In response to various stress factors affecting the cell, the p53 protein activates transcription of genes involved in cell cycle regulation, apoptosis, and DNA repair. Therefore, it is called the main suppressor of tumorigenesis and the "guardian of the genome" as it provides the stability of the genetic material and prevents cells with mutations from dividing that can lead to malignant transformation. The *p53* gene has been one of the most studied human genes over the past three decades.

Relatively recently, it has been demonstrated that expression of the *p53* gene occurs with the use of a number of transcriptional promoters, the transcripts are alternatively spliced, and alternative translation initiation codons are employed. Consequently, this leads to generation of a number of p53 isoforms. What is essential, it has recently been observed that the disturbed expression of p53 isoforms plays an important role in the development of cancer, cell differentiation, and cellular response to pathogens.

Expression of various isoforms of p53 can be regulated at many levels: the synthesis of p53 mRNA variants and their different stability in the cell, different efficiency of the synthesis of specific isoforms of p53, their post-translational modifications, and different susceptibility to degradation. It is believed that, compared to control at the level of transcription, regulation of translation enables the cell to much faster respond to changes caused by stress or to anti- or pro-apoptotic factors.

Although the translation process is regulated at each of the three stages: initiation, elongation and termination, the major regulation stage is that of initiation when the ribosome binds to mRNA and the initiation codon is selected. Translation initiation is a complex process which is under the control of several protein factors which interact not only with the ribosome, but also with the regulatory elements of mRNA. In addition, elements of the secondary and tertiary structure present in 5' non-coding regions of mRNA are the binding sites for multiple proteins and short non-coding or antisense RNAs that can affect translation.

The aim of the proposed project is to elucidate the role of the proteins that bind to the 5' non-coding region of human p53 mRNA in the regulation of expression of the full-length protein p53 and its major isoforms Δ40p53 at the translational level. The hypothesis will be verified that the distribution of p53 isoforms in a cell and the cell response to stress are regulated at the translational level, and this occurs primarily through specific interactions between the 5' non-coding region of the p53 mRNA and protein factors.

In the project, proteins will be identified that bind to major variants of the 5' non-coding region of p53 mRNA, which are possibly involved in the regulation of the functioning of this mRNA. It will be very important to determine which of these proteins interact specifically, and which non-specifically. In addition, in functional assays, the role of selected proteins in translation of the full-length p53 and its major isoform Δ40p53 will be tested.

The proposed studies will help to understand the role of the proteins that interact with the 5' non-coding region of p53 mRNA in the regulation of expression of the p53 protein and its Δ40p53 isoform under normal and stress conditions. The mechanisms that determine the level of individual isoforms of p53 in the cell under different conditions have not yet been known. Moreover, the newly identified proteins will be used to search for the relationship between the expression of p53 and other cellular processes in which these new proteins are involved. The obtained information will be applied in further studies to elucidate the role of the newly identified proteins in regulating the activity of p53 in the cell, malignant transformation and cellular response to bacterial and viral infections.