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**Supplemental information**

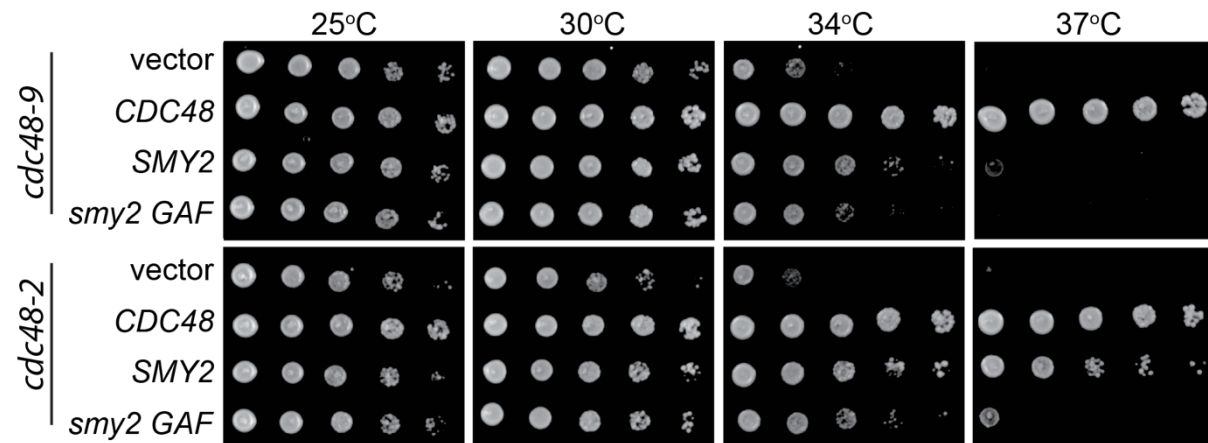
**Yeast Smy2 and its human homologs GIGYF1 and -2**

**regulate Cdc48/VCP function**

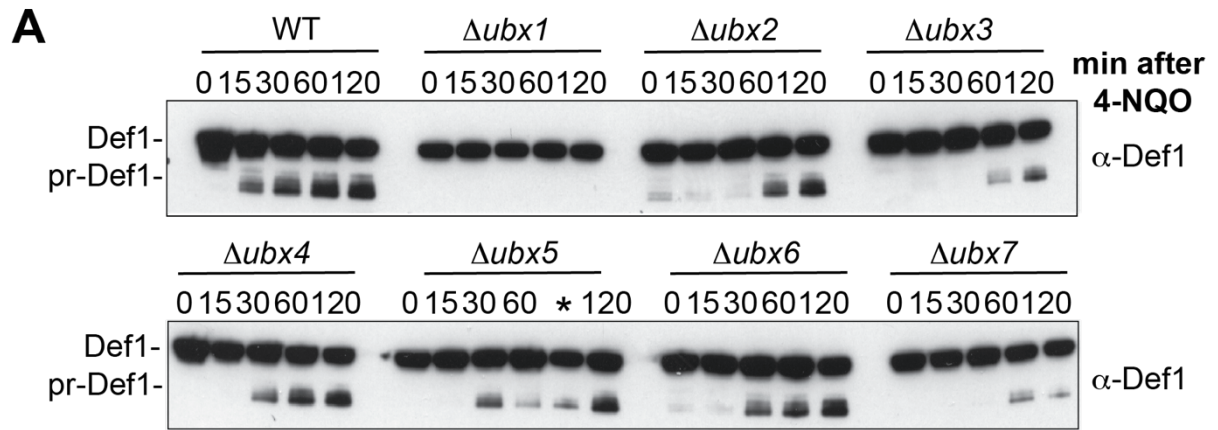
**during transcription stress**

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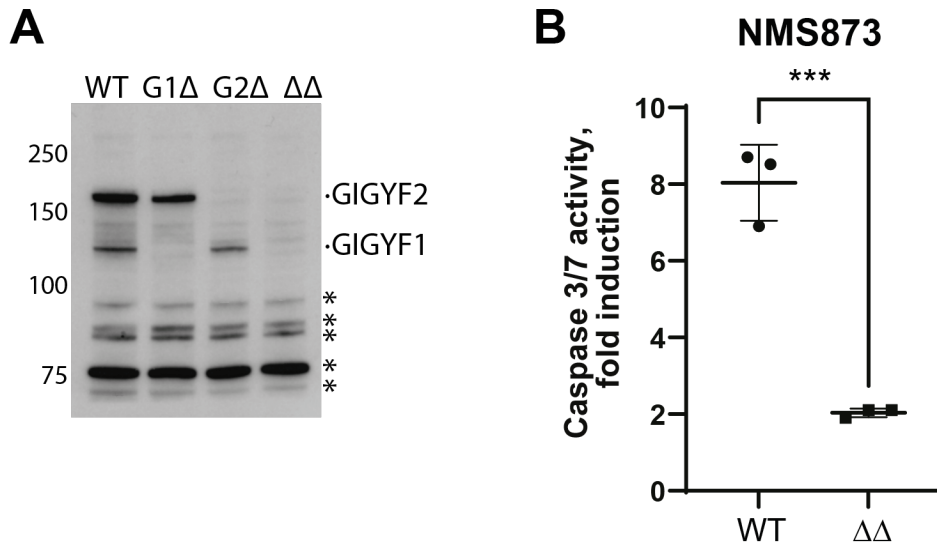
## Supplemental Figures with Legends



**Supplementary Figure S1, related to Figure 2. *SMY2* also affect growth of other *cdc48* mutants.** Dilution series of *cdc48-9* and *cdc48-2* yeast cells (carrying the indicated *SMY2* or *CDC48* plasmids) plated on minimal media and grown at the stated temperatures for 2-4 days.



