



**CALIFORNIA STATE SCIENCE FAIR
2014 PROJECT SUMMARY**

Name(s) Elan E. Filler	Project Number 34696
Project Title Transcription Factors that Regulate Antimicrobial Resistance in Candida glabrata	
<p style="text-align: center;">Abstract</p> <p>Objectives/Goals The fungus <i>Candida glabrata</i> is part of the normal human flora. In hospitalized patients with weakened immune systems, the fungus can enter the bloodstream from the GI tract and cause a serious, frequently fatal infection. Both white blood cells and cells lining the GI tract contain antimicrobial peptides that kill <i>C. glabrata</i> and prevent infection. Patients infected with <i>C. glabrata</i> are treated with the antifungal drug, caspofungin, but some strains are resistant. My hypothesis is that <i>C. glabrata</i> has specific transcription factors that enable it to resist antimicrobial peptides and caspofungin.</p> <p>Methods/Materials To identify these transcription factors, a collection of <i>C. glabrata</i> mutants, each of which lack a different transcription factor, was screened for increased susceptibility to the antimicrobial peptide, protamine, or the antifungal drug, caspofungin. The ability of each mutant to grow on agar plates containing either protamine or caspofungin was compared to the control wild-type strain. Mutants that were susceptible to either compound, as compared to the control strain, were retested to verify the results. Using bioinformatics, the genes that were absent in the susceptible mutants were searched in the <i>Candida</i> Genome Database to determine their function.</p> <p>Results Of the 91 <i>C. glabrata</i> transcription factor mutants that were tested, 3 were susceptible to protamine only and 6 were susceptible to caspofungin only. Seven mutants were susceptible to both protamine and caspofungin. Notably, 3 of these 7 mutants lacked Spt8, Ada2, or Gcn5. My bioinformatics research revealed that in other organisms, these proteins are known to form part of the SAGA histone acetyltransferase complex. This complex acetylates histones, exposing DNA and leads to the transcription of downstream genes that are responsible for resistance.</p> <p>Conclusions/Discussion Therefore, the Spt8-Ada2-Gcn5 complex plays a key role in governing the ability of <i>C. glabrata</i> to resist both antimicrobial peptides and caspofungin, and is a promising target for new antifungal drugs.</p>	
Summary Statement I found that the SAGA histone acetyltransferase complex governs the resistance of the fungus, <i>Candida glabrata</i> , to antimicrobial peptides and caspofungin.	
Help Received Used lab equipment at the Los Angeles Biomedical Research Institute under the supervision of Dr. Liu.	