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D. 研究発表

1. 論文発表

なし。

2. 学会発表

稲葉佐知子、大橋一晶、永沼 章: 酵母細胞膜に存在する鉄還元酵素 Frel によるパラコート毒性の増強. フォーラム 2003 : 衛生薬学・環境トキシコロジー2003.

稲葉佐知子、大橋一晶、永沼 章: 酵母細胞膜に存在する鉄還元酵素 Frel によるパラコート毒性発現機構の解析. 第 42 回日本薬学会東北支部大会, 2003.

稲葉佐知子、大橋一晶、永沼 章: 酵母細胞膜上の鉄還元酵素群によるパラコートに依存した活性酸素産生. 日本薬学会第 124 年会, 2004.

岩橋芳樹、大橋一晶、永沼 章: 酵母における multivesicular body sorting pathway によるパラコート毒性の軽減. 日本薬学会第124年会, 2004.

E. 知的財産権の出願・登録状況
なし。

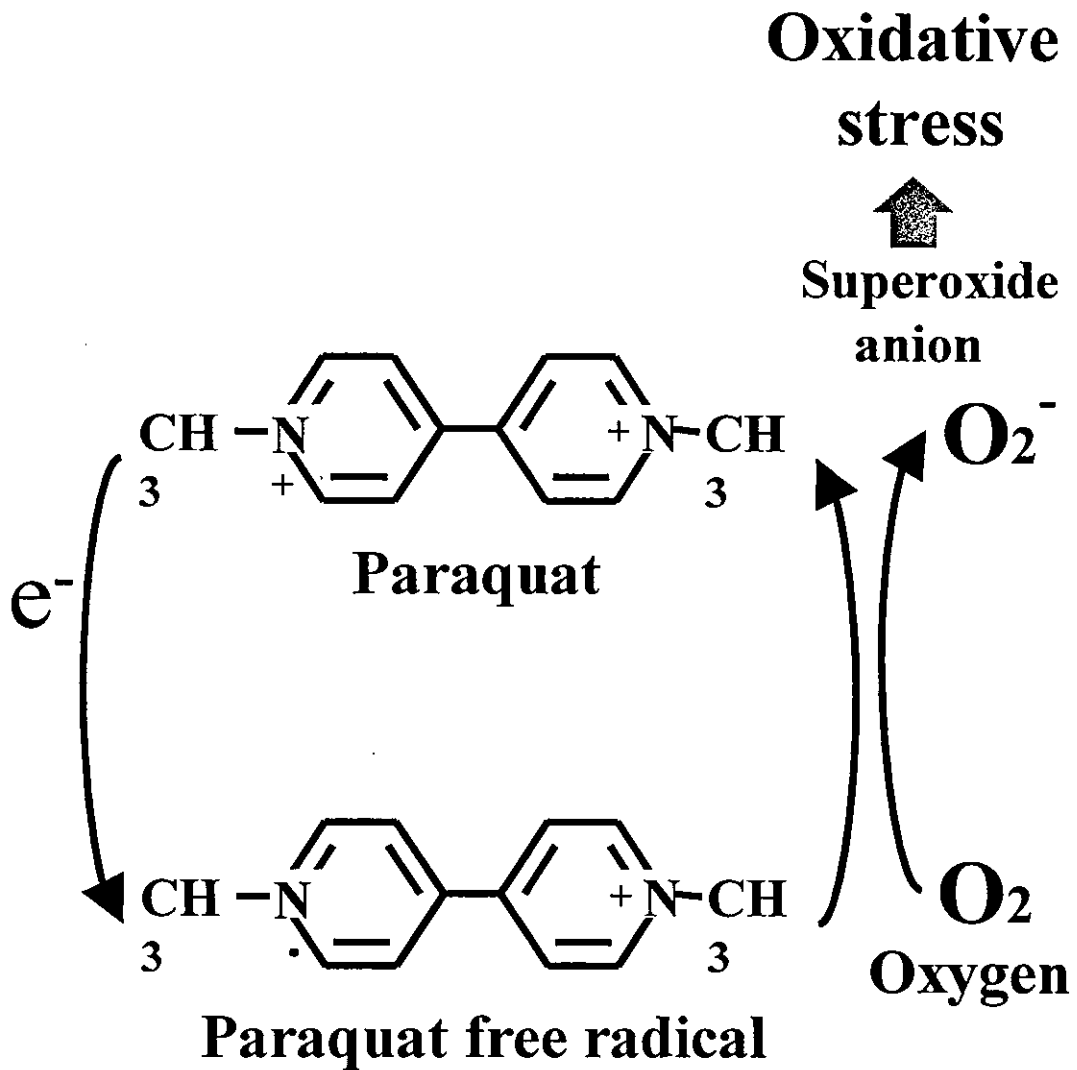
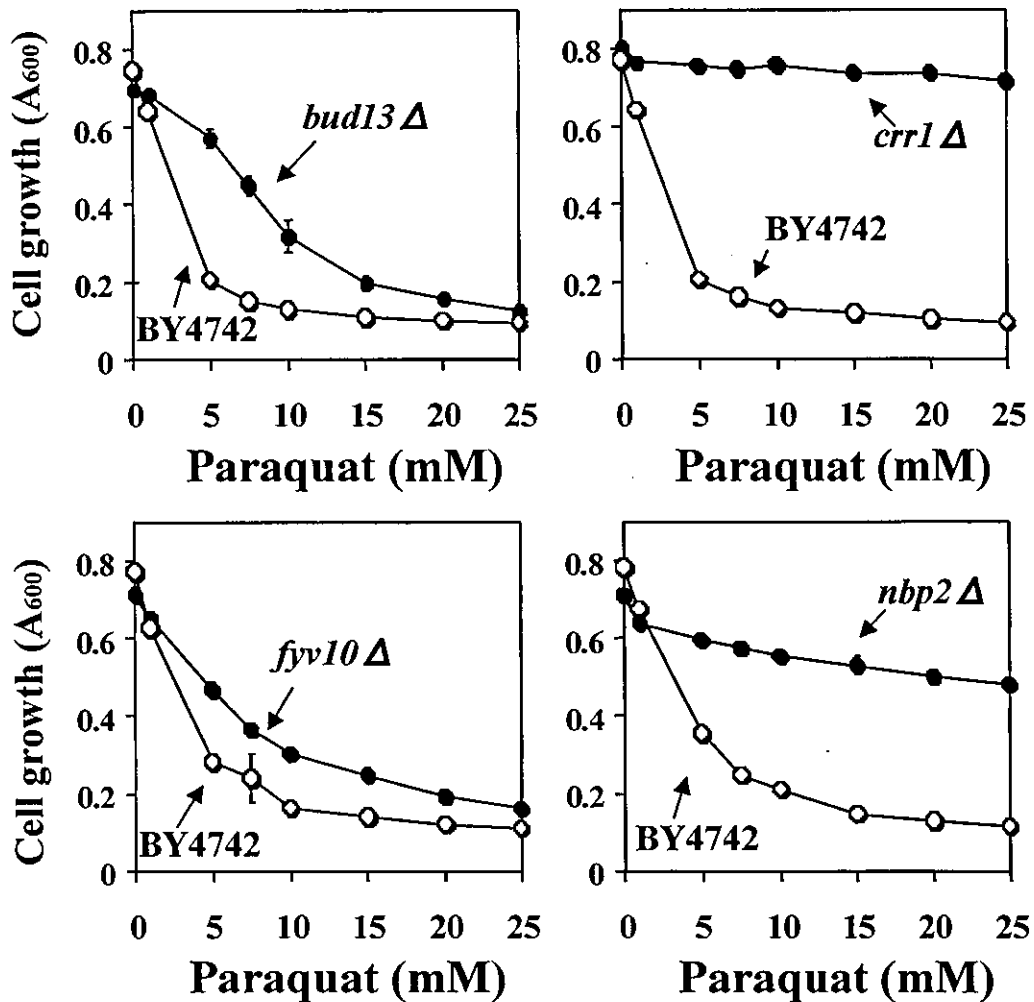


