BIOINFORMATIC STUDY OF GENES RESPONSIBLE FOR FAMILIAL MEDITERRANEAN FEVER

Aysel Mammadova[1], Ayaz Mammadov[1]
[1]Western Caspian University, Baku/Azerbaijan

Abstract: This article is a bioinformatics study of the MEFV gene. Bioinformatics involves the study of genetic variations and their association with diseases using computational tools used to analyze biological data. To understand what diseases the MEFV gene causes due to mutations, the gene was analyzed using various bioinformatics programs. By comparing MEFV sequences from different species using BLAST and Clustal Omega programs, the extent to which the gene is conserved across organisms was studied. The study performed a bioinformatics analysis of the MEFV genes from *Homo sapiens* (humans), *Mus musculus* (house mouse), and *Prionailurus bengalensis* (Bengal cat). The gene length, number of nucleotides, and percentages were analyzed for all three species, and although these values are different, it was found that the gene is orthologous, meaning it performs the same functions.

Keywords: MEFV gene, nucleotide sequence, mutation analysis, orthologous genes, bioinformatics analysis.

***Corresponding Author:** kamalovaaysel@gmail.com

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Introduction:

Familial Mediterranean Fever (FMF) is a group of hereditary inflammatory diseases and is widespread mainly in the Mediterranean region (Ozdogan & Ugurlu, 2019; Onen, 2006; Bakkaloglu, 2003). The disease is accompanied by fever, abdominal, chest and joint pain, which seriously impairs the quality of life. FMF is an autosomal recessive hereditary disease, that is, the disease is transmitted from parents to offspring by transmitting mutations in the FMF gene. The FMF gene provides the synthesis of the pyrin protein, which plays an important role in the regulation of inflammation in the body (Richards & ets, 2001; Bertin & DiStefano, 2000; Srinivasula & ets, 2002). When the function of the pyrin protein is impaired, abnormal inflammatory reactions occur in the body, which leads to FMF.

Different mutations of the MEFV gene can lead to different phenotypes of FMF disease with different symptoms. Determining the location and effect of these mutations is important for understanding the disease at the molecular level and developing treatment strategies. For this reason, research on the MEFV gene is one of the main areas of research in the diagnosis and treatment of FMF disease. Bioinformatics serves as an important tool for better understanding the genetic basis of diseases.

Bioinformatics is an interdisciplinary field that uses mathematical and computational methods to collect, store, analyze, and interpret biological data ((Luscombe & ets, 2001; Morgan & ets, 2024; Yamashita & ets, 2023)). This field is particularly concerned with the analysis of genetic and protein sequences, prediction of structure and function, study of

genetic variations, and understanding of disease mechanisms at the molecular level. Bioinformatic analysis of the MEFV gene involves the use of various programs and methods to better understand the structure and function of this gene and its association with disease through mutations.

The MEFV gene is studied not only in humans but also in other species, studying how the gene is preserved during evolution and the functional similarity of orthologous genes. In this study, a comparative analysis of the MEFV gene was conducted in species such as *Homo sapiens* (humans), *Mus musculus* (house mouse) and *Prionailurus bengalensis* (Bengal cat). Comparison of the nucleotide sequences of the MEFV gene, the regions susceptible to mutations, as well as the structure and function of the encoded protein pyrin among these species revealed which organisms have the most common mutations associated with the disease.

The bioinformatic analyses performed may provide more information about the molecular basis of FMF disease and contribute to the development of modern methods, such as gene therapy, for the treatment of this disease in the future. In this article, based on the analysis of the MEFV gene mutations, we consider the role of this gene in the development of FMF disease, how it is conserved in the evolutionary process in different species, and how the results obtained by bioinformatics methods can be used in the study of methods for treating the disease.

Materials and Methods:

In this study, a bioinformatic analysis of the MEFV gene responsible for Familial Mediterranean Fever (FMF) was performed. Various computational methods and bioinformatics tools were applied to study the structure, function and association of the MEFV gene with diseases due to mutations. The study conducted a comparative analysis of the MEFV gene in three major species - *Homo sapiens* (human), *Mus musculus* (house mouse) and *Prionailurus bengalensis* (Bengal cat).

Gene Sequences Obtained DNA and protein sequences of MEFV gene were obtained from databases such as NCBI (National Center for Biotechnology Information) and Ensembl. These data served as the main source for analyzing gene length, nucleotide sequence, and genetic variations among species.

