Candida albicans is an opportunistic fungal pathogen found in the oral mucosa, the gut, the vaginal mucosa, and the skin of humans. While C. albicans can cause mild and superficial infections, severe invasive infections can occur in immunocompromised patients. Understanding the survival and pathogenesis of C. albicans is critical for novel antifungal drug discovery, and is the main objective of this project. The goal of this research is to take a two pronged approach to discover new strategies for antifungal treatment: 1) a genetic strategy focused on genetic interaction analysis to uncover combinations of fungal stress response genes with negative genetic interactions or synthetic lethal interaction, to uncover putative targets for combination antifungal therapy, and 2) a chemical strategy using a natural product screening to identify new compounds that work singly or in combination with existing antifungals. For the genetic strategy, I will exploit a CRISPR-Cas9-based genome editing platform to create stress response deletion libraries in C. albicans, in order to study their role in pathogen survival. This library of single and double stress response mutants will be screened under diverse growth conditions to assess their relative fitness. Genetic interaction analysis will be exploited to map out genetic interactions between fungal genes involved in growth, survival, and pathogenesis. For the chemical strategy, a natural product library will be screened singly, to discover novel antifungal properties, or in combination with known antifungal drugs to discover synergistic effects between the natural product and the antifungal drug.