Fig. 1 The mechanism for paraquat toxicity



BUD13 : Protein that may be involved in bipolar and bud site selection
CRR1 : Sporulation specific protein with similarity to Crt1p cell wall protein
FYV10 : Protein involved in the degradation of fructose-1,6-bisphosphatase (FBPase)
NBP2 : Nap1p-binding protein involved in cell wall integrity and mitosis elevated temperatures

Fig. 2 Sensitivity of *BUD13*, *CRR1*, *FYV10*

● : Deletion mutant of yeast cell

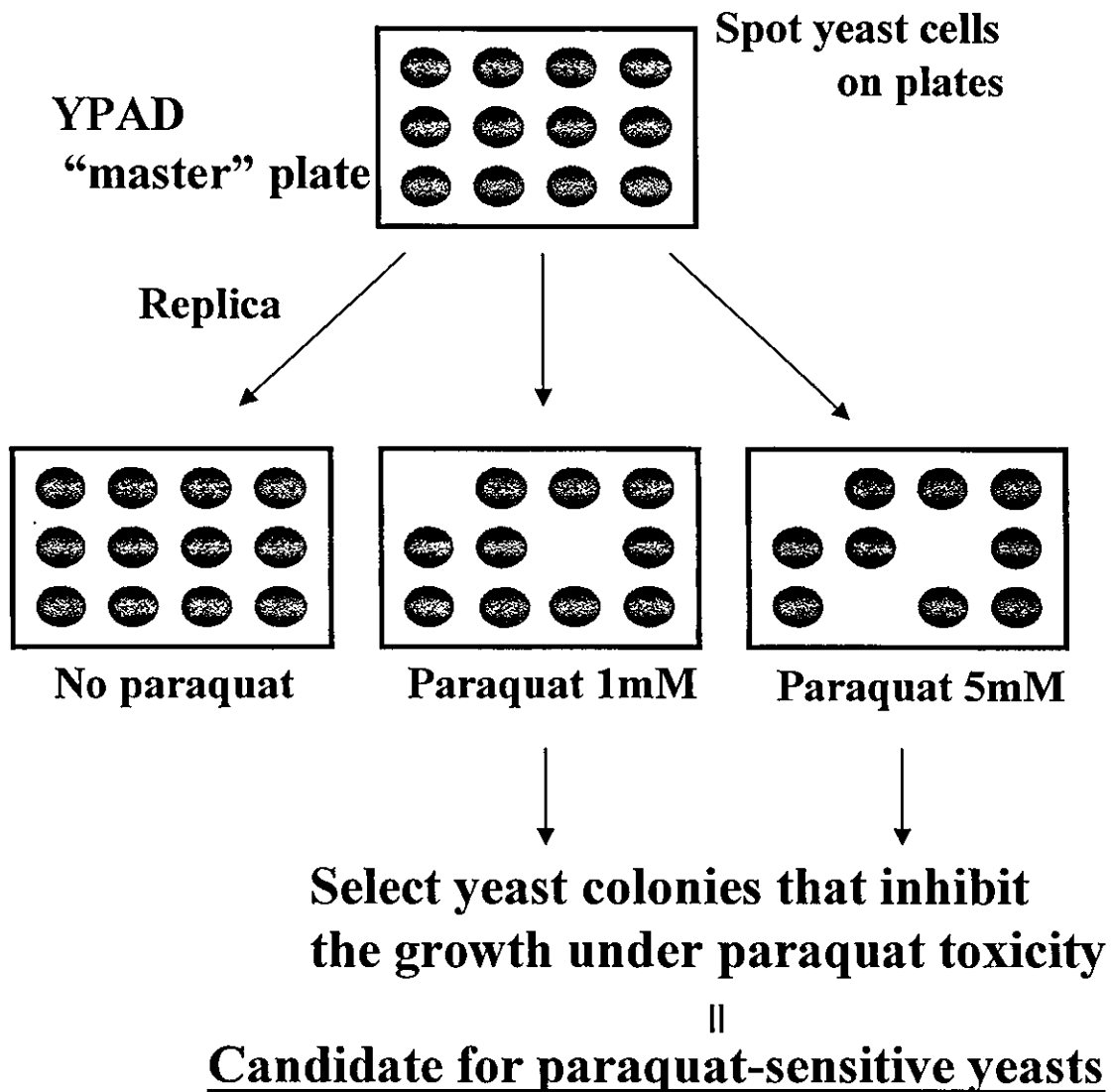


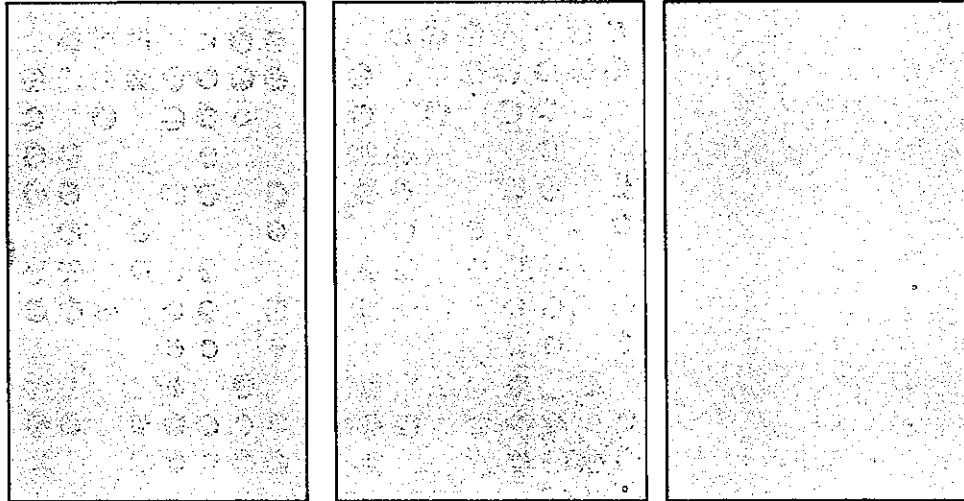
Fig. 3 Screening for paraquat-sensitive yeasts with replica-printing method

