**Supplemental Table 1. Yeast strains used in this study.**

| Strain | Genotype* | Source |
|---|---|---|
| RSY10 | | [1] |
| RSY1696 | *cnc1::KANMX6* | [2] |
| RSY1701 | *med13::HIS3* | [3] |
| RSY1707 | *mid2::HIS3 mtl1::TRP1 wsc1::KANMX4* | [4] |
| RSY1770 | *grr1Δ::his5*$^{+}$ | [5] |
| RSY1726 | *cdk8Δ::KANMX4* | [3] |
| RSY1949 | *gal83::KANMX4* | This study |
| RSY2080 | *snf1::KANMX4* | This study |
| YPDahl17 | *sak1::KANMX4* | [6] |
| MML1445 | *sip1::natMX4 sip2:: KANMX4* | [7] |
| MSY557 | *sip1::HIS3 sip2:: HIS3 gal83::HIS3* | [8] |
| JGY1 | | [9] |
| JGY4 | *psk1::HIS3 psk2Δ:: KANMX4* | [10] |
| PJ69-4 | *LYS2::GAL1-HIS3 GAL2-ADE2 met2::GAL7-lacZ gal4Δ gal80Δ* | [11] |

Genotype of all strains is *MAT***a** *ade2 ade6 can1-100 his3-11,15 leu2-3,112 trp1-1 ura3-1* except YPDahl17, MML1445, JGY1 and JGY4 which are *MAT***a** *ade2-1 can1-100 his3-11,15 leu2-3,112 trp1-1 ura3-1 and* PJ69-4 which is *MAT***a** *trp1-901 leu2-3,112 ura3-52 his3-200 gal4Δ gal80Δ.*

**Supplemental Table 2. Plasmids used in this study.**

| Plasmid Name | Gene | Epitope Tag | Marker | Promoter | 2µ/ CEN | Reference |
|---|---|---|---|---|---|---|
| pBK38 | *CNC1* | YFP | *URA3* | *ADH1* | CEN | [12] |
| pKC337 | *CNC1* | *CNC1* | *TRP1* | *ADH1* | CEN | [13] |
| pKC801 | *MED13* | 3HA | *URA3* | *TRP1* | CEN | [5] |
| pLR166 | *CNC1*$^{S266A}$ | *CNC1* | *TRP1* | *TRP1* | CEN | [14] |
| pKC803 | *MED13* | 3HA | *LEU2* | *ADH1* | CEN | [5] |
| pKC805 | *MED13*$^{571\text{-}650degΔ}$ | 3HA | *URA3* | *ADH1* | CEN | This study |
| pKC814 | *MED13*$^{742\text{-}844degΔ}$ | 3HA | *URA3* | *ADH1* | CEN | This study |
| pDS8 | *GAL4AD-MED13*$^{571\text{-}906}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | [5] |
| pDS15 | *GAL4AD-MED13*$^{571\text{-}650}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | [5] |
| pDS16 | *GAL4AD-MED13*$^{651\text{-}906}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | [5] |
| pDS32 | *GAL4AD-MED13*$^{742\text{-}844}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | [5] |
| pDS44 | *GAL4AD-MED13*$^{571\text{-}650\ S636}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS51 | *GAL4AD-MED13*$^{571\text{-}650\ S636,\ S634A}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS55 | *GAL4AD-MED13*$^{571\text{-}650\ S587A}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS56 | *GAL4AD-MED13*$^{571\text{-}650\ S58A7,\ S636A,\ S634A}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS45 | *NLS-Med13*$^{1\text{-}306}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS46 | *NLS-Med13*$^{306\text{-}570}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS47 | *NLS-Med13*$^{907\text{-}1420}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS52 | *NLS-Med13*$^{307\text{-}570}$ | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| pDS54 | *GST-Med13*$^{571\text{-}650,S608A}$ | GST | *AMP* | - | - | This study |
| pJG1215 | *HIS*$_6$*-PSK1-KD* | HIS$_6$ | *AMP* | - | - | [10] |
| pUM504 | *CDK8* | 1HA | *TRP* | *GPD* | CEN | [15] |
| pACT2 | *GAL4AD* | 1HA | *LEU2* | *ADH1* | 2*µ* | [16] |
| pAS2 | *GAL4BD* | 1HA | *TRP* | *ADH1* | 2*µ* | [16] |
| pAS2-Grr1 | *GAL4BD-GRR1* | 1HA | *TRP* | *ADH1* | 2*µ* | [17] |
| pAS2-Grr1ΔLΔF | *GAL4BD-GRR1Grr1ΔLΔF* | 1HA | *TRP* | *ADH1* | 2*µ* | [17] |
| pJG1465 | *GAL4AD-MED13*$^{504\text{-}703}$ | 1HA | *TRP* | *ADH1* | 2*µ* | [9] |
| pAS2-Psk1 | *GAL4BD-PSK1* | 1HA | *TRP* | *ADH1* | 2*µ* | [9] |
| JG1193 | Snf1 | 8Myc | *URA3* | *Snf1* | CEN | [18] |
| JG1338 | Snf1$^{K84R}$ | 8Myc | *URA3* | *Snf1* | CEN | [19] |
| | Snf1 | 8Myc | *URA3* | *GAL1-10* | 2*µ* | [19] |
| | Snf1$^{K84R}$ | 8Myc | *URA3* | *GAL1-10* | 2*µ* | [19] |
| pNLS-HA | SV40 NLS | 1HA | *LEU2* | *ADH1* | 2*µ* | This study |
| Mt-Cherry | Mito-targeting | mCherry | *TRP1* | *ADH1* | CEN | This study |
| pRS314 | - | - | *TRP1* | - | CEN | [20] |
| pRS316 | - | - | *URA* | - | CEN | [20] |

