**Table S1. DNA oligoes used for PCR in this study**

| Name | Sequence (5'-3') | Used for |
|---|---|---|
| 1-3F | gggg-ccgcgg (*Sac*II)-AGGTATTCGTTTGTTTACTA (nt -600 of *FLO11*) | *FLO11* promoter dissection |
| 1-3R | atat-cccggg (*Xma*I)-AGTGTGCGTATATGGATTTT (nt -1 of *FLO11*) | *FLO11* promoter dissection |
| 6F | gggg-ccgcgg (*Sac*II)-AATTAAGGTTTTTTTCTTC (nt -1200 of *FLO11*) | *FLO11* promoter dissection |
| 6R | aagtaaatattagtaaacaaacgaatacct (nt -571 of *FLO11*)-GTCCATTCTTAGCCCCAAAG (nt -1001 of *FLO11*) | *FLO11* promoter dissection |
| 9-10F | gggg-ccgcgg (*Sac*II)-ATTCTCATCGAGAGCCGAGC (nt -2000 of *FLO11)* | *FLO11* promoter dissection |
| 9-10R1 | aagtaaatattagtaaacaaacgaatacct (nt -571 of *FLO11*)–GATTAGCGCATTCACATTCG (nt -1601 of *FLO11*) | *FLO11* promoter dissection |
| 9-10R2 | ttaagaaaacagaagaaaaaaaccttaatt (nt -1171 of *FLO11*)–GATTAGCGCATTCACATTCG (nt -1601 of *FLO11*) | *FLO11* promoter dissection |
| ADH2-F | CGTTCCAGTCAGGAATGTTCCACGTG (nt -800 of *ADH2*) | *ADH2* promoter cloning |
| ADH2-R | TGTGTATTACGATATAGTTAATAGTTG (nt -1 of *ADH2*) | *ADH2* promoter cloning |
| ADH2S-F | gggg-ccgcgg (*Sac*II)-CGTTCCAGTCAGGAATGTTC (nt -800 of *ADH2*) | For $P_{ADH2}$-*URA3* reporter |
| ADH2X-R | ccat-cccggg (*Xma*I)-TGTGTATTACGATATAGTTA (nt -1 of *ADH2*) | For $P_{ADH2}$-*URA3* |
| Flo11ex-F | GAAAGCTGTGCGGGAAAAC (nt -1650 of *FLO11*) | Replacing *FLO11* ORF |
| Flo11ex-R | GTATTTTCGTTGTAACCGTAT (nt 350 of *FLO11*) | Replacing *FLO11* |
| FLO11-F | cccc-gaattc (*Eco*rI)-AGTCTTCGTTTCCTATCTCCACATACC (nt -3000 of *FLO11*) | *FLO11* promoter amplification |
| FLo11-R | atat-ccgcgg (*Sac*II)-AGTGTGCGTATATGGATTTTTGAGGCC (nt -1 of *FLO11*) | *FLO11* promoter amplification |
| FLO11S-F | gggg-ccgcgg (*Sac*II)-AGTCTTCGTTTCCTATCTCC (nt -3000 of *FLO11*) | *FLO11* promoter dissection |
| Flo11ura3-R | gtattttcgttgtaaccgtatagttggacggtacctttggaccagtgac (nt 350 of *FLO11*)-TAATAACTGATATAATTAAATTG (nt 879 of *URA3*) | Replacing *FLO11* ORF |
| FLO8F | gcg-tctaga (*Xba*I)-ATGAGTTATAAAGTGAATAGT ( nt 1 of *FLO8*) | PCR-amplifying *FLO8* |
| FLO8R | ccc-cccggg (*Xma*I)-A-GCCTTCCCAATTAATAAAAT(nt 2397 of *FLO8*) | PCR-amplifying *FLO8* |
| HO-F | CATTTTTGTTTCTTTTGGACAAATGTTG (nt -2000 of *HO*) | *HO* promoter amplification |
| HO-R | TTTAAAGTATAGATAGAATTGATTGCTG (nt -1 of *HO*) | *HO* promoter amplification |
| HOS-F | gggg-ccgcgg (*Sac*II)-CATTTTTGTTTCTTTTGGAC (nt -2000 of *HO*) | For $P_{HO}$-*URA3* reporter |
| HOX-R | ccat-cccggg (*Xma*I)-TTTAAAGTATAGATAGAATT (nt -1 of *HO*) | For $P_{HO}$-*URA3* reporter |
| mCherry-F | acga-cccggg (*Xma*I)-GACTAGAGGTGAGCAAGGGC | mCherry amlification |
| mCherry-R | cgcg-ctcgag (*Xho*I)–CTACTTGTACAGCTCGTC | mCherry amlification |
| URA3-F | ATGTCGAAAGCTACATATAAGG (nt 1 of *URA3*) | *URA3* ORF amplification |
| URA3-R | TTAGTTTTGCTGGCCGCATCTTC (nt 804 of *URA3*) | *URA3* ORF amplification |

