

Supplemental Figure 1. Standard curves for *C. albicans* strains spiked into mouse kidneys. Serial dilutions of conidia from CAI-12 (Fig. 2A),  $\Delta$ irs4 (Fig. 2B) and *IRS4* reinsertion (Fig. 2C) strains were spiked into mouse kidneys, and extracted genomic DNA was used for qPCR. Standard curves were also generated for conidia suspended in sterile saline (not shown).







Supplemental Figure 2. Growth curves in YPD medium at  $30^{\circ}$ C. Growth curves for CAI-12,  $\Delta$ irs4 null and mixtures of CAI-12 and  $\Delta$ irs4 were indistinguishable (Fig. 3A), as slopes of curves during exponential growth were 0.64, 0.65 and 0.67, respectively (p=0.38 and 0.18 for CA-12 *vs.* mixed inoculum and CA-12 *vs.*  $\Delta$ irs4, respectively). Results were corroborated by using qPCR to quantify genome equivalents (GE) at specific time points. The growth of CAI-12 and  $\Delta$ irs4 was comparable when cultured alone (Fig. 3B) or in a 1:1 mixture (Fig. 3C). Similar results were obtained in SD medium at 30°C and at 37°C (not shown). WT: strain CAI-12. Error bars represent standard deviations.



**Supplemental Figure 3. Recovery of CAI-12 and** *IRS4* **reinsertion strains from mouse kidneys.** Genome equivalents per gram of tissue (GE/g) were determined during competitive infections at days one and four. Error bars represent SD.



Expected

Supplemental Figure 4. Significance analysis of microarray (SAM) plot for gene expression by  $\Delta$ irs4 and CAI-12 in blood. Scatter plot of the observed relative difference in gene expression (y-axis) vs. the expected relative difference (x-axis). The solid line indicates the situation in which the observed difference is identical to the expected. The dotted lines are at a threshold distance  $\Delta$ =0.4 from the solid line. Even with this low  $\Delta$ , which maximized the number of genes called significant, only 14 genes were identified as differentially expressed (~0.2% of unique ORFs on the array). The median number of falsely significant genes was 3.5, yielding a false discovery rate (FDR) of 25%. Increasing the  $\Delta$  would lower the FDR, at the expense of further reducing the number of genes identified as significant.