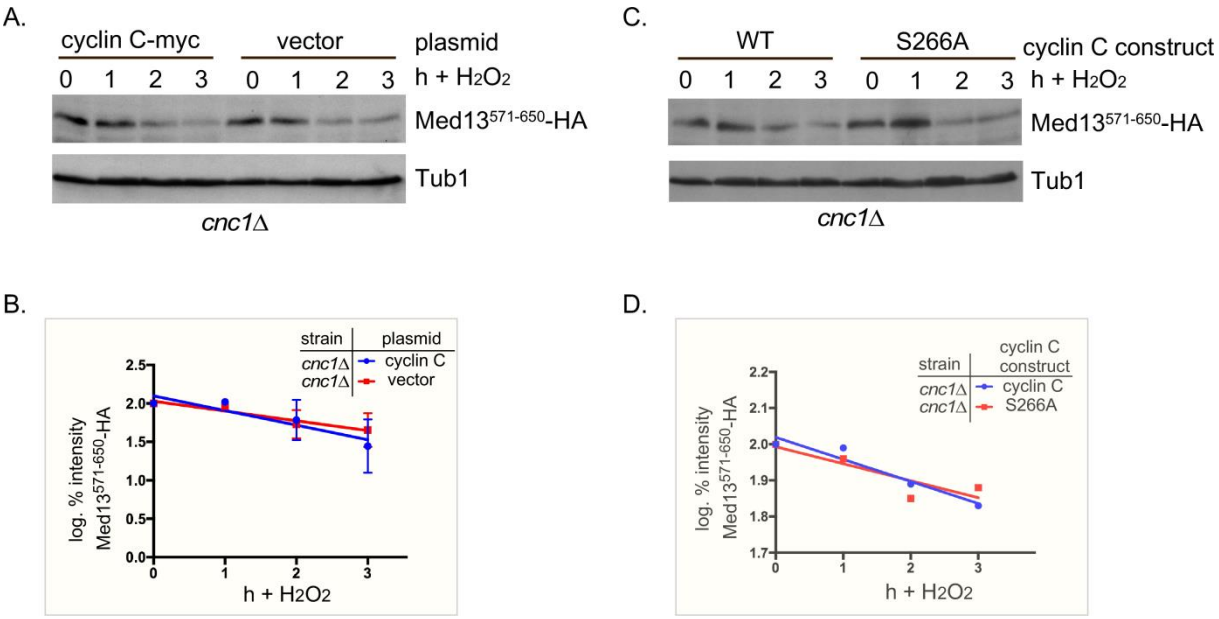


**FIGURE S1: Phosphorylation of cyclin C is not required for degradation of Med13$^{571-650}$.: (A)** *cnc1*Δ cells (RSY1696) harboring degron$^{571-650}$ (pDS15) and either wild-type cyclin C (pKC337) or a vector control (pRS314) were treated with 0.4 mM $H_2O_2$ for the timepoints indicated and Med13$^{571-650}$-HA levels analyzed by Western blot. Tub1 levels were used as loading controls. **(B)** Degradation kinetics of the degron$^{571-650}$ constructs shown in (A). Values represent averages ± SD from a total of at least two Western blots from independent experiments. **(C)** As in (A) except that *cnc1*Δ harboring either wild-type cyclin C (pKC337) or a phospho-mutant (cyclin C S266A, pLR166) was examined. **(D)** Degradation kinetics of results shown in (C).

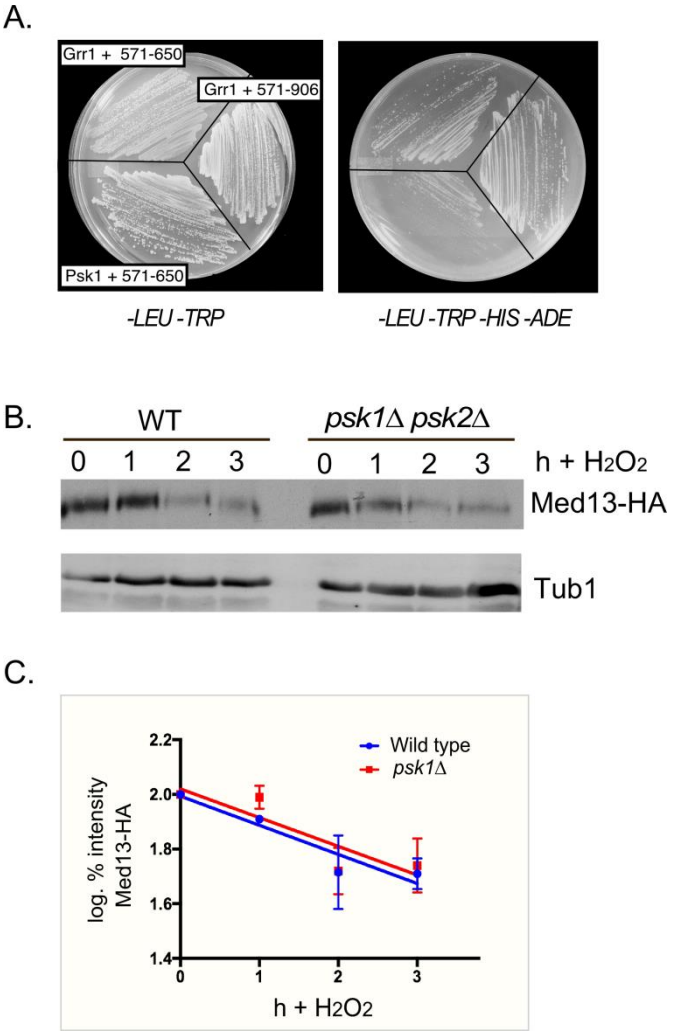


**FIGURE S2: The PAS kinase can associate with Med13 but is not required for its $H_2O_2$ mediated degradation. (A)** Y2H analysis of cells harboring the Med13 construct shown with either Grr1 or Psk1. PJ69-4 cells harboring the Med13-activating domain constructs shown and either pAS-Grr1 or pAS2-Psk1 which has previously been shown to interact with Med13$^{505-703}$ [9]. The cells were grown on *-LEU, -TRP* drop out medium to select for both plasmids (left panel) or *-TRP, -LEU, -HIS –ADE* (right panel) to test for Med13-Grr1 interaction. **(B)** Wild-type (RSY10) and *psk1*Δ *psk2*Δ (JGY4) cells harboring Med13-HA (pKC801) were treated with 0.4 mM $H_2O_2$ for the timepoints indicated and Med13 levels analyzed by Western blot. Tub1 levels were used as loading controls. **(C)** Degradation kinetics of the results shown in (B). Values represent averages ± SD from a total of at least two Western blots from independent experiments.