**Note:** Primers for DNA sequencing are not listed. Capital bases match the template. The lower-case bases are attached sequences with restriction sites underlined. Starting positions (from 5') are indicated in the brackets behind each homologous sequence, with the upstream positions as "-" and the downstream as "+' taking the base A of the start code as 1. In the primer names, "F" and "R" mean forward and reverse, respectively.

**Table S2. Plasmids used in this study**

| Name | Marker | Replicon | Promoter | Used for | Source |
|---|---|---|---|---|---|
| *p2HGhsp104* | *HIS3* | *2 micron* | *GPD* | overexpression of Hsp104 | (Li & Lindquist, 2000) |
| *p413GAL1* | *HIS3* | *CEN6/ARSH4* | *GAL1* | empty vector | ATCC |
| *p413GAL1-NQYFP* | *HIS3* | *CEN6/ARSH4* | *GAL1* | expression of Swi1 NQ-YFP | this study |
| *p413GAL1-NYFP* | *HIS3* | *CEN6/ARSH4* | *GAL1* | expression of Swi1 N-YFP | this study |
| *p413TEF* | *HIS3* | *CEN6/ARSH4* | *TEF1* | empty vector | ATCC |
| *p413TEF-NmCherry* | *HIS3* | *CEN6/ARSH4* | *TEF1* | expression of Swi1 N-mCherry | this study |
| *p413TEF-NQmCherry* | *HIS3* | *CEN6/ARSH4* | *TEF1* | Swi1 NQ-mCherry expression | this study |
| *p413TEF-NQYFP* | *HIS3* | *CEN6/ARSH4* | *TEF1* | expression of Swi1 NQ-YFP | this study |
| *p413TEF-NYFP* | *HIS3* | *CEN6/ARSH4* | *TEF1* | expression of Swi1 N-YFP | this study |
| *p415ADH2-URA3* | *LEU2* | *CEN6/ARSH4* | *ADH2* | expression of Ura3 | this study |
| *p415F1369-URA3* | *LEU2* | *CEN6/ARSH4* | *F1369* | expression of Ura3 | this study |
| *p415F136-URA3* | *LEU2* | *CEN6/ARSH4* | *F136* | expression of Ura3 | this study |
| *p415F139-URA3* | *LEU2* | *CEN6/ARSH4* | *F139* | expression of Ura3 | this study |
| *p415F13-URA3* | *LEU2* | *CEN6/ARSH4* | *F13* | expression of Ura3 | this study |
| *p415F16-URA3* | *LEU2* | *CEN6/ARSH4* | *F16* | expression of Ura3 | this study |
| *p415F19-URA3* | *LEU2* | *CEN6/ARSH4* | *F19* | expression of Ura3 | (Du *et al.*, 2015) |
| *p415FLO11-URA3* | *LEU2* | *CEN6/ARSH4* | *FLO11* | expression of Ura3 | this study |
| *p415HO-URA3* | *LEU2* | *CEN6/ARSH4* | *HO* | expression of Ura3 | this study |
| *p415SL* | *LEU2* | *CEN6/ARSH4* | *SUC2-LEU2* | empty vector | (Du *et al.*, 2015) |
| *p415SL-URA3* | *LEU2* | *CEN6/ARSH4* | *SUC2-LEU2* | expression of Ura3 | (Du *et al.*, 2015) |
| *p415TEF* | *LEU2* | *CEN6/ARSH4* | *TEF1* | empty vector | ATCC |
