SUPPORTING INFORMATION

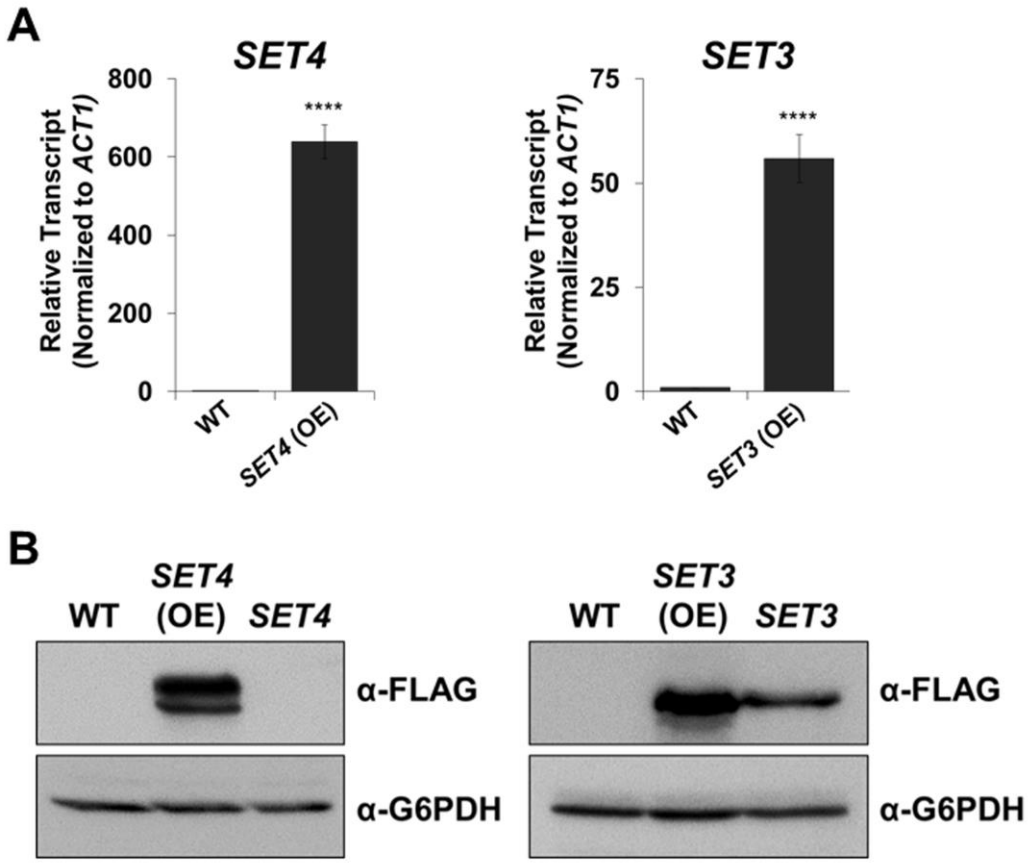

Figure S1. Set4 and Set3 are overexpressed in strains that have an integrated *PYK1* promoter upstream of *SET4* and *SET3.* A. Gene expression analysis of BY4741 WT and the overexpressed *SET4* and overexpressed *SET3* strains by qRT-PCR. The mRNA transcript levels were set relative to the WT strain and *ACT1* was used as an internal control to normalize expression levels. Data were analyzed from three biological replicates with three technical repeats each. Error bars represent the standard deviation. Four asterisks represents a $p<0.0001$. B. Western blot analysis of WT and the endogenous and overexpressed *3xFLAG-SET4* and overexpressed 3xFLAG-*SET3* strains. Set4 and Set3 expression levels were detected using an α-FLAG antibody and G6PDH was used a protein loading control.

