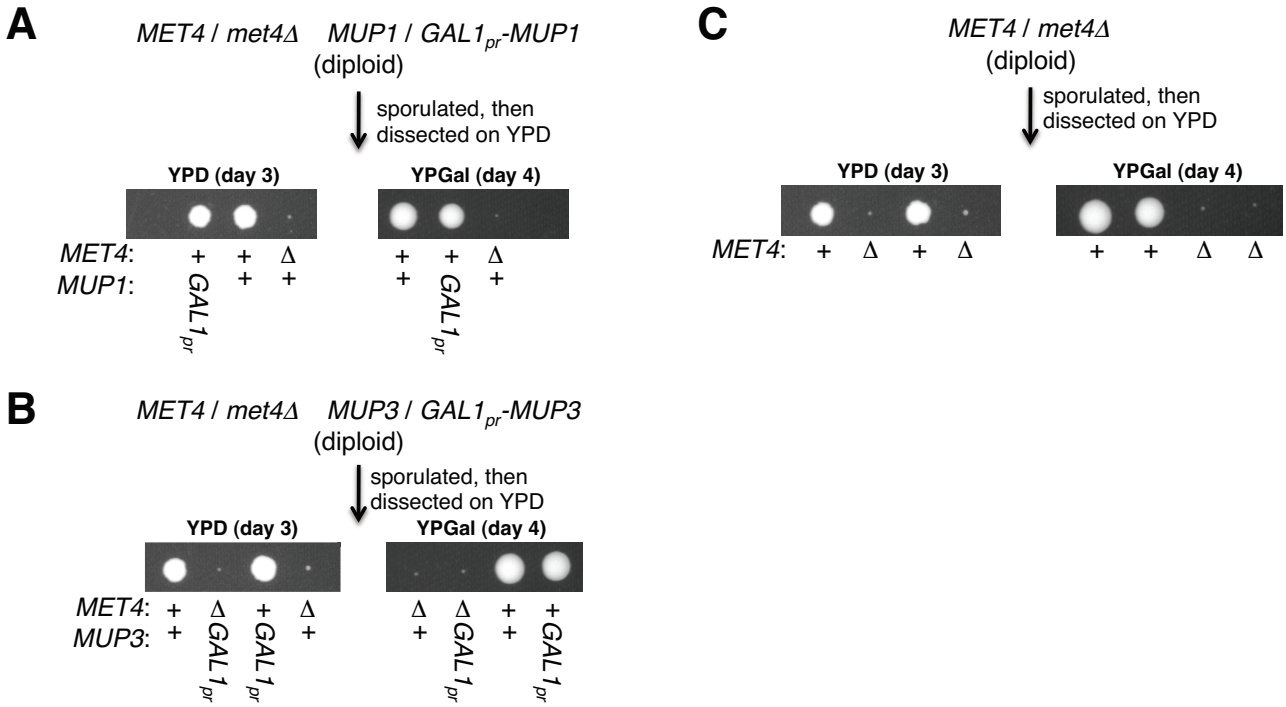

Figure S1. A *met4Δ* mutant grows slowly, but not due to a defect in methionine import. (A) Manipulating expression of the high-affinity transporter gene, *MUP1*, appears lethal to *met4Δ* cells. A *MET4*/*met4Δ MUP1*/*GAL1*$_{pr}$-*MUP1* diploid (strain DBY12230) was sporulated and the resulting diploids were dissected on YPD (to repress *GAL1*$_{pr}$, left panel) or YPGal plates (to induce *GAL1*$_{pr}$right panel). A representative tetrad is shown. We did not obtain a viable *met4Δ GAL1*$_{pr}$-*MUP1* spore on either YPD or YPGal, even after testing many tetrads. We speculate that a *met4Δ* cell cannot cope with the limited or excess methionine. (B) Overexpressing the low-affinity transporter gene, *MUP3*, does not rescue the growth defect of *met4Δ* cells. A *MET4*/*met4Δ MUP3*/*GAL1*$_{pr}$-*MUP3* diploid (strain DBY12231) was sporulated and the resulting diploids were dissected on YPD (left panel) or YPGal plates (right panel). (C) The carbon source has no effect on the *met4Δ* growth defect. A control *MET4*/*met4Δ* diploid (strain DBY12043) was sporulated and the resulting diploids were dissected on YPD (left panel) or YPGal plates (right panel).