| *p415TEF-NQYFP* | *LEU2* | *CEN6/ARSH4* | *TEF1* | expression of Swi1 NQ-YFP | (Du *et al.*, 2010) |
| *p416TEF-NQYFP* | *URA3* | *CEN6/ARSH4* | *TEF1* | expression of Swi1 NQ-YFP | (Du *et al.*, 2010) |
| *p416TEF-NYFP* | *URA3* | *CEN6/ARSH4* | *TEF1* | expression of Swi1 N-YFP | (Du *et al.*, 2010) |
| *p416TEF-SWI1YFP* | *URA3* | *CEN6/ARSH4* | *TEF1* | expression of Swi1-YFP | (Du *et al.*, 2008) |
| *p423GAL1* | *HIS3* | *2 micron* | *GAL1* | empty vector | ATCC |
| *p423GAL1-NmCherry* | *HIS3* | *2 micron* | *GAL1* | expression of Swi1 N-mCherry | this study |
| *p423GAL1-NQmCherry* | *HIS3* | *2 micron* | *GAL1* | Swi1 NQ-mCherry expression | this study |
| *p423GAL1-NQYFP* | *HIS3* | *2 micron* | *GAL1* | expression of Swi1 NQ-YFP | this study |
| *p423GAL1-NYFP* | *HIS3* | *2 micron* | *GAL1* | expression of Swi1 N-YFP | this study |
| *p423GPD* | *HIS3* | *2 micron* | *GPD* | empty vector | ATCC |
| *p423GPD-NYFP* | *HIS3* | *2 micron* | *GPD* | overexpression of Swi1 N-YFP | this study |
| *p423GPDSSE1* | *HIS3* | *2 micron* | *GPD* | overexpression of Sse1 | Morano K lab |
| *p425GPD* | *LEU2* | *2 micron* | *GPD* | empty vector | ATCC |
| *p425GPD-HSP104* | *LEU2* | *2 micron* | *GPD* | overexpression of Hsp104 | (Park *et al.*, 2006) |
| *p425GPD-NQYFP* | *LEU2* | *2 micron* | *GPD* | Swi1 NQ-YFP overexpression | this study |
| *p425GPD-NYFP* | *LEU2* | *2 micron* | *GPD* | overexpression of Swi1 N-YFP | this study |
| *p425GPD-SSE1* | *LEU2* | *2 micron* | *GPD* | overexpression of Sse1 | this study |
| *p425GPD-SWI1YFP* | *LEU2* | *2 micron* | *GPD* | overexpression of Swi1-YFP | this study |
| *p426GAL1-NQYFP* | *URA3* | *2 micron* | *GAL1* | Swi1 NQ-YFP overexpression | (Du *et al.*, 2015) |
| *p426GPDSSE1* | *URA3* | *2 micron* | *GPD* | overexpression of Sse1 | Morano K lab |
| *p426GPD-SWI1* | *URA3* | *2 micron* | *GPD* | overexpression of Swi1 | (Du *et al.*, 2008) |
| *pCUP1-NMGFP* | *URA3* | *CEN6/ARSH4* | *CUP1* | expressing Sup35 NM-GFP | (Park *et al.*, 2006) |
| *pCUP1-RNQ1GFP* | *URA3* | *CEN6/ARSH4* | *CUP1* | expression of Rnq1-GFP | (Sondheimer & Lindquist, 2000) |
| *pRS303-FLO8* | *HIS3* | | *FLO8* | expression of Flo8 | (Du *et al.*, 2015) |
| *pRS313-FLO8* | *HIS3* | *CEN6/ARSH4* | *FLO8* | expression of Flo8 | (Du *et al.*, 2015) |
| *pRS316CUP1-NMCFP* | *URA3* | *CEN6/ARSH4* | *CUP1* | expression of Sup35 NM-CFP | (Du & Li, 2014) |
| *pRS413CUP1-NMGFP* | *HIS3* | *CEN6/ARSH4* | *CUP1* | expressing Sup35 NM-GFP | Lindquist lab |