SUPPORTING INFORMATION

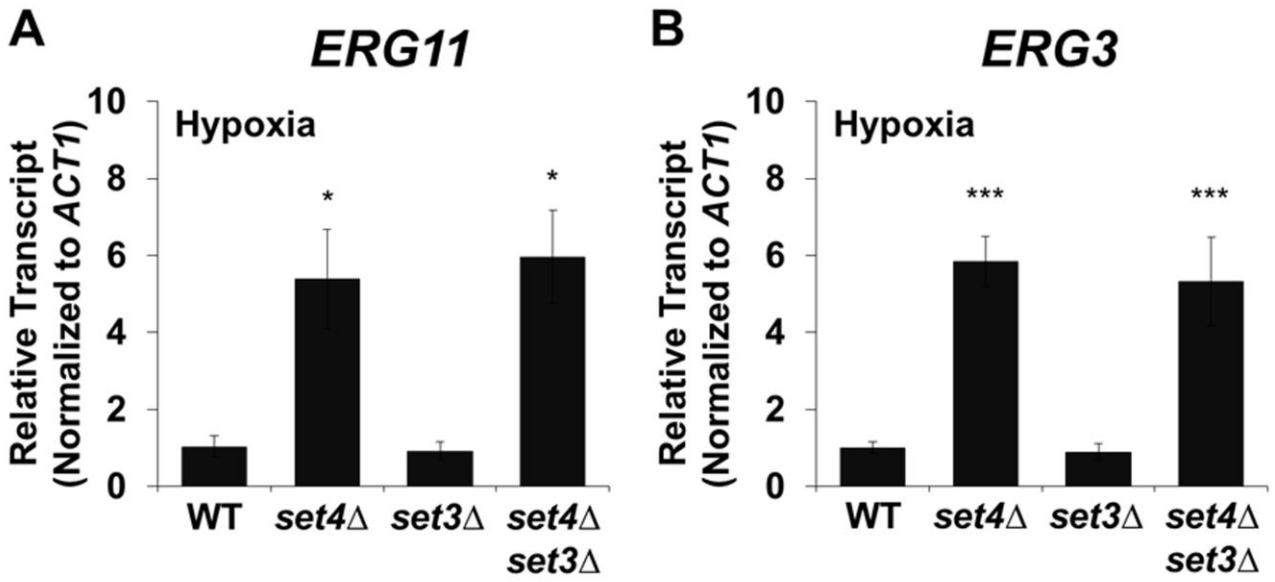

Figure S2. Set4 but not Set3 is required for *ERG11* and *ERG3* gene repression under hypoxic conditions. A-B. Expression of *ERG11* and *ERG3* was analyzed by qRT-PCR analysis in the BY4741 WT, *set4*Δ, *set3*Δ and *set4*Δ*set3*Δ strains following 8 hours of hypoxia. Gene expression analysis was relative to the WT strain and *ACT1* was used as an internal control to normalize expression levels. Data were analyzed from three biological replicates with three technical repeats each. Error bars represent the standard deviation. One asterisks represents $p<0.05$ and three asterisks represents $p<0.005$.

