Testing conservation of a messenger RNA localization pathway in yeast

Kevin Chi, Class of 2021

Candida albicans is a harmless organism that commonly lives on the skin or inside the body [1]. *C. albicans* becomes an infectious organism, however, when it grows out of control, or when it enters deep inside the body. This ability of *C. albicans* to infect the host has been linked to its ability to transform its shape [1, 2]. It typically exists in an oval-shaped "yeast" form, but under stress, adapts an elongated, filamentous form, called a hypha [3]. In this filamentous form, *C. albicans* can anchor into host tissues, invade host tissues and migrate into the bloodstream to cause widespread infections [4, 5].

In the form change of *C. albicans*, protein synthesis and location play important roles. Some of the key proteins for hyphal function arrive at the tip of the hypha via messenger RNA (mRNA) localization: mRNAs — molecules that carry genetic information from DNA — are specifically transported from the nucleus to the tip of the hypha, where they transfer the genetic information onto chains of amino acids, or protein [6]. This way, protein activities are restricted to a certain place within the cell [7].

Our understanding of the molecular mechanism of mRNA localization in *C. albicans* still remains incomplete. *Saccharomyces cerevisiae*, also called baker's yeast, serves as a useful model organism to study this process. Baker's yeast is a relatively well-characterized yeast species that can also adopt a filamentous form and displays a high degree of similarities with *C. albicans* in cellular mechanisms [8, 9]. In baker's yeast, localization of mRNAs occurs via the She-mediated transport system, in which proteins called She3 and She2 facilitate the asymmetric localization of the mRNA by binding to specific mRNAs and to a motor protein that mobilizes this complex [9].

In *C. albicans*, localization of mRNAs occurs via similar pathway but without the presence of the She2 protein [10]. This observation suggests that the She3 proteins in baker's yeast (ScShe3) and *C. albicans* (CaShe3) may have differences in the mechanism of function. Specifically, how the CaShe3 protein binds to and localizes mRNAs remains unclear [11]. Thus, my main research question is, "Can CaShe3 protein replace ScShe3 protein's role in localizing mRNA to specific locations in baker's yeast cells?". Addressing this question will show how similarly the CaShe3 protein and the ScShe3 protein function and illuminate the possibility that the yet-to-be identified She2-like protein exists in *C. albicans*.

This summer, I have conducted a thorough literature review of the She-mediated mRNA transport system in yeast and developed detailed plans for experiments that will address my main research question. Conducting the literature review, I have built a solid current understanding of this transport system and became familiar with commonly used methods in yeast research. Developing the detailed experimental plan has compelled me to think more creatively and more independently to imagine different ways to address the research question. I have planned two experiments – a growth assay and a localization experiment. The former will reveal whether baker's yeast cells that contain the CaShe3 protein instead of the ScShe3 protein will induce the same physical form as baker's yeast cells containing the ScShe3 protein. The latter experiment will allow me to visualize RNA movements in live cells. Visualizing RNA movements will demonstrate on a molecular level whether cells that contain the CaShe3 protein instead of the ScShe3 protein will display similar mRNA movement patterns as do cells containing the ScShe3 protein. With a slight modification to this experiment, I can also detect which proteins associate with the mRNAs that are transported to the tip of elongated yeast cells, which will show whether the CaShe3 protein interacts with the She2 protein, or other proteins, in baker's yeast. As I am pursuing an honors project on the same topic during the academic year, the work I have done for the fellowship has prepared me well. In the fall, when I have access to necessary laboratory equipment, I will be able to transition smoothly into executing the planned experiments.

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