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MOLECULAR-GENETIC ASPECTS OF FAMILIAL MEDITERRANEAN FEVER AND THE ROLE OF THE ETHNIC FACTOR IN THE MANIFESTATION OF THIS DISEASE IN THE REPUBLIC OF CRIMEA

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Abstract

The study and diagnosis of monogenic diseases is based on population analysis of the frequency of pathological genes. One of the rarest hereditary pathologies in the Russian Federation is Familial Mediterranean Fever (FMF). This monogenic disease is prevalent among Sephardic Jews, Turks, Arabs, Armenians, Italians, and peoples of the North Caucasus. It is characterized by recurrent short episodes of fever and serositis, resulting in abdominal pain, chest pain on inspiration, joint pain, muscle pain, and heel pain. Fever is accompanied by nausea, vomiting, diarrhea, erythematous spots on the extremities, and in males — swelling of the scrotum and penis. Neurological disorders may also develop. One of the main symptoms is amyloidosis, which, if untreated, can lead to renal failure. FMF results from mutations in the MEFV gene, located on the short arm of chromosome 16. It encodes the protein pyrin, which participates in immune defense. According to the 2021 All-Russian Population Census, the Republic of Crimea is home to 352,000 Crimean Tatars (14.1% of the total population, ranking 2nd among all nationalities), 41 Arabs, 7,717 Armenians, and 1,655 Jews — all potential carriers of this disease. Indeed, 17 cases of the disease have been recorded in the region (Zhogova O.V. et al., 2019). All patients identified themselves as Crimean Tatars.

Keywords: familial Mediterranean fever, monogenic disease, MEFV gene, pyrin protein.

Aim of the Article

The aim of the article is to summarize current scientific knowledge on the genetic mechanisms of FMF, to describe mutations of the MEFV gene and structural changes in the pyrin protein among representatives of the Crimean Tatar ethnic group, and to outline possible diagnostic methods.

Research Problems and Hypotheses

Research Problems

Research Problem 1: Underestimation of the true prevalence of FMF among the Crimean Tatar population

Despite the fact that Crimean Tatars constitute 14.1% of the population of the Republic of Crimea and belong to one of the high-risk ethnic groups for FMF, only 17 clinical cases have been officially documented (Zhogova O.V. et al., 2019). Given the estimated size of the at-risk population (352,000 Crimean Tatars, 7,717 Armenians, 1,655 Jews, and 41 Arabs), this number appears disproportionately low. The problem lies in the **absence of systematic population-level molecular-genetic screening** for MEFV mutations in Crimea, which makes it impossible to determine the actual carrier frequency and disease prevalence in this region. The lack of epidemiological data prevents the development of adequate preventive and diagnostic strategies.

Research Problem 2: Ethnic specificity of the MEFV mutational spectrum in Crimean Tatars

The MEFV gene harbors over 100 known pathological variants, and their distribution differs significantly between ethnic groups. Among Crimean Tatar patients, two specific mutations

have been identified: **p.Met694Val** and **p.Arg202Gln** (Zhogova O.V. et al., 2019). However, it remains unclear whether these two variants represent the **complete mutational spectrum** of FMF in this population, or whether additional, currently undetected mutations contribute to the disease burden. The absence of comprehensive next-generation sequencing (NGS) data for the Crimean Tatar population makes it impossible to establish a full ethnic-specific mutational profile, which is essential for designing targeted diagnostic panels.

Research Problem 3: Atypical manifestation of FMF in heterozygous carriers among Crimean Tatars

FMF follows a classical **autosomal recessive** inheritance pattern; however, symptomatic heterozygotes have been documented among Crimean Tatar patients carrying the p.Met694Val mutation (Zhogova O.V. et al., 2019; Seza Özen et al., 2017). This contradicts the expected recessive model and raises unresolved questions about the **molecular mechanisms underlying incomplete recessiveness** in this ethnic group. It is unclear whether this phenomenon is attributable to modifier genes, epigenetic regulation, gene-environment interactions, or structural features of the pyrin protein specific to the Crimean Tatar genetic background. The absence of functional studies on pyrin variants in this population leaves this problem unresolved.

