RaDiChal'21
FINAL

2021 Rare Disease Challenge

Suppression of DNA Methylation in the Promoter Region by CRISPR Cas9 Nickase and Graphene with Gene Therapy and Epigenetic Approach for MEFV Gene M694V Mutation

Resesif 16

Affiliation

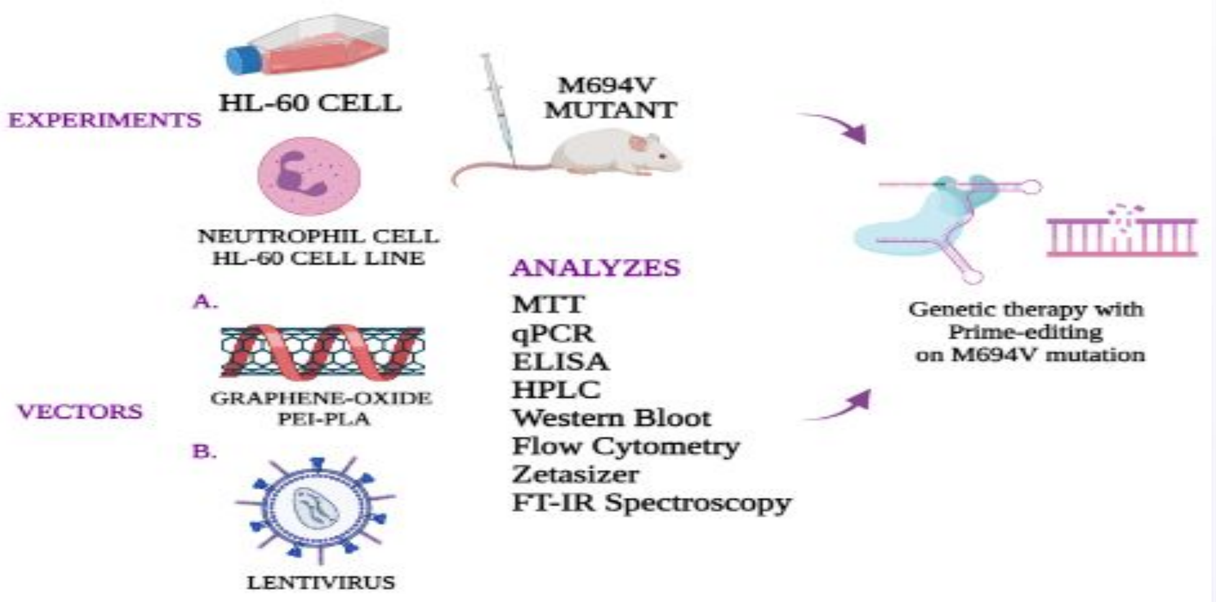
Kübra Nur GÖKDEMİR.Elif KARAKİŞİ. Menekşe YAMAÇ.
Dilara BULUT.Melike EKŞİ

