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mRNA degradation is an important step in gene expression that is traditionally thought to occur in the cytoplasm. However, a recent genome-wide study uncovered a class of genes whose transcripts are predicted to be primarily degraded in the nucleus. Yet, it is unclear how and why these mRNAs undergo nuclear degradation. Dr. Chantal Guegler will use both candidate- and screening-based approaches to determine which pathways are important for nuclear mRNA degradation, and how this process influences cellular physiology. Dr. Guegler will conduct this research in <u>Dr. Stirling Churchman's lab</u> at Harvard Medical School. This work will reveal the key determinants of nuclear mRNA degradation and how this process contributes to gene expression regulation.

As a graduate student, Guegler studied bacterial toxin-antitoxin (TA) systems and their role in protecting against bacteriophage infection in <u>Dr. Michael Laub's lab</u> at the Massachusetts Institute of Technology. There, Dr. Guegler demonstrated that the <u>RNase toxin ToxN cleaves phage mRNAs to disrupt the translation and assembly of viral particles</u>. Interestingly, Guegler also demonstrated that <u>T4 phage can combat ToxN using the phage-encoded antitoxin TifA that sequesters RNA-bound ToxN to prevent it from degrading additional phage mRNAs</u>. With her background in RNA degradation in bacterial TA systems, Dr. Guegler will now investigate nuclear mRNA degradation in eukaryotic cells.

