The Use of Prime Editing To Induce and Correct the CFTR-F508del Mutation in Induced Pluripotent Stem Cells

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According to the Cystic Fibrosis (CF) Foundation, over 70,000 people across the globe suffer from CF, and the life expectancy of patients with CF drops to about the age of 44. CF is an autosomal recessive inherited condition that makes a patient's mucus thicker and stickier, which can lead to lung damage and infection. Approximately 70-90% of these cases are caused by a 3-bp deletion known as CFTR-F508del. Given the critical need for novel therapeutic interventions with greater efficacy, I aimed to model this mutation using prime editing and iPSCs to later differentiate and use these cells for studying CF. iPSCs serve as excellent models for disorders that affect different parts of the patient's body, due to their pluripotency. Prime editing serves as a powerful genetic editing alternative to the more traditional CRISPR/Cas9 method, as prime editing is safer and more reliable. Here, I report the successful reprogramming of fibroblasts into iPSCs and cloning of the pegRNAs required for prime editing. I then attempted to use prime editing to both induce and correct this mutation. The efficiency of the correction was higher than that of the induction; however, it was still very low. I am working to optimize the prime editing of the iPSCs via new and improved prime editing methods. Successful demonstration of prime editing in iPSCs holds great potential for not only studying CF in models, but for a wide range of genetic disorders in both research and clinical practice to soon help many patients.

Awards Won:
Third Award of $1,000