.



**Figure S2:** A schematic representation of biosynthesis of glutathione (GSH) and phytocheletins (PCs) and their roles in cadmium chelation and detoxification of ROS. (1) Two steps biosynthesis of GSH; in first step glutamate (Glu) and Cysteine (Cys) are combined together to form γ-glutamylcysteine (γ-Glu-Cys) to which glycine is attached in second step at its C-terminal end to form GSH. Both these reactions are energy dependent and catalyzed by gamma glutamylcysteine synthase (γ-GCS) and glutathione synthase (GS), respectively. (2) GSH is degraded by two different ways catalyzed by γ-glutamyle transpeptidase (GT) and phytocheletin synthase (PS). GT cleaves the γ-linkage between glutamate and cysteine thus splitting GSH into Glu and Cys-Gly moieties. Whereas, PS cleaves γ-Glu-Cys moiety of GSH then transfers it to another GSH molecule for PC synthesis. (3-4) Both PCs and GSH have the ability to sequester cadmium ions through their thiol groups forming PC-Cd+2 and GSH-Cd+2 complexes respectively, (5) which are subsequently transported into vacuole via YCF1 in yeasts. (6) PCs are missing in bacteria where GSH actively participate in Cd sequestration forming complexes which are secreted to cell exterior via unknown transporters. (7) GSH detoxifies the cadmium-induced ROS (*e.g.,* H2O2) reducing it to H2O acting as a strong reducing agent and gets itself oxidized to GSSG catalyzed by glutathione peroxidase (GPx). GSSG is subsequently reduced to GSH by glutathione reductase (GR) using NADPH as a reducing agent.

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**Figure S3**: Schematic view of glutathionylation of protein via GSSG mediated disulfide exchange mechanism. Sulfhydryl group of protein cysteine residue (PSH) reacts directly with GSSG forming PSSG which is then reduced to GSH thus connecting two proteins via disulfide linkage. This disulfide exchange reaction may occur within same protein. GSH plays a significant role in quick deglutathionylation of proteins.