

To Find the Mechanism of Familial Mediterranean Fever (FMF) will Help Us to Solve Many Inflammatory Problems

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Familial Mediterranean Fever (FMF) is an autosomal recessive disorder that frequently affects Turkish, North African Jewish, Arabic, and Armenian populations. However, it is basic and a small model of the inflammation. This model consists not only the flares of the inflammation but at the same time miss model of spontaneous and nonterminating inflammation too. So, if we solve this puzzle and find the members of the puzzle it may help us to discover secrets of the inflammation. To find out every steps of the cascade of this inflammation probably will bring out the reasons of the auto-inflammatory and auto-immune diseases and, even help the treatment of cancer too.

FMF has heterogeneous symptoms and subjective laboratory findings. So, the diagnosis of the disease basically was done with the clinical symptoms and history of the patients. The discovery of the pyrin gene mutations (Figure) in the patients with FMF caused some expectations for to solve the accurate mechanism of the disease. However, pyrin gene mutations helped us to understand the disease but there are still so many dark points to completely solve the mechanism.

So, it is believed that mutations in pyrin gene is not enough to produce FMF phenotype. There may be some another genetic problems to set up the manifest disease. The most probable candidate for these mutations is Endoplasmic Reticulum Aminopeptidase-1 (ERAP-1) mutations (especially in exon10). Because one of the most important process for the recognition of the antigens by immune system which cleaves many types of proteins into small peptides. The reason of the importance of this step for inflammation is the probability of mis-response by immune system instead of ignorance or tolerance, if the wrong cleaving of antigens happen. These cleaved peptides in to the small particles are exported to the cell surface where they attach to major histocompatibility complex (MHC) class I proteins. MHC class I proteins display the peptides to

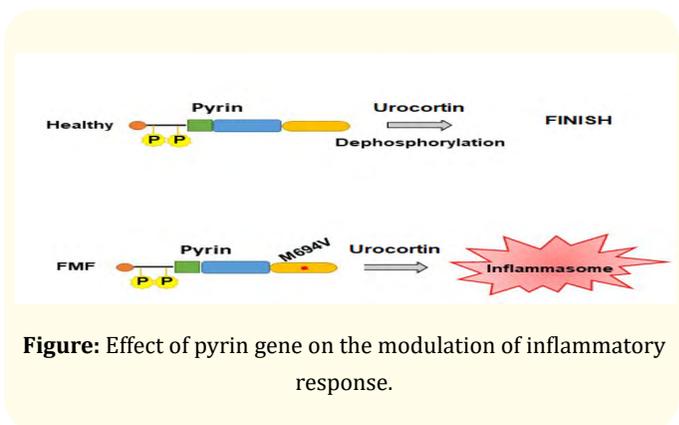


Figure: Effect of pyrin gene on the modulation of inflammatory response.

the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides) it responds by triggering the infected cell to self-destruction.

As a result, relationship between ERAP-1 mutations and pyrin gene still needs some more studies. However, to obtain all details of these relations will light many dark points of the inflammation.

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