0 h

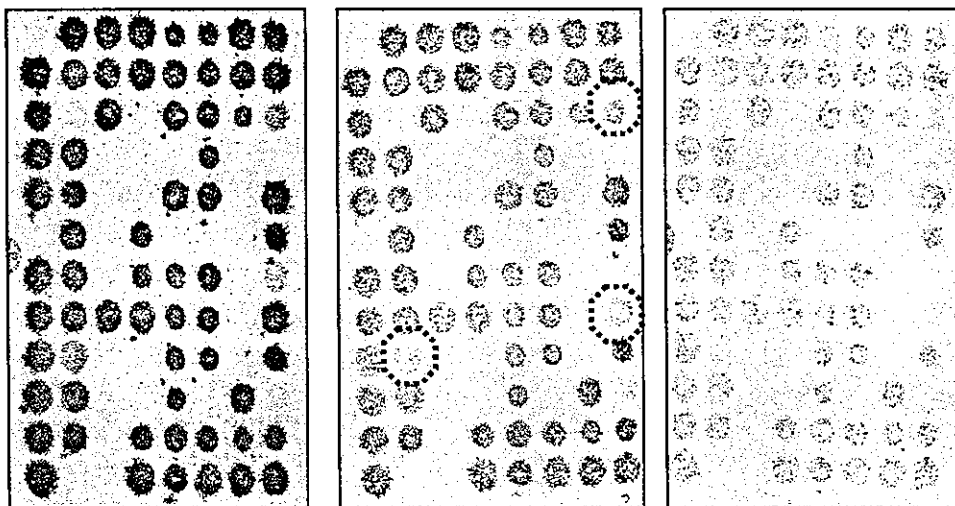
No paraquat

Paraquat 1mM

Paraquat 5mM

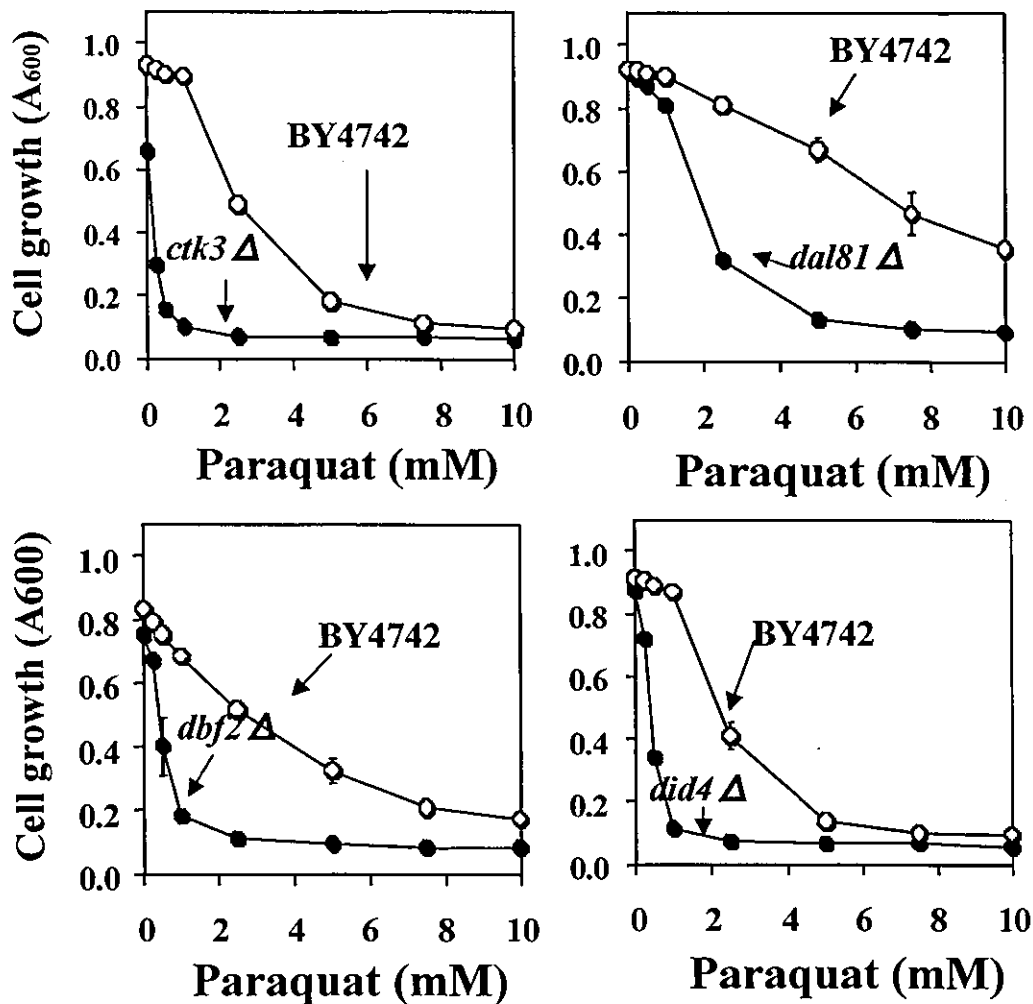


48 h



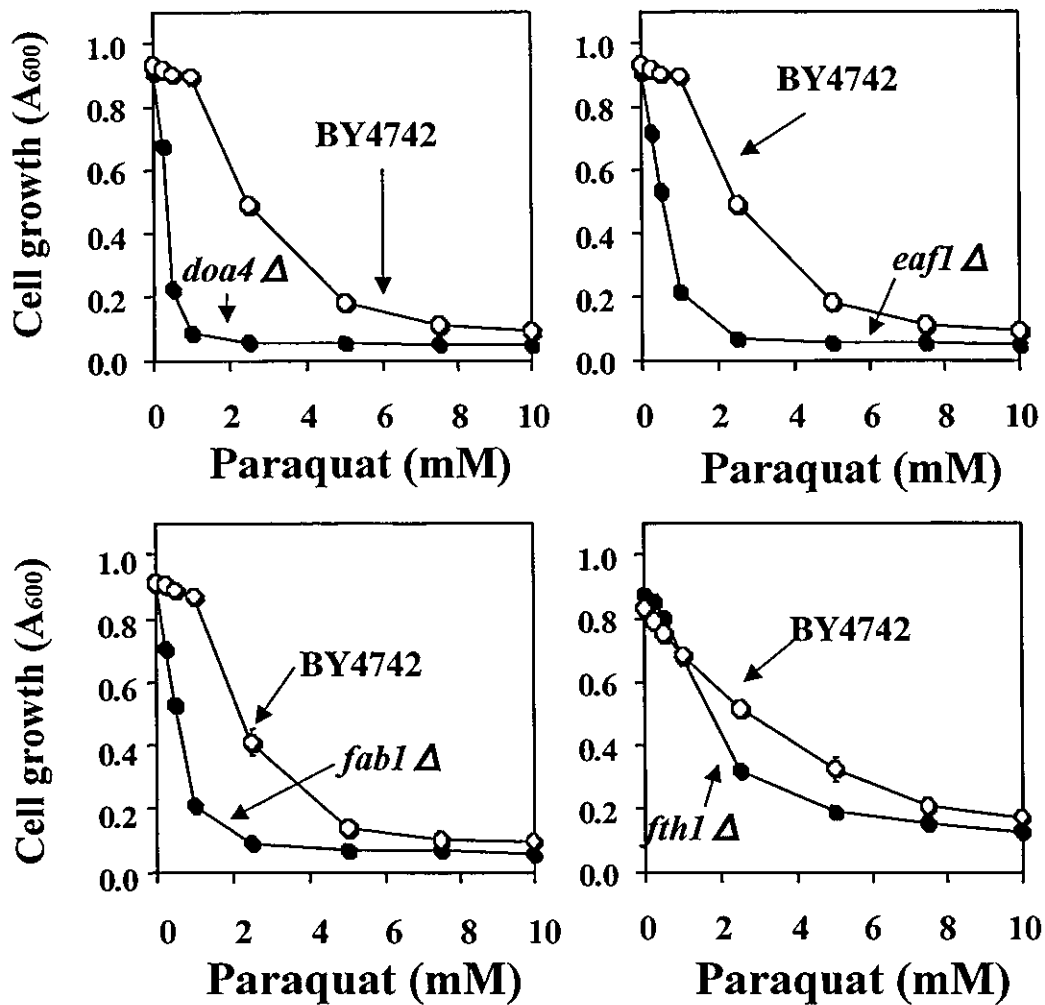
○: Candidate for paraquat-sensitive yeast

