Cryptococcus neoformans is an encapsulated opportunistic fungal pathogen known to cause lethal cryptococcal meningitis in immunocompromised individuals (e.g., HIV/AIDS). Treatment for this infection consists of three categories of antifungal drugs: polyenes, pyrimidine analogs and azoles. However, the availability of these drugs is limited in certain regions, leading to the prolonged use of fluconazole, an azole antifungal, that is readily available in most countries. Recently, there has been increased cases of fluconazole-resistant strains of *C. neoformans* found clinically caused by long periods of fluconazole monotherapy. Research conducted in the JGM laboratory at the University of Guelph has revealed that ClpX has an essential role in the mechanism of fluconazole-resistance in *C. neoformans*. ClpX is a molecular chaperone that partners with ClpP, a compartmentalized serine protease, to form the ClpXP complex that functions to maintain cellular protein homeostasis. ClpX is also a heat shock protein that is known to prevent protein misfolding and it is involved in metabolism, starvation and oxidative stress responses. Disruption of ClpX through gene deletion or inhibition has shown to significantly reduce resistant strains of *C. neoformans* growth in the presence of fluconazole, once again causing the pathogen to become susceptible to the drug. Using quantitative proteomics, ClpX will be characterized by analyzing the proteomes of resistant strains of *C. neoformans* with ClpX disrupted to further reveal the mechanism of resistance. ClpX disruption will be further tested using *in vitro* and *in vivo* models to assess its potential to be a therapeutic target.