Infection and inflammation are accompanied by an increase concentration ofgranulocyte-macrophage colony stimulating factor (GM-CSF), stimulating the differentiation of monocytes into macrophages, which then by classical activation, for example in response to bacterial endotoxin, polarize the cells in proinflammatory macrophages M1. Phenotype of M1 in response to the penetration of foreign pathogen into the body, characterized by a high expression of the factors include proinflammatory cytokines, such as IL1β and TNFα, which primary function is to activate other immune cells to accumulate in the site of the inflammation. Proximal and distal (enhancers) *cis*-regulatory regions play an important role in the process of differentiation characterized by immense dynamics of chromatin structure. *Cis*-regulatory regions intensifying transcription of factors responsible for the course of differentiation and/or specific to particular cell type.

Preliminary results obtained by Applicant and literature data allow to draw the hypothesis about participation ADP-ribosylation process within the *cis*-regulatory regions of *IL1β* and *TNFα* genes in preservation these regions in an inactive form, and reducing the level of PARP1 protein during the process of differentiation monocytes into proinflammatory macrophages M1 has functional significance for predisposing macrophages to an increased expression of proinflammatory cytokines.

Poly-ADP-ribose polymerases (PARP) are enzymes involved in a number of processes that are vital for every living cell. PARP 1 is the best characterized enzyme of this family, which is located mainly in the nucleus, where it occurs in the form of partly associated with chromatin, allowing the ADP-ribosylation of histones and other proteins involved in the conditioning chromatin structure. Thereby this enzyme also plays important role in regulating chromatin access for transcription factors, which in turn affects the level of expression of the certain gene. Now, there is no information on the course and the mechanism responsible for change the status of the proximal and distal *cis*-regulatory regions of *IL1β* and *TNFα* genes during differentiation and polarization of proinflammatory macrophages M1. Therefore, the main scientific goal of submited project is the identification of molecular mechanisms underlying the effect of poly(ADPribose)polimerase-1 (PARP1) on the readiness and/or activation of the proximal and distal *cis*-regulatory regions of *IL1β* and *TNFα* genes playing an important role in the innate immune response.

Project comprises four thematically ordered steps dedicated to identification of enhancers undergoing activation during differentiation, functionally involved in the expression of cytokines tested. determination of the physiological significance of reduction of PARP 1 protein expression for arrangement and activation of selected *cis*-regulatory regions. Identification of promoter and enhancer elements undergoing ADP-ribosylation during differentiation of monocytes into proinflammatory phenotype of macrophages M1 and the activation of endotoxin and to determine their impact for the repression of gene transcription *IL1β* and *TNFα* In order to accomplish all above enumerated goals the following modern cellular and molecular biolgy technics would be utilized: gene silencing with shRNA and siRNA, gene overexpression (cDNA-carrying expression vectors, western blot, *real-time* PCR, chromatin immunoprecipitation coupled to detection by quantitative *real-time* PCR analysis (ChIP-qPCR) and chromosome conformation. The results will have a significant impact on the extension of knowledge about the regulation of gene expression, which in the future may be used in research projects in various fields of science, including molecular biology, immunology, genetics and genomics.