Fig.4 Replica prints of yeast



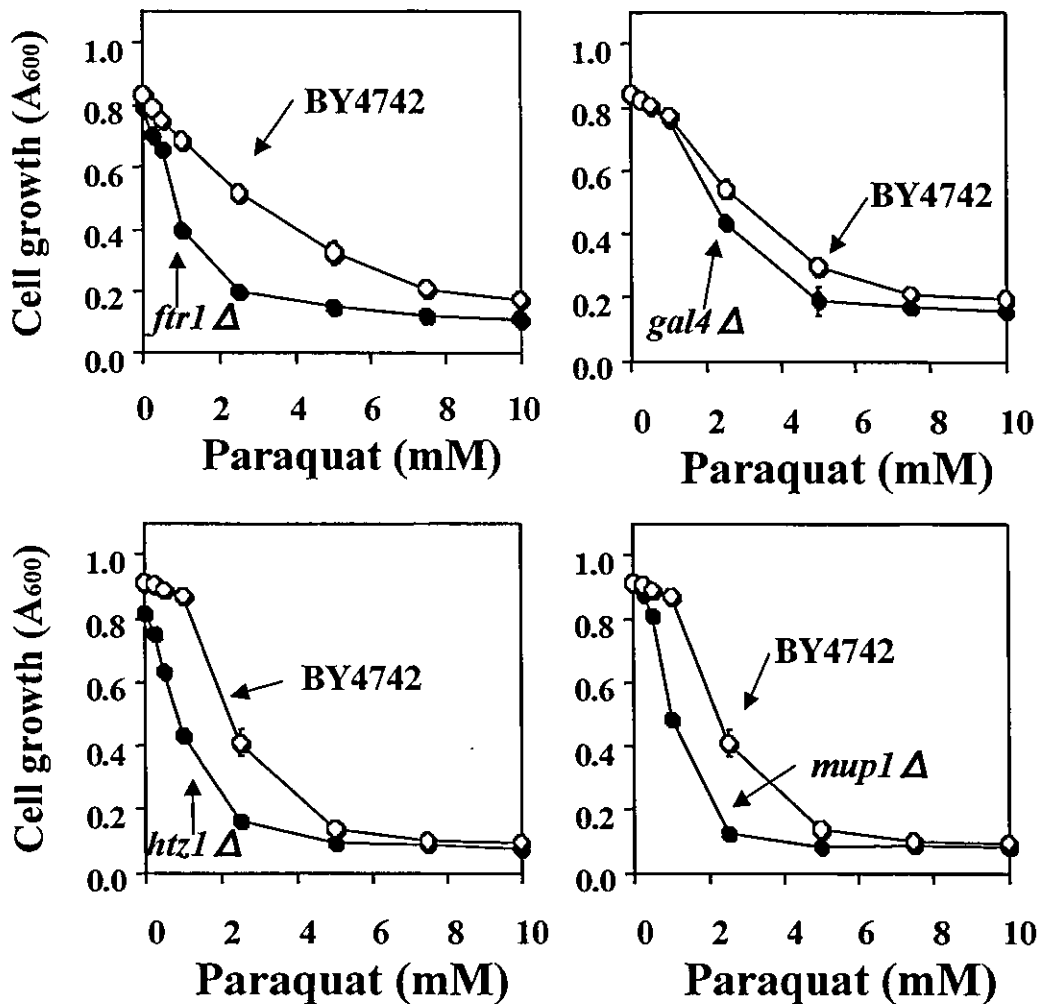
CTK3 : C-terminal domain (RNA-polymerase II CTD) kinase gamma subunit
DAL81 : Transcriptional activator for allantoin, GABA, and urea catabolic genes
DBF2 : Serine/threonine protein kinase
DID4 : Vps factor involved in endosome to vacuole transport, component of ESCRT-III complex

Fig. 5-1 Sensitivity of *CTK3*, *DAL81*, *DBF2* or *DID4* deletion mutant to paraquat



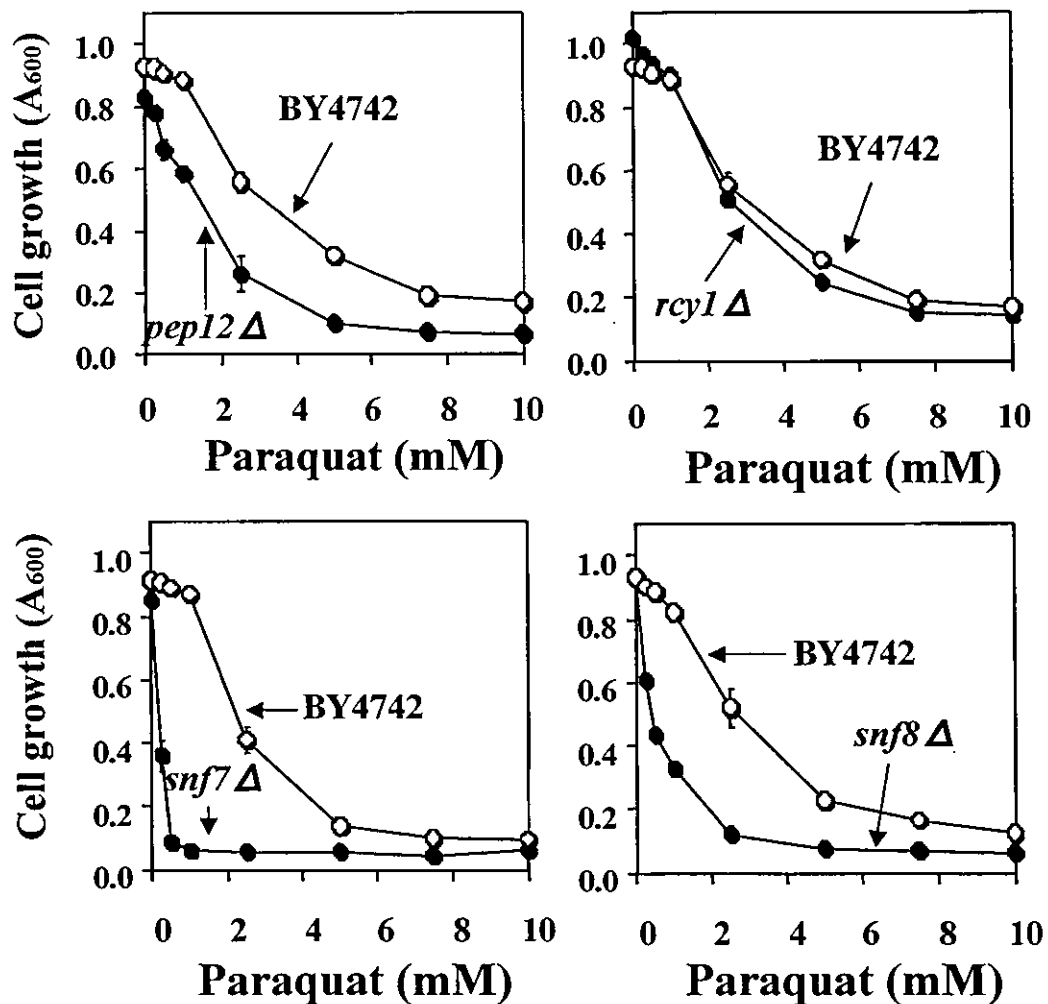
DOA4 : Ubiquitin-specific protease, involved in recycling ubiquitin from the proteasome and the vacuole
EAF1 : unknown function
FAB1 : Phosphatidylinositol-3-phosphate 5-kinase
FTH1 : Vacuolar iron transporter with similarity to Ftr1

