Exploring signals for transport of a pathogenic fungi mRNA using baker's yeast

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Candida albicans (*C. albicans*), a microscopic fungus living in humans, has the potential to cause a range of diseases. The pathogenicity of *C. albicans* is linked to the cell's ability to switch from its normal, circular shape to an elongated form known as a hypha that invades tissues, adheres to cells, evades host immune cells and can eventually lead to disease (Verma-Gaur and Traven, 2016). The mechanism of the hyphal growth in *C. albicans* is influenced by asymmetric transport of genetic information called messenger RNA (mRNA) to the hyphal tip by several key proteins (Inglis and Johnson, 2002). At the hyphal tip, the transported mRNA called *ASH1* undergoes translation, a process whereby proteins are synthesized from mRNA, to make Ash1p, which is essential for hyphal growth. *C. albicans* hyphal growth is widely studied, but the role of mRNA transport in hyphal growth is not. Understanding the mRNA transport mechanism can help us understand pathogenicity in *C. albicans.*

Studies on baker's yeast, a related fungus, provides insight for the mechanism of mRNA transport in *C. albicans*. In baker's yeast, directional *ASH1* mRNA transport to the bud tip is facilitated by proteins She2p and She3p. Briefly, She2p recognizes parts of the *ASH1* mRNA known as localization elements (LEs). Both *ASH1* and She2p then bind to She3p that is attached to motor proteins for the mRNA transport to the bud tip (Long et al., 2000). Four LEs have been identified in baker's yeast where the structure of the LEs acts as a signal for She2p recognition (Chartrand et al., 1999; Jambhekar et al., 2005; Olivier et al., 2005).

Interestingly, She2p is not found in *C. albicans* even though She3p has been identified (Elson et al., 2009). This suggests that *C. albicans ASH1* is bound by other proteins that may fulfill the role of She2p. The absence of She2p in *C. albicans* indicates that proteins that bind to *C. albicans ASH1* are likely to recognize structures that are different than LE in baker's yeast. However, one study found that *C. albicans ASH1* was able to travel to the bud in baker's yeast (Munchow et al., 2002). This result shows that even though *C. albicans ASH1* may not contain baker's yeast LE, there are still signals on *C. albicans ASH1* that can be recognized by proteins in baker's yeast for localization.

I am interested in the question: what are the localization-like elements in *C. albicans ASH1* that signal for protein recognition and localization? To further understand localization of *ASH1*, I used web-based software to align *ASH1* mRNAs from different yeast species. Alignment compares mRNA between different species to find similarities that may suggest a functional or structural conservation. Species with and without She2p that are related to baker's yeast or *C. albicans* were selected for *ASH1* alignment. Results showed that there were little to no similarities in *ASH1* mRNA among species with or without She2p suggesting that there is limited functional or structural conservation of *ASH1* between species. Next, I focused on one of the most studied LE in baker's yeast called E3. From the alignment, I selected the segment of *ASH1* mRNA that aligns with baker's yeast E3 and predicted the structure of that segment from *C. albicans*. Confirming the alignment results, the E3 structure was not similar between *C. albicans* and baker's yeast.

All these results suggest that *C. albicans ASH1* does not have an LE similar to baker's yeast. However, as mentioned previously, *C. albicans ASH1* can localize to the bud when studied in baker's yeast. Therefore, to further understand how *C. albicans ASH1* localizes and what localization-like elements are in *C. albicans ASH1*, I can design an experiment to visualize *C. albicans ASH1* movement in baker's yeast to perform in the McBride lab next summer or in my senior year.

Through literature search, computer alignment experiments, and weekly meetings with the McBride lab, I have built important skills such as presenting on literature sources, keeping laboratory notebooks, designing experiments and communicating with members of the McBride lab.

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