Bioengineering Day Poster Addendum (ABET)

1. Desired Needs:

(1) Need for an RNA therapeutic that will reverse the progression of neurodegenerative diseases due to age. **(2)** Need to create a more stable U1 snRNA variant that would help the spliceosome complex remain normal functioning. **(3)** Need to demonstrate proof of concept for RNA mutagenesis as a therapeutic approach.

2. Constraint (to be considered with the continuation of this project into therapeutic settings):

a. Safety/Regulatory Affairs: potential off-target splicing effects and challenges meeting FDA requirements for RNA therapeutics.
b. Risks: variable guide performance, limited translation of reporter results to endogenous MAPT splicing, and possible toxicity from engineered snRNAs.
c. Global Impact: potential treatment applications for neurodegenerative diseases involving tau dysfunction.
d. Manufacturability: maintaining stable and consistent production of RNA constructs or viral vectors.
e. Quality Control/Marketability: therapeutic success depends on proving improved safety and efficacy over existing treatments.

3. Engineering Standards:

Engineering standards were not a major focus during the early proof-of-concept stage of this project, but they would become critical if the engineered U1 snRNA system were developed into a therapeutic. FDA guidelines for gene and RNA-based therapies would require extensive testing and standardization, including proof-of-concept studies, toxicity analysis, tumorigenicity testing, animal studies, cell distribution studies, and determination of safe and effective dose levels. These standards would ultimately constrain the design, safety, performance, and clinical application of the therapeutic.

4. Ethical, Environmental, and Societal Concerns:

Engineered U1 snRNA therapeutics could cause unintended changes in RNA splicing, raising concerns about long-term safety and genetic manipulation. The production and disposal of genetically modified materials and viral vectors must be carefully controlled to prevent environmental contamination. Although this technology could help treat neurodegenerative diseases, the high cost and complexity of RNA therapeutics may limit accessibility for many patients.

5. Active Teamwork and Leadership

a. Collaboration: weekly meetings encouraged open discussion of ideas and data analysis.
b. Delegation: tasks were divided based on strengths; Emily focused more on coding while I handled detailed lab protocols and technicalities. Wet lab work was shared evenly.
c. Goals and Deadlines: weekly meetings helped set project goals and keep it on schedule.
d. Constructive Feedback: regular meetings with our mentor allowed for constructive feedback and problem-solving discussions.

6. Motivating Factors

a. New Knowledge: gaps in knowledge that would surface during more difficult wet lab work and data analysis would call for deeper literature review and self-study.
b. Self-Initiating: eagerness to learn and master new lab skills would call for self-initiating, as well making sure to keep the project on track if we were falling behind.
c. Persistence: in light of setbacks, review of previous steps and immediate planning of the next steps was done to ensure the same mistakes wouldn't be done again to keep us on track.