Fig. 5-2 Sensitivity of *DOA4*, *EAF1*, *FAB1*, or *FTH1* deletion mutant to paraquat



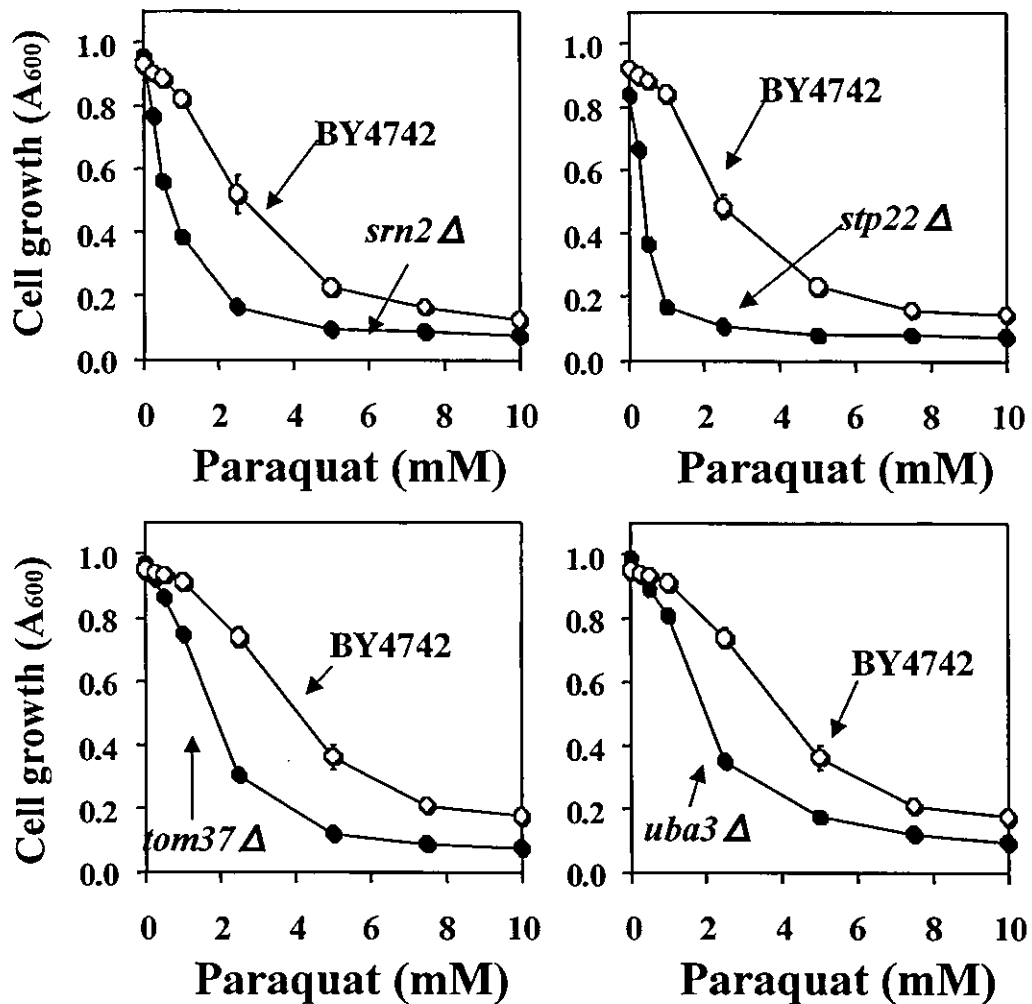
FTR1 : Iron permease that mediates high-affinity iron uptake
GAL4 : Transcription factor involved in expression of galactose-induced genes
HTZ1 : Histone-related protein, involved in silencing, required for GAL gene induction
MUP1 : High-affinity methionine permease

Fig. 5-3 Sensitivity of *FTR1*, *GAL4*, *HTZ1*, or *MUP1* deletion mutant to paraquat



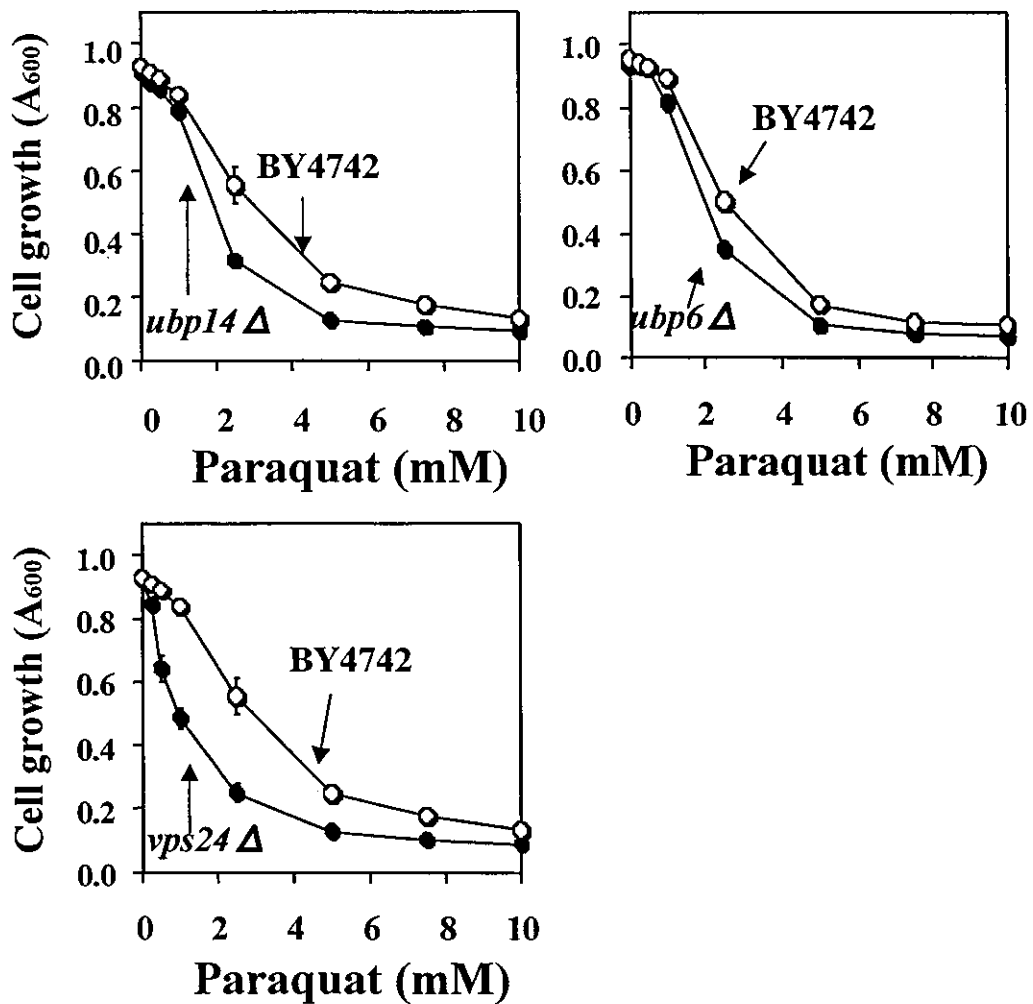
PEP12 : t-SNARE involved in Golgi to vacuole transport
RCY1 : F-box protein involved in endocytic membrane traffic and recycling out of early endosome
SNF7 : Involved in protein sorting in the pre-vacuolar endosome component of the ESCRT-III complex
SNF8 : Class E vacuolar sorting protein, component of the ESCRT-II complex