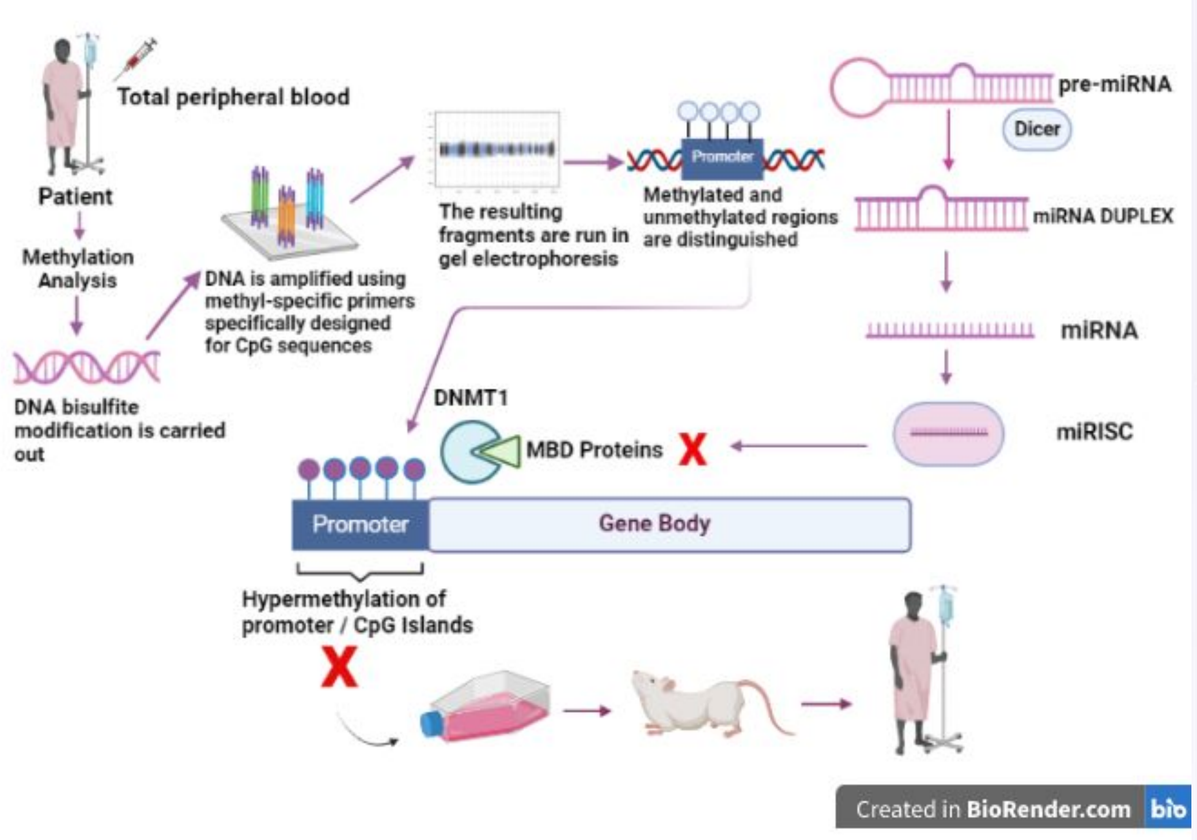
Abstract

Familial Mediterranean Fever (FMF) is an autosomal recessive autoinflammatory disease. It is characterized by recurrent episodes of fever and accompanying serositis. The disease occurs as a result of mutations in the MEFV gene [1]. Its incidence in Turkey is 1/1000. The most common mutations in the MEFV gene are M694V(51.4%), E148Q(16.41%), M680I(13.5%), V726A(13.43%) in exons 2,3,5 and 10.[2]

In this project, it is aimed to perform neutrophil-targeted genetic therapy, which is one of the basic cells of the immune system, in which the pyrin protein, which is known to be important in the regulation of inflammation in Familial Mediterranean Fever Disease, is mainly expressed, by prime-editing method. [3] The most commonly used cell line in neutrophil studies is the HL-60 cell line obtained from a female patient with acute promyelocytic leukemia[4] [5]. By targeting this cell line, vectorial transfer is aimed with the biocompatible Graphene Oxide-PEI-PLA. On the other hand, it is known that methylation in Fmf patients is 1.5 times higher than in healthy controls and that methylation is associated with the pathology of the disease [6]. In this part of our project, total peripheral blood will be drawn from patients in order to analyze the methylation status in CpG islets.Methylation specific PCR method will be preferred because it is a fast and sensitive method [7].After identifying the methylated and unmethylated regions as a result of these analyzes, it was aimed to silence hypermethylation in the promoter region by using RNAi directed against methyl binding proteins.

Projects





Social Impact

Followers: 872	381	162	-
Likes: 8052	2500	387	-
Sharings: 1000	-	-	-
Watchs: 5375	-	3949	-

Conclusion

In the first step of our project; The M694V mutation, which causes the development of various complications in Familial Mediterranean Fever Patients, will be corrected by targeting neutrophils from immune cells and performing genetic therapy with prime-editing, which is only one of the breakthrough innovations in genome engineering. With the GO modification, which is biocompatible, it is planned to transfer with lentivirus despite the problems that may occur in genetic therapy.

Since methylation must be present at certain levels in a healthy individual, hypermethylation in the promoter will be suppressed by passive demethylation mechanisms.

Since our participation in the competition, we have always aimed to create awareness in the most original, different and various fields by working together with patients and their relatives in our social awareness activities. The feedback we receive is one of the most important factors that motivate us in this process.

References

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