

## **Anti-inflammatory effect of vitamin K: mechanism of action**

The main functions of vitamin K are: regulation of calcium metabolism and participation in blood clotting. Recent studies, show that the functions of vitamin K go beyond coagulation and calcification, including, among others, anti-inflammatory activity, the mechanism of which has not been fully understood. In addition, our preliminary studies indicate that the anti-inflammatory effect of vitamin K covers a much wider spectrum of effects than previously reported. In this project, we will describe in detail the anti-inflammatory action of the vitamin selected members of the vitamin K group (K1, K3, K2MK-4, K2MK-5, K2MK-7, K2MK-9). The experiments will be carried out on the cell line of mouse subpopulations of M1 and M2 macrophages polarized by the use of appropriate cytokines. In the second part of the project, we will examine the mechanism of anti-inflammatory action of selected members of the vitamin K group with the strongest anti-inflammatory potential. We will characterize the presence of vitamin K dependent proteins in macrophages (M1, M2) and determine the importance of vitamin K-dependent carboxylation in the regulation of inflammation by silencing enzymes (VKOR, GGCX). We will characterize the effect of vitamin K on the regulation of the NF $\kappa$ B pathway by determining the level of the phosphorylated form of IKK $\alpha$  /  $\beta$ . In addition, we will define a number of parameters defining mitochondrial function (mitochondrial respiration and glycolysis, maximum respiration, proton leakage and ATP production) in M1 / M2 macrophages in presence and absence of vitamin K. The results will be verified by a simple in vivo model of peritonitis in mice on a control diet and enriched with vitamin K.

Macrophages are involved in the inflammatory process in many diseases, such as diabetes, cancer or atherosclerosis, so the project's results will shed new light on role of vitamin K in regulating the immune response and it will important part of basic research in immunology, pharmacology and cell biology.