SUPPORTING INFORMATION

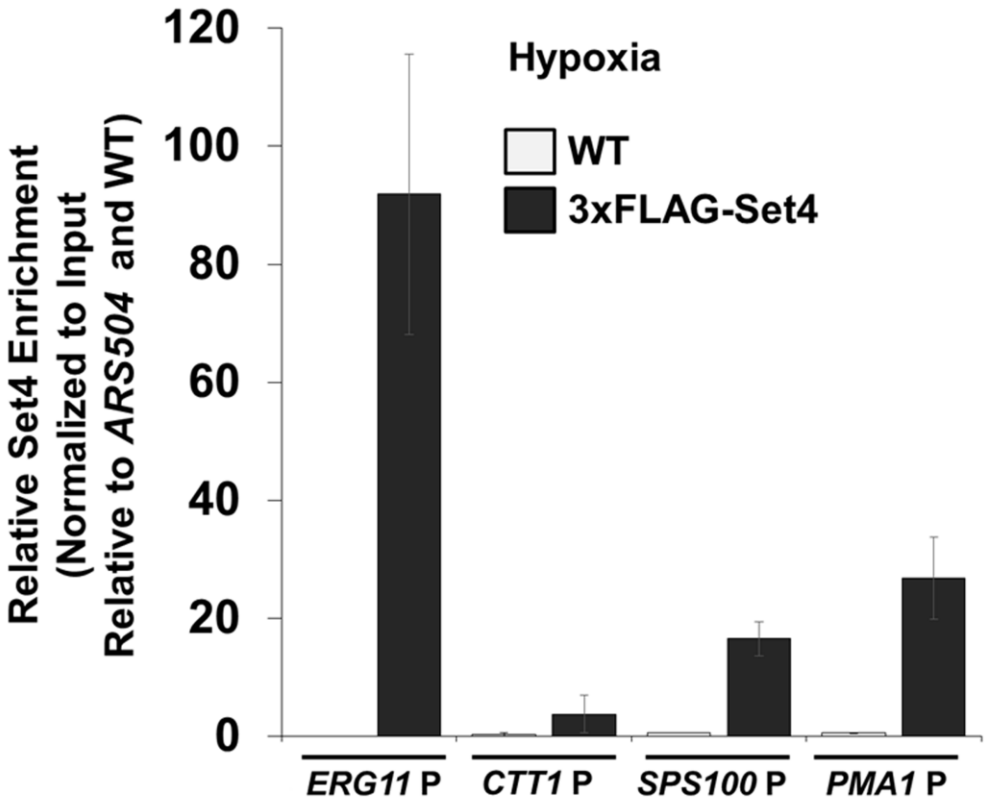

Figure S3. Set4 ChIP analysis at the promoters of *ERG11*, *CTT1, SPS100* and *PMA1* loci under hypoxic conditions. ZipChIP analysis was performed using BY4741 WT and 3xFLAG-Set4 strains at the promoter regions of *ERG11, CTT1, SPS100* and *PMA1* under hypoxic conditions. Both *CTT1* and *SPS100* were differentially expressed in the RNA-seq analysis when comparing the *set4*Δ and WT strains under hypoxia whereas *PMA1* was not differentially expressed. Set4 enrichment was normalized to DNA input and set relative to the untagged WT and *ARS504.* Data were analyzed from three biological replicates with three technical repeats each. Data represents low Set4 binding relative to enrichment observed at *ERG* promoters under hypoxia. Error bars represent the standard deviation. Set4 enrichment at the promoters was 92-fold at *ERG11*, 4-fold at *CTT1*, 16-fold at *SPS100* and 26-fold at *PMA1*.

SUPPORTING INFORMATION

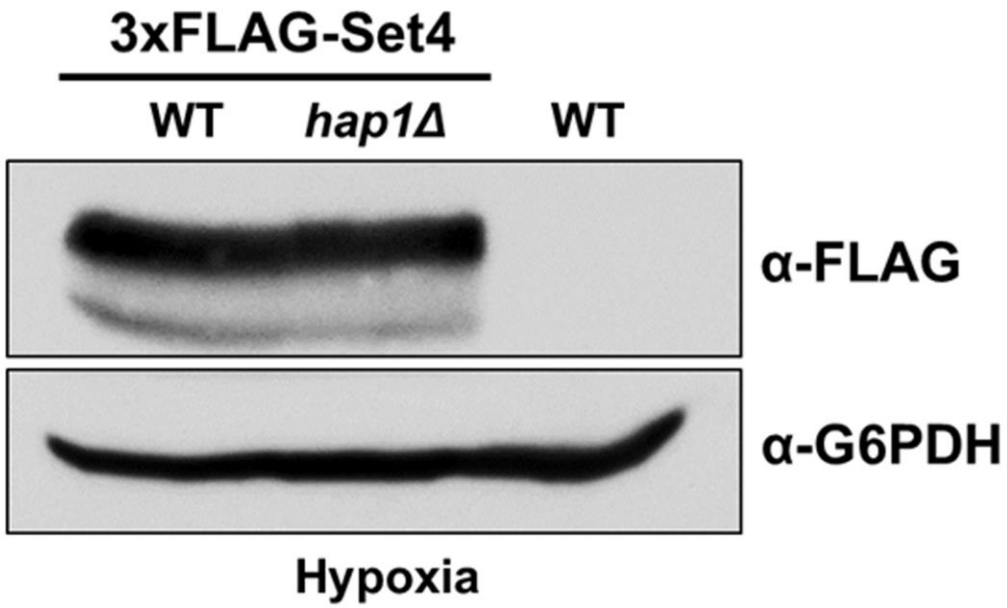

Figure S4. Set4 protein expression levels are unaffected in a *hap1*Δ strain under hypoxic conditions. Western blot analysis of the 3xFLAG-Set4 protein levels in FY2609 WT and FY2611 *hap1*Δ strains grown under 8 hours of hypoxia. Set4 protein levels were detected using the polyclonal anti-FLAG specific antibody (Sigma). The untagged WT was used as a negative control and G6PDH was used as a loading control.