Research Problem 4: Diagnostic delays and misdiagnosis due to insufficient clinical awareness

FMF is characterized by recurrent episodes of fever and serositis that closely mimic common surgical and rheumatological conditions, including acute appendicitis, pleuritis, and rheumatoid arthritis. In the Republic of Crimea, where the disease is considered extremely rare, **clinical awareness among physicians remains low**, leading to diagnostic delays that can span years. During this period, patients may undergo unnecessary surgical interventions, and the risk of developing amyloidosis — the most severe complication of untreated FMF — increases

significantly. The problem is compounded by the absence of standardized regional diagnostic algorithms that integrate molecular-genetic testing with clinical criteria.

Research Problem 5: Optimization of PCR-based molecular diagnostics for ethnically specific MEFV mutations

While PCR remains the gold standard for molecular diagnosis of FMF, the **selection of optimal primer sets** for detecting ethnically specific mutations (p.Met694Val and p.Arg202Gln) in the Crimean Tatar population has not been systematically validated. The Primer3Plus-generated primer candidates proposed in the literature have not been comparatively evaluated for sensitivity, specificity, and amplification efficiency under standardized laboratory conditions applicable to clinical settings in Crimea. Furthermore, the relative diagnostic value of conventional PCR versus Sanger sequencing versus NGS for this specific population context has not been established, leaving clinicians without clear evidence-based guidance on the most cost-effective and accurate diagnostic strategy.

Research Hypotheses

Hypothesis 1:

The actual prevalence of FMF among the Crimean Tatar population of the Republic of Crimea is significantly higher than the 17 officially documented cases, and systematic molecular-genetic screening using PCR-based MEFV mutation panels will reveal a carrier frequency consistent with that observed in genetically related Turkish and Middle Eastern populations (estimated 1:500 to 1:1,000).

This hypothesis is based on the genetic proximity of Crimean Tatars to Turkish and other Turkic populations, in which FMF carrier rates are well established. The discrepancy between the expected and observed case numbers strongly suggests systematic underdiagnosis rather than a genuinely low disease burden.

Hypothesis 2:

The mutational spectrum of the MEFV gene in the Crimean Tatar population is not limited to p.Met694Val and p.Arg202Gln, and comprehensive NGS analysis will identify additional pathogenic variants — including rare or population-specific mutations in exons 2, 3, 5, 9, and 10 — that contribute to the full clinical and genetic heterogeneity of FMF in this ethnic group.

This hypothesis is supported by the fact that only conventional targeted genotyping has been applied to Crimean Tatar patients to date. NGS-based studies in other Mediterranean and Turkic populations have consistently revealed a broader mutational landscape than that detected by panel-based approaches.

Hypothesis 3:

The symptomatic manifestation of FMF in heterozygous carriers of the p.Met694Val mutation among Crimean Tatars is mediated by a gain-of-function mechanism of the mutant pyrin protein, resulting in constitutive, low-level NLRP3 inflammasome activation that is sufficient to produce clinical symptoms even in the absence of a second pathogenic allele.

This hypothesis is grounded in the known molecular consequences of p.Met694Val: reduced CASP1 interaction and impaired NLRP3 degradation. In heterozygotes, the presence of one mutant allele may produce enough dysfunctional pyrin to disrupt the balance between

inflammasome activation and suppression, particularly under conditions of infectious or environmental stress common in the Crimean Tatar population.

Hypothesis 4:

Implementation of a standardized regional diagnostic algorithm integrating clinical scoring (Tel Hashomer criteria), acute-phase reactant profiling (ESR, leukocytosis, fibrinogen), and targeted MEFV PCR genotyping will reduce the average time to FMF diagnosis in the Republic of Crimea by at least 50% compared to the current non-standardized approach, and will prevent unnecessary surgical interventions in affected patients.

This hypothesis is supported by evidence from other countries with high FMF prevalence (Turkey, Israel, Armenia), where the introduction of structured diagnostic protocols incorporating molecular testing has dramatically reduced diagnostic delays and improved patient outcomes, including prevention of amyloid nephropathy.

Hypothesis 5:

Among the PCR primer sets designed for the detection of p.Met694Val and p.Arg202Gln mutations in the MEFV gene, primer combinations targeting exon 10 (for p.Met694Val) and exon 2 (for p.Arg202Gln) with amplicon sizes between 150–300 bp will demonstrate the highest analytical sensitivity and specificity under standardized thermocycling conditions, making them the most suitable candidates for routine clinical molecular diagnostics in the Crimean Tatar population.

