Title of Project	RNA interference in *Cryptococcus neoformans*
Cell Mechanism Supervisor Name	Liz Bayne
Quantitative Supervisor Name	Sander Granneman

Summary of project

RNA interference is a fundamental mechanism of genome regulation mediated by small RNAs, which direct silencing of complementary target RNAs at either transcriptional or post-transcriptional levels. RNAi pathways are conserved from yeast to human, and play important roles in gene regulation and genome stability, as well as in host-pathogen interactions.

Cryptococcus neoformans is an opportunistic human fungal pathogen responsible for ~1 million cases of meningitis per year in immunocompromised individuals. It is evolutionarily distant from more commonly studied yeast model systems such as *Schizosaccharomyces pombe*, and also appears to have a more complex RNAi pathway, with two of each of the core components, Dicer and Argonaute, each operating on distinct targets according to our preliminary analyses.

The aim of this project is to further investigate the RNAi pathway in Cryptococcus, to understand the molecular mechanisms involved, and the potential roles of RNAi in regulation of gene expression and genome stability in this human pathogen. We have already generated Cryptococcus strains bearing deletions or tagged versions of various RNAi-related genes; by employing a range of genome-wide approaches including RNA-seq, CRAC (RNA-protein crosslinking) and ChIP-seq we will investigate which genomic loci are targeted by RNAi, whether different genomic loci are targeted by different elements of the RNAi machinery, and whether they are subject to different mechanisms of regulation. To investigate possible roles of RNAi in the adaptive response to changes in growth conditions we will conduct experiments on Cryptococcus grown in a variety of different conditions, including conditions mimicking infection.