Fig. 5-4 Sensitivity of *PEP12*, *RCY1*, *SNF7*, or *SNF8* deletion mutant to paraquat



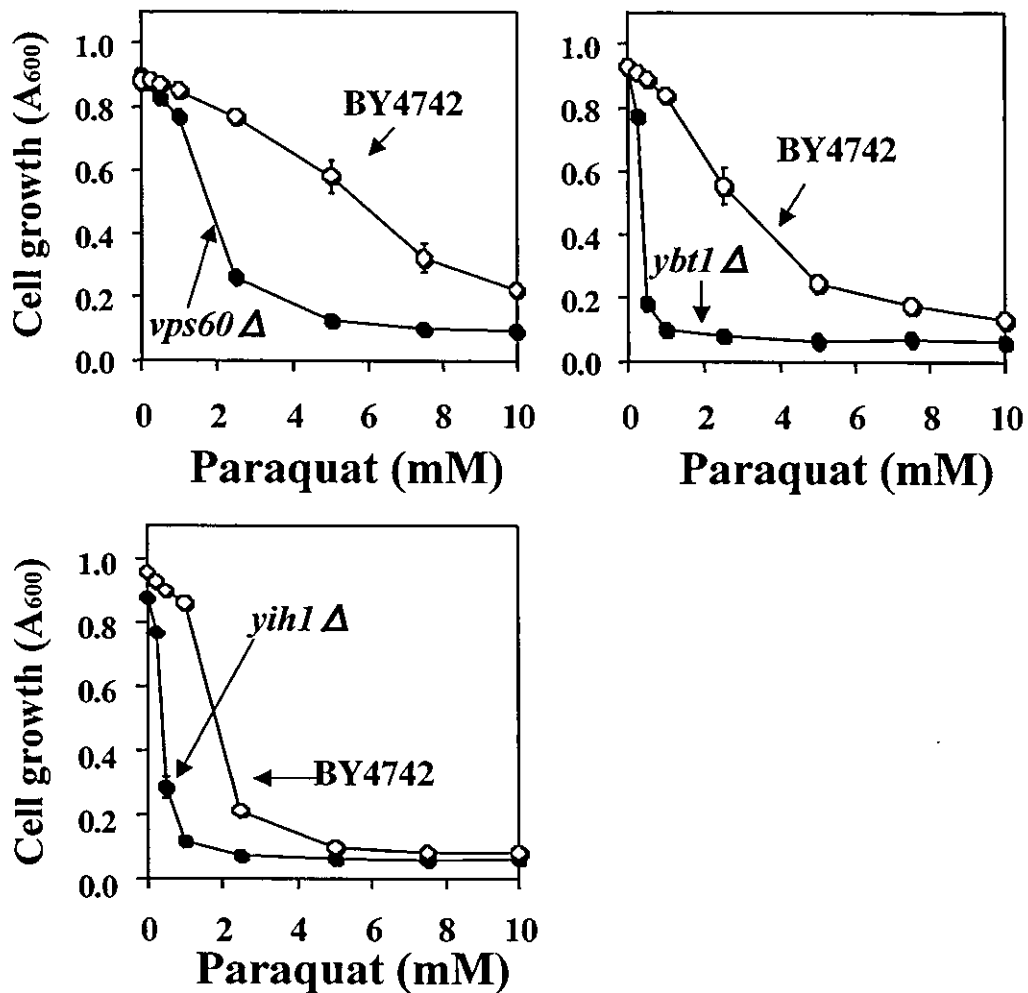
- SRN2*** : Class E vacuolar sorting protein, component of the ESCRT- I complex
- STP22*** : Required for vacuolar targeting of plasma membrane protein, component of ESCRT- I complex
- TOM37*** : Component of the mitochondrial outer membrane receptor (TOM) complex
- UBA3*** : Rub1-activating enzyme, similar to ubiquitin-activating E1-like protein

Fig. 5-5 Sensitivity of *SRN2*, *STP22*, *TOM37* or *UBA3* deletion mutant to paraquat