This hypothesis is based on the known structural organization of the MEFV gene, the localization of the target mutations within specific exons, and established principles of PCR primer design (optimal GC content, melting temperature, and absence of secondary structure formation), as evaluated using the Primer3Plus platform.

General Information on the Gene and Protein

Familial Mediterranean Fever (periodic disease) is caused by a mutation in the MEFV gene, located on the short arm of chromosome 16 (16p13.3). The coding region of the gene comprises 10 exons encoding a sequence of 781 amino acids (according to the GenBank database: https://www.ncbi.nlm.nih.gov/nuccore/?term=MEFV).

This gene encodes the protein pyrin (also referred to as marenostrin in some scientific publications). It regulates the mechanism of autophagy by influencing the cytoskeleton of leukocytes (Centola M. et al., 2000), as indicated by its localization in these structures. Pyrin participates in the formation and degradation of inflammasome components (macromolecular complexes that mediate inflammatory reactions and cell death responses to pathogens, as well as signals of cellular stress), serves as a platform for the assembly of proteins from the ULK1, Beclin 1/BECN1, ATG16L1, and ATG8 families, and recognizes specific autophagy targets, coordinating target recognition with the assembly of the autophagy apparatus and the initiation of autophagy (Chae J.J. et al., 2006). By binding to AIM2, it acts as a mediator of pyroptosis, necroptosis, and apoptosis (Mansfield E. et al., 2001; Centola M. et al., 2000). These processes collectively underlie the body's defense against pathogens in response to bacterial infection.

This protein is expressed in peripheral blood leukocytes, particularly in mature granulocytes (Tidow N. et al., 2000). Through infiltration of these cells, pyrin has been detected in the spleen, lungs, and muscles (Centola M. et al., 2000). Protein expression has been found in several cell lines in myeloid leukemia, colorectal cancer, and prostate cancer, but has not been detected in the thymus, testes, ovaries, small intestine, colon, heart, and a number of other organs (Papin S. et al., 2000).

Pathological Mutations in the Gene

According to the ClinVar database (https://www.ncbi.nlm.nih.gov/clinvar/), approximately 100 mutations occur in the transcribed region of the gene. The vast majority of these mutations are represented by single nucleotide polymorphisms (SNP – Single Nucleotide Polymorphism). In particular, the following SNPs have been identified: MEFV c.*1096A>T; MEFV c.*1080A>G, and others. However, insertions (Insertion, 2% of cases: MEFV c.*836*_837insACT),

duplications (Duplication, approximately 2% of cases: MEFV c.2330dup), and deletions (Deletion, approximately 6% of cases. Example: MEFV c.2330_2331del) are also present. Pathological mutations have been registered in exons 2, 3, 5, 9, and 10. They lead to more than 50 different variants of pathological proteins (UniProt database, https://www.uniprot.org/uniprotkb/O15553/entry#expression), which become the cause of the described pathology.

Pathological Forms of the Protein

The main symptoms of FMF are amyloidosis, fever, and serositis with developing peritonitis. Their development is caused by pathological changes in the primary structure of the protein, conditioned by the corresponding mutations.

Familial Mediterranean Fever is characterized by an autosomal recessive type of inheritance. Nevertheless, according to the results of research conducted at Hacettepe University in Turkey (Seza Özen et al., 2017), heterozygotes with a pathological phenotype carrying a mutated recessive gene were documented. It is presumed that the cause of disease manifestation in heterozygotes is the substitution of Methionine for Valine at position 694 (p.Met694Val). This mutation was detected among indigenous residents of Crimea (Zhogova O.V. et al., 2019). The cause of this substitution is a single nucleotide substitution of Thymine for Adenine, Cytosine, or Guanine (rs61752717), representing a missense mutation. Additionally, among the 17 hospitalized patients (Zhogova O.V. et al., 2019), another change in the amino acid sequence was identified — p.Arg202Gln, caused by a single nucleotide substitution of Cytosine for Guanine or Thymine (rs224222). This mutation can also be classified as a missense mutation. It is characteristic of recessive homozygotes.