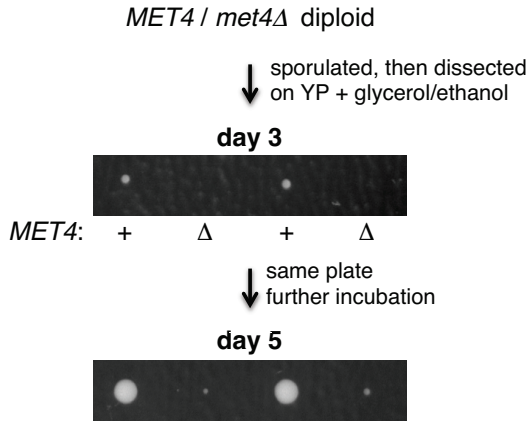

Figure S2. A *met4Δ* mutant can undergo aerobic respiration. A *MET4*/*met4Δ* diploid (strain DBY12212) was sporulated and the resulting diploids were dissected on plates with a non-fermentable carbon source (YP + glycerol + ethanol). Plates were grown at 30°C for 5 days. Shown are days 3 and 5 of a representative tetrad.

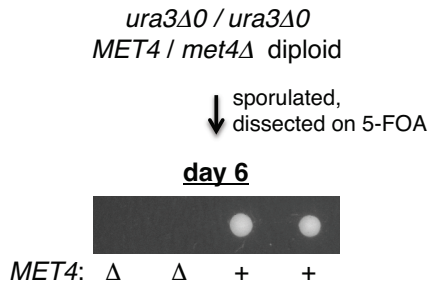

Figure S3. A *met4Δ* haploid does not grow at all on 5-floroorotic acid (5-FOA). A *met4Δ*/*MET4* heterozygote (DBY12212) was sporulated and the resulting tetrads were dissected on 5-FOA plates. A representative tetrad of many dissections is shown. Pictures were taken after 6 days of growth.

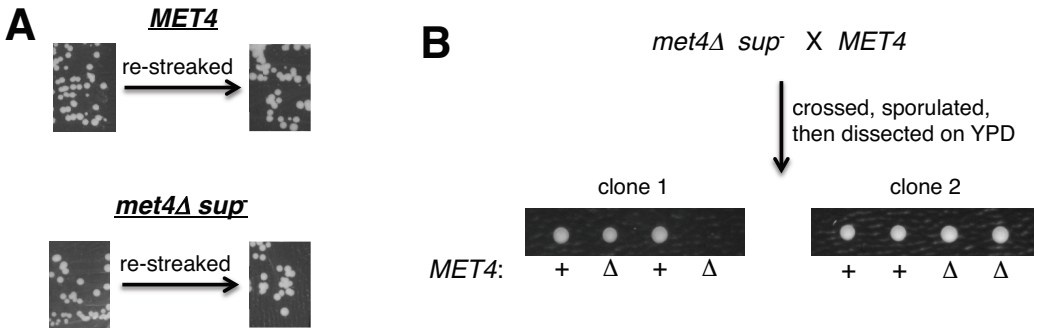

Figure S4. The suppression of the *met4Δ* growth defect is inherited and caused by a single-gene mutation. (A) The suppression of the *met4Δ* growth defect is mitotically inherited and stable. A suppressed *met4Δ* haploid (DBY12219, lower panels) was re-streaked onto YPD several times. A wild-type *MET4* haploid (upper panels, FY4) was used as a control. Shown are representative plates of many re-streaks and many strains. (B) The suppression of the *met4Δ* growth defect is meiotically inherited and caused by a mutation in a single-gene. To show this, we crossed two independently suppressed *met4Δ* strains by wild-type and sporulated the resulting diploid (left panel: DBY12215 crossed to FY5, right panel: DBY12222 crossed to FY4). The tetrads were dissected on YPD plates and the spores were grown for 2 days. It was expected that half of the *met4Δ* spores would be large if the suppressor mutation was in a single gene. Indeed, twenty-three of the *met4Δ* spores showed small colonies, while 19 showed large colonies.