Software for comparative analysis of nucleotide and protein sequences, such as Clustal Omega and BLAST (Basic Local Alignment Search Tool), were used to compare the nucleotide sequences of the MEFV gene between different species. Using these tools, similarities and differences between gene sequences of different species were visualized, and whether a gene was orthologous or not was determined. The results were used to analyze how disease-causing mutations are maintained throughout evolution.

Identification of genetic variations. Genetic variants of the MEFV gene, including single nucleotide polymorphisms (SNPs), insertions, deletions, and structural variations, were identified using programs such as GATK (Genome Analysis Toolkit), SAMtools, and BCFtools. These analyses identified potential disease-causing mutations.

Gene expression analysis. Transcriptomic data were obtained from databases such as GTEx (Genotype-Tissue Expression), TCGA (The Cancer Genome Atlas) and ArrayExpress to study how gene expression changes in different tissues, cell types and conditions. These data were used to understand under what conditions and to what extent the MEFV gene is active in FMF disease.

Homology modeling or AB initio modeling methods were used to predict the three-dimensional structure of the pyrin protein. Structural bioinformatics tools such as Swiss-Model and PyMOL were used for this process. In this way, it was analyzed how the identified mutations affect the structure and function of the pyrin protein. Evaluation of the impact of mutations. Programs such as PyMOL and Swiss-PdbViewer were used to evaluate the impact of mutations on the pyrin protein. These tools played an important role in investigating how disease-causing mutations affect protein stability and function.

Phylogenetic Analysis and Population Genetics MEGA (Molecular Evolutionary

Genetics Analysis) software was used to construct a phylogenetic tree, calculate FST, and analyze allele frequencies. This analysis allowed us to study the evolutionary history of the MEFV gene and the prevalence of mutations in different populations.

Using these methods, a detailed study was conducted to understand how the MEFV gene is evolutionarily conserved, genetic variations in different species, and the role of this gene in the development of FMF disease.

Results and discussions:

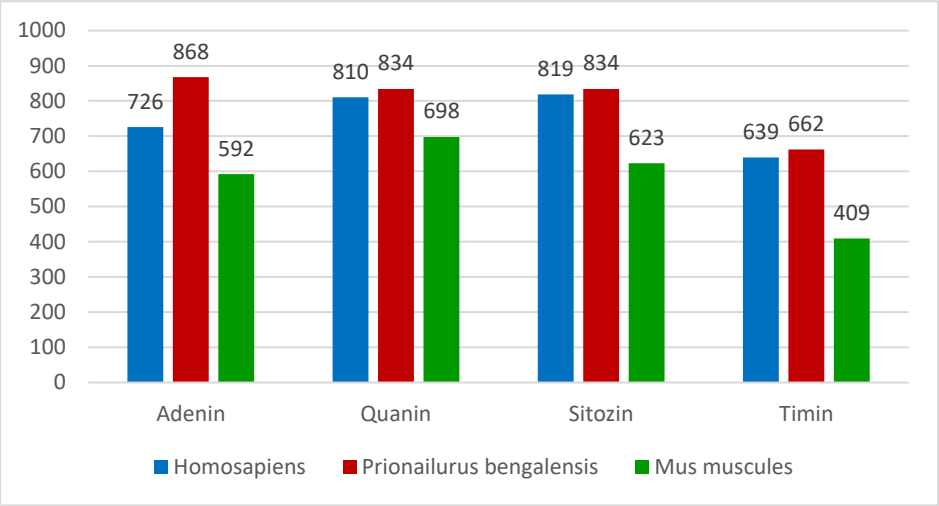
Bioinformatics analysis of the MEFV gene. Bioinformatics is an interdisciplinary field that combines biology, computer science, mathematics and statistics to analyze and interpret biological data. The main focus of bioinformatics is the development of methods and tools for understanding biological processes at the molecular level. This includes the analysis of DNA, RNA and protein sequences, prediction of protein structures and functions, the study of genetic variations and their association with diseases, modeling of biological pathways, etc. includes.