SUPPORTING INFORMATION

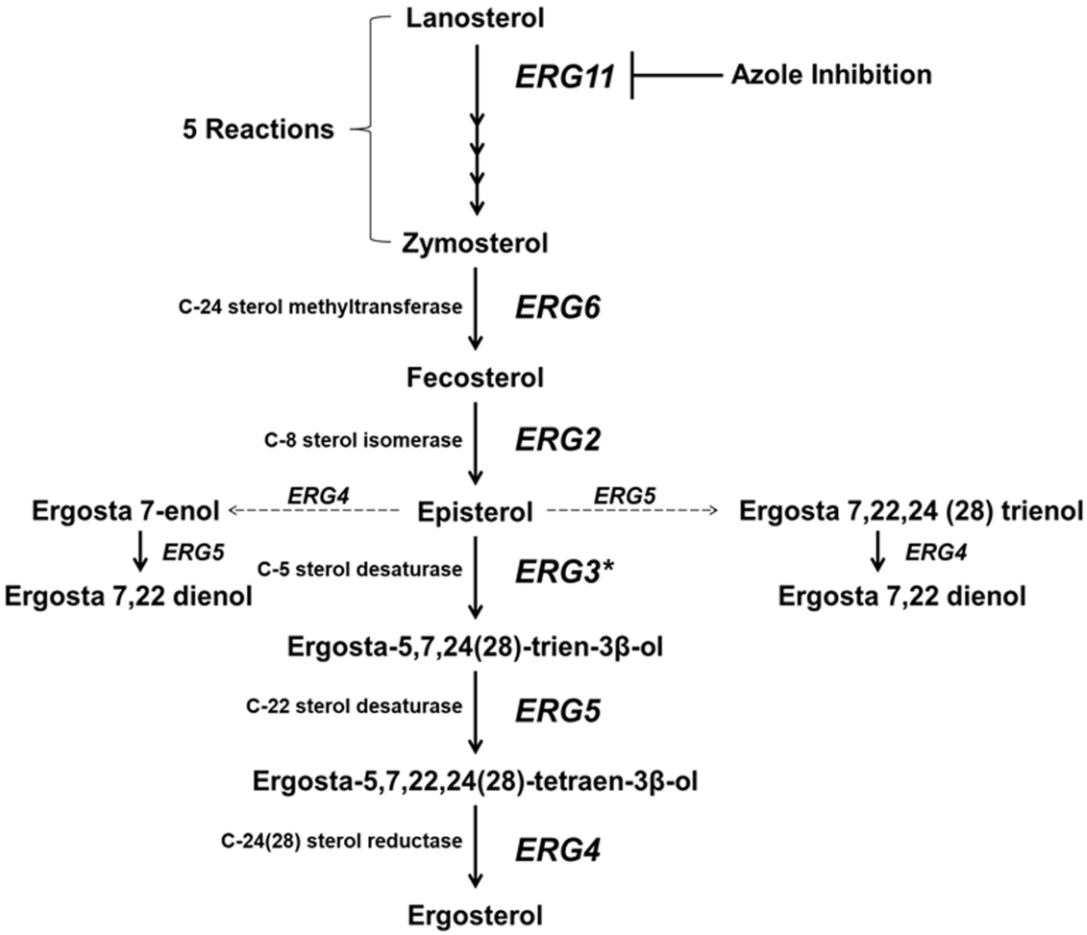

Figure S5. Ergosterol precursors observed in an *erg3*Δ strain. The last steps of ergosterol biosynthesis. When *ERG3* is deleted (represented by the asterisk on *ERG3*) the indicated sterol precursors are generated by Erg4 and Erg5. Erg11 is inhibited by azole drug treatment and occurs upstream of the final five steps of ergosterol biosynthesis.