**Note:** all the listed plasmids contain an amplicilin resistant gene ($AMP^R$) for selection in *E. coli*

**Table S3. Yeast strains used in this study**

| Name | Background | Description | Source |
|---|---|---|---|
| LY422 | 74D-694 | *MATa ade1-14 trp1-289 his3-200 ura3-52 leu2-3, 112* | (Chernoff *et al.*, 1995) |
| LY421 | 74D-694 | *MATa ade1-14 trp1-289 his3-200 ura3-52 leu2-3, 112 [PIN$^+$]* | (Chernoff *et al.*, 1995) |
| LY420 | 74D-694 | *MATa ade1-14 trp1-289 his3-200 ura3-52 leu2-3, 112 [PSI$^+$][PIN$^+$]* | (Chernoff *et al.*, 1995) |
| DY902 | 74D-694 | *MATa ade1-14 trp1-289::TRP1::P$_{TEF1}$-RNQ1CFP his3-200 ura3-52 leu2-3, 112 [SWI$^+$]* | (Crow *et al.*, 2011) |
| DY362 | 74D-694 | *MATa ade1-14 trp1-289 his3-200 ura3-52 leu2-3, 112 [PSI$^+$]* | (Du & Li, 2014) |
| LY722 | 74D-694 | *MATa ade1-14 trp1-289 his3-200 ura3-52 leu2-3, 112 [SWI$^+$]* | (Du & Li, 2014) |
| DY587 | 74D-694 | *MATa ade1-14 trp1-289 his3-200 ura3-52 leu2-3, 112 [SWI$^+$][PSI$^+$]* | (Du & Li, 2014) |
| LY746 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8 [PIN$^+$]* | ATCC |
| DY902 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8* | this study |
| LY720 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8 swi1Δ::KanMX4* | (Du *et al.*, 2008) |
| LY742 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8 [SWI$^+$]* | (Du *et al.*, 2008) |
| DY767 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8 flo11Δ::P$_{F139}$-URA3* | this study |
| LY740 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8 flo11Δ::P$_{F139}$-URA3 [SWI$^+$]* | this study |
| LY741 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 [SWI$^+$]* | (Du *et al.*, 2015) |
| DY759 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 flo11Δ::P$_{F139}$-URA3* | this study |
| LY744 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 flo11Δ::P$_{F139}$-URA3 [SWI$^+$]* | this study |
| LY737 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 flo11Δ::P$_{FLO11}$-URA3 [SWI$^+$]* | (Du *et al.*, 2015) |
| DY758 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 flo11Δ::P$_{FLO11}$-URA3* | (Du *et al.*, 2015) |
| DY755 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 flo1Δ::P$_{FLO1}$-URA3* | (Du *et al.*, 2015) |
| LY735 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 flo1Δ::P$_{FLO1}$-URA3 [SWI$^+$]* | (Du *et al.*, 2015) |
| DY761 | BY4741 | *MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 flo8::FLO8::HIS3 swi1Δ::KanMX4* | (Du *et al.*, 2015) |
| LY278 | CY396 | *MATalpha swi12::HIS3::SWI2-HA-6xhis::URA3 HO-lacZ* | Lindquist Lab |

**Reference**


Chernoff, Y.O., S.L. Lindquist, B. Ono, S.G. Inge-Vechtomov & S.W. Liebman, (1995) Role of the chaperone protein Hsp104 in propagation of the yeast prion-like factor [*PSI*$^+$]. *Science* **268**: 880-884.

Crow, E.T., Z. Du & L. Li, (2011) A small, glutamine-free domain propagates the [SWI+] prion in budding yeast. *Molecular and cellular biology*.

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Li, L. & S. Lindquist, (2000) Creating a protein-based element of inheritance. *Science* **287**: 661-664.

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Sondheimer, N. & S. Lindquist, (2000) Rnq1: an epigenetic modifier of protein function in yeast. *Molecular cell* **5**: 163-172.