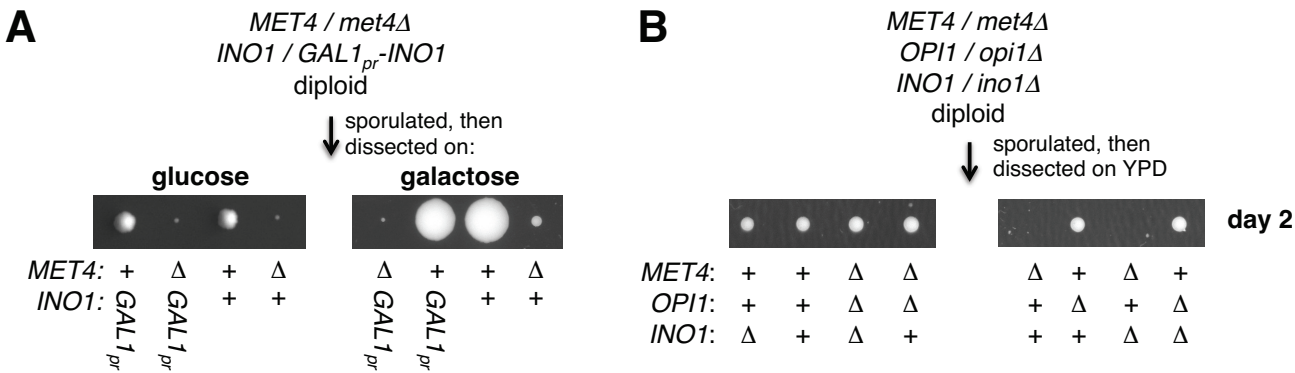

Figure S5. Ino1 is not required for the slow growth of a *met4Δ* strain. (A) The *met4Δ* cells grow slowly even when *INO1* expression is controlled by the *GAL* promoter. A *met4Δ*/*MET4 GAL1*$_{pr}$-*INO1*/*INO1* diploid (DBY12228) was sporulated and the resulting tetrads were dissected on glucose (to turn off *INO1*) or galactose (to turn on *INO1*). The glucose panel shows spores grown on YPD plates for 3 days, while the galactose panel shows spores grown on YPGal plates for 5 days. Representative tetrads of many dissections are shown. The slow phenotype segregated solely with the *met4Δ* genotype. (B) Deleting *INO1* has no effect on the growth of *met4Δ* or *met4Δ opi1Δ* strains. A *met4Δ*/*MET4 opi1Δ*/*OPI1 ino1Δ*/*INO1* diploid (DBY12229) was sporulated and the resulting tetrads were dissected on YPD plates. The spores were grown for 2 days and two representative tetrads are shown, containing the relevant genotypes. All markers were tested and were as expected (data not shown).

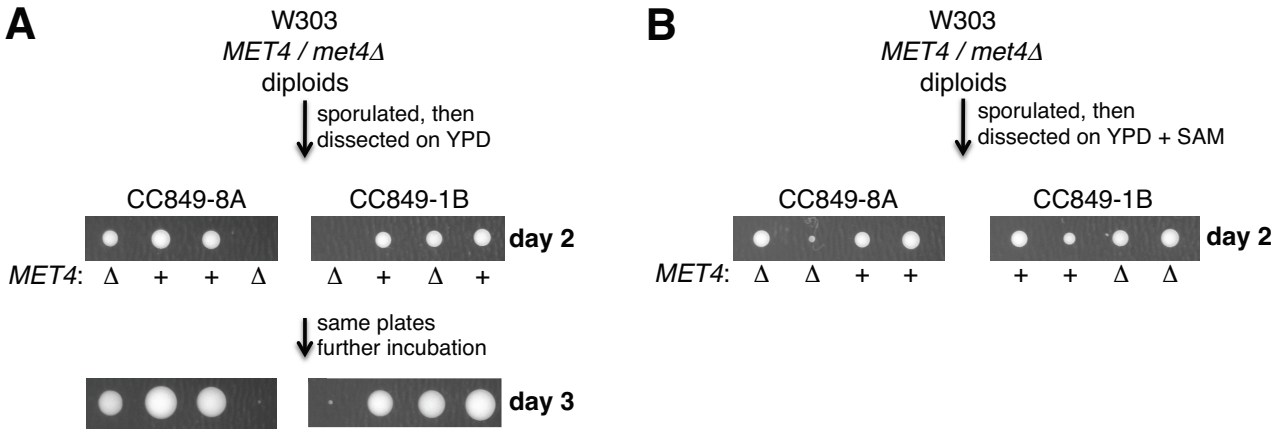

Figure S6. Deleting *MET4* causes slow growth in the W303 strain background. (A) A *met4Δ* allele causes slow grow and is suppressed in two commonly used W303 strains. Two different *met4Δ* haploids (CC849-8A and CC849-1B) were crossed with a *MET4* wildtype haploid (yMT-234). The resulting *met4Δ*/*MET4* heterozygotes were sporulated and the tetrads were dissected on a YPD plate. Representative tetrads are shown. All of the relevant auxotrophies were as expected (data not shown). Approximately half of the *met4Δ* spores formed small colonies while the other half formed large colonies, indicating that there is a suppressor mutation in another gene. Indeed, we identified frameshift mutations in the *OPI1* coding sequence in both *met4Δ* haploids (Deleted "A" at +500 in CC849-8A, and deleted "A" at +654 in CC849-1B). (B) The *met4Δ* strains are suppressed by adding SAM to the media. The *met4Δ*/*MET4* heterozygotes from panel A were sporulated and the tetrads were dissected on a YPD plate with 0.2 mM SAM. Representative tetrads are shown. All *met4Δ* spores formed large colonies, indicating that SAM suppressed *met4Δ* slow growth. All of the relevant auxotrophies were as expected (data not shown).