Bioinformatic analysis of the MEFV gene involves a number of computational methods to understand its structure, function, and association with diseases caused by gene mutation. For this purpose, the DNA or protein sequence of the MEFV gene was first obtained from databases such as NCBI or Ensembl and visualized using programs such as BLAST or Clustal Omega, which will be necessary for comparing MEFV sequences between different species. Genetic variants of the MEFV gene, including single nucleotide polymorphisms (SNPs), insertions, deletions, and structural variations, can be identified using programs such as GATK, SAMtools, or BCFtools. In addition, the frequency and distribution of MEFV gene variants, genetic diversity, population structure, and evolutionary dynamics can be estimated using methods such as allele frequency analysis, FST calculation, or phylogenetic tree construction. Using transcriptome data from databases such as GTEx, TCGA or ArrayExpress, it is possible to analyze MEFV gene expression patterns in different tissues, cell types and conditions, and generate a 3D structure of pyrin using protein structure prediction programs such as homology modeling or AB initio modeling and simultaneously determine that we can analyze how variants may affect protein structure, stability and function using structural bioinformatics programs such as PyMOL or Swiss-PdbViewer.

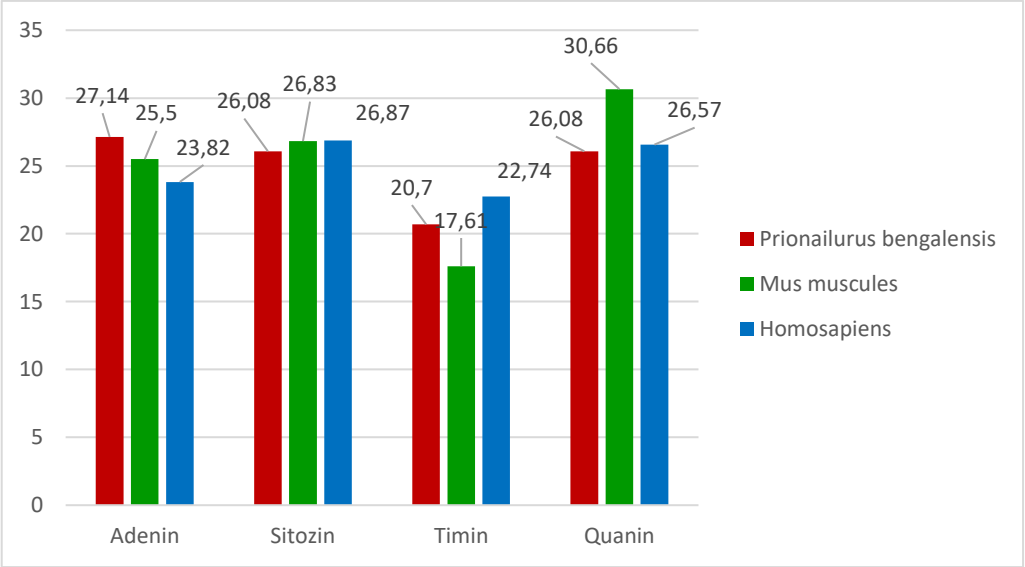
Bioinformatic analysis of the MEFV genes of *Homo sapiens* (human), *Mus musculus* (house mouse) and *Prionailurus bengalensis* (Bengal cat) revealed differences in gene length, nucleotide sequence, nucleotide count, nucleotide content and codon arrangement, and clearly showed promoter regions (Tables 1, 2; Schemes 1, 2, 3). Comparison of the MEFV gene will tell us whether these organisms are orthologous, which will form the basis for the use of methods such as gene therapy to eliminate mutations that cause AAA disease.

Table 1. Gene length, number of nucleotides and percentage values.

Name	Lenght	A	C	T	G	A%	C%	T%	G%
Prionailurus bengalensis	3198	868	834	662	834	27.14	26.08	20.70	26.08
Mus musculus	2322	592	623	409	698	25.50	26.83	17.61	30.66
Homo sapiens	3048	726	819	693	810	23.82	26.87	22.74	26.57