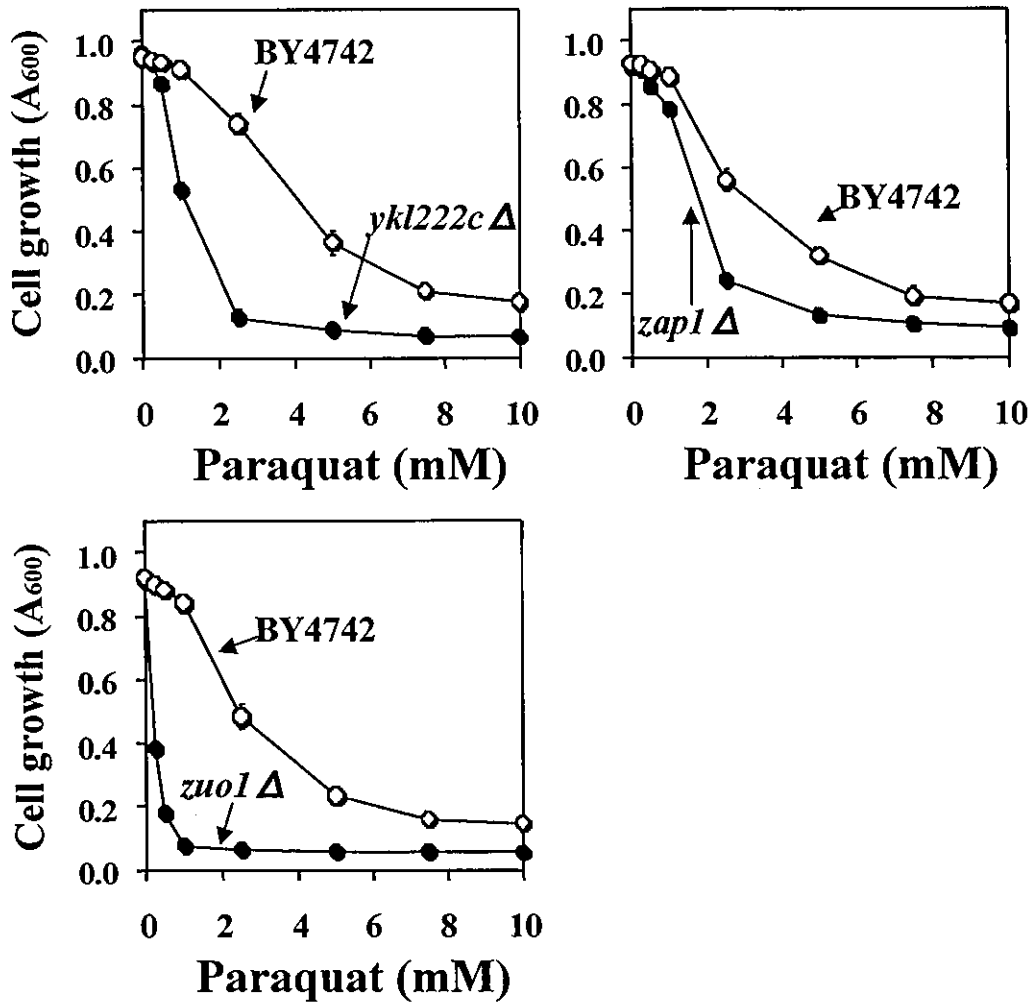
UBP14 : Ubiquitin-specific protease, ubiquitin C-terminal hydrolase
UBP6 : Ubiquitin C-terminal hydrolase associated with the 26S proteasome, involved in ubiquitin turnover
VPS24 : Component of the ESCRT-III complex

Fig. 5-6 Sensitivity of *UBP6*, *UBP14* or *VPS24* deletion mutant to paraquat



VPS60 : Protein with possible role in vacuolar protein sorting, has similarity to Snf7p
YBT1 : Similarity to mammalian ATP-dependent bile acid transporter
YIH1 : Protein with a possible function in general amino acid control response

Fig. 5-7 Sensitivity of *VPS60*, *YBT1* or *YIH1* deletion mutant to paraquat



YKL222c: protein with similarity to transcriptional factors
ZAPI : zinc-responsive transcriptional activator, regulates genes involved in zinc uptake
ZUO1 : zuotin (Z-DNA-binding protein)

