Bessie Kebaara and Erich Baker
Biology / College of Arts & Sciences

Identification of alternatively 3'-end processed messenger RNAs (mRNA) in Sacchromyces cerevisiae

Messanger ribonucleic acid (mRNA) decay is important in the regulation of gene expression. The amount of mRNA present at a specific time in a cell is dependent on the rate of synthesis and decay of that specific mRNA. mRNA processing determines the 3'-end of each mRNA and the length of the 3' untranslated region (3' UTR). Typical Saccharomyces cerevisiae cellular mRNAs have 3′ UTRs that range in size from 50-350 nucleotides, with most of the mRNAs 3′-UTRs in the 100 nucleotide range. We have shown that natural mRNAS containing atypically long 3'-UTR are rapidly degraded by the nonsense-mediated mRNA decay pathway in S. cerevisiae. The nonsense mediated mRNA decay pathway (NMD) is a specialized mRNA decay pathway that recognizes and rapidly degrades mRNAs with premature stop codons and some natural mRNAs as well. Natural (non-nonsense codon containing) mRNAs degraded by NMD have been identified in Saccharomyces cerevisiae, Drosophila melanogaster and humans. 5-10% of the S. cerevisiae transcripts are affected when this pathway is inactivated. Additionally, there are physiological consequences associated with the degradation of natural mRNAs by this pathway. It is important to understand the role the nonsense-mediated mRNA decay pathway plays in natural mRNA degradation because in humans this pathway is currently being targeted to treat genetic diseases caused by genes that contain nonsense mutations. Thus, it is important to understand the role the NMD pathway plays in regulation of natural mRNAs in order to facilitate development of therapies that are specific to nonsense-mRNA while causing the minimal side effects.

This grant will be used to: 1) Evaluate the extent to which natural mRNAs in the yeast S. cerevisiae undergo alternative 3'-end processing producing different isoforms of the same mRNAs, 2) Determine the extent to which these mRNAs are degraded by the nonsense-mediated mRNA decay pathway.