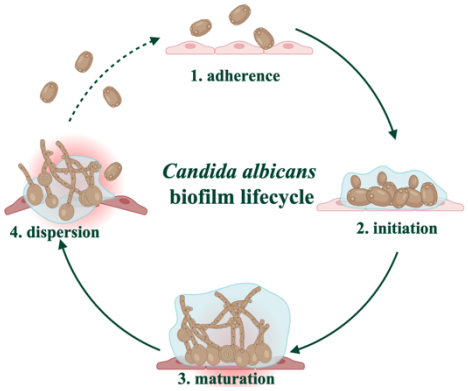
**Supervisor:** Dr. John Allingham

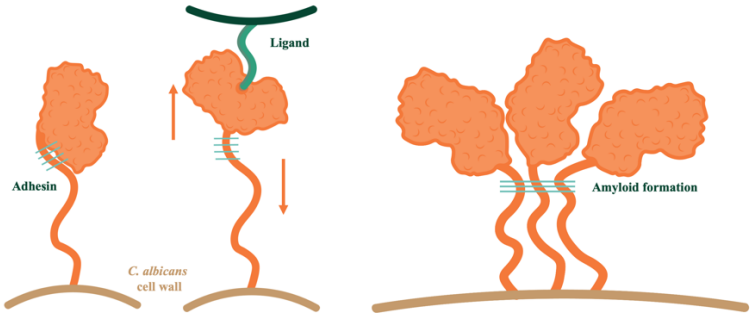
**Project #2 Title:** Structural basis for adhesin involvement in biofilm formation by *Candida albicans*

**Project Outline:** Adhesins are proteins linked to the outer surface of bacteria or fungi that help them attach to biotic and abiotic surfaces[1]. The human pathogen *Candida albicans* uses adhesins to colonize mucosal surfaces and form biofilms on prostheses and other medical devices. If *C. albicans* growth on such surfaces cannot be controlled, oropharyngeal and vulvovaginal candidiasis can develop, and deadly bloodstream infections can arise. The agglutinin-like sequence (Als) family of *C. albicans* adhesins are important in all these processes[2,3], however, the structural basis of their binding interactions with specific biotic and abiotic surfaces has not yet been studied. This research project will provide insight into how *C. albicans* adheres to host surfaces, forms biofilms, and invades host cells. This information is needed to the develop of new ways to prevent and treat *C. albicans* infections.




**Project Goals:**

1. Elucidate high-resolution structures of the Als1, 3, and 5 adhesins from *C. albicans*
2. Determine the structural basis for the substrate binding specificity of each Als isoform
3. Determine the interactions and architecture of Als-based amyloids that form in *C. albicans* biofilms
4. Design peptide-based inhibitors of Als adhesins to prevent or disrupt *C. albicans* biofilms




**Experimental Approaches:** The student involved in this project will learn research approaches from multiple disciplines, including microbiology, biochemistry, structural biology, and drug design. They will learn to use genetic engineering methods, such as a CRISPR gene editing system, to develop *C. albicans* strains that lack or have mutated Als adhesins to understand the roles of each Als adhesin in binding specific biotic and abiotic surfaces, and their importance in biofilm formation[5]. The student will gain expertise in recombinant adhesin protein expression and purification. They will also learn to perform studies that assess binding of purified adhesins or adhesin-deficient mutant cells to different surfaces using optical biosensing technologies like bio-layer interferometry. Adhesin protein structures will be determined by X-ray crystallography and cryo-EM to elucidate the structural basis of adhesin binding to specific substrates.

**References:**


1. Willaert, R. (2018) Adhesins of Yeasts: Protein Structure and Interactions. Journal of Fungi, Oct 27;4(4):119.
2. Golan, N., Schwarts-Perov, S., Landau, M., Lipke, P. (2022) Structure and Conservation of Amyloid Spines From the *Candida albicans* Als5 Adhesin. Front Mol Biosci. Jul 6;9:926959.
3. Ho, V. *et al*. (2019) An Amyloid Core Sequence in the Major Candida albicans Adhesin Als1p Mediates Cell-Cell Adhesion. mBio, Oct 8;10(5):e01766-19.
4. Shoukat, I., Frazer, C., Allingham, J.S. (2019) Kinesin-5 Is Dispensable for Bipolar Spindle Formation and Elongation in Candida albicans, but Simultaneous Loss of Kinesin-14 Activity Is Lethal. *mSphere* Vol. 4, No. 6.