**Figure S1**

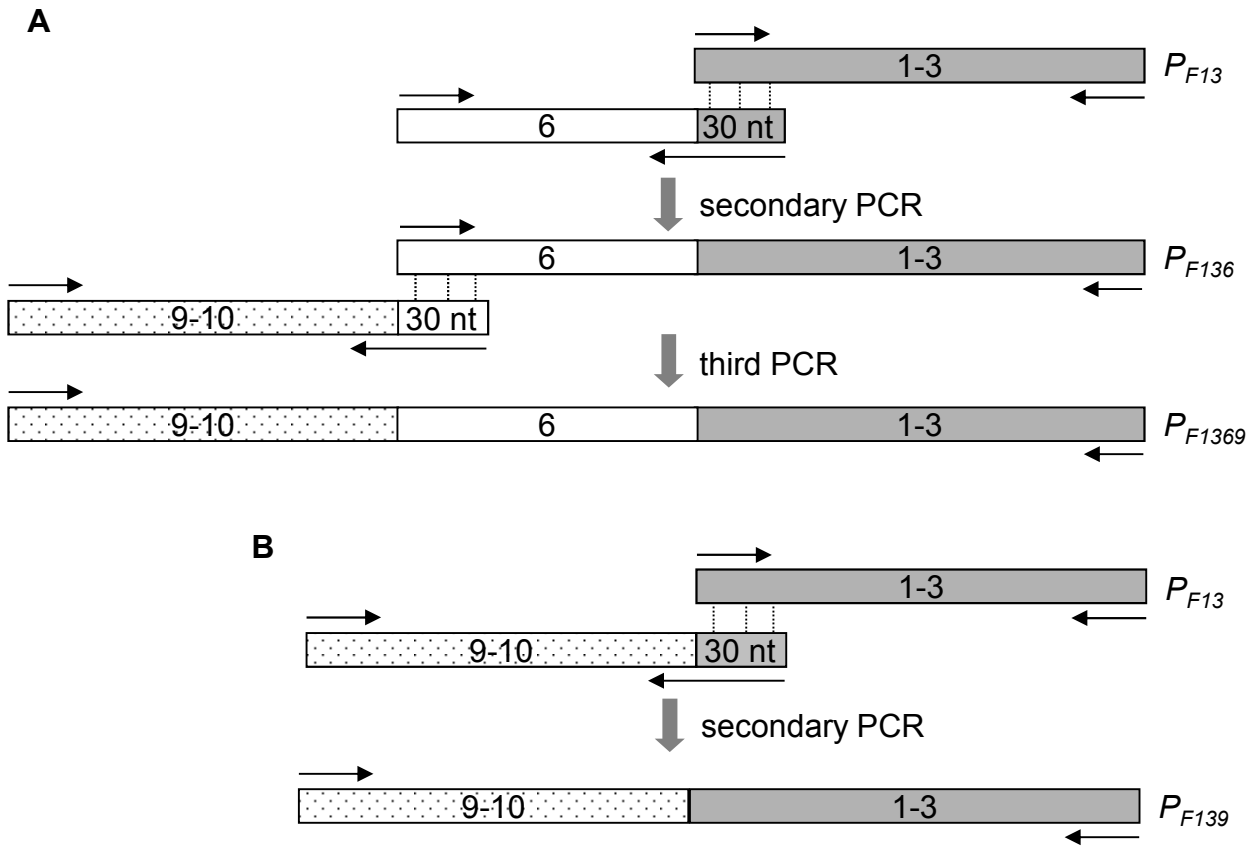



**Figure S1.** Programmatic illustration of the strategies to create truncated *FLO11* promoters. A bridge-PCR was used to generate $P_{F136}$ and $P_{F1369}$ **(A),** and $P_{F139}$ **(B).** Arrows represent primers used in PCRs. The *FLO11* gene promoter spans a 3-kb upstream sequence that can be divided into 15 0.2-kb sub-regions. The sub-regions of 1-3, 6, and 9-10 include major upstream activation sites (UASs) (also see Figure 1A for details).