**Supplementary Figure S2, related to Figure 5. Effects of *UBX* genes and *SMY2*.** A. Western blot analysis of Def1 from extracts of wild type and deletion strains of the seven yeast Ubxs. Logarithmically growing cells were incubated with 4-NQO for the indicated times. \*Denotes a gel loading error. There is variability in Def1 processing assays, but only *ubx1* deletion consistently had a dramatic effect in such experiments.



**Supplementary Figure S3, related to Figures 6 and 7. A *GIGYF1/2* knockout and its effect on p97/VCP inhibitor. A.** Step-wise generation of *GIGYF1* and *GIGYF2* double knockout cells. **B.** The apoptosis-inducing effect of p97/VCP inhibitor NMS873 and the dependence on the GIGYF proteins, 15 hours after adding inhibitor. Only clone C12 tested. Data from 3 biological replicates; data is average of 3 independent wells in each condition in each experiment. \*\*\*P-value <0.001. Results were analysed using GraphPad Prism 9 Software and statistical analysis by the unpaired t-test showed a p-value of 0.0005.

**Supplementary Table S2. Oligonucleotides.** Related to STAR Methods and Key Resources Table.

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
Forward SMY2	CCAATATCTACCGCCAGTGATGC	N/A
Reverse SMY2	GGGTAGACGCATCTTATTACCCGC	N/A
Forward Smy2 deletion	CCTTGAGCTTTTACCTTCCTTCCTCCCCTATATACTC AACTTCTCAGCCCACATCAATATCCGGTTCTGCTGCTAG T	N/A
Reverse Smy2 deletion	GTATATAACAATAACAATAAATGATAAAGAAATATGCAG TGAAAAGAAAAAATTATGAAGCTTTTCCTTCCTCGAGGC CAG AAGAC	N/A
Forward FLAG-Smy2	CGGATCCACTAGTAACGGCCGCAATGGATTACAAGGA TGACGACGATAAGGGCGGAATAGCACCAGACTCGCAA GATT ATTCG	N/A
Reverse FLAG-Smy2	TCCGCCCTTATCGTCGTCATCCTTGTAATCCATTGGCGG CCGTTACTAGTGGATCCGAGCTCG	N/A
Forward Smy2 GAF mutant	CATAGGTGGCGCTTTTGCTTCAACC	N/A
Reverse Smy2 GAF mutant	TACCATTGTGACATCATTG	N/A
Forward GST-Smy2 GYF domain	GCAGGGCTGGCAAGCCACGTTTGGTGG	N/A
Reverse GST-Smy2 GYF domain	GACCGTCTCCGGGAGCTGCATGTGTCAGAGG	N/A
Forward GST-Smy2 GYF domain GAF mutant	GGTCCATTTACTACCCAAATGATGTCACAATGGTACATA GGTGGCGCTTTTGCTTCAACCC	N/A
Reverse GST-Smy2 GYF domain GAF mutant	CCCAATCTTGAAATCTGAAGGGTTGAAGCAAAGCGCC ACCTATGTACCATTGTGACATCATTG	N/A
Forward FLAG-Cdc48 integration	CCACTAGCTAAAAAGTGGAACGATCATTCAAGAGATCC CCGTTATATGCCAGGTATATTTTTATTTAAATCGTAA ATT CAAGTC	N/A
Reverse FLAG-Cdc48 integration	GACTTGAATTTACGATTTAAAATAAAAATATACCTGGCA TATAACCGGGGATCTCTTGAATGATCGTTCCACTTTTTA GC TAGTGG	N/A
Forward Cdc48	CTGGCAAGCTTGAAGTAAAAGGACAATCAGCACGCCTT CC	N/A
Reverse Cdc48	CGGATCTCGAGCCAATAACATTAGCGACAAGTTTTCTCC GCG	N/A
Forward Pre1-myc	GGGCGTCATTGTTAAAATCGTGGATAAAGATGGCATAA GACAAGTAGATGACTTCCAGGCACAGTCCGGTTCTGCT GCTA GT	N/A
Reverse Pre1-myc	GGAAGATAATTACTTTAGTATATCATTAGCAATCACCTT TTCCGTGTGATTACACTGAATATCTTTCACCTCGAGGCC AG AAGAC	N/A

Forward FLAG-Spt23	GATTATAAAGATGACGATGACAAGATGATGAGTGGCAC AGGAAAC	N/A
Reverse FLAG-Spt23	CTTGTCATCGTCATCTTTATAATCCTTATCGTCGTCATCC TTG	N/A
GIGYF1 gRNA	TGACTACCGTTATGGGCGAG	N/A
Forward GIGYF1	ACTCGAGCTTCCCATCTCCT	N/A
Reverse GIGYF1	CCGAAATAAGCACCCCCAGA	N/A
GIGYF1 Sequencing	GGCGGGAGTGAGGACCCAGGC	N/A
GIGYF2 gRNA	ATTTCTGCCTATCCTCCAGG	N/A
Forward GIGYF2	TCACTTGAGAAGCTGGGGAGT	N/A
Reverse GIGYF2	AGGATGGTTCCCAATGTCCTT	N/A
GIGYF2 Sequencing	CTGGGGAGTATTGACTGGGGT3	N/A