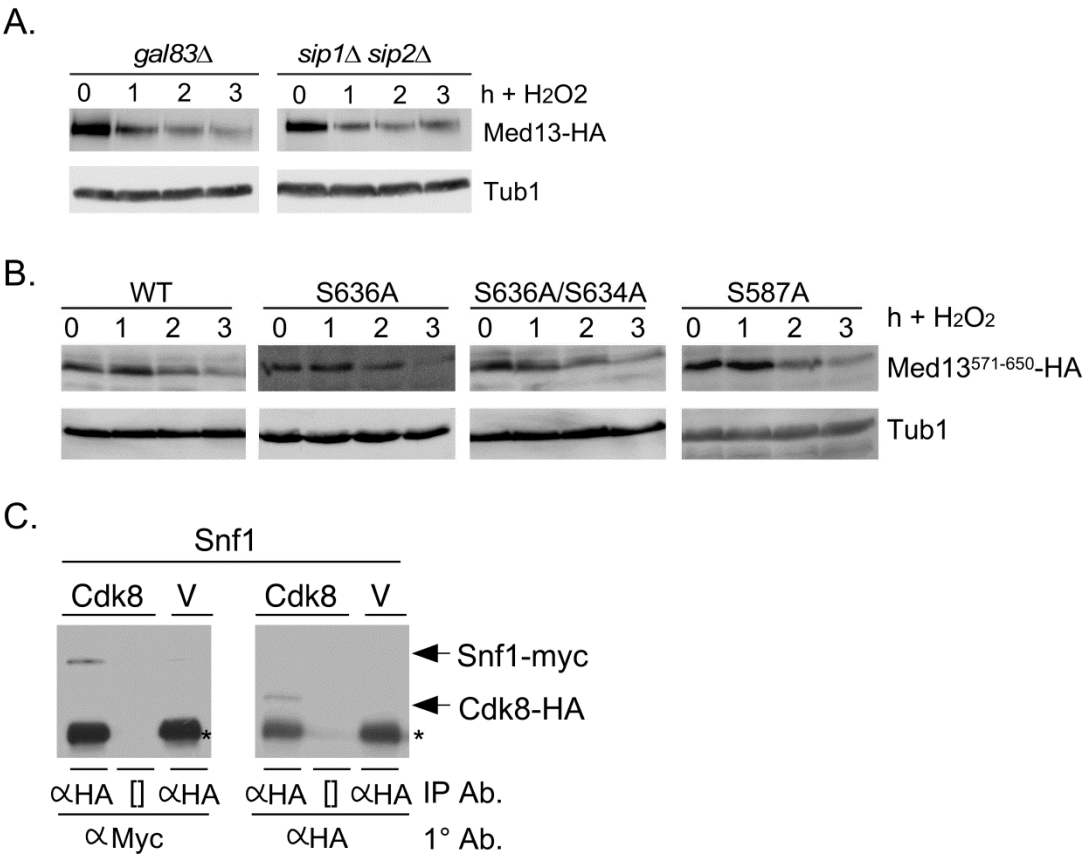


**FIGURE S3**: **(A)** Cells with the genotypes shown harboring Med13-HA (pKC801) were treated with 0.4 mM $H_2O_2$ for the timepoints indicated and Med13 levels analyzed by Western blot. Tub1 levels were used as loading controls. **(B)** Wild-type (RSY10) cells harboring either degron$^{571-650}$ (pDS15) or with the mutations shown were treated with 0.4 mM $H_2O_2$ for the timepoints indicated and analyzed by Western blot. Tub1 levels were used as loading controls. **(C)** Control experiment for the co-immunoprecipitation analysis shown in Fig. 5D showing that cells harboring a vector control are unable to pull down Snf1-myc whereas Cdk8-HA can.

