Personal statement: I am a perfect fit for this F32 fellowship project because it leverages my past experience and will position me well for my ideal next steps. My ideal career is to lead a lab that focuses on using a mixture of massively parallel assays and computational modeling to understand biological questions. I value the ability to pursue fundamental questions but also want to see the answers to those questions make a difference in the lives of people. Because of this, I aim to work at a university or research institute where I can study both the fundamental and the applied sides of problems. I am broadly interested in asking questions about how information encoded in the sequence of biological molecules controls the phenotypes we observe and in working on applications in human health or climate. Through these topics, I hope to be able to both contribute to our understanding of biology and to apply that knowledge to real problems. My proposed project leverages massively parallel splicing assays to provide an unbiased look at sequence elements that are important for establishing mutual exclusivity between exons 9 and 10 in pyruvate kinase M. I will follow up this work with both targeted experiments and modeling to elucidate the mechanisms of mutual exclusivity. My previous research has given me the skills I will need for this project. During my Ph.D. I performed a massively parallel growth assays to identify genes involved in the CO_2 concentrating mechanism in a chemoautotroph and measure their phenotypes as a function of CO_2 concentration. I followed up these experiments with detailed mechanistic experiments including reporter strain growth experiments,[1,2] I also used a mixture of massively parallel growth assays and modeling to map the fitness landscape of dihydrofolate reductase and design new functional variants in work that is in prep. I further demonstrated my ability at biochemical identifying the zinc binding behavior of the newly discovered CasX.[3] Finally, I applied kinetic modeling to design signal amplification strategies for cas13-based detection of RNA viruses.[4] These experiences prepared me well to use massively parallel assays, focused genetic and biochemical experiments, and modeling to characterize splicing regulation. This project will help me achieve my scientific goals by broadening my experience. My previous work has focused on applying massively parallel techniques and modeling to the study of microbiology and protein engineering. This project will allow me to explore applications in RNA biology, in the human-cell context, and with long read sequencing read outs. Further, this experience will allow me to grow and strengthen my experience with computational modeling by enabling me to work in the Kinney lab and in the Cold Spring Harbor Laboratory Simons Center for Quantitative biology, where I can work with world class experts on modeling of biological systems.

[1] John J Desmarais et al. "DABs are inorganic carbon pumps found throughout prokaryotic phyla". en. In: *Nat Microbiol* 4.12 (Dec. 2019), pp. 2204–2215. ISSN: 2058-5276. DOI: 10.1038/s41564-019-0520-8.

[2] Avi I Flamholz et al. "Trajectories for the evolution of bacterial CO_2-concentrating mechanisms". In: *Proceedings of the National Academy of Sciences* 119.49 (2022), e2210539119. DOI: 10.1073/pnas.2210539119.

[3] Jun-Jie Liu et al. "CasX enzymes comprise a distinct family of RNA-guided genome editors". en. In: *Nature* (Feb. 2019), p. 1. ISSN: 0028-0836. DOI: 10.1038/s41586-019-0908-x.

[4] Tina Y Liu et al. "Accelerated RNA detection using tandem CRISPR nucleases". en. In: *Nat. Chem. Biol.* (Aug. 2021), pp. 1–7. ISSN: 1552-4450. DOI: 10.1101/2021.03.19.21253328.