The pathological mutation p.Met694Val leads to a reduction in the interaction of CASP1 (an enzyme of the cysteine protease family) (Shohat M. et al., 1999), which cleaves precursors of inflammatory cytokines (acts as an inducer of pyroptosis, performs an immune function) and ULK1 (an enzyme that activates autophagy) (Tomonori K. et al., 2015), and leads to a reduction in the degradation of NLRP3 (a cytosolic protein, a Nod-like receptor of the NALP family, the

main component of the eponymous type of inflammasomes, involved in the activation of caspases 1 and 5). As a result, amyloidosis is observed — the accumulation of coarse protein structures leading to disruptions in the normal functioning of organs.

The mutation p.Arg202Gln leads to the replacement of the large amino acid Arginine, carrying a positive charge, with a medium-sized amino acid with pronounced polarity — Glutamine, which leads to the transformation of protein isoform 2 into isoform 3 and uninhibited activity of pyrin (Masters S.L. et al., 2016). As a result, uncontrolled production of Interleukin-1 and excessive inflammation are observed, accompanied by fever, peritonitis, and other characteristic symptoms (Gunesacar R. et al., 2014).

Post-Translational Modification Disorders

Some researchers also consider that the cause of the disease is a disruption of post-translational modification, but this remains only a hypothesis at present. As a result of the changes, cleavage of the CASP1 protein occurs. The N-terminal cleavage product localizes in the nucleus as a filamentous network and in the cytoplasm, interacts more strongly with RELA and NFKBIA than the full-length protein, enhances the nuclear localization of RELA, and induces proteolysis of NFKBIA. The C-terminal cleavage product localizes in the cytoplasm (Serdobintsev K.V., 2016).

Disease Diagnosis

For the diagnosis of the disease, a blood test is used, aimed at detecting elevated erythrocyte sedimentation rate, increased concentration of leukocytes, and fibrinogen in the blood serum. In addition, colchicine therapy is often used for diagnosis (Seza Özen et al., 2017). It is conducted over a period of 6 months and is aimed at preventing the deposition of amyloid and the development of fever.

However, the most reliable method for diagnosing hereditary diseases is the PCR method (Polymerase Chain Reaction). This is a method of medical genetics designed for the diagnosis of monogenic and polygenic diseases by significantly increasing the number of copies of certain nucleic acid fragments in a biological sample. To perform this testing, it is necessary to know the sequence of DNA primers, which serve as a starting point for the synthesis of complementary chains using DNA polymerase. The Primer3Plus website (https://www.primer3plus.com/index.html) facilitates this work. More than 10 primer variants were proposed for the detection of each of the mutations. For example:

Left Primer: 1. GATAGGTTGAAGGGGCCCAG; 2. GAAGGGGCCCAGAGAAAGAG; 3. TCCCAGGGCTGAAGATAGGT; 4. GTGGGATCTGGCTGTCACAT; 5. CCCAGAGAAAGAGCAGCTGG; 6. GATGTGGGATCTGGCTGTCA; 7. TGAAGATAGGTTGAAGGGGCC; 8. GGGCCCAGAGAAAGAGCAG; 9. CCAGGGCTGAAGATAGGTTGA

Right Primer: 1. CTCCGAGTTTCCTCTCTGGC; 2. CATTGTTCTGGGCTCTCCGA; 3. GTTCTGGGCTCTCCGAGTTT; 4. TGATGGCCCGCAAAGATTTG; 5. GGCTCTCCGAGTTTCCTCTC; 6. CCGCAAAGATTTGACAGCTGT; 7. TACTGGGAGGTGGAGGTTGG; 8. TGGGCTCTCCGAGTTTCCT; 9. GGAGGTGGAGGTTGGAGACA (p.Met694Val)

Left Primer: 1. AATTTCTGGATTTGCGGGCG; 2. AGGAGAATTTCTGGATTTGCGG; 3. CGCCTTCTCCCCTGTAGAAA; 4. GATTTGCGGGCGCCTTCTC; 5. CAGCTGTCTTTTCCTCTAGAGTCA; 6. TGTCTTTTCCTCTAGAGTCAGGA; 7. CCTCTAGAGTCAGGAGAATTTCTGG; 8. CCTCAAGGCTTCTAGGTCGC; 9. TAGGTCGCATCTTTCCCGAG; 10. GTCTTTTCCTCTAGAGTCAGGAGAA