SUPPORTING INFORMATION

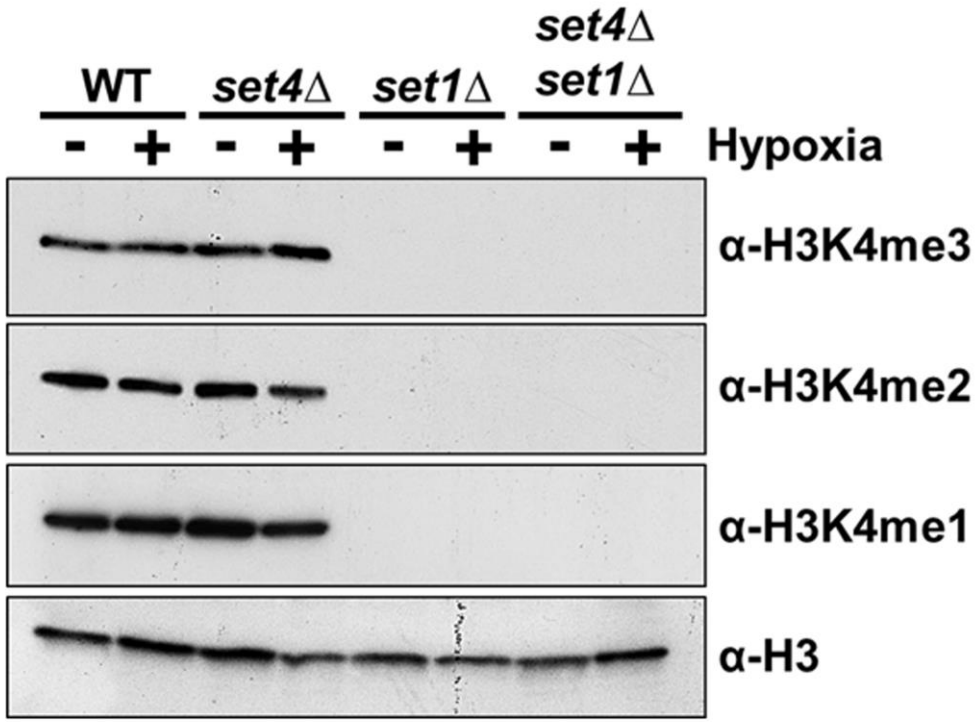

Figure S6. Set4 does not affect global H3K4 methylation levels under hypoxic conditions. Western blot analysis of BY4741 WT, *set4*Δ, *set1*Δ, and *set4*Δ*set1*Δ strains under hypoxia. H3K4 methylation was determined using antibodies specific to H3K4 mono-, di- and trimethylation. The *set1*Δ strain was used as a negative control for H3K4 methylation under aerobic conditions and H3 was used as a loading control.

