

Inflammation is the body's natural defense against infection caused by all pathogens. The defense includes non-specific response cells - those that correspond to all types of infections, and these are among others monocytes, macrophages and granulocytes, NK cells, etc., and the specific response - that recognize specific type of pathogen, eg. T cells and B cells to produce an intruder-specific antibody. Then the antibodies dispose of unwanted guests in your body. Upon contact with the pathogen, our specific cells of the immune system "remember" which organism had to deal with, and during the next infection they combat the intruder much more quickly and effectively - this is so-called "immunological memory". During childhood people often get sick, it is because our body learns to recognize and fight microbes and viruses that are invading us. Similarly, cancer cells. In the first phase, when cells are scarce, our immune system treats it as if it were hurt, trying to fix broken cell or eliminate them. Unfortunately, after a while, the cancer begins to cheat our natural defenders, forcing them to cooperate. The innate immune system cells secrete specific molecules, so-called. pro-inflammatory cytokines (eg. IL-1, IL-6) and factors tempt cells to the place of the infection, but in the case of cancer compounds - they help cancer cells with uncontrolled growth and spread.

A few years ago, scientists discovered a new protein MCPIP1 encoded by the gene *Zc3h12a*. This protein has RNase activity, which has the ability to degrade mRNA (messenger RNA). We found that the protein appears in the cell in a much larger amount than normally occurs after treatment of lipopolysaccharide (LPS) molecule - a component of the cell wall of many bacteria. In addition, it was discovered that MCPIP1 has the ability to degrade RNAs of many viruses like HIV-1, HCV, and other such as dengue virus - thereby inhibiting the replication of viruses. During infection immune system generates many molecules inducing an inflammatory response (inflammation). It is a natural defense but after fighting infection, inflammation must be suppressed. In order to quench inflammatory response, the protein MCPIP1 acting as an RNase degrades the mRNA molecules triggering inflammation, eg. IL-1, IL-6 etc. The generalised inflammation is accompanied by a cancer. However, there is little information on the role of MCPIP1 in that process. First reports suggest that in tumor cells there is significant reduction of the protein level of MCPIP1.

Another protein that appears to be involved in the functioning of the innate immune response is HAX-1 protein. Scientists discovered that a mutation in the gene encoding this protein occurs in people with the Kostmann disease - heavy recessive hereditary neutropenia. What's more, it is now known that this protein interacts with many proteins of various types of viruses, eg. Influenza A virus, HIV-1, etc.

In the view of the fact that both proteins HAX-1 and MCPIP1 evolved only in vertebrates, it can be concluded that both of them can be very important to the proper functioning of our immune system. Therefore, the main objective of the project is to understand how the two proteins interact with each other and which mRNAs they can regulate in the context of the inflammatory response and the carcinogenesis process.

The basic research made in this project are designed to broad knowledge of the basic mechanisms of inflammation and carcinogenesis process. Conduct those experiments will have resulted in receiving set of data that can be presented at national and international scientific conferences, as well as published in a scientific journal. The interaction of proteins HAX-1 and MCPIP may lead to degradation of the factors that cause an inflammatory response, which would result in quenching that process. Many other molecules can participate in that mechanism. On this basis, it can be assumed that, thanks to basic research, this project could serve as a basis for further experiments eg. in the clinical field.

The modern equipment will allows us to observe the location of proteins interaction in the cell under the confocal microscope and also to find molecules interacting with both HAX-1 and MCPIP and analyze them – during this project.

We have undertaken this theme because it allows to explore unknown connection between the inflammatory response and carcinogenesis process, which will contribute to a better understanding of both of these phenomena occurring in the human body.