Right Primer: 1. CCTGAGCAAACGCAGAGAGA; 2. AAACGCAGAGAGAAGGCCTC; 3. GAGGGGGCTGTCGAGGAA; 4. AGGAAGCCCCTGAGCAAAC; 5. AGCAAACGCAGAGAGAAGGC; 6. AGAGAGAAGGCCTCGGAGG; 7. CCCCTGAGCAAACGCAGA; 8. CAAGCCTCGGACCCGGAG; 9. CAGGGCAAGCCTCGGACC; 10. CTGCAGGGCGCTAGAGG. (p.Arg202Gln)

The sequencing method can also be used, ranging from Sanger sequencing to high-throughput NGS (Next-Generation Sequencing). This method is based on determining the nucleotide sequence by extracting DNA, fragmenting it, reading the information, and assembling the data.

Conclusions

Conclusion 1: Familial Mediterranean Fever is a monogenic autosomal recessive disease caused by mutations in the MEFV gene (16p13.3), encoding the pyrin protein, which plays a central role in the regulation of inflammasomes, autophagy, and cell death pathways. The multifunctional nature of pyrin — as a mediator of pyroptosis, necroptosis, apoptosis, and autophagy — explains the systemic and multi-organ character of the clinical manifestations of FMF, including fever, serositis, peritonitis, and amyloidosis. Understanding the molecular functions of pyrin is a prerequisite for the development of targeted therapeutic strategies aimed at correcting specific dysfunctional pathways rather than merely suppressing general inflammation.

Conclusion 2: The two predominant mutations identified in Crimean Tatar patients — p.Met694Val and p.Arg202Gln — exert their pathological effects through distinct and well-characterized molecular mechanisms. The p.Met694Val mutation impairs CASP1 and ULK1 interactions and reduces NLRP3 degradation, ultimately leading to amyloidosis through the accumulation of coarse protein aggregates in target organs. The p.Arg202Gln mutation, by contrast, transforms pyrin isoform 2 into isoform 3, resulting in uninhibited pyrin activity, uncontrolled IL-1 production, and excessive systemic inflammation manifesting as fever and peritonitis. The co-existence of these two mechanistically distinct mutations within the same ethnic population underscores the molecular heterogeneity of FMF even within a geographically confined cohort.

Conclusion 3: The ethnic composition of the Republic of Crimea, with over 360,000 individuals belonging to high-risk populations for FMF — including 352,000 Crimean Tatars, 7,717 Armenians, 1,655 Jews, and 41 Arabs — creates a substantial epidemiological basis for the occurrence of this disease in the region. However, only 17 officially documented cases have been recorded to date (Zhogova O.V. et al., 2019), a figure that is disproportionately low relative to the size of the at-risk population and the known carrier frequencies in genetically related ethnic groups. This discrepancy strongly indicates the presence of systematic underdiagnosis attributable to insufficient clinical awareness, the absence of population-level molecular-genetic screening programs, and the lack of standardized regional diagnostic algorithms integrating PCR-based MEFV genotyping with clinical criteria.

Conclusion 4: The atypical symptomatic manifestation of FMF in heterozygous carriers of the p.Met694Val mutation among Crimean Tatars challenges the classical autosomal recessive inheritance model and represents an unresolved scientific problem of considerable clinical importance. The documented occurrence of symptomatic heterozygotes in this population necessitates further molecular, functional, and epidemiological investigations to elucidate the underlying mechanisms — which may include gain-of-function effects of the mutant pyrin, the influence of modifier genes, epigenetic regulation, or gene-environment interactions specific to the Crimean Tatar genetic background. Until these mechanisms are clarified, the clinical management of heterozygous carriers in this population cannot be based on standard recessive inheritance assumptions.

Conclusion 5: PCR-based genotyping, complemented by Sanger sequencing or next-generation sequencing (NGS), represents the most reliable and definitive diagnostic approach for FMF in the Crimean Tatar population. The development and validation of ethnically targeted primer sets for the detection of p.Met694Val (exon 10) and p.Arg202Gln (exon 2) mutations, using tools such as Primer3Plus, is an essential step toward establishing a standardized molecular diagnostic protocol for the region. The integration of such molecular testing into a comprehensive regional diagnostic algorithm — combining clinical scoring (Tel

Hashomer criteria), laboratory markers (ESR, leukocytosis, fibrinogen), colchicine therapeutic testing, and MEFV genotyping — is urgently needed to reduce diagnostic delays, prevent unnecessary surgical interventions, and minimize the risk of amyloidosis-related renal failure in affected patients in the Republic of Crimea.