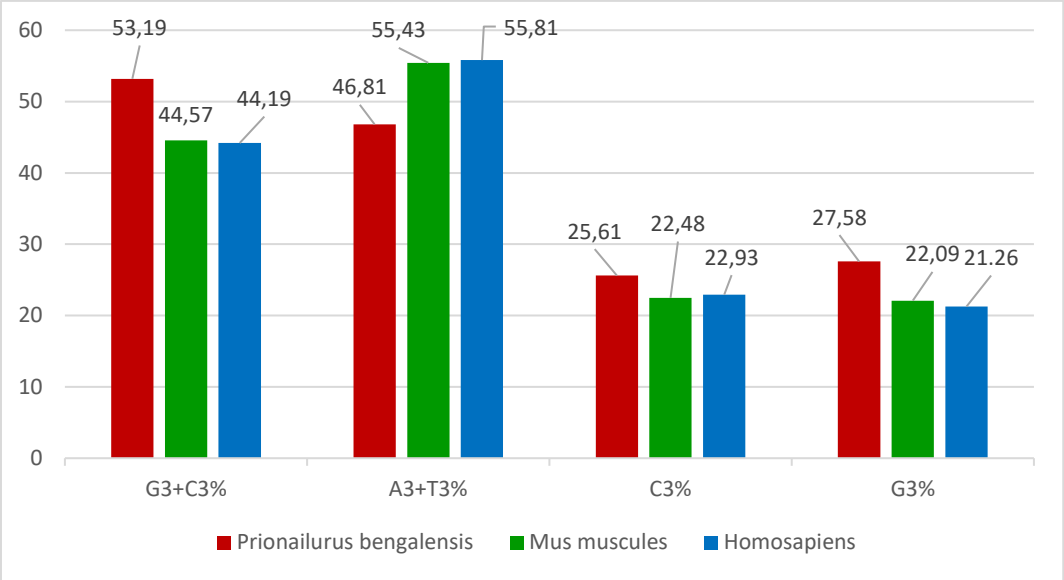
Scheme 1. Schematic estimation of the number of nucleotides.



Scheme 2. Schematic assessment of nucleotide percentages.

Table 2. Percentage of mutable nucleotides.

Name	G+C %	G+A %	G+T %	A+T %	A+C %	C+T %	G3+C 3%	A3+T 3%	C3%	G3%
Prionailurus bengalensis	52.16	53.22	46.78	47.84	53.22	46.78	53.19	46.81	25.61	27.58
Mus musculus	56.89	55.56	47.67	43.11	52.33	44.44	44.57	55.43	22.48	22.09
Homo sapiens	53.44	50.39	49.31	46.56	50.69	49.61	44.19	55.81	22.93	21.26

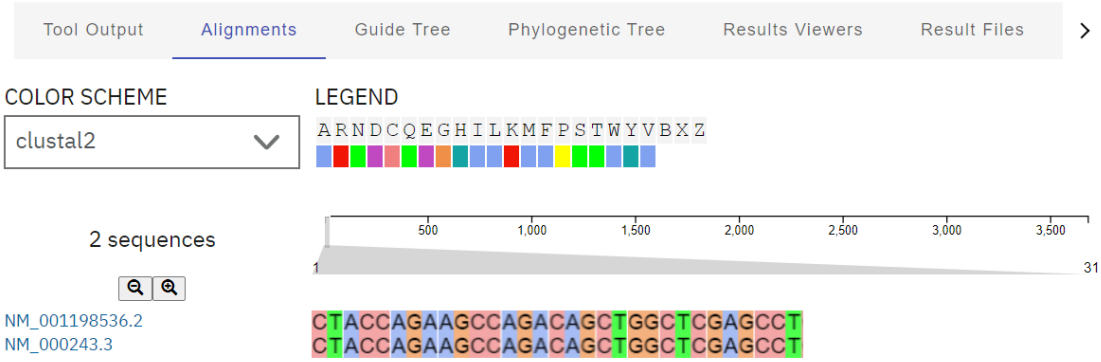


Scheme 3. Percentage of mutable nucleotides.