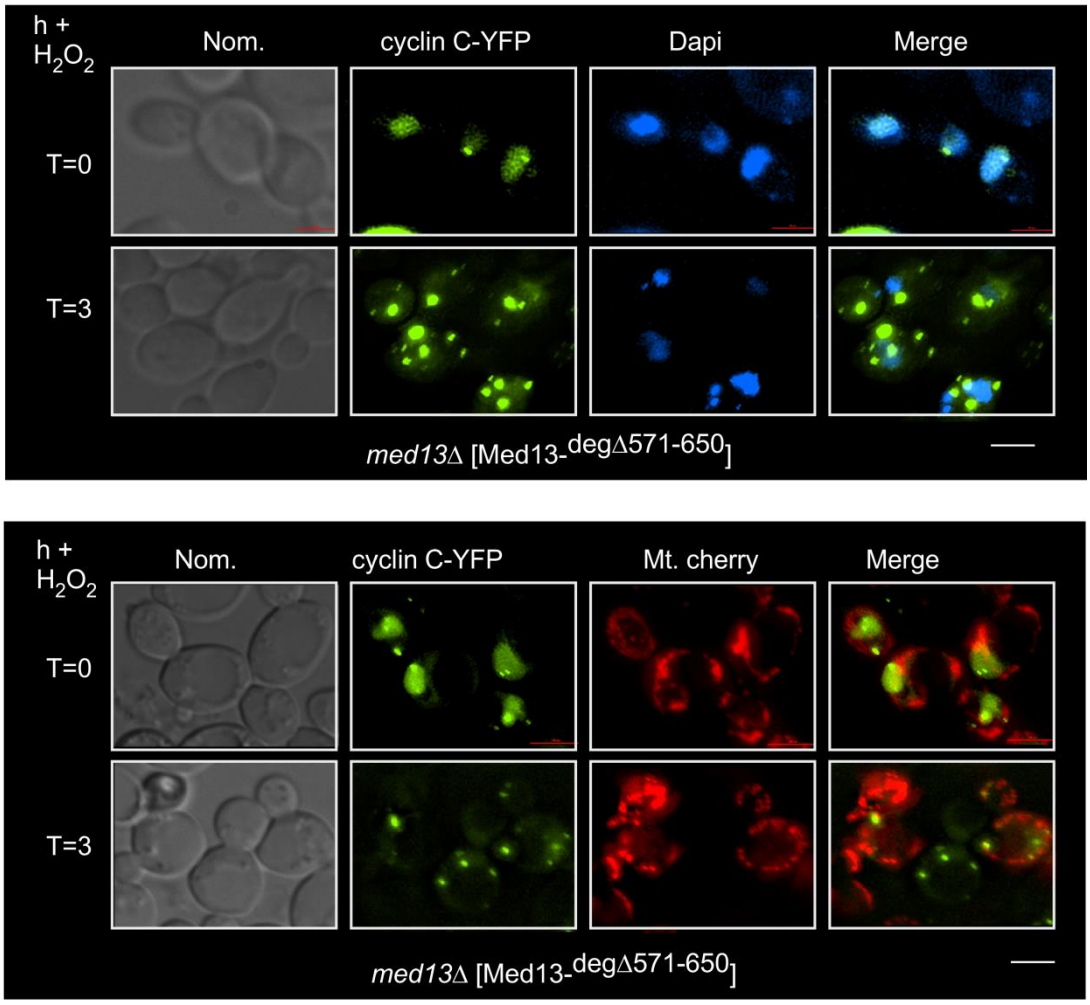


**FIGURE S4**. Upper panel: cyclin C is released from the nucleus following $H_2O_2$ stress in *med13*Δ cells harboring Med13$^{571\text{-}650\text{deg}\Delta\text{-}}$HA (pKC805) as the only source of Med13. Fluorescence microscopy of mid-log phase *med13*Δ harboring pKC805 and cyclin C-YFP (pBK38) were analyzed as shown before and after 0.4 mM $H_2O_2$ stress. Cells were stained with Dapi to visualize the nucleus. Lower Panel: as in upper panel except that the mitochondrial marker mCherry was also expressed. Bar = 13 µM.

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