ASPIRE League Partnership Seed Fund
2nd (2020) Round – Project 1
Research Project Summary

Q1. Title of Research Project
Investigation of primate-specific RNA-editing using single-cell RNA-seq
Q2. Timeframe
Project Start: 01/10/20 Project Completion: 01/04/22
Q3. Project Synopsis

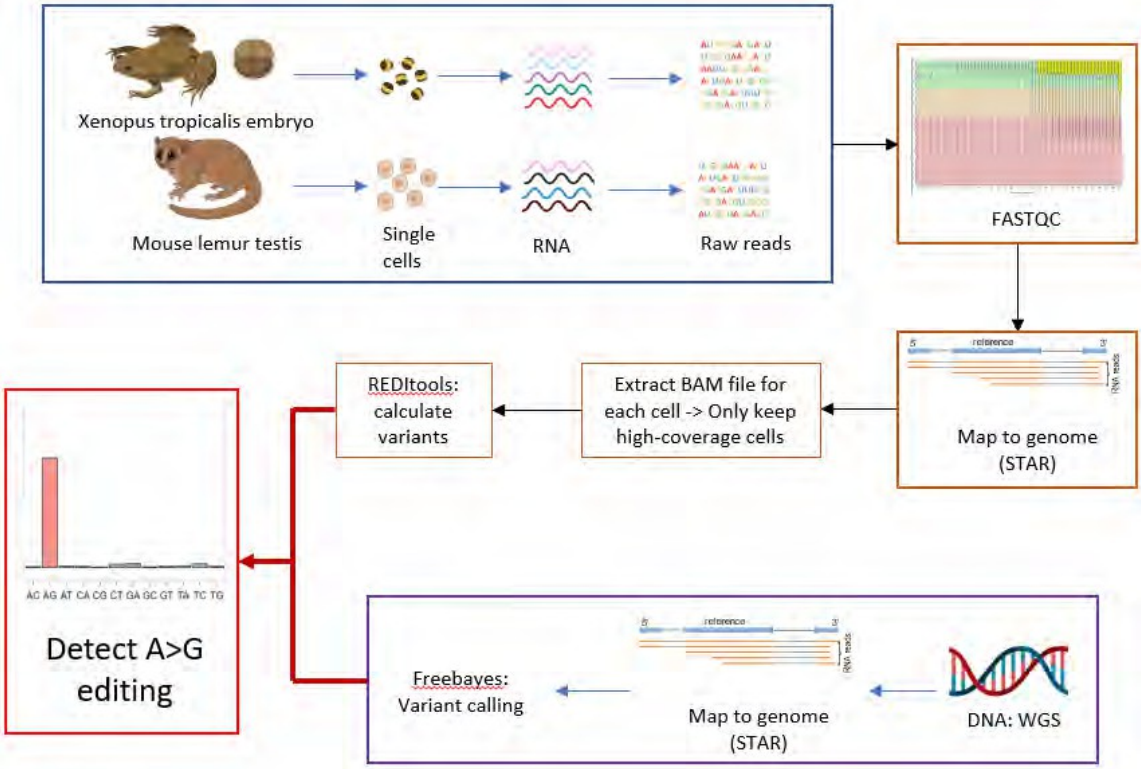

Figure 1. An overview of our research study.

RNA editing is a fundamental but incompletely understood molecular process in the cell. It has been observed in organisms across the evolutionary tree, but its functions can differ widely from organism to organism. Existing literature has shown that RNA editing plays an important role in environmental adaptation, and evolutionarily is associated with the emergence of complex biological functions in higher species. Furthermore, RNA editing mis-regulation has also been implicated in myriad diseases, including brain-associated pathologies such as autism and Alzheimer's, cancer, and autoimmune disorders. Hence, there is great interest in studying RNA editing, of which the dominant type is an adenosine to inosine (A-to-I) conversion mediated by the ADAR family of enzymes. However, studies that examined A-to-I editing in vivo have largely explored the molecular process only in whole embryos and bulk tissues. While some understanding of RNA editing can be gained in such studies, much useful information is unfortunately lost because embryos and tissues are highly complex and are made up of heterogeneous cell types. Hence, many critical signals are lost in bulk analysis. To address the problem, we sought to leverage on single-cell RNA-seq (scRNA-seq), which is a new technology that can dissect tissue heterogeneity and has proven insightful for studies on embryos as well as normal and diseased samples. In this project, we performed RNA editing analysis on three different scRNA-seq datasets – GM12878, mouse lemur testis, and *Xenopus tropicalis* embryos (Figure 1). Of note is the mouse lemur, which is a small primate that is currently being

explored as a new animal model to study human biology and diseases. Our analysis revealed some challenges with the analysis of RNA editing in single cells from outbred animal embryos and tissues using existing scRNA-seq technologies. The insights gained will lay the groundwork for future studies on RNA editing in heterogeneous samples.