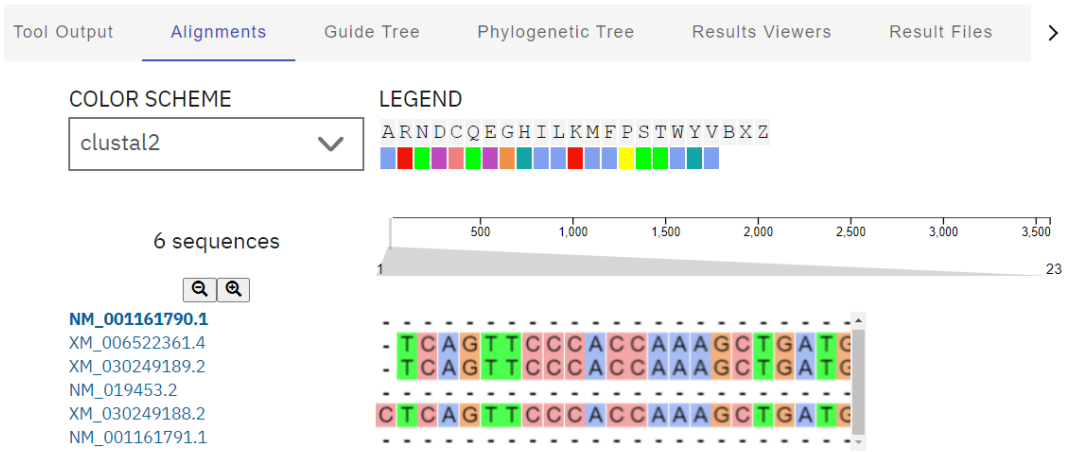
As can be seen from the diagrams, there were no significant changes in the number of nucleotides in these organisms. This indicates that the gene has not changed much over the years in orthologous organisms. These visualized results allow us to determine which organism is more prone to mutations. will be the basis for the application of methods such as gene therapy.

The studies and bioinformatics analysis show that the nucleotides in the 3rd position of the codon are more prone to mutations. If the disease is caused by a point mutation, then most likely it is associated with cytosine and guanine in the last position of the nucleotides. This can affect the structure and function of the pyrin protein. The specific effects of each mutation may vary, but they usually lead to increased inflammation and characteristic symptoms of FMF.

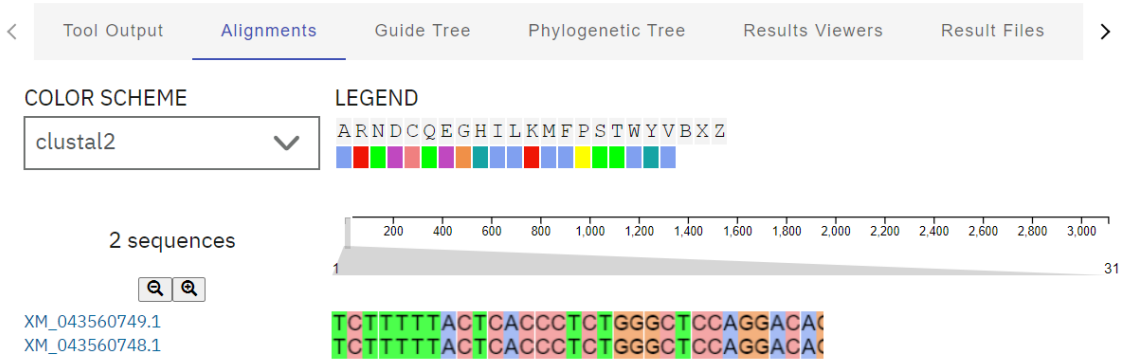
Visualization of the nucleotide sequence showed that these organisms do not have DNA with the same nucleotide sequence, but are composed of different codons encoding the same amino acid, and that although these compositions are different, they cause slight changes in the structure and function of the protein. . There are codons that code for the same amino acid, although they have different nucleotide sequences, indicating that the organisms are orthologous. Studying orthologs of the MEFV gene in different species helps researchers understand the evolutionary conservation of this gene and its importance in health and disease.



Nucleotide sequence of the *Homosapiens* MEFV gene.



Nucleotide sequence of the *Mus musculus* MEFV gene.



Nucleotide sequence of the *Prionailurus bengalensis* MEFV gene.

Conclusıon:

According to the results of this study, the bioinformatic analysis of the MEFV gene has great significance for understanding the genetic basis of FMF disease. The ortholog of the gene in Homo sapiens, Mus musculus and Prionailurus bengalensis and the conservation of genetic variations indicate that the gene plays important functions in the evolutionary process. The fact that the third nucleotides of codons are more prone to mutations plays an important role in the development of the disease. The obtained results indicate that mutations in the MEFV gene can cause AAA disease by changing the structure and function of the pyrin protein. Such bioinformatic analysis can lead to a more accurate understanding of the relationship between genetic variations and diseases, as well as to the development of treatment methods such as gene therapy. Thus, research conducted in this area opens up new prospects for the treatment of FMF disease, and it may be possible to apply potential genetic approaches to the treatment of this disease in the future.

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