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To Whom It May Concern:

I met Dr. Barry Williams (Barry) about 3 years ago when he came to me to discuss technical aspects of yeast molecular genetics. At this time, he was beginning an ambitious but well-considered project to examine the relationship between changes to specific genes during evolution and the quantitative effects on the fitness of an organism. His idea seemed smart and timely to me—the whole genome sequences and the experimental possibilities in yeast that far surpass those available in any other type of organism seemed ideal for the types of experimental-evolution questions he hoped to pursue.

My own lab pursues mechanistic questions in *Saccharomyces cerevisiae* centered on the structure and function of a highly conserved protein complex called the origin recognition complex (ORC). The essential role for ORC, and the role that generates the most publicity, is in marking chromosomal positions as replication origins, the sites at which DNA replication initiates. This basic functional role is highly conserved and so are the protein-protein interactions between ORC and other players in DNA replication. However, ORC has a second "non-essential" role (in terms of cell viability) in controlling specialized chromatin structures. This basic role is also conserved at some level among eukaryotic organisms, although the types of chromatin-mediated functions and the protein partners that are involved appear to vary substantially. My lab concentrates on this second role for ORC in *S.cerevisiae* with the goal of understanding how it is specified and related to ORC's primary role in DNA replication. We have examined a specific protein-protein interaction in mechanistic detail between ORC and a chromatin-protein in yeast called Sir1p, including recently solving the structure of a complex between two relevant domains in these proteins. One of the reasons this interaction is interesting is that, although the region on ORC that is involved is conserved, the Sir1p is not. In fact, a Sir1p cannot be found outside the *Saccharomyces* genus! Barry is particularly intrigued by this, as is my lab, and he sees real advantages to studying the *SIR1* gene using his fitness approaches because he can, ultimately, relate these studies to hard molecular, biochemical and structural data obtained in my lab for relevant complexes in *S.cerevisiae* and other related species.

Barry and I have had many discussions about this joint venture and I have found him to be a thoughtful colleague and a strong communicator. We each come from two very different backgrounds yet I find it easy to communicate with Barry. I am more than happy to provide data and technical expertise on the experimental manipulation of yeast to help Barry pursue his interesting experiments. From my experiences with Barry I anticipate that he will be very successful at what he does and will make a wonderful faculty colleague.

Sincerely,

Catherine A. Fox
Associate Professor