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Tumakov I.V. — literature search, data analysis, manuscript preparation.

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Dolomatov S.I. — conceptualization, scientific supervision, critical revision of the manuscript.

Zukow W. — editorial review, critical revision of the manuscript.

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This article is a review study based exclusively on previously published data. No new human or animal subjects were involved in the research. Accordingly, no ethical approval was required.

Data Availability Statement:

All data discussed in this article are derived from publicly available sources, including the NCBI GenBank database (https://www.ncbi.nlm.nih.gov/nuccore/?term=MEFV), the ClinVar database (https://www.ncbi.nlm.nih.gov/clinvar/), and the UniProt database (https://www.uniprot.org/uniprotkb/O15553/entry#expression).

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List of Russian-language References

Zhogova O.V., Lagunova N.V., Ivanovsky S.V., Salugina S.O., Kostik M.M. Familial Mediterranean fever in the Republic of Crimea: description of a series of cases with analysis of historical and ethnographic aspects of the disease. // Scientific and Practical Rheumatology. — 2019. Vol. 57, No. 3. — P. 339–344.

Serdobintsev K.V. The complement system. Pathology, diagnostics, treatment. // Allergology and Immunology in Pediatrics. — 2016. Vol. 3, No. 46. — P. 33–39.

List of English-language References

Centola M., Wood G., Frucht D.M. et al. The gene for familial Mediterranean fever, MEFV, is expressed in early leukocyte development and is regulated in response to inflammatory mediators. // Free article — 2000. pmid: 10807793.

Chae J.J., Wood G., Masters S.L. et al. The B30.2 domain of pyrin, the familial Mediterranean fever protein, interacts directly with caspase-1 to modulate IL-1beta production. // Proc Natl Acad Sci U S A — 2006. doi: 10.1073/pnas.0602081103.

Gunesacar R., Celik M.M., Arica V. et al. Frequency of MEFV gene mutations in Hatay province, Mediterranean region of Turkey and report of a novel missense mutation (I247V). // GENE. — 2014. Vol. 546, No. 2. — P. 194–199. doi: 10.1016/j.gene.2014.06.019.

Mansfield E., Chae J.J., Komarov H.D. et al. The familial Mediterranean fever protein, pyrin, associates with microtubules and colocalizes with actin filaments. // Free article — 2001. pmid: 11468188. doi: 10.1182/blood.v98.3.851.

Masters S.L., Lagou V., Jeru I. et al. Familial autoinflammation with neutrophilic dermatosis reveals a regulatory mechanism of pyrin activation. // Free article — 2016. doi: 10.1126/scitranslmed.aaf1471.

Papin S., Duquenoy P., Kaznev K. et al. Alternative splicing at the MEFV locus involved in familial Mediterranean fever regulates translocation of the marenostrin/pyrin protein to the nucleus. // Human Molecular Genetics. — 2000. Vol. 9. — P. 3001–3009. doi: 10.1093/hmg/9.20.3001.

Seza Özen, Batu E.D., Demir S. Familial Mediterranean Fever: Recent Developments in Pathogenesis and New Recommendations for Management. // Frontiers in Immunology. — 2017. doi: 10.3389/fimmu.2017.00253.

Shohat M., Magal N., Shohat T. et al. Phenotype-genotype correlation in familial Mediterranean fever: evidence for an association between Met694Val and amyloidosis. // European Journal of Human Genetics. — 1999. Vol. 7, No. 3. — P. 287–292. doi: 10.1038/sj.ejhg.5200303.

Tidow N., Chen X., Muller C. et al. Hematopoietic-specific expression of MEFV, the gene mutated in familial Mediterranean fever, and subcellular localization of its corresponding protein, pyrin. // Free article — 2000. pmid: 10666224.

Tomonori K., Ashish J., Song Won Choi et al. TRIM-mediated precision autophagy targets cytoplasmic regulators of innate immunity. // Journal of Cell Biology. — 2015. Vol. 210, No. 6. — P. 973–989. doi: 10.1083/jcb.201503023.