**Figure S2**

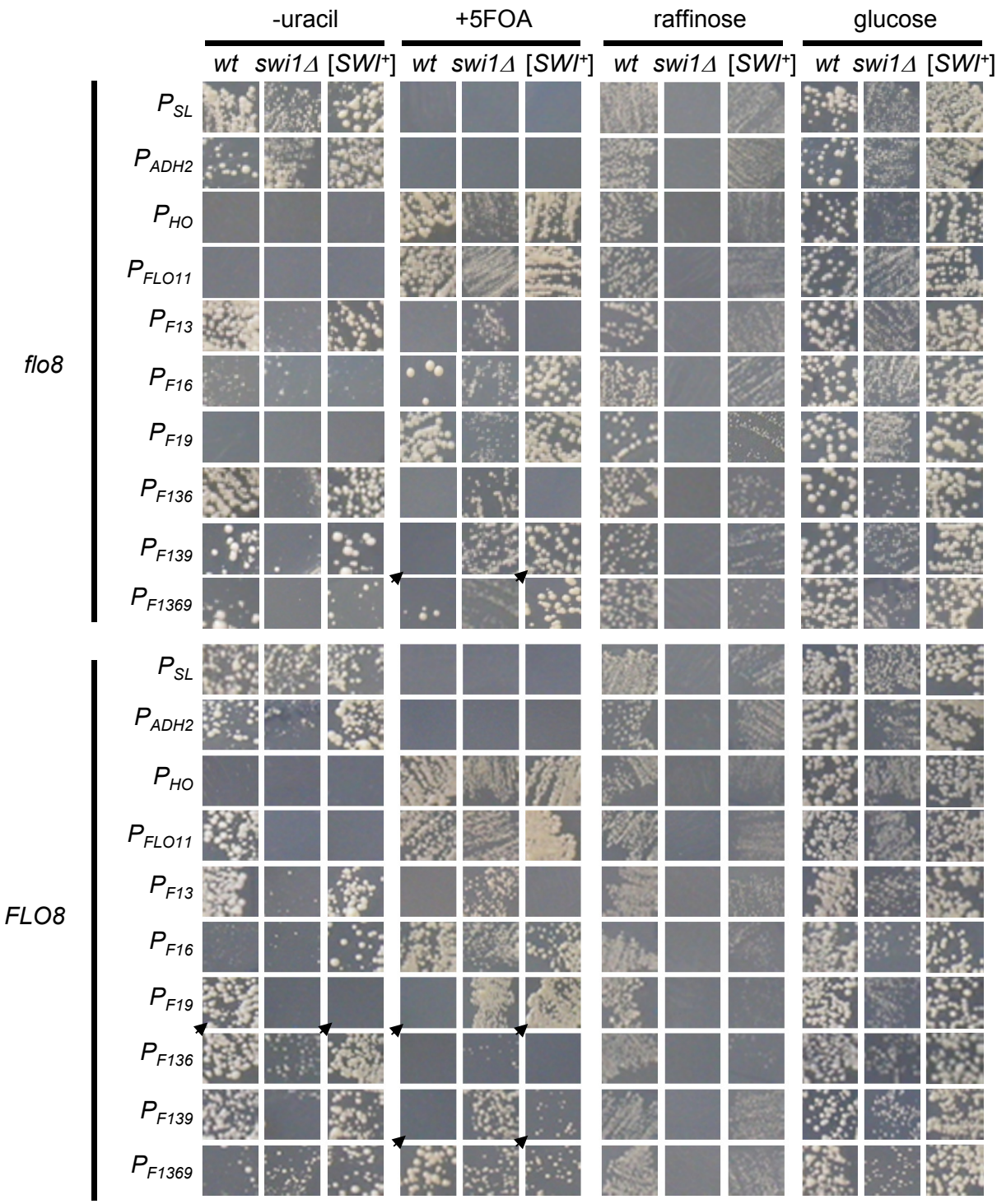



**Figure S2.** Growth of *flo8* (upper) and *FLO8*-repaired (lower) BY4741 strains with the indicated Swi1 prion states on synthetic complete (SC) plates without uracil (-uracil), with 5 FOA (+5FOA), non-selective SC with raffinose as the sole carbon source (raffinose) or with glucose (glucose). As indicated, all cells carry a *CEN*-plasmid expressing *URA3* gene driven by promoters of *SUC2-LEU2* ($P_{SL}$), *ADH2*, *HO*, or *FLO11* (wild-type and engineered). Arrowheads highlight the distinguishable growths of wild-type [*swi*$^-$] and [*SWI*$^+$] strains under the tested conditions.

**Figure S3**

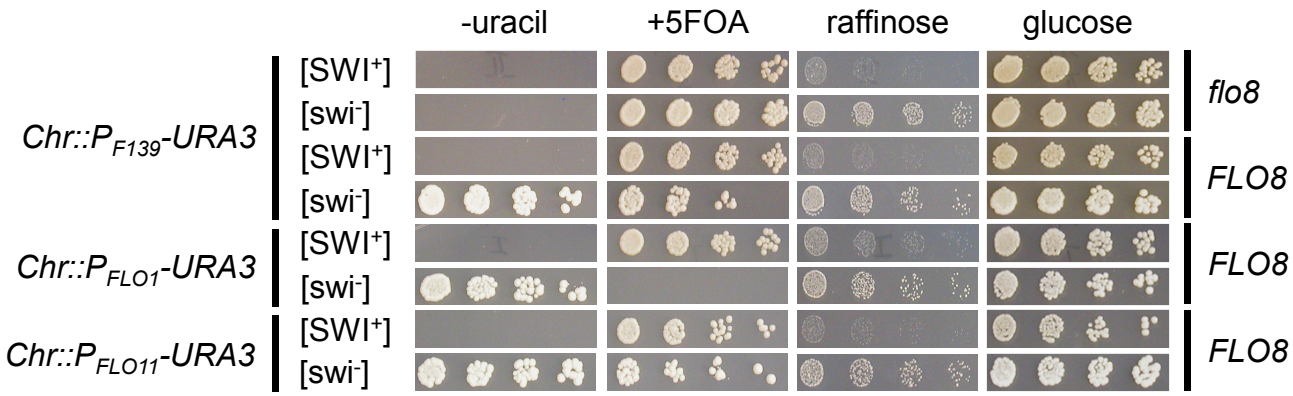



**Figure S3**. As described in Experimental Procedures, the indicated cassettes containing *URA3* gene driven by wild-type (*Chr::$P_{FLO11}$-URA3*) or engineered (*Chr::$P_{F139}$-URA3*) *FLO11* promoter, or wild-type *FLO1* promoter (*Chr::$P_{FLO1}$-URA3*) were used to replace the *FLO11*- or *FLO1*-ORF including the putative promoter regions at their corresponding chromosomal loci in isogenic [*SWI*$^+$] and [*swi*$^-$] cells with (*FLO8*) or without (*flo8*) repairing *FLO8*, respectively. Mid-log phase cultures of these strains were properly diluted and spotted for growth assays on glucose-containing SC selective medium (glucose), without uracil (-uracil), or with 5-FOA (+5FOA). Raffinose plate was also used to verify the Swi1 status. Shown are representative images of at least three independent experiments, which were taken 3 days post spotting onto the indicated plates.