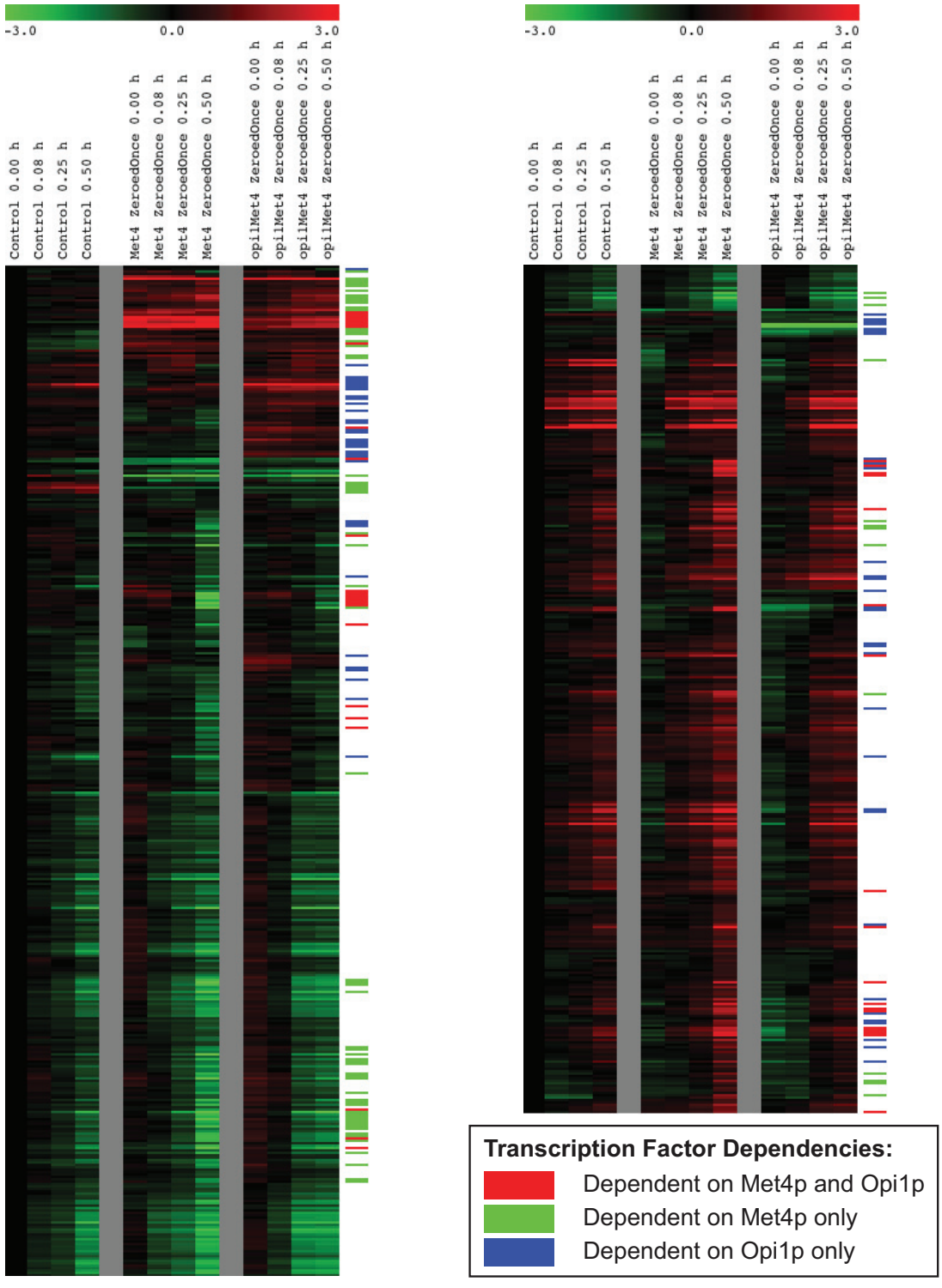

Figure S7. Hierarchically clustered gene expression data. Gene expression data collected during the first 30 minutes of treatment with 1uM estradiol are shown. Genes that change by at least 1.5-fold in at least one time course (Materials and Methods) were hierarchically clustered using the Pearson correlation coefficient as the distance metric. The gene sets further discussed in the paper (Materials and Methods) are indicated using colored boxes (Red, genes dependent on Met4p and Opi1p; Green, genes dependent on Met4p only; Blue, genes dependent on Opi1p only).