SUPPORTING INFORMATION

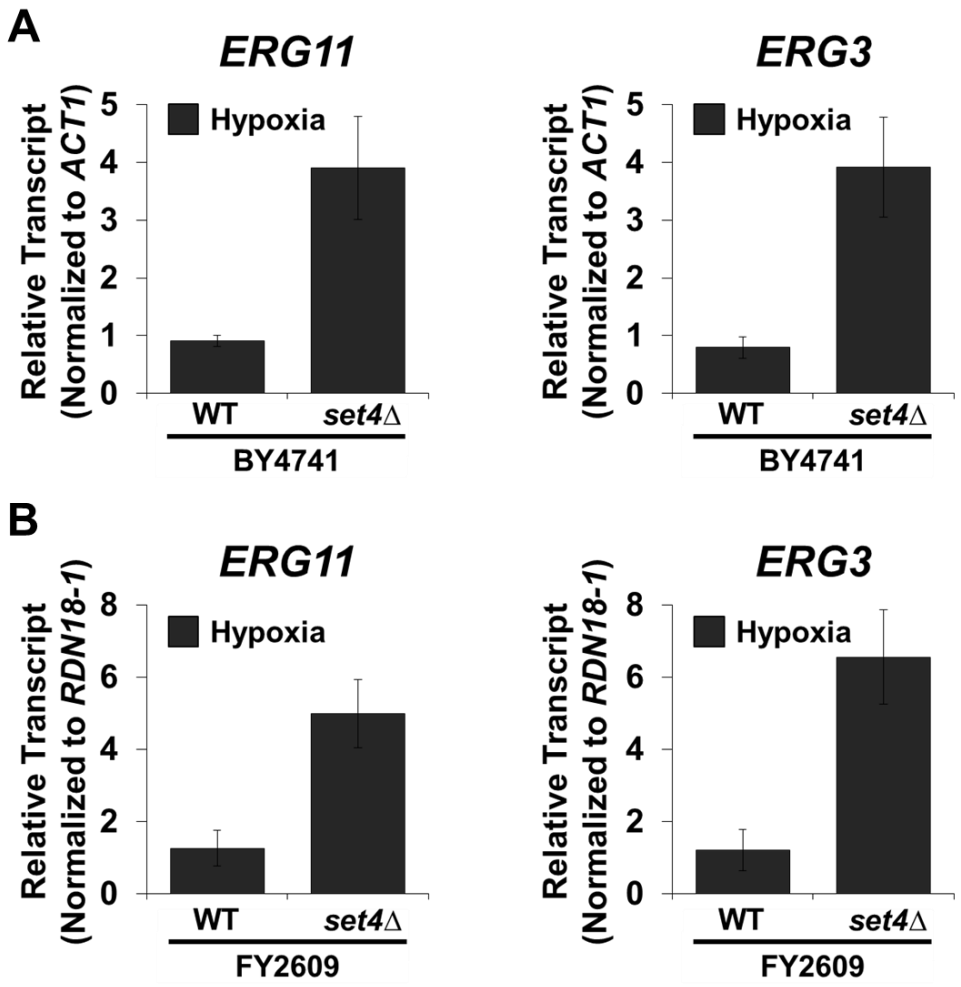

Figure S7. *ERG11* and *ERG3* expression increases in a *set4*Δ strain in the BY4741 and FY2609 strains . Expression of *ERG11* and *ERG3* was analyzed by qRT-PCR in the WT and *set4*Δ strains for the BY4741 and FY2609 parent strains under hypoxic conditions . The BY4741 contains the mutant *hap1* allele and the FY2609 WT contains a full length *HAP1.* Gene expression analysis was relative to hypoxia and *ACT1* or *RDN18-1* was used as an internal control to normalize mRNA levels. Data were analyzed from three biological replicates with three technical repeats each. Error bars represent the standard deviation.

SUPPORTING INFORMATION

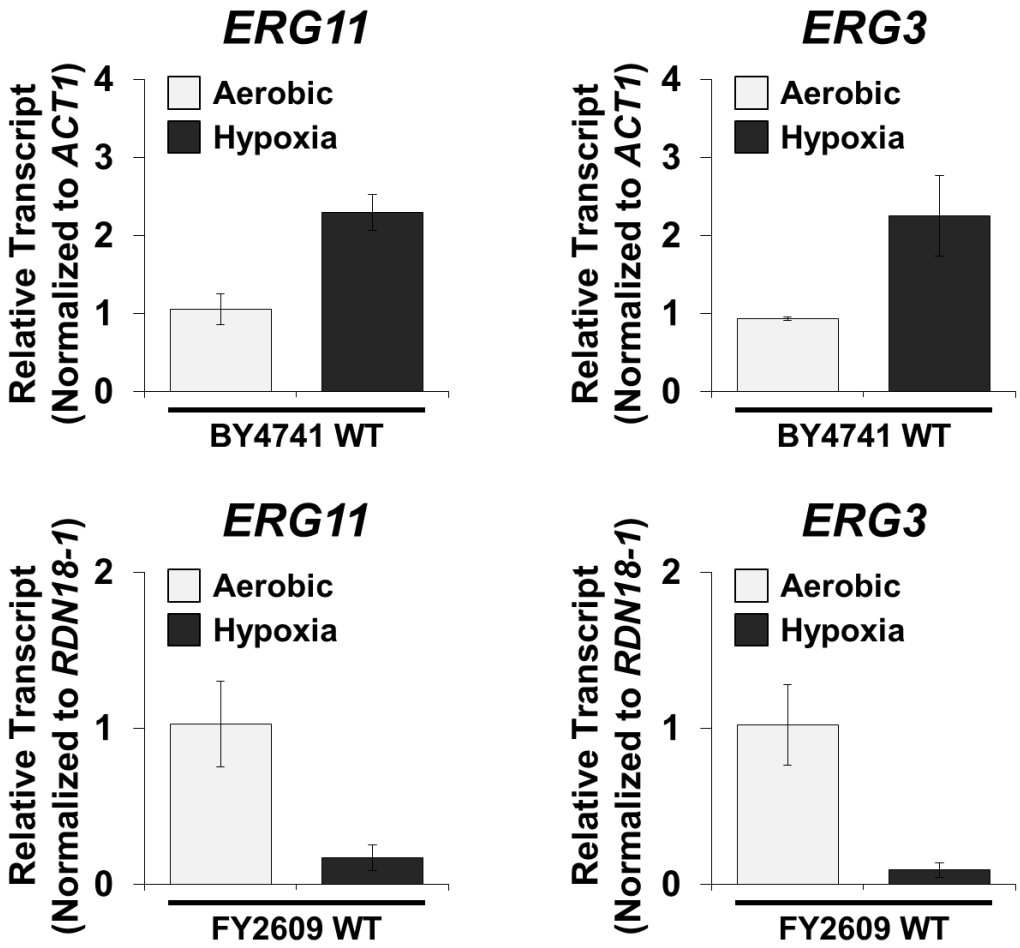

Figure S8. *ERG11* and *ERG3* expression are repressed in strains containing a full length Hap1. Expression of *ERG11* and *ERG3* was analyzed by qRT-PCR analysis in the BY4741 WT and FY2609 WT strains under aerobic and hypoxic conditions . The BY4741 contains the mutant *hap1* allele and the FY2609 WT contains a full length *HAP1.* Gene expression analysis was relative to the aerobic condition and *ACT1* or *RDN18-1* was used as an internal control to normalize expression levels. Data were analyzed from three biological replicates with three technical repeats each. Error bars represent the standard deviation.