**Figure S4**

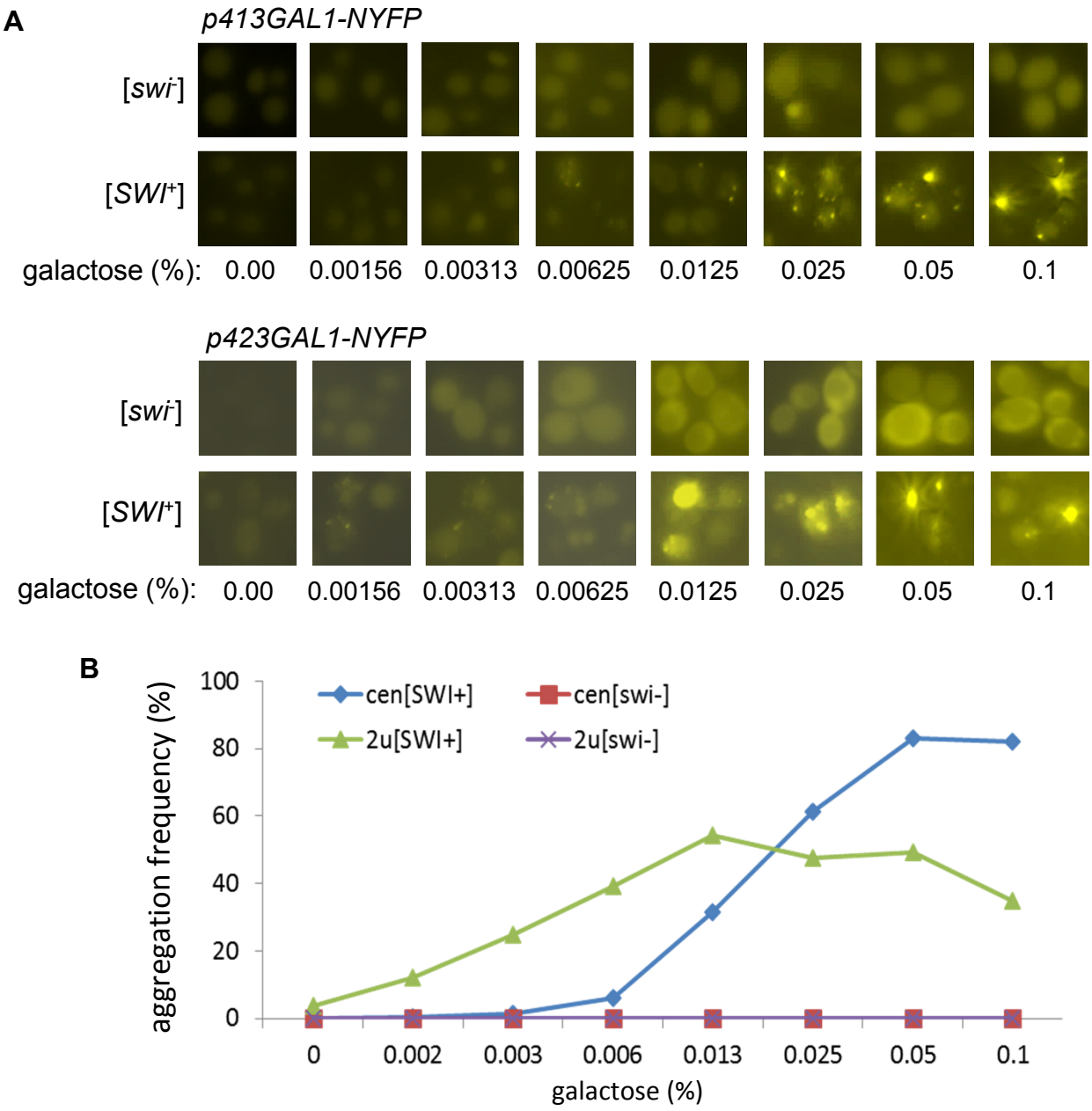
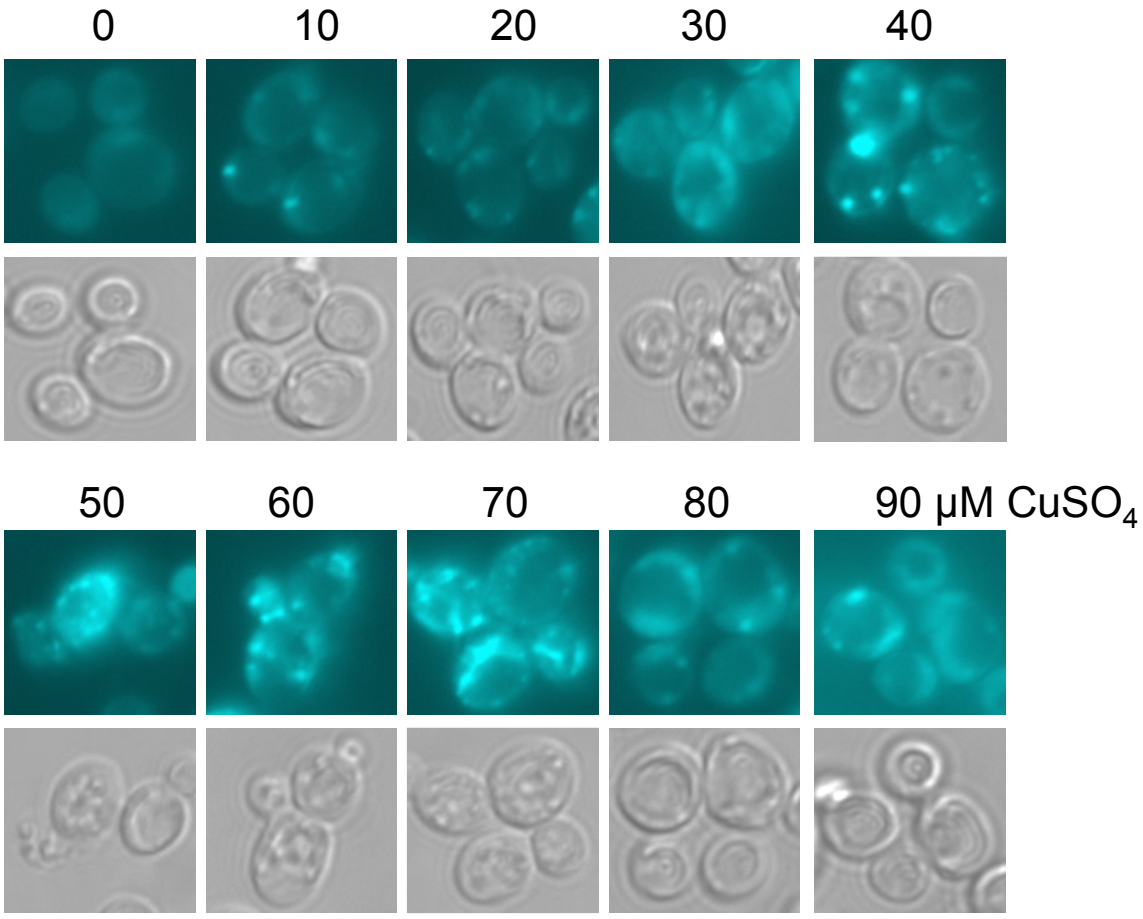



