Gene expression dynamics have provided foundational insight into almost all biological processes. We have analyzed expression of environmentally responsive genes and transcription factor genes to infer signals and pathways that drive pathogen gene regulation during invasive *Candida albicans* infection of a mammalian host. Environmentally responsive gene expression shows that there are early and late phases of infection. The early phase includes induction of zinc and iron limitation genes, genes that respond to transcription factor Rim101, and genes characteristic of invasive hyphal cells. The late phase includes responses related to phagocytosis by macrophages. Transcription factor gene expression also reflects early and late phases. Transcription factor genes that are required for virulence or proliferation in vivo are enriched among highly expressed transcription factor genes. Mutants defective in six transcription factor genes, three previously studied in detail (Rim101, Efg1, Zap1) and three less extensively studied (Rob1, Rpn4, Sut1), have been profiled during infection. Most of these mutants have distinct gene expression profiles during infection as compared to in vitro growth. Infection profiles suggest that Sut1 acts in the same pathway as Zap1, and we verify that functional relationship with the finding that overexpression of either *ZAP1* or the Zap1-dependent zinc transporter gene *ZRT2* restores pathogenicity to a *sut1* mutant. Perturbation with the cell wall inhibitor caspofungin also has distinct gene expression impact in vivo and in vitro. Unexpectedly, caspofungin induces many of the same genes that are repressed early during infection, a phenomenon that may contribute to drug efficacy. The pathogen response circuitry is tailored uniquely during infection, with many relevant regulatory relationships that are not evident during growth in vitro. Our findings support the principle that virulence is a property that is manifested only in the distinct environment in which host-pathogen interaction occurs.