Fig. 5-8 Sensitivity of *YKL222c*, *ZAP1* or *ZUO1* deletion mutant to paraquat

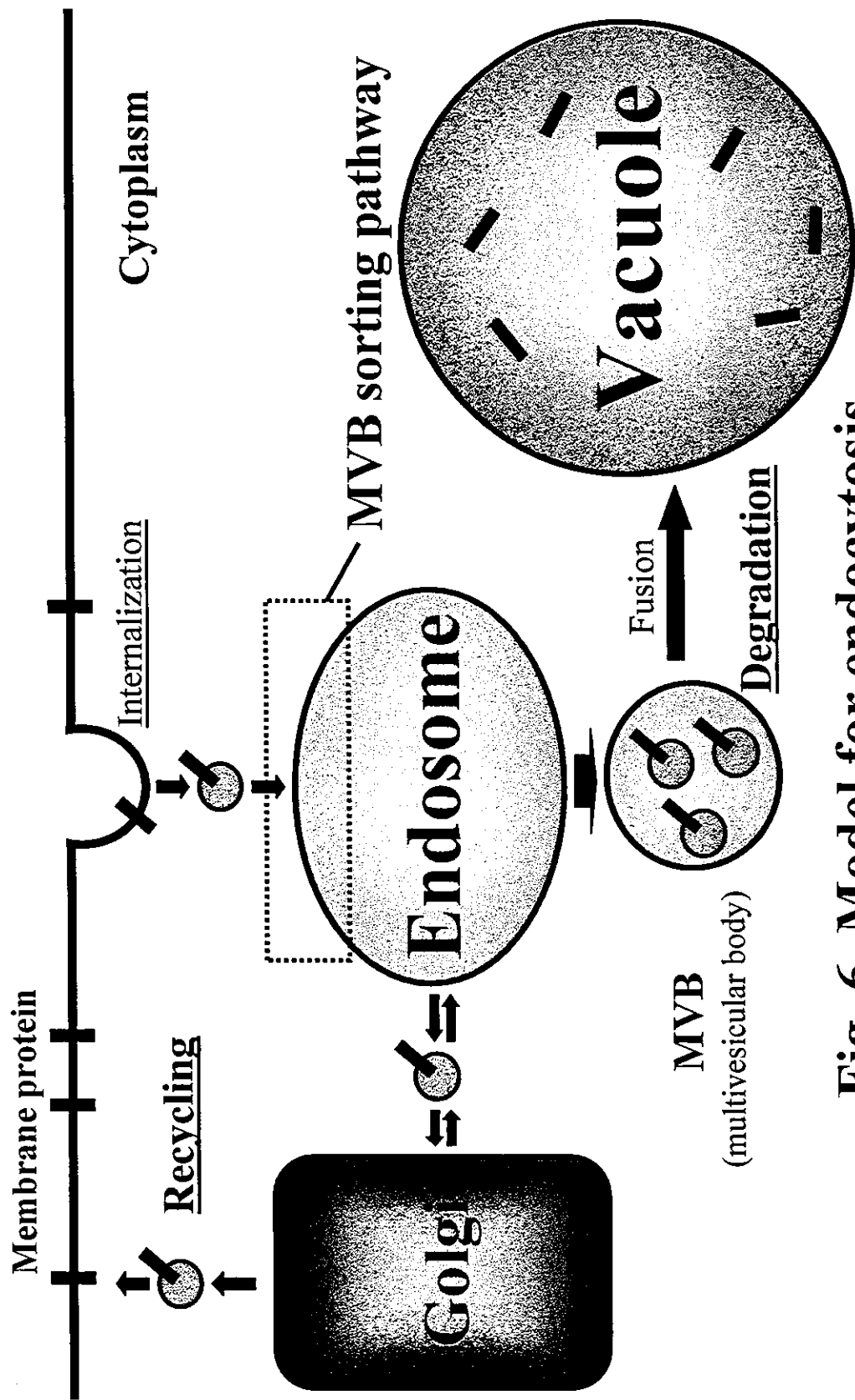


Fig. 6 Model for endocytosis

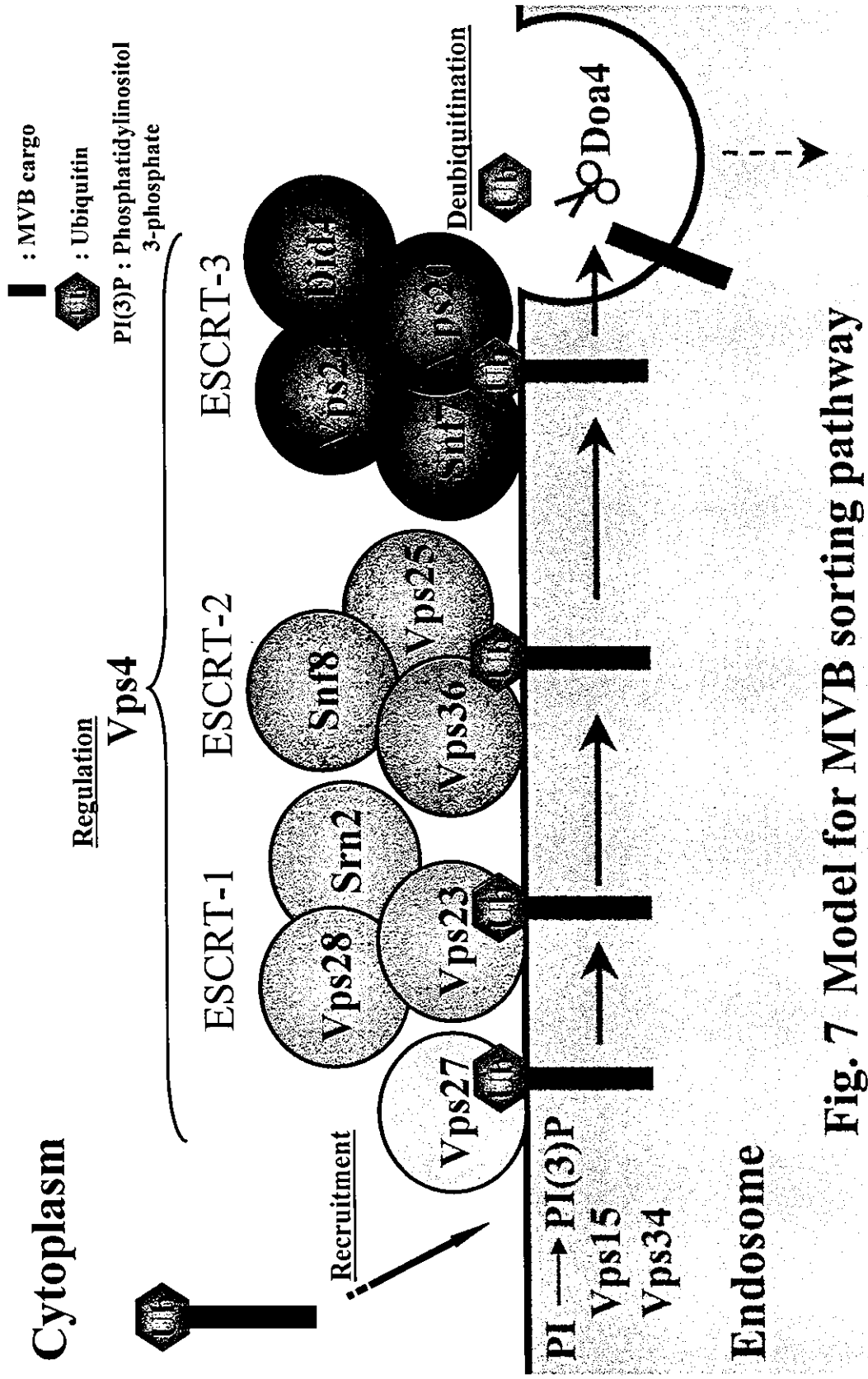


Fig. 7 Model for MVB sorting pathway

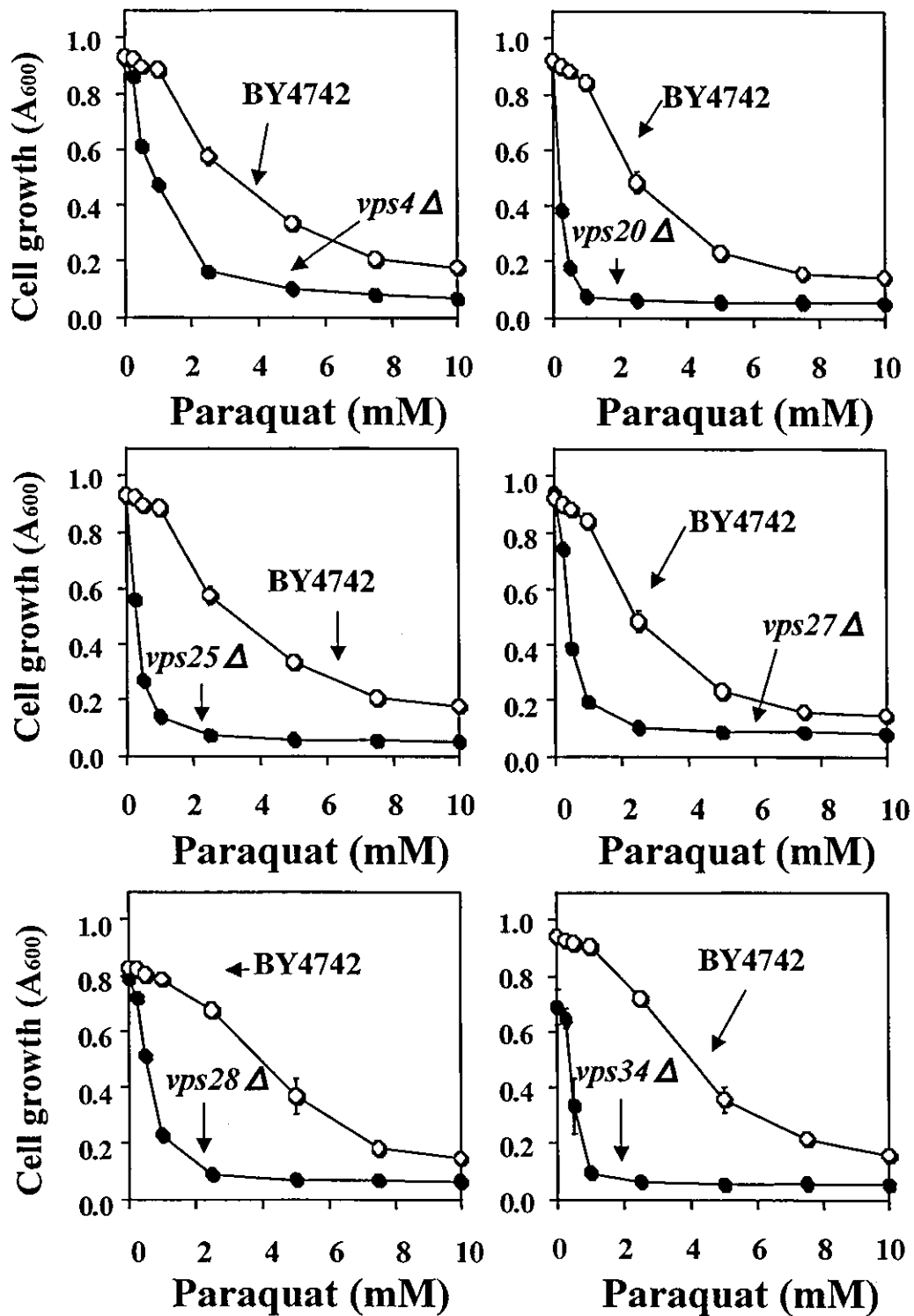


Fig. 8 Sensitivity of *VPS4*, *VPS20*, *VPS25*, *VPS27*, *VPS28* or *VPS34* deletion mutant to paraquat