**Figure S4.** Determination of the minimal galactose concentration in a *GAL1*-driven *SWI1 N-YFP* expression experiment that can effectively distinguish the aggregation status of [*swi*$^-$] and [*SWI*$^+$] cells. **(A)** Isogenic 74D-694 [*swi*$^-$] and [*SWI*$^+$] strains carrying plasmid *p413GAL1-NYFP* (upper) or *p423GAL1-NYFP* (lower) were streaked to SC-his plates containing the indicated amount of galactose. N-YFP aggregation was assayed by fluorescence microscopy after three days of growth. **(B)** Cells containing N-YFP aggregates in (A) were quantified.

**Figure S5**




74D-694 ([*PSI*$^+$][*PIN*$^+$]): *p316CUP1-NMCFP*

**Figure S5.** Determination of the minimal amount of the *CUP1* promoter inducer ($CuSO_4$) that can be used to visualize Sup35 NM-CFP aggregates in a [*PSI*$^+$][*PIN*$^+$] 74D-694 strain. Overnight SC-ura culture of the strain containing plasmid *p316CUP1-NMCFP* was diluted into the same medium to ~$10^6$ cells/mL and grown for 3 h before adding the indicated amounts of $CuSO_4$. The NM-CFP aggregation was observed after overnight (24 h) of induction.