Mitochondria are small structures inside cells that are essential for many important functions, like producing energy, controlling cell death, sending signals, and managing calcium levels. When mitochondria don't work properly, it can lead to serious diseases such as heart problems, autoimmune conditions, neurodegenerative disorders, metabolic diseases, and cancer.

To function well, mitochondria need many proteins, most of which are made from instructions in the cell's nucleus and then transported into the mitochondria. If these proteins are made incorrectly or don't fold properly, they can build up and cause stress inside the mitochondria. In response, the cell activates a protective system called the **mitochondrial unfolded protein response (mtUPR)**, which is similar to a well-known system in the endoplasmic reticulum (ER) called the **unfolded protein response (UPR)**.

Recent studies suggest that during mtUPR, the cell slows down protein production to reduce stress. However, it's still unclear how the cell controls the levels of mRNAs (the messages that tell the cell which proteins to make) for mitochondrial proteins. If translation restarts too quickly after the stress ends, it could lead to too many mitochondrial proteins being made, causing more stress.

My early research shows that mtUPR activates a protein called **IRE1**, which is known to break down RNA during ER stress. This leads to my main idea: **there may be special mechanisms during mtUPR that help break down mRNAs for mitochondrial proteins**, preventing their overproduction. These mechanisms might involve IRE1 or small regulatory RNAs called **miRNAs**, which are controlled by a protein called **ATF5**.

This project aims to discover how RNA is broken down during mtUPR, through two main goals:

Aim 1:
To find out if miRNAs activated by mtUPR help reduce the amount of mitochondrial proteins. I will use sequencing to identify these miRNAs, and test whether they target mRNAs for mitochondrial proteins.

Aim 2:
To test if IRE1 helps reduce mRNAs for mitochondrial proteins during mtUPR. I will block IRE1 with a specific inhibitor and use RNA sequencing to see which mRNAs are affected. I'll confirm the results with lab techniques like qPCR and Western blot, and also test how blocking IRE1 affects cell survival and energy production.

Currently, we know very little about how mRNA is controlled during mtUPR. To my knowledge, no one has studied the roles of IRE1 or ATF5-related miRNAs in this process. This makes the project highly original and potentially important for understanding how cells keep mitochondria healthy — which could lead to new ways to diagnose or treat many diseases.